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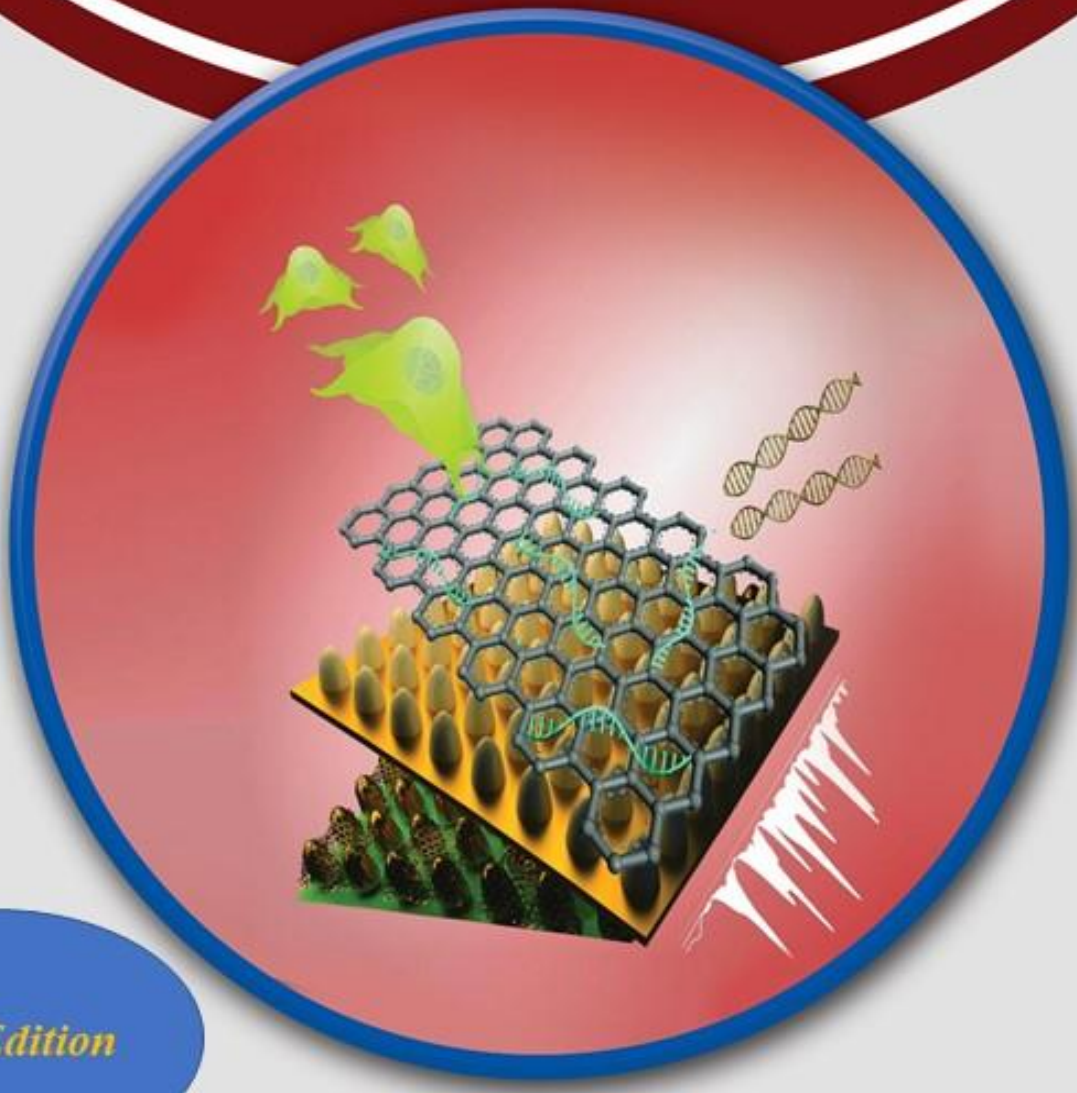

First Edition

Abstract Book

Abstracts of oral presentation

OBa-1

Abstract Type: Original Research

Broth Microdilution Antibacterial Assay of Chitosan Nanoparticles as a Carrier for the Supernatant of Mesenchymal Stem Cells against Multidrug-Resistant Clinical Isolates

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Abstract

Background and Aim: The threat of antimicrobial resistance (AMR) is a major public health problem worldwide. Considering the increasing prevalence of multidrug-resistant (MDR) bacteria, non-antibiotic treatment methods are required to treat these infections. This study focused on the antimicrobial activity of mesenchymal stem cell conditioned medium (MSCs CM) encapsulated in chitosan nanoparticles (CS NPs) against multidrug-resistant clinical isolates.

Methods: Scanning electron microscopy (SEM), zeta potential (ZP), and dynamic light scattering (DLS) techniques were used to characterize CS NPs. MSCs CM was incorporated into CS nanoparticles, and its release rate from the composite (MSCs CM-CS NPs) was estimated. Antibacterial properties of MSCs CM, CS NPs, and MSCs CM-CS NPs were assessed by microbroth dilution technique.

Results: The mean particle size of most CS NPs was 85.2 nm, and their zeta potential was 32.1 mV. SEM findings supported the morphology of the prepared CS nanoparticles and the synthesized composite (MSCs CM-CS NPs). Entrapment efficiency of the prepared composite was 71%. The antimicrobial activities of the new construct (MSCs CM-CS NPs: 1000 µg+0.05%) against multidrug-resistant bacteria were significantly higher compared to (MSCs CM: 1000 µg), (CS NPs: 0.05%) each alone. These results highlight the synergistic antimicrobial activity of the new construct (MSCs CM-CS NPs).

Conclusion: This composite exhibited the synergistic antibacterial activity of CS NPs and MSCs CM, resulting in a more potent dose-dependent antibacterial activity against multidrug-resistant clinical isolates. The use of this composite is suggested as a new treatment method to combat multidrug-resistant bacteria.

Keywords: Antibacterial, Mesenchymal stem cells, Chitosan, Nanoparticle, Multi-drug resistant

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OBa-2

Prevalence of plasmid-mediated AmpC β-lactamase gene (*bla*$_{FOX}$) in *Klebsiella pneumoniae* isolates collected from different clinical specimens in Mazandran province, north Iran

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Background and Aim: *Klebsiella pneumoniae* is a versatile pathogen causing a wide range of infections, including pneumonia and systemic bacteremia, particularly in immunocompromised individuals. The acquisition of virulence factors increases the pathogenicity of certain strains, complicating treatment in the context of antimicrobial resistance. Extended-spectrum beta-lactamases (ESBLs), produced by some bacteria, degrade β-lactam antibiotics, such as penicillins and third-generation cephalosporins, rendering them ineffective and complicating treatment, especially in hospitalized patients. ESBL-producing strains often form biofilms more readily than non-ESBL-producing strains, thereby increasing their virulence. Conversely, non-ESBL strains are more likely to harbor virulence genes (e.g., *rmpA* and *iutA*) that are associated with hypervirulence and severe infections. Base on previous study, phenotypic tests identified ESBL-producing *Kp* strains in 40% of the isolates, with 20% producing AmpC β-lactamases. So. The aim of this study was to evaluate of antimicrobial resistance profiles and the presense of *bla*$_{FOX}$ gene in *Kp* strains recovered from hospitalized patients in Mazandaran province.

Methods: Clinical samples, including 100 isolates (blood, stool, sputum, wound, and CSF), were obtained from patients hospitalized in Sari from March to September 2023. The isolates were identified by conducting biochemical and differential tests, including cultivation in TSI, SIM, Simons citrate, MRVP, catalase, and oxidase. The disk diffusion method was mainly used to test the antibiotic susceptibility of bacteria using the CLSI guidelines with 14 antibiotic disks. DNA was extracted using the boiling method. To detect bla-AmpC (FOX) β-lactamase, bacterial colonies were suspended in distilled water to obtain a homogeneous solution. The *bla*$_{fox}$ genes were investigated using PCR with specific primers. A DNA ladder was used to identify PCR products with the target band sizes, which were then placed in a gel doc system for confirmation, and the DNA bands were visualized and analyzed for size. The data collected from the results of this study were imported into SPSS v. 23. The chi-square test was used for statistical analysis of the data. Statistical significance was set at $P < 0.05$.

Results: *Kp* isolates showed the highest rates of resistance to cefotaxime (69%), piperacillin (68%), ceftazidime (67%), ceftriaxone (66%), and aztreonam (77%). In contrast, the isolates were the most susceptible to imipenem (39%), cefoxitin (39%), amikacin (55%), and gentamicin (61%). A phenotypic confirmatory test (CDT) was used to examine the presence of Amp-C β-lactamase. Of the 61 cefoxitin-resistant isolates (61%), 26 (42.62 %) tested positive for AmpC production. Moreover, 14 of the 61 cefoxitin-resistant isolates (22.95%) had the bla-Amp-C- (fox) gene, according to molecular analysis.

Conclusion: Further research is needed to ascertain antibiotic resistance patterns of *Kp* in patients across different hospital departments and isolate sources. It is also important to identify the prevalence of other beta-lactamase genes involved in the AmpC resistance mechanism in *Kp*, such as plasmid-mediated genes DHA, MOX, and ACT. Additionally, studies should focus on understanding resistance mechanisms and developing new therapeutic strategies. Effective infection control and prevention of drug-resistant isolates require precise drug prescription management and screening of resistant strains.

Keywords: *Klebsiella pneumonia*; extended-spectrum beta-lactamase; Multi-drug resistant

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OBa-3

Abstract Type: Original Research

Investigation of the inhibitory effects of IgY antibody against key epitopes of *Helicobacter pylori UreB* recombinant protein

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Abstract

Background and Aim: *Helicobacter pylori* (*H.pylori*) is considered to be the most important gastrointestinal pathogen in causing gastritis, gastric ulcers and even gastric cancer. The treatment of these infections has failed due to the rapidly increasing antibiotic resistance to standard treatment regimens and the lack of an effective vaccine. Immunotherapy has been considered as one of the alternative treatments recently. This study was conducted to produce and evaluate the inhibitory effects of IgY antibody against *Helicobacter pylori* urease B recombinant protein, an essential virulence factor.

Methods: In the present study, *Helicobacter* UreB gene fragments containing key epitopes as antigens to stimulate immune response were cloned in the pET32b vector and expressed in *E. coli* BL21 (DE3). After extracting and purifying the desired peptide by Ni-NTA affinity chromatography, it was used as an antigen along with Freund's adjuvant to produce IgY

antibodies in chickens. IgY was purified from egg yolk powder by polyethylene glycol method (PEG) and evaluated by SDS-PAGE, ELISA and western blot tests, and the inhibitory effects of UreB-IgY on the growth of *Helicobacter pylori* and its urease activity were evaluated in laboratory conditions.

Results*:* The recombinant UreB protein was successfully expressed and purified. The results of ELISA for blood serum obtained from chickens immunized under UreB injection showed a high preference for UreB recombinant protein ($P < 0.001$).

Based on this, in the group immunized with recombinant urea-B, the highest antibody response was observed at a concentration of 1:100 and the lowest at 1:12800. Western blot results show that IgY is correctly bound to HRP-conjugated anti-chicken IgY secondary antibody.

At a concentration of 10 mg/ml, IgY-UreB significantly ($P<0.001$) inhibited urease activity. Specifically, at this concentration, it reduced urease activity by 84.53%. Experiments on the inhibition of *H.pylori* growth by agar dilution method exhibited that IgY-UreB at a concentration of 5 mg/ml has inhibitory activity on *H. pylori* growth.

Conclusion: According to these findings, UreB-IgY can be proposed as an alternative therapeutic candidate for *H.pylori* infections and overcome its antibiotic resistance.

Keywords*:* IgY antibodies; Urease B; Recombinant protein; *Helicobacter pylori*; Gastritis; Gene cloning

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OBa-4

Abstract Type: Review Research

Effect of natural nanoparticles on VRSA

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Vancomycin Resistant *Staphylococcus aureus* (VRSA) is a bacterium that belongs to the genus *Staphylococcus*, which is one of the most common infections and diseases in the community. The difference between this bacterium and other *Staphylococcus aureus* is in the *vanA* gene, which makes it resistant to vancomycin antibiotic. This bacterium causes effects such as respiratory tract infection and blood-borne infections in the body. In this review, we summarize treatment approaches for VRSA, including novel nanoparticle design techniques for improved therapeutic outcomes.

Methods: According to the articles that were surveyed from databases such as Google Scholar, PubMed, Web of Sciences and Scopus from February 2015 to June 2024, it was found that due to the increase in antibiotic resistance, tests regarding the sensitivity of S*taphylococcus aureus* to Gold (AuNPs), silver and zinc were explored. The keywords, we used, were nanoparticles, VRSA, Gold (AuNPs), ZnO, silver, *Staphylococcus aureus* and therapeutic.

Results: The results obtained from the studies, out of 19 strains collected from VRSA, 13 strains recorded an inhibition zone of 9 to 13 mm when exposed to silver nanoparticles, while the other 6 strains recorded an inhibition zone of 5 to 6 mm. In another study each of the 34 isolated samples of VRSA became inactivated when exposed to ZnO and from another analysis 19 samples isolated from this bacterium were greatly reduced their activation when exposed to Gold (AuNPs) nanoparticles

Conclusion: In this study, it was found that in general, nanoparticles such as Gold (AuNPs), silver and ZnO have good and significant effects on VRSA strains, and overall they are effective in inhibiting their growth process. This study gives a good prospective for the treatment of antibiotic-resistant bacteria by using natural nanoparticles.

Keywords: VRSA, nanoparticles, Gold (AuNPs), ZnO, silver, *Staphylococcus aureus*.

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OBa-5

Abstract Type: Original Research (Times New Roman, font size 12)

Impact of heavy metals on Intestinal Microbiome in Tehran and suburbs

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Abstract
(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Heavy metals are a special group of metals that enter the environment through various processes. The increase in human industrial activities may cause heavy metals to enter the atmosphere and water. Many of these metals, such as cadmium are harmful to humans. Moreover, certain elements, such as zinc, iron, copper and selenium, are necessary for the body's biochemical reactions. Consuming large amount of these elements or disrupting their elimination process may have harmful consequences, including affecting the microbial pattern of the digestive system and/or changing the bacterial population**.**

Methods: Considering the profound importance of heavy metals in the human environment, It is observed increasing reports of natural resource pollution and human poisoning with these metals.In this study, several specific heavy metals, including zinc, cadmium, chromium, iron, copper and selenium, were detected in the of a human population of 50 residing both in the polluted area of Tehran and Firoozkooh as the clean area. For this purpose, first DNA stool extraction was performed according to kits' instructions. In order to determine the frequency of bacteria such as Escherichia, Bacteroides, Bifidobacterium, Lactobacillus and Akkermansia was used qPCR and microbiota population was investigated at the branch level category. The one-way ANOVA is used to compare between groups. The t-test was evaluated of elements in the serum of two independent groups in people living in Tehran as a polluted area and Firoozkooh as a healthy area.

Results: In this study, the presence of species such as Escherichia, Bacteroides, Bifidobacterium, Lactobacillus and Akkermansia indicated the relationships between these metals and the microbial composition and pattern of the digestive tract using biochemical,

microbial and molecular methods. The results showed that there is a relationship between some heavy metals and the gut microbiota pattern in the human body.

Conclusion: The results have shown that heavy metals disrupt the balance of the normal human intestinal flora. As a result, we see a decrease in probiotics such as Lactobacillus and Bifidobacterium.

Keywords: Microbiota/Heavy metals/Tehran/Firoozkooh

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OBa-6

Effects of Sub-inhibitory Concentrations of Antibiotics and Oxidative stress on the expression of type II TA system genes in *Klebsiella pneumoniae*

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Abstract

Objectives: Sub-inhibitory concentrations (sub-MICs) of antibiotics reflect the conditions bacteria encounter in tissues and the natural environment. Sub-MICs of antibiotics can induce stress and alter the expression of different bacterial genes. Bacteria react to stress conditions using different mechanisms one of which is Toxin-Antitoxin (TA) systems. This study investigated the expression of TA system genes under oxidative and antibiotic stress in *Klebsiella pneumoniae*.

Methods: To determine the effects of sub-MIC of gentamicin, nalidixic acid, ceftazidime, and certain concentrations of H_2O_2 on bacterial survival and growth, colony forming unit was quantitated and turbidity was assessed following the treatment of *K. pneumoniae* with ½ MIC of antibiotics and 5mM H_2O_2 at different time intervals. Moreover, the expression of TA system genes in *K. pneumoniae* was evaluated one hour after treatment using qRT-PCR method.

Results: Our results revealed the reduced *K. pneumoniae* growth in the presence of sub-MICs of antibiotics and 5 mM H_2O_2 compared to the control. Furthermore, according to the results

of qRT-PCR assay, only the presence of gentamicin could increase the expression of TA system genes.

Conclusion: Although the exact role of the TA systems in response to stress is still unclear, our study provided information on the effect of the type II TA systems under the oxidative and antibiotic stress conditions.

Keywords: *subinhibitory antibiotic concentrations; oxidative stress; K. pneumonia*; TA system; Realtime PCR

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OBa-7

Original Research

Wound healing properties and antimicrobial activity of platelet Wound derived biomaterials

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Abstract

Background and Aim: Treatment of burn wound infections has become a global challenge due to the spread of multidrug-resistant bacteria; therefore, the development of new treatment options for the mentioned infections is essential. Platelets have drawn much attention for this purpose because they are a safe and cost-effective source of different antimicrobial peptides and growth factors. The present study evaluated antibacterial effects and wound healing properties of Platelet-derived Biomaterial (PdB) against S. aureus and P. aeruginosa burn wound infections.

Method: The third-degree burn wound healing effects of PdB was also studied. Blood samples were obtained from 10 healthy volunteers and biological assays of the PdB were performed and the antimicrobial activity against MRSA and P. aeruginosa was determined using disk diffusion (DD), broth microdilution (BMD), and time-kill assay methods. 48 Wistar albino rats were burned and infected with MRSA. Two groups were injected PdB, the control groups were treated with plasma and received no treatment respectively. In the next step, the rats were euthanized and skin biopsies were collected and histopathologic changes were examined.

Result: The results of DD and BMD showed that both PdB performed very well on MRSA, whereas P. aeruginosa was only inhibited by F-PdB and was less susceptible than MRSA to PdBs. The time-kill assay also showed that F-PdB has an antibacterial effect at 4 hours for two

strains. Histopathological studies showed that the treated groups had less inflammatory cells and necrotic tissues.

Conclusion: Our data suggest that PdB may possess a clinical utility as a novel topical antimicrobial and wound healing agent for infected burn wounds.

Keywords: burn, wound infection, Platelet-derived biomaterial, P. aeruginosa

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OBa-8

Systematic Review

The Use of Lactic Acid Bacteria in Cancer Treatment

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Abstract

Background: Current treatments for various types of cancer include surgery, chemotherapy, and radiotherapy. Due to the toxic effects of some treatments, including chemotherapeutic agents, much research has been done recently to reduce their side effects in treatment protocols. Researchers have reported that substances secreted by certain bacteria, including lactic acid bacteria, can be used as alternative treatments alongside mainstream therapies such as chemotherapy and radiotherapy.

Methods: Data on the use of lactic acid bacteria in the treatment of various cancer cell lines in vitro and in vivo from 2015 to 2024 were collected and analyzed from websites such as SID, PUBMED, NATURE, and Scopus via the Google Scholar search engine.

Results: In vitro studies on cell lines such as Caco-2, HT29, CT26, A549, K562, AGS, SiHa, KB, and OSCC have shown that bacterial extracts and cell walls of *Lactobacillus casei*, *Lactobacillus paracasei*, *Lactobacillus plantarum*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, *Lactobacillus brevis* isolated from local dairy products sometimes alone and sometimes in combination with certain drugs such as coumarin and cisplatin and the toxin microcystin inhibited tumor cell proliferation and induced dose-dependent apoptosis. In-vivo studies *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, and *Lactobacillus plantarum* were added to the diet of a group of mice inoculated with tumors. The size of the tumors was subsequently measured, and it was found that the tumors had become smaller after several weeks of feeding with these probiotics.

Conclusion: Cellular extracts from lactic acid bacteria have a growth-inhibiting effect and induce apoptosis in various cancer cell lines including Caco-2, HT29, CT26, K562, A549, AGS, SiHa, KB, and OSCC. They can be used as compounds alongside chemotherapy and radiation therapy in the dietary regimen of cancer patients.

Keywords: Cancer, Novel Treatment, Lactic Acid Bacteria

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OBa-9

Abstract Type: Original Research

Novel Pseudomonas putida-derived nanoliposomes improve the efficacy and toxicity of doxorubicin in MCF-7 breast cancer cells

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Abstract

Background and Aim: In this study, we aimed to extract phospholipids from the bacterium Pseudomonas putida (PP), which serves as a safe, abundant and available source of phospholipids commonly used in nanoliposome production. These phospholipids do not pose any toxicity risks or adverse effects on the environment. We used them to produce nanoliposomes to encapsulate doxorubicin (Dox) and deliver it to MCF-7 breast cancer cells.

Methods: Molecular dynamics (MD) simulations were first performed to assess the feasibility of this approach and to analyze the DOX interaction with the phospholipids. The PP-derived phospholipids were then obtained using Folch's technique. Then, Dox-loaded PP-derived nanoliposomes (PNL-Dox) were fabricated via the thin-film method. After the determination of the physicochemical characteristics, the anticancer effects of this system were tested on MCF-7 cells.

Results: MD indicated that Dox formed hydrogen bonds with all of the phospholipids. These interactions did not affect the stability, fluidity, or thickness of the membrane. Additionally, a significant number of Dox molecules were found inside the nanocarrier, while only a small fraction interacted with the nanocarrier membrane. PNL-Dox exhibited a zeta potential of 8.8 ± 3.3 mV and an average particle size of 271.7 ± 7.1 nm. Scanning electron microscopy indicated that the particles were spherical with no aggregation. The release of the drug from PNL-Dox was higher at pH 6.5 compared to pH 7.4. In vitro studies demonstrated the successful uptake of PNL-Dox by MCF-7 cells, resulting in cytotoxic effects observed within 24 and 48 hours of treatment. Furthermore, PNL-Dox increased apoptosis and decreased the production of reactive oxygen species (ROS) in these cells.

Conclusion: Our study revealed the potential of PP phospholipids to make a promising anti-cancer drug delivery system, opening up new possibilities for the treatment of all types of cancers**.**

Keywords: Breast cancer; Nanoliposome; Doxorubicin; Molecular dynamics simulations

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OBa-10

Investigating the affinity of compounds identified in cinnamon essential oil (Cinnamomum verum) for beta-lactamase OXA-48 of Klebsiella pneumoniae bacteria using molecular docking methods

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Abstract

Background and Aim: The problem of bacterial resistance to antibiotics is one of the biggest challenges in the field of health and sanitary, which leads to the death of many people every year. In recent years, molecular modeling and computational biology have been considered as the main tools in drug design and discovery. Virtual screening is a computational method used to identify effective compounds from large chemical libraries and is faster and more cost-effective than experimental methods. In this study, the aim of bioinformatics is to investigate the possible molecular mechanism of inhibition of beta-lactamase OXA-48 of *Klebsiella pneumoniae* by the compounds in cinnamon essence (Cinnamomum verum) using molecular docking methods.

Methods: For this purpose, first, the crystallographic structure of OXA-48 in the presence of imipenem was obtained from RCSB database, and then the sequence, secondary structures and interaction of OXA-48 with imipenem ligand were investigated. In the next step, the protein structure of OXA-48 was extracted from the 7KH9.pdb file. The structure of imipenem was also obtained from RCSB database and after preparation, it was converted to PDBQT format for docking process. The chemical compounds identified in cinnamon essential oil were downloaded from PubChem database and prepared for docking in PDBQT format. Molecular docking was performed using AutoDock-Tools and Vina autodock software, and compounds were classified based on binding energy (ΔG of binding). After identifying the compounds effective in inhibiting the carbapenemase enzyme, the physicochemical, pharmacokinetic and toxicity properties of the three compounds with the highest affinity were determined by the SwissADME and PASS servers.

Results: Acquired results showed that the compounds in cinnamon essential oil and specifically Cadalene, gamma-Muurolene and alpha.-Calacorene can be used as a specific drug for the treatment of infections caused by *Klebsiella pneumoniae* with OXA-48 gene with high affinity and suitable therapeutic properties when one of the carbapenems is used. This research is an effective step towards discovering new drugs and dealing with antibiotic resistance.

Pharmacokinetic and toxicity analyzes showed that the identified compounds have favorable medicinal properties and low toxicity, which indicates their high safety and efficacy in therapeutic applications. The use of computational and bioinformatics methods in this study has accelerated the process of discovering new drugs and reduced costs, and can be a model for similar researches in the future.

Conclusion: Finally, this study showed that the compounds in cinnamon essential oil have a high potential for the development of new antibacterial drugs and can be used as alternative or complementary drugs in the treatment of antibiotic-resistant infections. According to the obtained results, it is suggested to conduct more research on these compounds in clinical and laboratory conditions to confirm their real effects on *Klebsiella pneumoniae* infections.

Keywords: Cinnamomum verum, OXA-48, *Klebsiella pneumoniae*, Molecular Docking, Pharmaceutical Properties.

OBa-11

Bioinformatic and pharmacological investigation of the potential of compounds identified in Shirazi thyme essential oil (Zataria multiflora) as a combination for beta-lactam antibiotics to inhibit the growth of Klebsiella pneumoniae bacteria carrying OXA-48 protein

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Abstract

Background and Aim: The growing challenge of antibiotic-resistant infections, especially those caused by multi-drug resistant (MDR) bacteria, is a significant global health concern.

One of the main mechanisms behind this resistance involves the production of enzymes such as carbapenemases, which deactivate antibiotics. Carbapenems, crucial antibiotics for treating MDR bacteria, have shown declining effectiveness due to increased resistance. The study focuses on the potential of compounds found in the essential oil of Zataria multiflora (Shirazi thyme) as adjuvants to β-lactam antibiotics in inhibiting Klebsiella pneumoniae that harbors the OXA-48 carbapenemase enzyme, thereby improving antibiotic efficacy and curbing bacterial growth.

Methods: Using bioinformatics and pharmacological approaches, this research assessed the interactions of compounds extracted from Zataria multiflora essential oil with OXA-48 protein through molecular docking methods. The study involved simulating the molecular binding of Zataria multiflora compounds to the OXA-48 protein, utilizing a crystal structure model (PDB ID: 7KH9) as the template. Various binding characteristics, such as free energy of binding, inhibitory constant, and binding efficiency, were evaluated to ascertain the efficacy of these compounds as potential inhibitors of the OXA-48 enzyme.

Results: The results revealed that certain compounds in Zataria multiflora essential oil, due to their favorable antimicrobial and low side-effect profiles, exhibit significant binding affinity to the OXA-48 protein. These compounds demonstrated a competitive binding energy and inhibition potential comparable to known antibiotics, indicating that they could serve as effective adjuvants in enhancing β-lactam antibiotic action. The docking analysis showed promising pharmacokinetic properties of these natural compounds, which may improve treatment efficacy against MDR K. pneumoniae infections.

Conclusion: The study highlights the potential of Zataria multiflora essential oil as a complementary treatment to combat carbapenem-resistant infections. With a focus on the molecular interactions that reduce bacterial growth, this research supports further investigation into clinical applications of these natural compounds. This alternative approach could present new avenues in developing strategies to manage antibiotic-resistant bacterial infections effectively. Future studies should explore clinical trials and additional pharmacokinetic analyses to confirm the therapeutic benefits of these compounds.

Keywords: *Zataria multiflora, OXA-48, Klebsiella pneumoniae, Molecular Docking, Pharmaceutical Properties*

OBa-12

Abstract Type: Original Research

Determination of immunogenic property of truncated MrpH.FimH.FliC as a vaccine candidate against urinary tract infections caused by *Proteus mirabilis and E. coli*

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Background and Aim:

E. coli and Proteus mirabilis are the common pathogens in Urinary tract infections (UTIs), an ideal vaccine is inevitably required. The N-terminal domain of MrpH and FimH (Truncated form of MrpH and FimH) lies between the most critical antigens of *P. mirabilis* and *E. coli* to consider as vaccine candidates. FliC of *Salmonella typhimurium* as an adjutant, induces several pathways of the immunity system, which leads to the production of antibodies and cytokines. In this study, adjuvant properties of FliC and efficacy of truncated MrpH and FimH as important antigens, in tMrpH.FimH.FliC was determined in *in vitro* and *in vivo* circumstances.

Methods:
E. coli (0073 strain), P. mirabilis (HI4320 strain), and *S. Typhimurium* (ATTCC 14028) were obtained from the Pasteur Institute of Iran. Bioinformatics methods selected the best model of fusion protein. Fusion *fimH*, *mrph*, and *flic* genes amplified by overlap PCR. All genes were cloned and expressed, then purified proteins, confirmed by SDS-PAGE and Western blot. Three proteins including FliC, and tMrpH.FimH.FliC was injected into mice and subsequently sera and supernatant of cell culture were collected to measure different immune responses compared to control. In addition, *Proteus mirabilis and E. coli* were injected into mice's bladders for challenging tests. For comparing the differences between the mean parametric values of the mice groups, SPSS software was used. In all experiments, $p < 0.05$ was considered significant.

Results:
According to our findings, tMrpH.FimH.FliC could stimulate both humeral and cellular immune responses, so that serum IgG, urine IgA, IL.4, IFN-γ, and IL.17 were increased significantly in comparison to FliC alone and control groups, this augmentation was considerable. Results of the challenging test showed a significant decrease of bacterial load in all of the challenged

groups compared to the control group, although this protective effect was the highest in mice vaccinated with tMrpH.FimH.FliC.

Conclusion:
Our results showed truncated MrpH and FimH without an unwanted domain is an ideal vaccine target and FliC, as an adjuvant, increases its immunogenic properties. Thus, fusion protein tMrpH.FimH.FliC can increase both humoral and cellular immune responses in UTIs and can be considered as promising vaccine against *P. mirabilis and E.coli*.

Keywords: *Proteus mirabilis*; *E. coli*; Urinary tract infections; MrpH; FliC; FimH.

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OBa-13

Original Research

Antibacterial effects of photoactivated flavonoid glycosides against *Acinetobacter baumannii*

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Abstract

Background and Aim: The rising antibiotic resistance of *Acinetobacter baumannii* complicates the treatment of infections, making the development of effective therapeutic strategies essential. This study investigates the potential of antimicrobial photodynamic therapy (aPDT) using Rutin-Gal(III) complex and Quercetin against *A. baumannii*.

Methods: The study measured the absorbance and fluorescence spectra, as well as the minimum inhibitory concentration (MIC) of the Rutin-Gal(III) complex and Quercetin. In addition, the effects on reactive oxygen species (ROS) production, extracellular polymeric substances (EPS), cell membrane permeability, and the expression of key resistance genes (*ompA* and $bla_{OXA\text{-}23}$) were analyzed, along with anti-biofilm and anti-metabolic activities.

Results: Both compounds exhibited visible absorption peaks and fluorescence at 524 nm for Quercetin and 540 nm for Rutin-Gal(III). The MIC for Rutin-Gal(III) complex was 64 µg/mL and for Quercetin, it was 256 µg/mL. aPDT using these compounds significantly reduced colony-forming units (58.4% and 67.5%), EPS production (47.4% and 56.5%), metabolic activity (30.5% and 36.3%), and downregulated gene expression of *ompA* (5.5- and 10.5-fold) and $bla_{OXA\text{-}23}$ (4.1-fold and 7.8-fold), with all results showing statistical significance ($P < 0.05$). Furthermore, aPDT enhanced biofilm degradation (36.2% and 40.6%), ROS production (2.55- and 2.90-fold), and membrane permeability (10.8- and 9.6-fold).

Conclusion: These findings suggest that Rutin-Gal(III) complex and Quercetin-mediated aPDT exhibit significant antibacterial activity and could be a promising adjunctive approach to conventional antibiotics for treating *A. baumannii* infections. However, the study was limited to testing on a standard strain, and further evaluation using clinical isolates would provide a more comprehensive assessment.

Keywords: *Acinetobacter baumannii*; Quercetin; Rutin-Gal(III) complex; Antimicrobial photodynamic therapy

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OBa-14
Original Research

Photoactive bio-theragnostic agent for *Enterococcus faecalis* biofilm destruction using aptamer decorated emodin nanoparticles-assisted delivery of dermcidin-derived peptide DCD-1L

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: The study addresses the issue of failures in root canal treatments, despite their overall high success rates. It emphasizes the need for innovative strategies, including new antimicrobial agents and drug delivery systems, to enhance treatment effectiveness. The research specifically investigates the antimicrobial properties of antimicrobial photodynamic therapy (aPDT) using a dermcidin-derived peptide (DCD-1L) encapsulated in aptamer-functionalized emodin nanoparticles (Apt@EmoNp-DCD-1L). The focus is on targeting *Enterococcus faecalis*, a common bacterium linked to recurrent treatment failures.

Methods: The study involved preparing EmoNp-DCD-1L and assessing the binding of a selected labeled aptamer to it, confirming its specificity for *E. faecalis*. The antimicrobial effectiveness of aPDT was evaluated after determining the minimum inhibitory concentration (MIC) of Apt@EmoNp-DCD-1L. Molecular docking analysis was conducted to investigate how EmoNp interacts with proteins related to *E. faecalis* pathogenesis. Lastly, the anti-virulence effects of Apt@EmoNp-DCD-1L-mediated aPDT were examined through quantitative real-time PCR (qRT-PCR), measuring the production of intracellular reactive oxygen species (ROS).

Results: The binding specificity of Apt@EmoNp-DCD-1L to *E. faecalis* was confirmed using flow cytometry. Results indicated that *E. faecalis* cell viability significantly decreased when treated with sub-MIC doses of Apt@EmoNp-DCD-1L (7.8 and 15.6 µM) compared to the control group ($P < 0.05$). Additionally, combining Apt@EmoNp-DCD-1L with blue laser light enhanced the anti-biofilm effects of aPDT against *E. faecalis* biofilm. Quantitative real-time PCR (qRT-PCR) analysis revealed a significant reduction in the expression of genes associated with bacterial biofilm formation following aPDT exposure ($P < 0.05$).

Conclusion: This in vitro study suggests that aPDT using the minimum concentration of Apt@EmoNp-DCD-1L can serve as an effective targeted bio-theragnostic agent for both detecting and eliminating *E. faecalis* in its dispersed and biofilm forms.

Keywords: Antimicrobial peptide; Antimicrobial photodynamic therapy; Aptamer; Biofilm; *Enterococcus faecalis*

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Abstract Type: Original Research (Times New Roman, font size 12)

OBa-15

Anti-biofilm Activity of a Lytic Phage Against Vancomycin-Resistant Enterococcus faecalis

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Abstract

Background and Aim:

This study aims to isolate a lytic bacteriophage against planktonic Enterococcus faecalis V583 culture and evaluate its ability to disrupt and inhibit biofilm.

Methods:

An anti-E. faecalis phage was isolated from sewage and visualized by electron microscopy, the vB_EfsS_V583 (V583) host range was determined by spot test on 13 E. faecalis clinical strains. Inhibition and degradation experiments were designed to investigate the effect of phage on biofilm. In the inhibition and degradation assay, biofilms were formed in the presence and absence of phage, respectively. Finally, crystal violet method tested the effect of phage on biofilm.

Results:

Phage V583 belongs to the Siphoviridae family and can infect all E. faecalis strains. Antibacterial activity has been shown to degrade and inhibit biofilm produced by V583. The study results showed that phage v583 is more efficient in biofilm inhibition than biofilm degradation. In both assays, phage-treated wells' absorption is less than untreated wells. These results were confirmed by Colony-forming unit reduction in the treated biofilm.

Conclusion:

The anti-biofilm activity showed that phage therapy using phage V583 might be an alternative tool to remove E. faecalis biofilms.

Keywords:

Bacteriophages, Biofilms, Enterococcus faecalis, PCR, Phage Therapy, Vancomycin Resistance

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OBa-16

Review Article

Latent Microbial Infections Leading to Myelin and Axonal Damage in Multiple Sclerosis: A Narrative Review

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Abstract:

Background: Multiple sclerosis (MS) is a complex autoimmune disease characterized by chronic inflammation, demyelination, and axonal damage in the central nervous system (CNS). This review specifically aims to investigate the role of latent microbial infections—such as those caused by *Epstein-Barr* virus, *Chlamydia pneumoniae*, and others—in contributing to myelin and axon damage in MS.

Methods: We evaluated recent studies from PubMed, Google Scholar, and Scopus databases that focus on the relationship between latent microbial infections and MS pathogenesis.

Results: In MS, emerging evidence suggests that latent microbial infections play a significant role in triggering and perpetuating the inflammatory processes associated with the disease. The potential mechanisms by which these infections contribute to the pathogenesis of MS, highlighting the interplay between the immune system, microbial agents, and the CNS are evaluated. These include molecular mimicry, where similarities in sequence or structure between viral, bacterial, or self-peptides can activate autoreactive T or B cells through cross activation by pathogen-derived peptides; chronic inflammation triggered by persistent infection, leading to immune-mediated damage; and disruption of the blood–brain barrier, allowing microbial agents or immune cells to infiltrate the CNS.

Conclusion: This review underscores the critical role of latent microbial infections in MS pathogenesis. By elucidating these mechanisms, we provide new insights that could inform the development of innovative therapeutic interventions and preventive strategies for MS.

Keywords: Multiple Sclerosis; Therapeutics; Demyelination; Axonal Damage; Latent Infections

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OBa-17
Original Research

Making a construct to deletion of DNT encoding gene in clinical *Bordetella pertussis* strain by homologous recombination

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Abstract

Background and Aim: Since**,** *Bordetella pertussis* strains are variable through the world, pertussis vaccines are challengeable to prevent the spread of this organism in communities. Nasal vaccine could be one of the alternative for whole cell and acellular vaccines nowadays. So in this research, we aimed to omit the deronecrotic toxin encoding gene (*dnt*) from a selected *B. pertussis* predominant strain in Iran.

Methods: According to the results of pulsed-field gel electrophoresis and virulence profile of 100 clinical *B. pertussis* strains from the biobank of Pasteur Institute of Iran, a *B. pertussis* strain with predominant genomic and virulence pattern was selected. In this study the construct including chloramphenicol resistant gene (*cat*) surrounded by downstream and upstream regions of *dnt* gene are created and confirmed via restriction enzyme analysis. This construct was designed in order to deletion of *dnt* gene via homologous recombination.

Results: First of all, 1300 bp of *cat* gene and its promotor amplified and cloned into puc19 and after that 700 bp and 800 bp region of downstream and upstream of *dnt* gene was amplified and cloned at the right and left side of cat gene, respectively. All of the steps was confirmed by restriction enzyme analysis.

Conclusion: This study was conducted in order to create an attenuated *B. perussis* from predominant circulating strains between Iranian people. For the next step, we will try to conjugate pss1129 vector into *B. pertussis* strain and delete the *dnt* gene by homologous recombination and advancing the study towards make an attenuated strain used in nasal vaccine composition.

Keywords: *Bordetella pertussis*, nasal vaccine, dermonecrotic toxin

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OBa-18
Abstract Type: Original Research

Monoclonal Antibody Targeting the PilQ-PilA DSL Region in Pseudomonas aeruginosa Enhances Survival in Infected Mice Treated with Antibiotic Combinations

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Abstract

Background and Aim: Infections caused by *Pseudomonas aeruginosa* are associated with significant mortality and morbidity among critically ill patients, largely due to the organism's multidrug resistance. This study investigates the effectiveness of a monoclonal antibody (mAb) targeting the PilQ-PilA DSL region (QA) in conjunction with antibiotics in a murine model of *P. aeruginosa* infection.

Methods: mAbs were produced from Hybridoma clone 2E1E6, and passive immunization was administered to groups of mice challenged with PAO1 and experiencing sepsis. The study included various groups: sepsis induced mice without treatment, those treated with 2E1E6, those treated with antibiotics and those receiving a combination of antibiotic and 2E1E6.

Results: We employed three clinically relevant antibiotics—levofloxacin, ceftazidime, and gentamicin—alongside the anti-QA mAb to treat mice suffering from *P. aeruginosa* sepsis. Notably, the combination of the antibiotic treatment with the anti-QA mAb significantly improved survival rates in mice infected with *P. aeruginosa* strain PAO1 compared to other treatment groups receiving either the antibody or antibiotics alone. This synergistic effect was attributed to enhanced bactericidal activity, which effectively curtailed bacterial spread to various organs.

Conclusion: Therefore, the combination of antibiotics and anti-QA mAb represents a promising therapeutic approach for managing *P. aeruginosa* sepsis, especially in cases involving highly virulent strains.

Keywords: Monoclonal Antibody; *Pseudomonas aeruginosa*; sepsis

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OBa-19
Abstract Type: Original Research

Rational Design of an Aureolysin Inhibitor: Molecular Docking Analysis of 5-[2-(4-Hydroxyphenyl) ethenyl]-2-(3-methylbut-2-enyl) benzene-1,3-diol as a Potential Therapeutic Agent against *Staphylococcus aureus*

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Abstract

Background and Aim: *Staphylococcus aureus* is a gram-positive bacterium, regarded as the most significant species of the genus *Staphylococcus*. This bacterium can lead to a range of diseases, from mild conditions like skin infections to life-threatening illnesses. Aerolysin is a crucial virulence factor in this bacterium; if targeted, it can inflict serious damage and significantly reduce its lifespan. Currently, antibiotic production industry faces challenges in inhibiting this bacterium, and research on the inhibition of this protein could serve as a foundation for treating this type of *Staphylococcus*. In this study, we attempted to determine the most effective inhibitory candidate through molecular docking analysis.

Methods: First, we downloaded the Aureolysine 3D structure in PDB format (PDB ID: 7skl) from the RCSB PDB database. Next, we obtained the resveratrol ligand (CID 445154), along with 20 similar structures exhibiting inhibitory properties, from the PubChem site in the SDF format to evaluate its potential as a drug. Subsequently, after preparing the protein and ligands, molecular docking was conducted using Molegro Virtual Docker version 6.0. The interactions were analyzed to identify the best binding with the lowest energy by the Molegro Molecular Viewer software. Finally, we assessed pharmacokinetic properties such as absorption, distribution, ligand excretion, and metabolism using the SwissADME.

Results: Among all the inhibitory analogs, the most effective analog for Aureolysin was identified as 5-[2-(4-Hydroxyphenyl) ethenyl]-2-(3-methylbut-2-enyl) benzene-1,3-diol with

CID442718. This compound has a molecular weight of 296.36 g/mol and a binding energy of -109.642 kcal/mol. This analog formed four steric interactions with the Aureolysin residues His356, Gln366, Arg320, and Leu365, along with three hydrogen bonds involving Asn364, Ser472, and His356. However, no electrostatic bonds were observed between CID442718 and Aureolysin. The ADME analysis revealed that CID442718 has a water solubility (logS) score of -5.00, lipophilicity (XLogP3) of 5.05, polarity (TPSA) of 60.69, and three hydrogen bond donors and three hydrogen bond acceptors.

Conclusion: Our results suggest that 5-[2-(4-Hydroxyphenyl) ethenyl]-2-(3-methylbut-2-enyl) benzene-1,3-diol is a promising candidate for the inhibition of Aureolysin in *Staphylococcus aureus*. Further in vitro and in vivo studies are required to confirm its efficacy and potential as a therapeutic agent.

Keywords: *Staphylococcus aureus*; Aureolysin; 5-[2-(4-Hydroxyphenyl) ethenyl]-2-(3-methylbut-2-enyl) benzene-1,3-diol; Molecular Docking.

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OBa-20
Abstract Type: Original Research

The antibacterial effect of adipose-derived stem cells on LL-37 resistant bacteria

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Abstract

Background and Aim: Previous studies have shown the effect of stem cells in reducing the growth of bacteria and one of their possible mechanisms is the secretion of the antimicrobial

peptide Since the antibacterial effect of stem cells on LL-37 resistanct bacteria has not been studied yet, the aim of this study is determining the antibacterial effect of human adipose-derived stem cells (hADSCs) on Pseudomonas aeruginosa (Gram-negative), Proteus mirabilis (Gram-negative) and MRSA (Grampositive) and its association with antimicrobial peptide LL-37.

Methods: After separation and culture of the hADSCs, they were confirmed by flow cytometric analysis of the cell surface markers and by differentiating into adipocytes and osteoblasts. All three bacteria were inoculated to the medium of unstimulated stem cells (supernatant), interferongamma-timulated stem cells (CM). and the bacterial growth was evaluated and compared by microdilution method and gentamicin. The LL-37 concentration was measured by ELISA method. One-way ANOVA followed by post hoc Tukey and Kruskal-Wallis tests were used for statistical analysis. P <0.05 was considered as significan.

Results: Supernatant and CM of the hADSCs reduced the growth all three bacteria (P<0.05, P<0.01). A significant amount of LL-37 peptide was found in both supernatant and CM of hADSCs. Also, the concentration of LL-37 peptide in supernatant and CM was reduced in the presence of each bacterium (P<0.05 and P<0.01). There was no significant difference between the growth of bacteria .and the amount of LL-37 production between supernatant and CM in control and all three bacteria.

Conclusion: Our results indicate that hADSCs-secreted factors demonstrate an antibacterial effect against Gram-negative and Gram-positive bacteria mediated in part by LL-37 secretion. This ability is too high, which can reduce the growth of resistant bacteria to antibiotics or bacteria secreting antiLL-37 enzymes.The results of this study revealed that the efficacy of mediums derived from unstimulated cells is comparable with interferon gamma-stimulated cells. It seems that the hADSC secreted factors can be considered in the treatment of antibiotic-resistant infections.

Keywords: stem cells; antibacterial effect; Pseudomonas aeruginosa; Proteus mirabilis; MRSA

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OBa-21

Abstract Type: Original Research

Investigating the antibacterial effects of human adipose derived stem cell (hADSCs) on E. coll ATCC 25922 and the role of hepcidin

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Abstract

Background and Aim: Several studies have shown the antibacterial effects of stem cells and these effects were mediated by antimicrobial peptides secretion such as LL-37.Since the antibacterial effect of human adipose tissue-derived stem cells (hADSCs) by hepcidin has not been investigated, the aim of this study was to evaluate the antibacterial effect of human adipose tissue-derived stem cells (hADSCs) on E. coli ATCC:25922 and the role of hepcidin.

Methods: Isolated hADSCs were evaluated by flow cytometric analysis and differentiatin into adipocytes and osteoblasts. Stem cells were cultured in 24-well plate and a suspension containing 300 CFUS/ml of E coli ATCC: 25922-prepared by serial dilution- was added each well and incubated for 6 hours at 37° C. The supematant of each well considered as conditioned medium (CM) and bacterial growth was measured in CM group. control group only bacteria) and heparin group (containing heparin). Hepcidin gene expression in stem cells was determined by real-time PCR One-way ANOVA. Tukey post hoc and Kruskal-Wallis tests were used for statistical analysis. $P<0.05$ was considered as a significant criterion.

Results: The growth of bacteria was (1494 + 173.2) 10 CFU/ml in control group, (242.7 +77.9) 10' CFU/ml in CM group and (533.3± 104) 10 CFU/ml in heparin group. Bacterial growth was significantly reduced in CM group compared to the control group ($P<0.05$). The expression of hepcidin gene was increased to 3.16 fold in CM group compared to control group. The expression of hepcidin was reduced in the presence of heparin. Also, heparin increased bacterial growth, but not significantly.

Conclusion: Our results showed that hADSCs reduce the growth of bacteria significantly. In the presence of bacteria the expression of hepcidin by hADSCs was increased .Heparin was able to reduce the expression of hepcidin and increase the bacterial growth, but this increase was not statistically significant. It seems that in addition to hepcidin, other secretory factors may be involved in the antibacterial effects of hADSCs.

Keywords: stem cells; antibacterial; Escherichia coli; Hepcidin

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OBa-22

Prevalence of colistin resistance in clinical isolates of *Pseudomonas aeruginosa*: a systematic review and meta-analysis

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Abstract

Aim: The emergence of resistance to colistin, the last resort for treating severe infections caused by *Pseudomonas aeruginosa*, poses a significant threat to public health. This meta-analysis aimed to investigate the prevalence of colistin resistance in clinical isolates of *P. aeruginosa.*

Method: A comprehensive search of MEDLINE (PubMed), Web of Science, and Scopus databases was conducted to identify relevant articles published until December 2023. Subsequently, a meta-analysis was performed using Stata software to examine the pooled prevalence of colistin resistance and to conduct subgroup analyses.

Results: A total of 619 studies were included in the meta-analysis, revealing a global prevalence of colistin resistance of 1% among all *P. aeruginosa* isolates. Furthermore, cystic fibrosis patients exhibited the highest resistance to colistin, with a prevalence of 7% among the examined diseases.

Conclusion: The increase in colistin resistance in *P. aeruginosa* in recent years from 2% (in the period of 2006–2010) to 5% (in the period of 2020–2023) underscores the need for implementing infection prevention programs, using appropriate treatment regimens, and disseminating comprehensive information on antimicrobial resistance patterns. These measures are crucial for addressing this growing public health concern.

Keywords: *Pseudomonas aeruginosa*; colistin; meta-analysis

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OBa-23

Abstract Type: Original Research

Investigation of the *Rv3065, Rv2942, Rv1258c, Rv1410c,* and *Rv2459* efflux pump genes expression among multidrug-resistant *Mycobacterium tuberculosis* clinical isolates

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Abstract

Background and Aim: Different resistance mechanisms for multidrug-resistant tuberculosis (MDR-TB) and extensively drug- resistant tuberculosis (XDR-TB) have been reported. Although mutations in target genes are the main cause of drug resistance, efflux pumps (Eps) also play an important role in this process. So far, limited information is available on the expression profile of genes encoding drug EPs in *Mycobacterium tuberculosis* (Mtb) clinical isolates. Here, we investigated the overexpression of five putative EP genes plus gene mutations in MDR-TB clinical isolates.

Methods: A total of 27 Mtb clinical isolates including, 22 MDR and 5 sensitive isolates were analyzed. Minimum inhibitory concentrations (MIC) were determined in the absence and presence of efflux inhibitor. The expression level of 5 EP genes including *Rv3065*, *Rv2942*, *Rv1258c*, *Rv1410c*, and *Rv2459* was investigated by quantitative real time PCR (RT-qPCR). DNA sequencing of *rpoB*, *katG*, and *inhA* promoter was done.

Results: Among the 22 MDR-TB isolates, 13 (59.1%) showed significant overexpression (>4-fold) for at least one EP gene. The expression levels of 5 genes were significantly higher ($P < 0.05$) in MDR-TB isolates than sensitive isolates. The *Rv3065* (22.7%), and *Rv1410c* (18.2%) were found to be the most commonly overexpressed EPs. The observed MICs were as follows: RIF (2 to >128 µg/ml) and INH (2–32 µg/ml). After efflux pump inhibitor exposure, 10/22 (45.45%) isolates showed a decrease in MIC of INH, and 17/22 (77.27%) isolates showed a decrease in MIC of RIF. Of the isolates that were overexpressed, 4 isolates lacked mutation in *inhA*, *rpoB*, and *katG* genes and 10 ones lacked mutation in *inhA* and *katG*.

Conclusion: Our data showed that drug resistance of MDR-TB is a combination of drug efflux and the presence of target gene mutations. Hence, the expressional differences of some EPs genes (*Rv2942*, *Rv3065*, *Rv1410c*, *Rv2459*, and *Rv1258c*) between MDR and sensitive isolates could be helpful in MDR-TB diagnosis and treatment. Efflux pump activity inhibitor CCCP can reduce the phenotypic level of INH and RIF resistance. In addition, to clarify the actual roles of EPs in drug resistance, further researches on more isolates and more EP genes regarding efflux pump inhibitors are required.

Keywords: Efflux pumps, MDR-TB, Mutation, Tuberculosis

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OBa-24

Abstract Type: Systematic Review

Exploring Topical Probiotics as an exciting new prospect for Managing Diabetic Foot Ulcers: A Systemic Review

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Abstract

Background and Aim:

Diabetic foot ulcer (DFU) is a common and severe complication of diabetes, affecting 19-34% of patients, with 25% requiring amputation and a 50% three-year survival rate. Probiotics may play a crucial role in managing chronic diseases and their complications, including diabetic foot ulcers. This study aims to review the effects of topical probiotics on diabetic foot ulcers management.

Methods:

This review article searched articles published on PubMed, Google Scholar, and Web of Science from 2021 to June 2024 using keywords such as diabetic foot ulcer,diabetes, gut-skin axis, and probiotic. About 26 articles were identified, with 14 excluded based on titles and abstracts and 12 articles were selected under the inclusion criteria.

Results: Finally,12 articles were included in the study. Topical application of a soybean-based probiotic effectively managed DFUs, achieving complete healing in over 80% of patients within 16 weeks. Topical application of Lactobacillus plantarum in chronic infected leg ulcers, diabetic and non-diabetic, reduced neutrophils, decreased bacterial load, and promoted wound healing. Perioperative probiotic supplementation accelerated skin healing by reducing inflammation, promoting neovascularization, and increasing type I collagen deposition. In a study involving 60 patients with Wagner grade 3 diabetic foot ulcers, probiotics significantly reduced ulcer length, width, and depth over 12 weeks. Probiotics also improved fasting plasma glucose, serum insulin concentrations, and HbA1c levels. Probiotics containing Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus fermentum, and Bifidobacterium bifidum safely aided in the therapy of infected diabetic wounds. Both topical application and oral intake of probiotics, particularly combined with antibiotics, appeared beneficial for enhancing the healing process of infected diabetic foot ulcers.

Conclusion: The findings suggest that probiotics hold promise as a novel adjuvant therapy for DFUs. However, clinical studies are limited due to challenges in identifying, isolating, stabilizing, and the high cost of probiotics. Further research is necessary on this topic.

Keywords: Diabetic foot ulcer, diabetes, gut-skin axis, probiotics

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OBa-25

Comparative Analysis of Cytotoxicity and Toxin Gene Profiles in Shigella Isolates: Insights into Pathogenicity and Clinical Impact

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Abstract

Background and Aim: Shigella species are known for their ability to cause dysentery and other gastrointestinal disorders through toxin production. This study investigates the cytotoxicity of Shigella isolates on cell lines to evaluate the toxic potential of different species and their correlation with the presence of specific toxin genes.

Methods: A total of 100 Shigella isolates, including *S. flexneri*, *S. sonnei*, and *S. dysenteriae*, were tested for cytotoxicity. Toxin-producing capacity was assessed by exposing cell lines to bacterial toxins and monitoring morphological changes such as cell rounding and color alteration. The presence of toxin genes (*sen*, *set1A*, *set1B*, and *sat*) was determined using PCR. Cytotoxic effects were quantified by comparing toxin-treated cells to positive controls at various time intervals (4, 8, 24, and 48 hours).

Results: Out of 100 isolates, 15 *S. flexneri*, 10 *S. sonnei*, and 1 *S. dysenteriae* exhibited cytotoxicity. Most isolates demonstrated 30% cell rounding compared to positive controls. Isolates harboring *sen*, *set1A*, *set1B*, and *sat* genes, particularly from hospitalized patients, exhibited over 50% cytotoxicity, with cell color changing from red to yellow. Notably, *S. dysenteriae* displayed the highest cytotoxicity, destroying over 70% of cells within 4 hours, followed by *S. flexneri*. In contrast, *S. sonnei* showed delayed and less stable cytotoxic effects, with some isolates losing toxicity after 8 hours. However, isolates from hospitalized cases retained toxicity at all time points (8, 24, and 48 hours).

Conclusion: These findings highlight the high cytotoxic potential of *S. dysenteriae* and *S. flexneri*, especially in isolates from severe cases. The transient cytotoxicity observed in *S. sonnei* isolates emphasizes variability in toxin stability. This study underscores the clinical significance of toxin genes in Shigella pathogenesis and their role in disease severity.

Keywords: Shigella; Cytotoxicity; Toxin Genes; Pathogenesis; Gastrointestinal Disorders

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OBa-26

Abstract Type: Original Research

Enhancing Antibiofilm Efficacy of Lysostaphin Against Staphylococcus aureus Wound Infections Using Niosomal Delivery Systems

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Abstract

Background and Aim: Staphylococcus aureus is the most common cause of wound infections and often presents biofilms with inherent resistance to antibiotics. In this regard, lysostaphin has emerged as a potent anti-staphylococcal enzyme with limitations in delivery and stability. Herein, we develop a new strategy based on niosomes encapsulating lysostaphin for enhanced efficacy against biofilms. By combining the active targeting capabilities of niosomes with the potent antimicrobial action of lysostaphin, we aim at enhanced wound healing and combating antibiotic resistance.

Methods: Clinical isolates of S. aureus were collected from wound infection specimens and confirmed by standard microbiological and molecular methods. Biofilm formation was quantified by crystal violet assay. The thin-film hydration method was used to prepare the lysostaphin-containing niosomes, which, after preparation, were characterized for size, encapsulation efficiency, and stability. The in vitro antibiofilm activities of the lysostaphin-loaded niosomes were conducted by measuring biofilm disruption using both the spectrophotometric and confocal microscopy analyses. Controls included free lysostaphin and empty niosomes. Moreover, statistical analysis was focused on the significance of the observed differences.

Results: Lysostaphin-loaded niosomes exhibited significantly higher antibiofilm activity compared to free lysostaphin and empty niosomes ($p < 0.01$). Confocal microscopy revealed extensive biofilm disruption and bacterial cell lysis upon treatment with lysostaphin-loaded niosomes.

Conclusion: This study has emphasized that lysostaphin-loaded niosomes may be an effective therapeutic strategy against S. aureus biofilms in wound infection. The niosomal formulations improve enzyme stability and target cells associated with biofilms, thus overcoming the major limitations of traditional therapies. These promising in vitro results call for in vivo studies to further establish the clinical applicability of this novel approach.

Keywords: Staphylococcus aureus; Biofilm; Niosomes; Wound infection.

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OBa-27

Abstract Type: **Narrative Review**

The health risks of illegal immigrants and the resurgence of infectious diseases in Iran

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Abstract

Background and Aim: In all the countries of the world, one of the main concerns about illegal immigrants is the health issue. For most of these immigrants, there is no access to medical records such as their vaccination schedule. In addition, for example, in some neighboring countries, vaccination programs are not mandatory and are mostly encouraged, so there is a potential risk of disease transmission from these immigrants.

Methods: Considering the above-mentioned points, it led us to look at the statistics of the health and treatment situation in Iran due to the arrival of illegal immigrants.

Results: According to the statistics of the World Health Organization and UNICEF in 2023, the situation of infectious diseases in Afghanistan and Iran has significant differences. In Afghanistan, polio is still a major health challenge, while Iran has been a country since 2001. It is known to be free of this disease. Measles in both countries has not yet been completely eradicated, but in Iran due to high vaccination coverage, its cases are very rare, while in Afghanistan, the lack of vaccination has caused a very high prevalence of this disease, especially among children. Malaria is common in Afghanistan, especially in the southern and eastern regions, and is still a serious threat to public health, while in Iran, this disease has been eradicated in many regions and is reported only in some southern and border regions. Tuberculosis (TB) is also considered as one of the major diseases in Afghanistan and requires strengthening control and treatment programs, while in Iran this disease is under control and

national programs are being implemented to reduce it. Acute diarrhea, which is one of the main causes of death of children under five years of age in Afghanistan and is extremely common due to health problems and lack of safe drinking water, has decreased in Iran due to the improvement of health conditions and access to safe water.

Conclusion: The arrival of a large number of illegal immigrants to Iran can put significant pressure on the country's healthcare system. These immigrants, who often live in unsanitary conditions, may need urgent medical services. In the event of an epidemic of infectious diseases, the capacity of hospitals and health centers is quickly saturated, and this issue can cause a shortage of hospital beds, medicines and medical resources. Therefore, continuous screening is necessary to prevent the illegal entry of immigrants.

Keywords: Illegal immigrants, outbreaks, infectious diseases

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OBa-28

Abstract Type: Original Research

Survey on *Lactobacilli* cell extract effects isolated from Guilan province dairy products on *PTEN*, *Caspase-3* and *P53* signaling pathways in HT-29 cancer cell line and HUVEC normal cells

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Abstract

Background and Aim: Colorectal cancer is one of the most common malignancies of the gastrointestinal tract worldwide. The death rate is increasing every year and new strategies are needed to control this deadly disease. Probiotics help to reduce or stop growth in cancer cells and cure cancer by inducing apoptosis. This study investigated the effects of *Lactobacillus* cell extracts isolated from dairy products in Guilan province on *PTEN*, *Caspase-3* and *P53* signaling pathways in HT-29 cancer cell line and normal HUVEC cells.

Methods: The survival of cells under the effect of isolated *lactobacillus* extract was investigated using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, Annexin V-FITC) test. *PTEN*, *Caspase-3* and *P53* were performed in the cells and flow cytometry with Annexin V-FITC kit was used for the analysis of the standard strain of *L. fermentum* PTCC 1744 was used.

Results: The isolated species was *Lactobacillus fermentum* (*L. fermentum*) with 88.61% homology and was registered as *Limosilactobacillus fermentum* GL strain. MTT results showed that the cytoplasmic extract of L. *fermentum* GL bacteria at a concentration of 1 mg/ml caused a 50% reduction in HT29 cancer cells, but had no toxic effect on normal HUVEC cells. Also, after comparison, it was observed that the cell extracts of both isolated *L. fermentum* GL strains and the standard *L. fermentum* PTCC 1744 strain reduced the growth of cancer cells to the same extent, and no significant difference was observed between the two strains.

Conclusion: Flow cytometry results confirmed the death of cancer cells through apoptosis. Accordingly, with further studies, *L. fermentum* GL can be used as a probiotic product in the treatment and prevention of colon cancer.
Keywords: *Lactobacillus*; dairy products; signaling pathway; cancer cell; normal cell
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OBi-1

Glutamine protected rats against acute liver injury by elevating the Gln-GSH axis and reducing the NF-kβ signaling

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Background and aims: Acute liver injury with a poor prognosis is a major health concern. Hepatotoxic compounds, such as carbon tetra chloride (CCl_4) can cause liver failure by increasing hepatic nuclear factor- kβ (NF-kβ) pathway signaling while decreasing endogenous antioxidant potential. Therefore, we conducted a study to investigate the effect of glutamine (Gln) on NF-kβ expression and indicators of oxidative stress and inflammation in a rat model of acute liver injury.

Materials and Methods: The study involved four groups, each consisting of nine rats: control (C), acute liver injury rat model (ALI), and those treated with Gln (1000 mg/L in drinking water for two weeks). Acute live injury was simulated by injecting CCl_4 (1 ml/kg) on the 15th day. The expression of hepatic NF-kβ was analyzed, and markers of oxidative stress and

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inflammation were measured. Additionally, biochemical markers of hepatic function were evaluated, and liver histopathological changes post-ALI simulation were examined.

Results: The results showed that Gln treatment effectively reduced liver histopathological changes due to ALI induction. The treatment decreased hepatic NF-kβ expression, liver dysfunction parameters, and indicators of oxidative stress and inflammation. Furthermore, it significantly enhanced systemic and hepatic antioxidant potential ($p < 0.001$).

Conclusions: The hepatoprotective effect of Gln included preventing liver necrosis and improving liver function by reducing NF-kβ signaling and increasing systemic and hepatic antioxidant potential by raising the GSH/GSSG ratio and antioxidant enzyme activities. Probably, a decrease the NF-kβ pathway and an enhancement of the Gln-GSH axis may be principal mechanisms for its hepatoprotective effects.

Keywords**:** Glutamine; Acute liver injury; Nuclear factor- kβ, Glutathione

OBi-2

Abstract Type: Original Research

Therapeutic potential of Dimethyl fumarate in preventing premature rupture of membranes

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Abstract

Background and Aim: The fetal membrane, containing amniotic fluid, plays a vital role in protecting the fetus and creating a suitable environment for its growth. Premature rupture of membranes (PROM) is defined as rupture of fetal membranes before the onset of labor. PROM is one of the most common pregnancy complications that can lead to serious complications for the mother and fetus. Recent studies have shown that inflammation and oxidative stress may be key factors in PROM development. Dimethyl fumarate (DMF), a fumaric acid ester, could ameliorate oxidative stress and inflammation through reducing the production of inflammatory cytokines and suppressing oxidative stress in the body. However, the role of DMF in preventing amniotic membrane degradation is not well defined. This study was conducted with the aim of evaluating the therapeutic potential of DMF in preventing rupture and amniotic membrane regeneration.

Methods: From human fetal membranes, we extracted human amniotic epithelial stem cells (hAESCs). The cells were exposed to oxidative stress by the use of hydrogen peroxide and mitochondrial damage. By monitoring the expression of apoptosis-related genes in vitro, we assessed the impact of DMF on the survival and growth of hAESCs. Using the western blot technique, we assessed the expression of the proteins fibroblast growth factor (FGF) and epidermal growth factor (EGF) to evaluate the repair and regeneration potential of DMF. By using ELISA, the levels of MDA, IL-6, and TNF-α were determined in order to assess the antioxidant and anti-inflammatory properties of DMF on cells.

Results: A dose-dependent effect was observed for DMF on the survival of hAESCs in vitro. DMF treatment improved cell survival by reducing the expression of genes associated with apoptosis markers (Bax, caspase 3, and cytochrome c) and increasing the anti-apoptotic marker Bcl2. DMF also improved the repair and regeneration of damaged cells in vitro by upregulating

the expression of fibroblast growth factor (FGF) and epidermal growth factor (EGF) proteins. DMF decreased inflammation and oxidative stress caused by hydrogen peroxide- in hAESCs by decreasing MDA, IL-6, and TNF-α.

Conclusion: Based to our study, DMF improved hAESCs' in vitro survival and proliferation as well as their capacity to combat inflammatory and oxidative stress. As a result, DMF may be a very effective therapy for treating and preventing membrane rupture.

Keywords: Dimethyl fumarate, premature rupture of membrane, regeneration, amniotic membrane,

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OBi-3

Abstract Type: Original Research (Times New Roman, font size 12)

Antioxidant and anti-inflammatory effects of cerium oxide nanoparticles

Fatemeh sadat Babaei, Ebrahim Abbasi, **, (Times New Roman, Bold, font size 10)**

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Abstract

Previous experiments have reported that cerium oxide nanoparticle has potential antioxidant effects. Hence, in this experiment, we evaluated the anti-hyperlipidemic, antioxidant, and anti-inflammatory effects of this nanoparticle in the high-fat diet (HFD) rats.

Background and Aim: Previous experiments have reported that cerium oxide nanoparticle has potential antioxidant effects. Hence, in this experiment, we evaluated the anti-hyperlipidemic, antioxidant, and anti-inflammatory effects of this nanoparticle in the high-fat diet (HFD) rats.

Methods: In this experiment, Wistar rats were randomly divided into 3 groups, including 1- healthy animals, 2: high-fat diet (HFD) group, and 3: HFD + cerium oxide nanoparticles. In the end of the experiment, the biochemical factors such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein, albumin, bilirubin, blood sugar, triglyceride, and cholesterol were determined. Oxidative stress markers, including malondialdehyde (MDA), total antioxidant activity (TAC), total oxidative status (TOS), glutathione levels, and tumor necrosis factor-α (TNF-α) levels were measured. Furthermore, morphological changes in the liver were evaluated by using hematoxylin and eosin (H & E). The results were analyzed using SPSS as mean ± SEM by ANOVA followed by Tukey as a post-hoc test.

Results: The levels of liver enzymes significantly increased by HFD, while treatment with cerium oxide nanoparticles normalized these factors. HFD also increased the malondialdehyde (MDA), total oxidative status (TOS), glutathione levels, and tumor necrosis factor-α (TNF-α)

levels, and reduced antioxidant activity (TAC) and glutathione levels. While treatment with cerium oxide nanoparticles normalized these factors. cerium oxide nanoparticles also alleviated morphological changes of liver.

Conclusion: : Our results showed that cerium oxide nanoparticles reduce inflammation and oxidative stress in HFD model and can be a propose as a potential treatment of hyperlipidemia.

Keywords: high-fat diet (HFD), rats, malondialdehyde

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OBi-4

Abstract Type: Original Research

Effects of licorice hydroalcoholic extract and glyceric acid on sex hormones, malondialdehyde, and testicular histomorphometry in NMRI adult male rats exposed to cyclophosphamide

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Abstract

Background and Aim: The present study aimed to investigate the effects of licorice hydroalcoholic extract (LHE) and Glyceric acid (GA) on sex hormones, Malondialdehyde (MDA), and testicular histomorphometry in NMRI adult male rats exposed to cyclophosphamide (CP)

Methods: Animals were divided into 8 groups, including (1) control: normal saline, (2) CP: 100 mg/kg, (3) LHE: 150 mg/kg, (4) GA: 0.5 mg/kg, (5) CP + 50 mg/kg LHE, (6) CP + 0.5 mg/kg GA, (7) CP + 150 mg/kg LHE, and (8) CP + 250 mg/kg LHE. Changes in testicular tissue were evaluated through Hematoxylin–Eosin staining. The serum levels of luteinizing hormone (LH)/follicle-stimulating hormone (FSH) and MDA concentrations were measured by an enzyme-linked immunosorbent assay (ELISA) kit.

Results: Histological findings showed the integrity of the seminiferous tubules and regular basement membrane in groups 1, 3, and 4. In group 2, the epithelium had an irregular shape with atrophy, edema, and immense, extensive inflammation. Group 5 had decreased tubular diameter. In group 6, edema with vacuolization of the interstitial tissue was observed. Slight spermatogenesis and Leydig cells with pyknotic nuclei were evident in groups 7 and 8. Group 2 had significantly decreased serum levels of LH and FSH compared to group 1. Groups 5, 6, 7, and 8 showed no significant changes in the LH level. Although the administration of 50 mg/kg LHE (group 5) increased the level of FSH compared to group 2, other doses, 150 mg/kg (group 7) and 250 mg/kg (group 8), had no significant difference from group 2. Furthermore, the FSH level increased in group 6 compared to group 2. The MDA level in group 2 was significantly increased compared to group 1 and significantly decreased compared to group 5.

Conclusion: Results demonstrate that administration of low doses of LHE (compared to high doses) and GA is highly effective. They can improve histological characteristics, sex hormones (LH/FSH), and the MDA level, as well as mitigate the side effects of CP. Eventually, it is essential to note that LHE effects are more prominent than GA effects.

Keywords: Glyceric acid; Licorice; Cyclophosphamide; Sex hormones; Histology

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OBi-5
Original Article

Evaluation of the protective effect of Omega-3 on the hepatotoxicity of Clavulanic Acid in mice

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Abstract

Purpose: Clavulanic acid (CA) is a weak beta-lactam antibiotic and a potent inhibitor of the beta-lactamase enzyme, which alone does not have much antibiotic power. Still, when combined with penicillin group antibiotics, it increases its effectiveness. This study aims to

investigate the protective effects of omega-3 on hepatotoxicity caused by clavulanic acid in male mice.

Methods: CA was administered intraperitoneally at 10 mg/kg, and omega-3 was administered orally to male mice at 125, 250, and 500 mg/kg for 21 days. Liver mitochondria were isolated to evaluate oxidative stress biomarkers such as reactive oxygen species (ROS), lipid peroxidation (LPO), and glutathione (GSH) content. Blood samples were collected, and Alanine transaminase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), and Lactate dehydrogenase (LDH) were quantified in the serum. Also, the histopathological changes of the liver tissue were examined.

Results: Oxidative stress biomarkers, including ROS and LPO, were significantly enhanced. Also, GSH content was significantly decreased by CA-treated groups in Liver mitochondria compared to the control group. CA administration elevated the serum levels of ALT, AST, ALP, and LDH compared with the control group. Omega-3 inhibits the toxicity of CA by Reducing the amount of ROS and LPO, increasing the amount of GSH, reducing the level of liver enzymes, and improving the histopathological damage of liver tissue (especially at high doses).

Conclusion: These findings suggest that omega-3 causes dose-dependent Reduction of hepatotoxicity of clavulanic acid in mice.

Keywords: Clavulanic acid, Omega-3, Hepatotoxicity, Liver enzymes, Oxidative stress

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OBi-6

Abstract Type: Clinical Trial

The effects of curcumin on hepatic T2* MRI and liver enzymes in patients with β-thalassemia major: a double-blind randomized controlled clinical trial

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Abstract

Background and Aim: Curcumin present in turmeric has been considered due to its cancer-preventive features, antioxidant and anti-inflammatory properties. This double-blind, randomized, controlled clinical trial with a reasonable sample size and longer intervention period was conducted to investigate how oral curcumin affected cardiac and hepatic T2*MRI and liver enzymes in patients with β-thalassemia major.

Methods: This clinical trial study was conducted on 171 patients over 5 years old. The subjects were randomly divided into a curcumin-treatment group and a placebo group to receive either curcumin capsules twice daily or placebo for 6 months. Patients were examined once a month for 6 months to receive capsules and measure the levels of alanine aminotransferase (ALT), aspartate transferase (AST), alkaline phosphatase (ALP), direct and total bilirubin, ferritin and cardiac and hepatic T2*MRI.

Results: There was a significant decrease in levels of AST, ALT, ALP, and bilirubin (direct and total) in the curcumin group compared with the placebo group by the end of the study ($p < 0.05$). The levels of serum ferritin remained unchanged in both groups at the end of the follow-up period ($p > 0.05$). No significant differences were observed between the curcumin and placebo groups at baseline values or at the end of the study of cardiac and hepatic T2*MRI and serum magnesium.

Conclusion: Administration of curcumin has some beneficial effects on liver function by reducing liver enzymes in patients with beta-thalassemia major.

Keywords: Thalassemia, Curcumin, Liver Enzymes

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OB-07

Ectopic expression of insulin in a type 1 diabetic rat model by injection of manipulated mesenchymal stem cells with an insulin construct driven by a glucose-sensitive romoter in the port vein

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Abstract

Background and Aim: The treatment of type 1 diabetes through islet cell transplantation is a complex process, facing challenges such as allograft rejections and a limited supply of donors. One potential solution is to utilize the liver as an alternative for natural insulin production, as hepatocytes can secrete proteins and respond to glucose levels. Recent research has shown promising results in using mesenchymal stem cells as a potential cure for diabetes. The study utilized a diabetic rat model, confirmed through blood sugar measurement.

Methods: A plasmid vector was designed with specific genetic components and synthesized. Bone marrow-derived mesenchymal stem cells (BM-MSCs) were cultured and transfected with

the plasmid. Transfection confirmed by PCR. For the animal study, 30 male Wistar rats were divided into six groups. All groupe recive MSCs or constract via Portal Vein Injection. The control group did not receive any treatment, while the second group received MSCs. The third group received MSCs transfected with a specific construct. The fourth group was induced to develop diabetes through streptozotocin (STZ) injection, the fifth group developed diabetes and received untransfected MSCs, and the sixth group received MSCs transfected with the specific construct. To manage Pain, appropriate pain control was administered to the rats for 3 days after the surgery. Fixed liver tissues obtained from the euthanized rats were utilized for immunohistochemistry

Results: In this study, immunohistochemical techniques were used to examine insulin expression in different groups of rats. The control groups showed high levels of insulin expression, while the diabetic groups exhibited lower expression. However, there was a significant difference between the diabetic groups treated with MSC and transgenic MSC cells. All groups had similar baseline glucose levels, but the diabetic groups showed a significant increase after STZ injection, whereas the control and MSC groups did not. Postintervention, both the control and MSC groups had similar glucose levels to the post-STZ levels. However, diabetes-induced groups experienced a significant decrease in glucose levels, with the transfected MSCs showing a greater decrease than the untransfected MSCs.

Conclusion: The study suggested that treatment with MSCs, especially transfected ones, can effectively reduce glucose levels in rats with diabetes. In this research, rat BMMSCs were utilized to create insulin-producing mesenchymal cells with glucosesensitive insulin expression. The cells were transferred to the liver of diabetic rats via portal vein injection,

leading to an increase in insulin expression. This study proposes a novel approach for cell therapy and delivery in the treatment of type 1 diabetes.

Keywords: bone marrow-derived mesenchymal stem cells , cell therapy, portal vein

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OBi-8
Abstract Type: Original Research

Evaluation of the effects of Melatonin on heart function and inflammatory and oxidant biomarkers in patients after coronary artery bypass graft surgery (CABG)

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Abstract

Background and Aim: Background: Oxidative stress and inflammation following the Coronary Artery Bypass Grafting (CABG) surgery have been identified to damage the myocardium and affect heart function. Therefore, this study aimed to evaluate Melatonin's effects on heart function and inflammatory and oxidant biomarkers in patients after CABG and whether the effects are dose-dependent

Methods: A total of 60 CABG patients in the postoperative period were included in this double-blind, randomized placebo control clinical trial. The patients were randomly divided into three groups: Group 1 (n= 20, 5 mg melatonin), Group 2 (n= 20, 10 mg melatonin), and Control (n= 20, placebo). The start of taking placebo and Melatonin was about 8 to 10 days after hospital discharge and continued for 60 days before and after all the participants underwent echocardiography, electrocardiography and taking systolic and diastolic blood pressure, blood collection for the measurement of biochemical markers (CK-MB, LDH, MDA, TNF-α, TAC, NO).

Results: Our results showed that melatonin treatment significantly increased EF and TAC levels in both the treatment groups compared to the control group ($P < 0.05$) while significantly decreasing the levels of inflammatory and oxidative biomarkers, including TNF-α, MDA, and

NO (P < 0.05). LDH and CK-MB levels had no significant changes. Also, there were no significant changes in systolic and diastolic blood pressure (P > 0.05). The serum biomarker comparison between the two treatment groups shows that the group with 10 mg was more effective than the group with 5 mg melatonin. However, they were not significant (P > 0.05).

Conclusion: The present study showed that Melatonin, as a potent antioxidant, reduces oxidative stress and inflammation associated with CABG and is essential in improving heart function due to increasing EF levels.

Keywords: Antioxidant, CABG, Oxidative stress, Inflammation, Melatonin

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OBi-9

Association Between Dietary Pattern Indices and Biochemical Parameters in infertile men

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Abstract

Background and Aim: The complex interplay between dietary quality and seminal biochemical parameters remains a significant focus of contemporary research. We undertook a cross-sectional analysis aimed at clarifying the correlations between dietary pattern indices and both seminal and serum biochemical parameters in male patients attending infertility clinic.

Methods: In the current study, we enrolled a cohort of 90 men diagnosed with idiopathic infertility. Semen samples were collected and subjected to analysis in accordance with the World Health Organization (WHO) 2010 guidelines. To assess dietary intake comprehensively, we utilized a 168-item semi-quantitative food frequency questionnaire (FFQ) specifically tailored for the Tehran Lipid and Glucose Study (TLGS). The statistical analysis involved independent samples t-tests to compare demographic characteristics, energy intake, and initial SA results between subjects with normal versus abnormal semen parameters. Furthermore, to elucidate the associations between dietary scores—including dietary total antioxidant capacity (dTAC) and dietary inflammatory index (DII)—and biochemical markers such as semen total antioxidant capacity (TAC) and tumor necrosis factor-alpha (TNF-α) levels, we employed one-way ANOVA followed by Tukey's post hoc test for multiple comparisons.

Results: The analysis revealed that a higher intake of advanced glycation end products (AGEs) may be associated with abnormal semen parameters. However, no other notable differences were detected in serum or semen biochemical parameters between the two groups. Furthermore, no significant associations were identified between dietary total antioxidant capacity (dTAC) and dietary inflammatory index (DII) scores and total antioxidant capacity (TAC) or tumor

necrosis factor-alpha (TNF-α) levels. Additionally, seminal plasma levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) and MDA did not show significant differences between the normal and abnormal semen groups. Lastly, no significant correlations were found between dTAC or DII scores and oxidative stress (OS) indices- TAC, MDA, 8-OHdG- and TNF-α in either serum or semen of infertile men.

Conclusion: This study highlights the relationship between diet and male fertility, specifically the link between AGEs and abnormal seminal parameters. Our research significantly contributes to the increasing evidence base concerning the relationship between dietary habits and male fertility. It underscores the critical importance of adopting a healthy dietary pattern as a fundamental aspect of achieving optimal reproductive health.

Keywords: dTAC; infertile men; Oxidative Stress; Dietary Pattern Index; DII, semen analysis.

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OBi-10

The upregulation of the anti-aging protein Klotho occurs during the neural differentiation of mesenchymal stem cells derived from bone marrow

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Abstract

Background and Aim: The Klotho protein, known for its anti-aging properties, plays a critical role in regulating oxidative stress, neuronal survival, and cognitive functions. Previous studies have shown Klotho's involvement in various tissues and its neuroprotective potential. However, its role during the differentiation of mesenchymal stem cells (MSCs) into neuron-like cells remains unclear. This study investigates the expression of Klotho and its relationship with neuron-specific markers during this differentiation process.

Methods: MSCs Isolation and Differentiation: Bone marrow-derived MSCs were isolated from mice and cultured. Differentiation into neuron-like cells was induced using a specialized medium over 14 days.Gene and Protein Analysis: Quantitative PCR (qPCR) was used to measure mRNA levels of Klotho and neuronal markers (Pax-6, NeuN, and NfL) on days 0, 7, and 14. Immunocytochemistry (ICC) and Western blotting assessed Klotho protein expression

and localization, Morphological Observations: Structural changes in MSCs were monitored to confirm differentiation into neuron-like cells.

Results: Morphological Changes: MSCs transitioned into neuron-like cells, forming interconnected cellular chains by the second week.Gene Expression: Neuronal markers (Pax-6, NeuN, NfL) showed significant upregulation over time, indicating successful differentiation.Klotho Expression: Klotho mRNA levels increased in a time-dependent manner (2.6-fold by day 7, 3.2-fold by day 14). ICC and Western blot revealed Klotho protein accumulation in neuron-like cells, primarily near the inner cell membrane. Protein Confirmation: Western blot confirmed the presence of Klotho (~130 kDa) and neuronal markers in differentiated cells.

Conclusion: The study demonstrates that Klotho expression is minimal in undifferentiated MSCs but increases significantly during neuronal differentiation, paralleling morphological and genetic changes. This suggests Klotho's crucial role in neuronal maturation and maintenance. Previous findings align with this study, indicating Klotho's involvement in regulating oxidative stress, promoting cellular survival, and enhancing differentiation pathways. These results position Klotho as a potential therapeutic target for neurodegenerative conditions by aiding neural regeneration and repair.

Keywords: antiaging, differentiation, gene expression, klotho, mesenchymal stem cells, neuron-like cells

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OBi-11

Abstract Type: Original Research

Mesenchymal stem cell therapy led to the improvement of spatial memory in rats with Alzheimer's disease through changing the expression of lncRNA TUSC7/ miR-449a/ PPARγ and CD36 genes in the brain tissue

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Abstract:

Background and Aim: Peroxisome proliferator-activated receptor gamma (PPARγ) in brain tissue plays a role in reducing inflammation caused by microglia activity and phagocytosis of Aβ plaques by the scavenging receptor CD36. Due to lack of definitive treatment, other treatments such as stem cells and non-coding RNAs have been considered as possible therapeutic approaches. This study aimed to investigate the effect of mesenchymal stem cell (MSC) treatment on PPARγ gene expression in the brain of an Alzheimer's disease (AD) animal model.

Methods: A total of 24 adult male Wistar rats were randomly divided into three groups: the control group, the group treated with Aβ (AD group), and the group treated with Aβ and MSC (AD + MSC group). The expression levels of PPARγ, lncRNA TUSC7, CD36, and miRNA-449a genes were evaluated using Real-Time PCR, also PPARγ and CD36 protein levels were evaluated using western blotting.

Results: This study shows that treatment with MSC led to behavioral improvement and spatial memory performance in the AD group ($p \leq 0.05$). The expression of PPARγ, lncRNA TUSC7, and CD36 genes increased in the AD + MSC group compared to the AD group ($P \leq 0.0001$), while the expression level of miR-449a decreased ($P \leq 0.0001$). The analysis of the data obtained from the western blot showed that the protein level of PPARγ and CD36 increased in the AD+MSC group compared to the AD group ($P \leq 0.0001$).

Conclusion: This study showed that MSC treatment probably leads to the expression level modulation of miRNA-449a by affecting the lncRNA TUSC7. Also, MSC treatment, led to the clearing of amyloid plaques and improvement of behavioral performance by affecting related genes such as PPARγ in the microglial phagocytosis pathway.

Keywords: Alzheimer's disease; mesenchymal stem cell; PPAR gamma; microRNAs; LncRNA.

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OBi-12

Abstract Type: Original Research

Resveratrol relieves hepatic steatosis and enhances the effects of atorvastatin in a mouse model of NAFLD by regulating the renin-angiotensin system, oxidative stress, and inflammation

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Abstract

Background and Aim: The classical renin-angiotensin system (RAS) axis is implicated in NAFLD development by promoting oxidative stress and inflammation, whereas the non-classical axis antagonizes its effects. In this study, we evaluated the effects of resveratrol (RSV), a well-known polyphenol antioxidant, alone and in combination with atorvastatin (AT) on the RAS axes in NAFLD mice.

Methods: Male C57/BL6 mice were fed a normal diet (control group) or a high-fat diet (HFD) for 12 weeks to induce NAFLD. Afterwards, the animals received AT (20 mg/kg), RSV (100 mg/kg/day), and AT + RSV (20 and 100 mg/kg/day) by oral gavage for four weeks.

Results: NAFLD animals exhibited swollen hepatocytes with numerous fat-containing vacuoles. HFD significantly increased oxidative stress, as manifested by high levels of malondialdehyde and low paraoxonase 1 activity. Additionally, NAFLD mice showed significantly increased IL-1β, IL-6, and TNF-α expression and reduced IL-10 expression. An imbalance among RAS axes was evident as high expression levels of angiotensinogen, renin,

and type 1 angiotensin receptor and reduced expression levels of angiotensin-converting enzyme 2 and angiotensin 1-7.

Conclusion: RSV ameliorated these changes in NAFLD mice, which was comparable with the beneficial effects of AT. Interestingly, the ameliorative effects of AT increased considerably when it was administered in combination with RSV. Overall, our findings indicate that RSV attenuates HFD-induced NAFLD in mice, particularly when co-administered with AT, at least by regulating the RAS axes, oxidative stress, and inflammation.

Keywords: non-alcoholic fatty liver disease; renin-angiotensin system,; resveratrol; atorvastatin; oxidative stress; inflammation

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OBi-13

Abstract Type: Original Research

Evaluating the Relationship Between Non-High-Density Lipoprotein Cholesterol and Cardiovascular Outcomes in Chronic Kidney Disease

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Abstract

Background and Aim: The global prevalence of chronic kidney disease (CKD) is rapidly rising and advanced CKD patients facing a 10-30 times higher risk of cardiovascular(CV) disease comparison with general population. Although high serum non-HDL-C levels are associated with an increased risk of adverse cardiovascular outcomes, their relationship in CKD remains underexplored.

Methods: The MASHAD study, conducted from 2010 to 2020, recruited 604 participants aged 35 to 65 with stage G3a CKD and no history of coronary artery disease, stroke, or peripheral arterial disease. Throughout the 10-year follow-up, participants were evaluated for cardiovascular events. CKD was defined by kidney damage or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², calculated using the CKD EPI equation. Non-HDL cholesterol levels were assessed against a cutoff of 130 mg/dl.

Results: Finally, 604 participants with a GFR of less than 60 mL/min/1.73 m² were enrolled in the study, including 76.3% women and 23.7% men, 84.1% without diabetes and 65.7% without hypertension. At the end of the study, 12.6% of the participants developed cardiovascular disease, predominantly affecting men (85.4%). Also, we found a significant association between elevated triglycerides and CVD risk ($p < 0.001$). In addition, lower cholesterol and higher non-HDL cholesterol levels were associated with higher CVD risk in CKD patients, p-value 0.013 and 0.025 respectively.

Conclusion: This study showed that the risk of CVD in patients with CKD increased with higher serum non-HDL-C levels. More research is needed with larger statistical samples. In conclusion, cardiovascular events in patients with CKD may be prevented by controlling serum non-HDL-C levels.

Keywords: Non-High-Density Lipoprotein, Chronic kidney disease, Cardiovascular disease.

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OBi-14

Title: Comparison of miR-155, miR-26a, miR-146a, and miR-132 expression in patients with Alzheimer disease and control

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Background: Alzheimer's disease is a neurodegenerative disease characterized by progressive cognitive impairment and memory loss. This disease has two neuropathological features, one is the accumulation of beta-amyloid plaque in the extracellular part of neurons, and the other is caused by the hyperphosphorylation of tau proteins and the formation of neurofibrillary tangles inside neurons. Disorders in the function of synapses are one of the most important features of AD, which leads to cognitive disorders in these patients. Creating functional disorders in mitochondria due to amyloid beta, which is considered a strong poison for mitochondria, eventually causes damage to neurons. miRNAs, which are among the neutralizing markers, play a role in regulating gene expression and preventing or progressing many diseases. In this study, we decided to use these miRNAs as biomarkers for the diagnosis and identification of AD.

Materials and Methods: In this study50 patients with Alzheimer diagnosed by a specialist doctor were selected and 50 healthy people who were free of any neurological and metabolic diseases were selected. In this study, we investigated the expression of several miRNAs in the group of Alzheimer's patients and healthy individuals. To check the expression of miRNAs,

we first took 5 cc of blood from AD and healthy people, and then we measured the gene expression with real-time PCR. For statistical analysis, we used graph pad PRISM 5.0 and SPSS 16.0 software. A significant difference was defined as $P<0.05$.

Results: Based on our study, by comparing the expression level of miR-26a, miR-146a and miR-132 in the serum of the control group and patients with AD, it was higher than the control group, but compared to the expression level of miR-155 in two cases, the level The expression of this gene was lower in the Alzheimer group than in the control group ($P < 0.001$).

Conclusion: According to this experiment and the information obtained from this study, it can be suggested that the expression of miR-155 enzyme decreases in AD and the expression of miR-26a, miR-146a and miR-132 increases in AD compared to the control group. According to the studies, these miRNAs play a role in inflammation in the body and the central nervous system. Impairment in the expression of these miRNAs and by increasing and decreasing these miRNAs causes disturbances in the central nervous system directly or through mediators that cause progression or prevention of neurological diseases such as Alzheimer's, Parkinson's, etc. These miRNAs can be used as biomarkers for the diagnosis and prognosis of AD.

Keywords: Alzheimer disease, miRNA, biomarker.

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OBi-15

Abstract Type: Original Research

Circulating miRNA-106b-5p As a Potential Biomarker for Coronary Artery Disease

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Abstract

Background and Aim: Coronary artery disease (CAD) is a major cause of death and presents a significant economic burden to the healthcare system. Despite extensive research and identification of several biomarkers, early detection continues a critical challenge. MicroRNAs (miRNAs) play a crucial role as epigenetic regulators, affecting gene expression and essential biological processes. The expression profiles of circulating miRNAs alter in response to CAD, making them promising candidates for diagnostic biomarkers due to their high sensitivity and specificity. This study aimed to predict and validate miRNA, which are significantly upregulated in CAD patients and to evaluate their potential as diagnostic biomarkers.

Methods: In this study, the CAD dataset (GSE113079) was analyzed, and 100 DEmRNAs were identified. Among them, only miRNAs with significant interaction with the DEmRNAs were selected for more study. By computational prediction method, miR-106b-5p, miR-20a-

3p and miR-17-3p were identified. Next, the predicted expression of these microRNAs was evaluated in CAD patients and healthy controls.

Forty-four male candidates for coronary artery bypass graft (CABG) were enrolled in the study at Shafa Hospital located in Kerman, Iran. A questionnaire was used to collect demographic data, including information on smoking habits, family health history, and past drug history. In addition, a standard healthy control group made up of 48 people of similar age was selected.

In the next step blood pressure, triglycerides, cholesterol levels, height, weight, body mass index (BMI), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) were assessed in all participants under standard conditions as part of the clinical measurements.

Results: We employed stem-loop qRT-PCR to evaluate the expression levels of miR-106b-5p, miR-17-3p and miR-20a-3p in both groups. Only the expression level of miR-106b-5p demonstrated a statistically significant increase in the CAD group compared to the control group ($p < 0.001$). In addition, the data revealed no significant differences in the expression levels of miR-17-3p and miR-20a-3p between the CAD group and the control group. Concerning the risk factors associated with CAD, we found a correlation between LDL cholesterol levels and miR-106b-5p expression in the control group ($r = -0.532$, $P = 0.023$). Furthermore, in the patient group, miR-106b-5p expression was associated with weight ($r = -0.358$, $P = 0.041$) and body mass index (BMI) ($r = -0.463$, $P = 0.015$).

Conclusion: Our findings revealed that there were no significant differences in the expression levels of the other predicted miRs (miR-17-3p, miR-20a-3p) between patients with CAD and those who are healthy individuals. Moreover, the miR-106b-5p expression level was increased in CAD group. This microRNA may become a valuable diagnostic tool for CAD diagnosis. However, further investigations are essential to affirm our conclusions.

Keywords: MicroRNA, coronary artery disease, miRNA-mRNA interaction**,** qRT-PCR

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OBi-16

Cyrtopodion Scabrum and protective effect on 5-FU-induced cardiotoxicity in rats

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Abstract

Background and Aim: Chemotherapy is the main approach for the treatment of different cancer but is often causes unpleasant oxidative damages in body. Therefore, effective and developing alternative therapy with improved tumor suppression efficiency and lower adverse effects is highly required. Recently we proved that *Cyrtopodion Scabrum* extract is an effective tumor suppressor medicine with no adverse effects on the other organs. In this study, the antioxidant activity of *Cyrtopodion Scabrum* extract (CsE) and homogenate (CsH), and their effects on 5-FU-induced heart dysfunction in rat was investigated. .

Methods: 60 Male rats were divided into six groups randomly and treated for 14 days. The positive and negative control groups were received 5-FU and distilled water, respectively. Four groups were administered by CsE, CsH, CsE+5-FU and CsH+5-FU, orally by gavages in a daily schedule in this study. 5-FU-induced oxidative damage was evaluated by changes in the weight, food and water intake during treatment and the antioxidant parameters in the heart and serum of the treated rats.

Results: Results indicated that the administration of CsH and CsE improved heart function and antioxidants defense system significantly by suppress level or activity of MDA, and increased of GSH, TAC, GPx, GR activities in the heart and serum in 5-FU-induced rats. Also, 5-FU caused of significant increased ($P < 0.05$) levels of CK-MB, LDH, LDL and significant decrease ($P < 0.05$) in the level of HDL in serum and heart, that CsE and CsH compounds suppress this oxidative damages, too.

Conclusion: Our data suggests that CsH and CsE play a protective role against the cardiotoxicity elicited by 5-FU and can be used as complementary supplementation with 5-FU to reduced oxidative stress parameters which is a consequence of ROS production in cancerous patients.

Keywords: *Cyrtopodion Scabrum*, 5-FU, Antioxidant parameters, Cardiotoxicity

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OBi-17

Investigation of the Effects of Crocin Supplementation on Glycemic Indices, Lipid Profile, Oxidative Stress Factors, and Inflammatory Biomarkers in Type 2 Diabetic Patients Under Metformin Treatment

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Abstract

Background and Aim: Diabetes is a metabolic disorder marked by high blood glucose levels, which can produce free radicals leading to cellular damage and oxidative stress. Crocin, an active compound in saffron, has anti-inflammatory and antioxidant properties that may enhance glycemic indices and reduce inflammation. This study investigates the effects of crocin supplementation on glycemic indices, lipid profiles, oxidative stress factors, and inflammatory biomarkers in type 2 diabetic patients treated with metformin.

Methods: This study was conducted as a double-blind, randomized clinical trial involving 60 diabetic patients receiving metformin. Participants were randomly assigned to either the intervention group (30 patients) or the placebo group (30 patients). The intervention group received two crocin tablets (15 mg each) daily for three months, while the placebo group

received a similar placebo. Serum levels of glycemic indices, lipid profile, oxidative stress factors, and inflammatory biomarkers were measured before and after the intervention to evaluate the therapeutic effects of crocin on these parameters.

Results: Crocin supplementation for three months significantly reduced serum fasting plasma glucose levels ($P < 0.001$), serum insulin levels ($P = 0.03$), and insulin resistance ($P < 0.001$), while markedly increasing insulin sensitivity ($P < 0.001$). These enhancements were also statistically significant relative to the baseline measurements within the crocin group. Crocin intake led to a reduction in triglycerides ($P = 0.04$) and VLDL -cholesterol ($P = 0.04$) compared to the placebo group. Additionally, significant decrease was observed in serum levels of high-sensitivity-CRP ($P = 0.03$) and malondialdehyde ($P = 0.04$) was observed in the intervention group, alongside a significant increase in plasma glutathione ($P = 0.008$) compared to the placebo group.

Conclusion: This study demonstrated that crocin supplementation enhances the effects of metformin, improving glycemic status and lipid profiles. Additionally, the administration of crocin reduces oxidative stress and chronic inflammation, potentially playing a significant role in preventing and slowing the progression of diabetes-related complications

Keywords: Crocin; Type 2 Diabetes; Metformin; Oxidative Stress.

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OBi-18

Effects of resveratrol on inflammatory cytokines in COVID-19 patients

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Abstract

Background and Aim: Resveratrol is one of the effective compounds of the plant that has anti-inflammatory and antioxidant properties. Studies show that combined herbal treatment significantly reduces the clinical symptoms of COVID-19 and the use of effective herbal medicines and supplements will be appropriate due to mild side effects. Therefore, the aim of this study was to investigate the effects of resveratrol consumption on biochemical markers, haematological parameters and some inflammatory cytokines in patients with COVID-19.

Methods: This study was a double-blind clinical study. A total of 44 patients with COVID-19 randomly were assigned to receive 750 mg/day resveratrol (n=24) orally or placebo (n=20) for 10 days. The biochemical markers, hematological parameters and plasma levels of IL-6 and TNF-α cytokines were measured at baseline and after 10 days.

Results: We observed a statistically significant reduction in the CRP *(P = 0.041)*, FBS *(P = 0.002)*, ALP *(P = 0.034)*, TNF-α *(P = 0.001)*, and WBC *(P = 0.043)*,PLT *(P = 0.042)*, NUT *(P = 0.015)* and an increase in LYM *(P = 0.010)* in the resveratrol treated group when compared with the placebo group.

Conclusion: The present study demonstrated that resveratrol as an herbal supplement may be useful in reducing markers of inflammation, neutrophils, low platelet count as well as lowering blood glucose levels in patients with COVID-19. The IRCT NO: IRCT20111119008129N13.

Keywords: Resveratrol; COVID-19; Cytokines; Inflammation

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OG-1
Abstract Type: Original Research

Exploring Two VUS Mutations on the X Chromosome as Possible Causes of Intellectual Disability in a Child

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Abstract

Seventy percent of intellectual disabilities (IDs) are attributable to genetics. The incidence of this condition is rising globally, impacting around 1 to 3% of the population in developing countries. The aim of this research is to uncover the potential genetic factors contributing to the child's ID. This study examines an 8-year-old boy with an ID who presents with limited speech (restricted to a few words), delayed walking, and hypotonia during early childhood. To identify genetic causes, whole exome sequencing was conducted for the child, followed by segregation analysis for family members. Analysis revealed two hemizygous VUS mutations on the X chromosome: BRWD3 (NM_153252.5): c.2656T>C p.(Ser886Pro) and USP9X (NM_001039591.3): c.1161+70_1161+71insA. Both genes follow an autosomal recessive inheritance pattern and align with the child's clinical symptoms. Segregation studies indicated that the child's mother and grandmother are heterozygous for these mutations. Additionally, the affected mother's uncle carries both mutations on his X chromosome, while the unaffected child's uncle does not. Although one of these mutations is located in an intronic region and is less likely to be pathogenic, the correlation of many symptoms with that gene cannot be

disregarded. These findings highlight the existing gaps in variant classification for accurate genetic counseling.

Keywords: Intellectual disability, Speech disorder, Novel mutations, Variant classification.

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OG-2
Abstract Type: Original Research

New Insights into HPD-Like Protein: Identification of A Novel Bi-allelic Mutation, Docking Simulation Study, and Literature Review

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Abstract

Background: Hereditary Spastic Paraplegia (HSP) is a rare neurodegenerative disorder causing progressive weakness and spasticity in the lower limbs. Mutations in the HPDL gene are linked to Spastic Paraplegia 83 (SPG83), an autosomal recessive form of HSP. While HPDL mutations are known to cause SPG83, the molecular mechanisms behind its role remains unclear, mostly due to rare nature of the condition. The aim of this study is to determine the genetic basis of HSP in two consanguineous families from Iran.

Methods: Whole-exome sequencing (WES) was employed to identify genetic variants in the probands. To confirm the pathogenicity potential of identified variants in the HPDL gene computational tools such as SIFT, CADD, Mutation Taster, Polyphen-2, and PANTHER were used. Conservation analysis of the HPDL protein sequence was performed using Clustal Omega and ConSurf tools, and the 3D structure of HPDL variants was predicted using the I-TASSER server. Protein-protein interactions involving HPDL were studied using the STRING database. Also, the DynaMut web server was used to analyze the effect of identified mutations on protein dynamics and stability. Additionally, the impact of the variants on protein stability was assessed using the I-Mutant and MUpro web servers. Finally, Molegro Virtual Docker (MVD), a cutting-edge integrated platform, was utilized to perform protein-ligand docking simulations.

Results: WES identified two biallelic missense mutations c.3G>C (p.Met1Ile) and c.128G>A (p.Arg43Pro) in HPDL. The c.128G>A mutation is novel and is documented here for the first time in an SPG83 patient. Trio-based Co-segregation analysis confirmed inheritance of variants. A comprehensive literature review revealed a significant consanguinity rate (49.55%) within families harboring HPDL mutations. Furthermore, based on the ΔΔG prediction and protein flexibility analysis, it was observed that the p. Arg43Pro variant resulted in a decrease in molecular flexibility.

Conclusion: This study strengthens the link between HPDL mutations and HSP, particularly SPG83. Furthermore, our bioinformatics findings serves as the initial step in validating the identified variant as a pathogenic mutation before undertaking functional studies.

Key Words: Hereditary spastic paraplegia, Spastic paraplegia 83, HPDL gene, Whole Exome Sequencing, Iran

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OG-3

The Expression of Cell Cycle Genes in Cell Senescent Models: New Insight into the Role of Mitosis in Aging Process

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Abstract

Background and Aim: Aging process increases the risk of chronic diseases such as heart disease, diabetes, neurodegenerative diseases, and cancer. The cellular senescence theory suggests that human aging emerges from the halted cells division. This process involves changes in DNA, epigenetics, mitochondria, and telomere length. Cellular senescence models help to investigate these changes, and provides a framework to understand the impact of senescence on health.

Methods: In this study, we collected the RNASeq data from bulk RNA sequencing (RNA-seq) from public repositories such as GEO, including GSE210140, GSE122079, GSE262932, and GSE252132. Data analysis was performed using R software (version R-4.4.2), utilizing packages including DESeq2, tidyverse, GenomicDataCommons, dplyr, and EnhancedVolcano. Subsequently, Enrichr, a comprehensive web-based tool for gene set enrichment analysis, was

employed to examine pathways to identify the correlation between senescence and cell cycle gene expression.

Results: Our analysis showed a significant number of DEGs related to cellular senescent, including CDC20, CCNA2, CDKN1B, RAD21, CHEK1, PLK1, CDK1, BUB1B, BUB1, CDC25B that are involved in cell cycle processes. These genes play diverse roles in various biological processes, particularly in mitotic spindle assembly checkpoint signaling. Through GO analysis, we identified several molecular pathways including cell cycle and cellular senescence pathways.

Conclusion: in conclusion, our results show that different genes and pathways dysregulate in cellular senescence. These results could help to develop new diagnostic approaches and treatment strategies for aging.

Keywords: Cell Cycle Genes; Cellular senescence; Mitosis; Aging Process.)

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OG-4

Abstract Type: Original Research

Enhanced Delivery of miRNAs into U87MG Glioma Cells Using Exosomes Derived from Umbilical Cord Mesenchymal Stem Cells

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Abstract

Background and Aim: MicroRNAs (miRNAs) are recognized as promising candidates for therapeutic interventions in various diseases, particularly cancer. However, the challenge of effectively delivering miRNAs to target cells persists. Exosomes, as natural nanovesicles, offer a promising platform for delivering therapeutic agents. In this study, we investigated the efficiency of exosomes derived from umbilical cord mesenchymal stem cells (UC-MSCs) in delivering fluorescently labeled oligonucleotides into U87MG glioma cells compared to the commonly used transfection reagent, Lipofectamine 3000.

Methods: Exosomes were extracted from the culture supernatant of UC-MSCs through the process of ultracentrifugation. U87MG glioma cells were subsequently cultured and transfected with fluorescently labeled oligonucleotides that were either complexed with exosomes or Lipofectamine 3000. Five experimental groups were formulated to analyze the combined effects of two primary factors: exosomes and Lipofectamine 3000, as well as the influence of fetal bovine serum (FBS) on cell treatment. The study specifically examined the role of FBS when it was added either during the cell treatment or introduced into the culture medium five hours following the treatment with exosomes or Lipofectamine. Moreover, we investigated the incorporation of dimethyl sulfoxide (DMSO) into the cell culture environment to assess its potential to improve transfection efficiency.

Results: The findings of our study indicated that the delivery of oligonucleotides into U87MG cells via exosomes was markedly more effective than the delivery achieved through Lipofectamine 3000. Notably, the introduction of FBS immediately following transfection resulted in an increase in transfection efficiency, implying that certain components within FBS may facilitate the transfection process. Furthermore, while the incorporation of DMSO alongside Lipofectamine 3000 improved transfection efficiency, it also led to considerable cytotoxicity. The higher transfection efficiency observed with exosomes can be attributed to multiple factors, including their inherent targeting properties, protection of the cargo from degradation, and ability to penetrate cell membranes.

Conclusion: Our findings suggest that exosomes derived from UC-MSCs provide a secure and efficient means for delivering therapeutic oligonucleotides to glioma cells. In summary, this research illustrates the enhanced efficacy of exosome-mediated oligonucleotide delivery in comparison to conventional transfection techniques. The results underscore the potential of exosomes as an innovative nanocarrier for targeted cancer treatment. Additional investigations are necessary to elucidate the mechanisms involved in exosome-mediated delivery and to assess the therapeutic possibilities of exosome-based drug delivery systems.

Key words: exosomes, mesenchymal stem cells, oligonucleotides, transfection, glioma, U87MG, drug delivery.

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OG-5

Title: Importance of Genetic tests in diagnosis, prognosis and management of patients with Leukemia

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Key Words: Leukaemia, Genetic tests, Karyotype, FISH, Sanger, NGS, Diagnosis, Prognosis, Management

Introduction:

Leukemia, as we know, is a heterogeneous group of malignancies characterized by the uncontrolled proliferation of leukocytes. The complexity of leukemia lies not only in its different subtypes such as AML, ALL, CML, and CLL but also in the unique genetic alterations that can drive these diseases. In recent years, the landscape of leukemia management has shifted dramatically thanks to advances in our understanding of the underlying genetic changes that influence the pathology of this disease. Genetic testing has emerged as a crucial tool in both the diagnostic process and in tailoring individualized treatment approaches.

Methods:

Key genetics tests comprise:

Karyotyping; Examines chromosome structure and number, Detects abnormalities like Philadelphia chromosome in CML.

Fluorescent In Situ Hybridization (FISH): Uses fluorescent probes for specific DNA sequences. Identifies gene rearrangements like BCR-ABL in CML.

Sanger Sequencing: Identifies specific DNA mutations with high accuracy. Common for mutations in genes such as FLT3 and NPM1 in AML.

Next-Generation Sequencing (NGS). Allows high-throughput mutation analysis. Crucial for comprehensive leukemia profiling and guiding personalized treatment.

Results:

Genetic tests in leukemia primarily serve two roles: establishing a definitive diagnosis and providing prognostic information. High-throughput sequencing techniques, including next-generation sequencing (NGS), allow us to identify specific genetic mutations, chromosomal abnormalities, and other molecular markers associated with various subtypes of leukemia. For instance, in AML, we often look for mutations in genes such as FLT3, NPM1, and IDH1/2, which not only assist in diagnosis but also help in determining prognosis. For instance, the presence of FLT3 internal tandem duplications (ITDs) is linked to a poorer prognosis and guides the decision to employ targeted therapies such as FLT3 inhibitors, including midostaurin and gilteritinib. Risk Stratification and Prognosis: Genetic testing does not merely aid in diagnosis; it also plays a critical role in risk stratification. Techniques such as fluorescent in situ hybridization (FISH) and chromosomal karyotyping help identify abnormalities like the Philadelphia chromosome, translocation 9/22, in CML.

Conclusion:

Genetic testing plays a vital role in the diagnosis and management of leukemia, providing us with valuable insights into tumor biology and enabling tailored therapies that offer the best chance for patient success. As we embrace this scientific advancement, we must remain committed to expanding our skill sets and embracing the beguiling complexities of genetic changes, ensuring that our patients receive the most effective and personalized care possible.

OG-6
Abstract Type: Original Research

The risk of developing colorectal cancer associated with colitis is influenced by the oncogenic effects of the KRAS gene status, cripto-1 activation, and epigenetic changes in miR-106a

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Abstract

Background and Aim: Chronic inflammation promotes cell transformation into a pro-tumorigenic state, influenced by Ulcerative colitis (UC) molecular patterns, which impacts tumor development in colorectal cancer (CRC) through a favorable environment.

Methods: A total of 200 tissue specimens, comprising UC biopsies, high-grade dysplasia, CRC, and normal tissue, were utilized to extract whole RNA to quantify mature miRNA by Real-time PCR analysis. The identification of KRAS and PIK3CA mutations, as well as aberrant overexpression of the Cripto-1 protein, was achieved through direct DNA sequencing and immunohistochemically (IHC) screening.

Results: The data indicate that the mutant phenotype of p. G12D in codon 12 contributes to 24.1% in UC, 26.6% in HGD, and 78% in CRC, specifically in the presence of different KRAS

mutations in codons 12, 13, and 61. This finding strongly suggests a significant association with disease activity. All individuals who had somatic mutations at codons 542, 547, and 1047 of the PIK3CA gene did not respond to treatment. The expression levels of miR106a were significantly higher in tissue samples from patients with UC, HGD, and CRC compared to normal samples ($p < 0.001$). Additionally, the expression levels of this miRNA were significantly higher in CRC and HGD compared to UC ($p < 0.001$). Additional results demonstrate a significant difference in the immunostaining of CR-1 protein between colorectal cancer CRC and severe dysplasia compared to normal IHC, ($p < 0.001$). There is also a significant difference between the HGD and paired-control groups ($p < 0.05$).

Conclusion: The research indicates that the existence of mutant KRAS oncogenes and distinct expression patterns of CR-1, miR106a might play a key role in developing and advancing colitis-associated colorectal cancer.

Keywords: KRAS gene, CR-1, miR106a, UC, CRC

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OG-7
Original Research

Genetic analysis of intellectual disability (ID) in consanguinity families using next generation sequencing (NGS)

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Abstract

Background and Aim: Intellectual disability (ID) is a common and highly heterogeneous neurodevelopmental disorder. It affects 1–3% of the world's population. Autosomal recessive intellectual disability (ARID), being the most common form of ID. In Iran, the rate of consanguinity is approaching 40% and this high rate results in higher rates of recessive disorders including ARID. Inbred families provide a unique opportunity to find pathogenic variants in known as well as candidate genes responsible for recessive disorders due to the extensive regions of homozygosity in the genomes of these individuals.

Methods: We enrolled 30 suspected consanguineous ARID families based on pedigree analysis and clinical evaluation. 29 families were investigated through whole exome sequencing (WES) and one family through microarray-based comparative genomic hybridization (aCGH). Bioinformatics analysis was carried out using Genome Analysis Tool Kit (GATK) based bioinformatics in-house and out-house pipelines. Variants were interpreted using wANNOVAR and ANNOVAR. Subsequent prioritization was carried out by application of various quality filters. Finally, the selected putative causative variants were validated by Sanger sequencing.

Results: Out of 29 families, known causative variants in six known genes (*HNMT*, *TBCD*, *SPR*, *ERCC6*, *ALDH3A2*, and *NAGLU*) were identified in six different families for ARID. Furthermore, novel variants in four known ID genes (*CNPY3*, *ANKH*, *CAPN10*, and *SLC1A4*) were found in four families. One potential likely pathogenic variant and one VUS were identified in two different families in two novel genes (*MYO7B* and *MED26*). For one family (NDD30), two CNVs were identified using aCGH. However, for the remaining 16 families, pathogenic/probably pathogenic variants in known/new genes were not identified.

Conclusion: This study showed that exome sequencing is a powerful technique to find out the causative variants in rare ARID families and can be used to discovery of candidate genes. The diagnostic yield of the strategy used in this study for ID was found to be approximately 41% (12/30). Furthermore, the present study showed that different variants are associated with a significant number of consanguineous ARID families from Iran, which indicates the high heterogeneity of ID in Iran despite the high rate of consanguineous marriage.

Keywords: Neurodevelopmental disorders, Intellectual disability, Next generation sequencing, Whole exome sequencing,

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OG-8
Abstract Type: Case Report Research

A Case of 49, XXXXY Syndrome: Early Diagnosis and Comprehensive Clinical Characterization

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Abstract

Background and Aim: Characterized by three extra X chromosomes, 49, XXXXY syndrome is a rare and severe aneuploidy, resulting in profound developmental delays and multisystem anomalies. While historically sometimes considered a variant of Klinefelter syndrome (KS), 49, XXXXY syndrome presents with a more severe and distinct clinical phenotype. We report a 2-year-old boy presenting with speech and motor delays, leading to genetic testing. A 49, XXXXY karyotype was identified. Notably, he also had microcytic anemia, leukocytosis, and severe unilateral renal impairment. This case expands the phenotypic understanding of 49, XXXXY syndrome, emphasizing early recognition for improved outcomes.

Methods: Karyotype analysis was performed on peripheral blood lymphocytes using standard G-banding (GTG) technique at a resolution of 450-500 bands. Twenty metaphase spreads were analyzed. Hematological parameters were assessed using a Sysmex KX-21N Hematology

Analyzer. Renal function was evaluated through imaging and functional studies. An anti-urinary reflux surgery was performed for this patient. Tests were repeated for reconfirmation.

Results: A 2-year-old male patient was referred to the physician with symptoms of growth and speaking disorder. He was directed to the lab for chromosome analysis, karyotyping, and further investigation. Cytogenetic analysis revealed a 49, XXXXY karyotype in all cells examined, confirming the diagnosis. The CBC showed leukocytosis (WBC 12.9 x 10^3/µl), microcytic hypochromic anemia (hemoglobin 11.6 g/dL, hematocrit 34.3%, MCV 72.8 fL, MCH 24.6 pg), and a borderline elevated red cell distribution width (RDW-CV 14.5%). The count of platelets was in a normal range. Renal imaging demonstrated severe unilateral renal dysfunction secondary to Vesicoureteral Reflux (VUR), and after further examination, it was determined that only 20% of one of his kidneys was functioning and the other kidney was normal. Urine Analysis (UA) and Urine Culture (UC) tests came back normal after the anti-urinary reflux surgery.

Conclusion: This case underscores the importance of considering rare chromosomal aneuploidies, 49, XXXXY syndrome, in young males presenting with developmental delay and dysmorphic features. The findings in this report, including the presence of significant hematological and renal abnormalities, contribute to the expanding phenotypic spectrum associated with 49, XXXXY syndrome and emphasize its distinction from classic Klinefelter syndrome. Early diagnosis facilitates timely intervention and anticipatory management of potential complications. Considering the rarity of this condition and the limitation of resources available, this report is valuable, indicating that more research should be conducted.

Keywords: 49, XXXXY Syndrome; Aneuploidy; Developmental Delay; Intellectual Disability; Renal Dysfunction; Case Report.

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OG-9

Abstract Type: Original Research

miR-124- loaded exosome derived from mesenchymal stem cells, effectively reduced LX-2 cells proliferation capacity dose and time-dependently

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Abstract

Background and Aim: Liver cirrhosis, which develops following liver fibrosis, is a major global health challenge that leads to organ failure through inflammation and the release of fibrotic biomarkers. One of the key factors in the progression of liver fibrosis is the high proliferative capacity of hepatic stellate cells (HSCs). Activated HSCs are the main source of

collagen in the liver and can produce large amounts of extracellular matrix proteins (ECM). The exosome, which is derived from cell membranes, contains several cellular macromolecules, including miRNAs. Mesenchymal stem cell-derived extracellular vehicles such as exosomes can be considered as possible carriers for perfect miRNA delivery. In this study, we aimed to investigate the effects of miR-124-enriched mesenchymal stem cell-derived exosomes (MSC-EX) on LX-2 cells.

Methods: The exosomes (EX) were isolated from the supernatant from cultured Wharton's jelly of the human umbilical cord-derived mesenchymal stem cell. Exosomes were isolated by commercial kit and characterized by scanning and transmission electron microscopy, and flow cytometry. The modified calcium chloride (CaCl2) method was applied for miR-124 loading in Exo (EX-miR-124). Confirmation of loading was assessed by real-time PCR. The impact of EX-miR-124 and exosomes on cell viability and proliferation in the LX-2 cell line was evaluated using the MTT assay. The measurements were performed at different concentrations and two time intervals (24 and 48 hours).

Results: The isolated exosomes were characterized using TEM and SEM imaging, revealing round or oval shapes with membrane-bound lipid bilayer structures. The majority of the exosomes were approximately 90 nm in size. Additionally, flow cytometric analysis of vesicles isolated from the stem cell culture supernatant demonstrated positivity for the exosomal markers CD81 and CD63, further confirming their identity. The expression of miR-124 was significantly higher in EX-miR-124 compared to unmodified exosomes, confirming the successful enrichment of exosomes with miR-124. Finally, the results demonstrated that the viability and proliferation of hepatic stellate cells were inhibited in a time- and dose-dependent manner following treatment with EX-miR-124.

Conclusion: Our findings show that the miR-124-3p mimic is effectively delivered into hepatic stellate cells (HSCs) by exosomes derived from mesenchymal stem cells, preserving the high functionality of miR-124-3p. This process efficiently suppresses HSC proliferation and viability.

Keywords: Liver fibrosis, Mesenchymal stem cells, Exosomes, miRNA delivery, microRNA.

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OH-1
Abstract Type: Original Research

Identification of the spectrum of alpha thalassemia mutations in southwest Iran

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5. Medical Student, Izmir University Of Economics, Izmir, Turkey.

Abstract

Background and Aim: There are many different disorders that can go along with alpha thalassemia, ranging from small problems that don't pose much of a threat to a person's life to big problems that could prove fatal.It is just important to identify the gene mutations that lead to alpha thalassemia. The disease is mainly inherited as an autosomal recessive trait. According to researchers' studies, -globin gene mutations are more common and more than 40 deletion mutations have been reported, including partial deletion to complete deletion of the -globin gene5. 3.7/ +-thalassemia is caused by single gene deletions 7 and 6, 0-thalassemia is caused by two gene deletions.

Methods: From 2008-2022, the records of alpha thalassemia patients who were sent to Baqaei 2 Hospital, a thalassemia treatment center in the southwestern part of the country, were studied attentively. The necessary information, which included age, gender, and mutation type, was gathered using PCR, GAP PCR, and alpha globulin strip and then analyzed with SPSS software.

Results: Out of 546 patients who were evaluated during this period, 261 were minors, 267 had silenced genes, and 18 had HbH. Over a 14-year period in terms of gender: 272 were male and 274 were female. The age range of people was from 4 years to 41 years. Patients with alpha thalassemia were divided into three categories: minor, silent and HbH. The most observed mutations were $\alpha^{-3.7}\alpha/\alpha^{-3.7}\alpha$ and $\alpha^{-3.7}\alpha/\alpha\alpha$. In the present study, the fewer observed mutations included α-3.7α/αPA4α, α-3.7α/αconstantspringα and α-4.2α/αPA6α mutations, In terms of HbH, the number of cases observed during the 14-year period was 18, of which 8 were female and 10 were male.

Conclusion: According to the findings of this study, the southwestern region of Iran has a large number of different alpha globin mutations. Identifying these mutations could help doctors make it easier to track and treat the disease, reduce the risk of babies being born with hemoglobin disorders, and improve the health of society as a whole. It should be added, according to the results of this research, and the existence of a variety of deletion and point mutations, especially for the rare types of a.a a/anti-3.7. And with the presence of a.a a/anti-3.7.and cd, the probability of thalassemia major has increased, so screening before marriage is very important.

Keywords: Mutation, Alpha thalassemia, Iran, hemoglobin, patients

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OH-2
Abstract Type: Original Research

ZnO Q-Dots Nanoparticles: Intensifying ROS Stress to Improve Anticancer Drug Efficacy

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Abstract

Background: Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia that is effectively treated with arsenic trioxide (ATO) combined with all-trans retinoic acid. However, ATO's toxic effects necessitate exploring safer therapeutic combinations. Nanotechnology offers potential enhancements in drug efficacy and safety. Zinc oxide quantum dots (ZnO Q-dots) exhibit properties like biocompatibility, selectivity, and the ability to induce reactive oxygen species (ROS), which can enhance anticancer drug effects. This study investigates the combination of ZnO Q-dots and ATO to improve anticancer outcomes in NB4 APL-derived cells.

Methods: NB4 cells were treated with varying concentrations of ZnO Q-dots and ATO, either individually or in combination. Cell viability was assessed using the Trypan blue exclusion assay and MTT assay. The BrdU proliferation assay and cell cycle distribution were analyzed by flow cytometry. Apoptosis and autophagy markers were assessed using qRT-PCR and ROS levels were measured using a fluorogenic dye.

Results: ZnO Q-dots enhanced ATO's anti-proliferative and apoptotic effects in a dose- and time-dependent manner. Combined treatment resulted in 83% cell viability inhibition compared to controls. Significant upregulation of apoptotic genes (e.g., p53, Bax) and downregulation of anti-apoptotic genes (e.g., Bcl-2) were observed. ROS production was markedly increased, alongside the induction of autophagy-related genes (ATG-7, Beclin-1).

Conclusion: The combination of ZnO Q-dots and ATO enhances anticancer efficacy in APL-derived NB4 cells, primarily through increased ROS production, apoptosis, and autophagy. This suggests a promising therapeutic strategy with improved efficacy over single-agent treatments.

Keywords: Acute promyelocytic leukemia, Zinc oxide quantum dots, Arsenic trioxide, Reactive oxygen species, Apoptosis, Autophagy

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OH-3

Abstract Type: Original Research

Royal jelly-induced ROS-mediated cell cycle disruption in Acute Lymphoblastic Leukemia (ALL)-derived Nalm-6 Cells

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Background and Aim: Acute lymphoblastic leukemia (ALL) is the most common subtype of leukemia in pediatrics, characterized by abnormal proliferation of immature lymphocytes. Considering that the chemotherapy regimen of ALL is accompanied by various challenges, there is a need for novel agents for treatments. Honey bee products such as RJ with various

anti-cancer properties are among the most interesting in this field. This study aimed to unravel the anti-leukemic effect of RJ on ALL-derived Nalm-6 cells.

Methods and Materials: The metabolic activity was assessed by MTT assay after 24, 48, and 72h. The flow cytometry analysis was performed to investigate cell cycle progression and intracellular reactive oxygen species (ROS) levels. Moreover, the gene expression assay was scrutinized using quantitative real-time PCR (qRT-PCR).

Results: RJ remarkably decreased the viability of Nalm-6 cells in a concentration and time-dependent manner. Of note, RJ reduced 50% of Nalm-6 cell proliferation (IC50) in 2.267±0.026 concentration after 48 h. Additionally, ROS production increased in Nalm-6 cells after RJ treatment while RJ resulted in a significant reduction of cell population in the S phase and halted the ability of ALL cells to replicate in a concentration-dependent manner. Finally, Molecular analysis data revealed the expression of FOXO4 and Sirt1 genes was raised in RJ-treated cells compared to the control counterpart as well as shown an apparent reduction in c-Myc expression coupled with the upregulation of p21.

Conclusion and discussion: Our data indicated that RJ significantly diminished the metabolic activity of the Nalm-6 cell line in a concentration and time-dependent way. The cytotoxicity of RJ can be attributed to ROS generation. In this study, we demonstrated that Nalm-6 pretreatment with RJ resulted in a rise in ROS level in flow cytometric analysis. Therefore, the cytotoxic properties of RJ can be related to its prooxidant activity which was accompanied by increased expression in oxidative stress-regulating genes, Sitr1 and FOXO4. The Sirt1 increases the expression of FOXO4 after deacetylating. Additionally, the increasing FOXO4 and Sirt1 could interact with p21 cyclin-dependent kinase inhibitors, leading to cell cycle alternation. Thus, the upregulation of Sirt1 and FOXO4 hinders the transition of cells from the G1 to S phase by upregulation of p21 that confirmed in PI staining. In contrast, Nalm-6 cell pretreatment with RJ led to c-Myc gene down-expression. The c-Myc is an oncogenic protein that inhibits p21 gene expression, resulting in cell cycle progression. Therefore, c-Myc downregulation fosters RJ antiproliferative capacity.

In conclusion, this research shed new light on the anti-leukemic effect of RJ against ALL-derived Nalm-6 cells. Overall, RJ inhibits the metabolic activity of Nalm-6 cells and exerts a growth-suppressive effect which is mediated by ROS generation. Although this study

reinforces the therapeutic potential of RJ, its effectiveness should be validated in ALL treatments.

Keywords: Acute lymphoblastic leukemia, Royal jelly, Reactive oxygen species, Cell cycle, Nalm-6

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OH-4

Original research (OH4-G1108)

Association between HLA-DRB1*04, HLA-DQB1*03, and HLA-DQB1*06 with alloimmunization in tansfusion-dependent patients with thalassemia

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Background and Aim: Transfusion therapy is crucial for treating Transfusion-dependent thalassemia (TDT) patients. However, the production of Alloantibodies presents a substantial challenge for these individuals and impacts their quality of life. The Rh and Kell blood group

antigens are particularly susceptible to alloantibody development. This study aims to establish the correlation between HLA-DRB1*04, HLA-DQB1*03, and HLA-DQB1*06 alleles and alloimmunisation in thalassemia patients from Iran.

Methods: Ninty-eight thalassemic patients were recruited for this study (49 alloimmunized and 49 non-alloimmunized). Alloimmunized patients developed Rh and Kell specificities alloantibodies. The two groups were compared based on the results of HLA-DRB1 and HLA-DQB1 genotyping conducted using Sequence-Specific Primers (SSP-PCR).

Results: The findings from the antibody screening revealed that the predominant alloantibody detected was Anti-K (95.9%), Anti-E (65.3%), Anti-C (30.6%), Anti-D (28.6%), Anti-c (10.2%), Anti-e (2%), and Anti-k (2%). There was a notable difference in HLA-DQB1*03 between alloimmunized and non-alloimmunized groups, 41.8% vs 58.2%, respectively. (P= 0.001, OR= 0.135, CI= 0.036-0.499). There was not any notable relationship between HLA-DRB1*04 and HLA-DQB1*06 alleles and alloimmunization.

Conclusion: Our findings indicate that HLA-DQB1*03 may have a protective role in preventing alloantibody production. Thus, HLA-typing, particularly focusing on DQB1*03, can significantly enhance the screening process, leading to improved blood transfusion management, reduced rejection of hematopoietic stem cell transplantation, and minimized blood transfusion complications.

Keywords: Thalassemia; Alloimmunization; HLA-DRB1; HLA-DQB1; Blood group antigens.

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OH-5
Abstract Type: Original Research

Targeting Microvesicles: Repurposing Imipramine to Boost Arsenic Trioxide Efficacy and Increase Drug Sensitivity in Acute Promyelocytic Leukemia

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Abstract

Background and Aim: Drug discovery is crucial in developing treatments for leukemia and translating basic research into clinical applications. While targeted therapies, such as arsenic trioxide (ATO) for acute promyelocytic leukemia (APL), have shown efficacy, they face limitations like lack of specificity, short half-lives, and adverse effects. These challenges call for new strategies to improve treatment effectiveness and combat drug resistance. Drug repurposing, which utilizes the known safety profiles of existing drugs, offers a promising approach to developing new therapies. This study explored the potential of repurposing the antidepressant imipramine (IMI) to enhance the chemosensitivity of APL cells (NB4 cell line) to ATO. We hypothesized that microvesicles (MVs) released by NB4 cells after ATO treatment contribute to resistance and that IMI could inhibit MV release, improving ATO efficacy.

Methods: In silico methods were employed to investigate IMI's interaction with proteins involved in MV release, focusing on the P2X7 purinergic receptor (P2X7R) and Src kinase (Src-K). Homology modeling predicted the 3D structures of P2X7R, which were assessed by several validation tools. Binding site analyses identified potential IMI interaction sites, and docking simulations were performed using HDOCK and Molegro Virtual Docker. The effects of IMI and ATO on NB4 cell viability were assessed using Trypan blue and MTT assays, while apoptosis and cell cycle changes were evaluated using flow cytometry. MV size, protein content, and number were determined through dynamic light scattering, atomic force microscopy, and BCA assay. Additionally, qRT-PCR was used to measure the expression of key genes involved in apoptosis and cell cycle regulation.

Results: In silico analysis identified acid sphingomyelinase (ASM), P2X7R, and Src-K as key IMI targets. Docking simulations revealed strong interactions between IMI and these proteins, suggesting inhibition of MV release. IMI enhanced NB4 cell sensitivity to ATO ($P<0.001$) resulting in increased cytotoxicity, cell cycle arrest at the G2/M phase, and apoptosis. The combination of IMI and ATO showed synergistic effects, lowering the IC50 of ATO. Flow cytometry revealed a significant increase in apoptotic cells with combination treatment ($P<0.0001$), while qRT-PCR indicated upregulation of pro-apoptotic genes (BAX, PTEN, P53, P21) and downregulation of anti-apoptotic Bcl-2 and cell cycle regulator Cyclin D1. IMI also significantly inhibited MV release, evidenced by reduced MV protein concentration ($P<0.01$) and particle count ($P<0.01$). Importantly, IMI showed no cytotoxicity toward normal peripheral blood mononuclear cells (PBMCs), indicating selectivity for leukemic cells.

Conclusion: This study demonstrated that IMI inhibits key proteins involved in MV release, potentiating ATO's cytotoxic effects on APL cells through multiple mechanisms, including MV inhibition, cell cycle modulation, and apoptosis induction. These findings suggest that combining IMI with ATO could be a promising strategy to enhance ATO efficacy and overcome drug resistance in APL patients. Further research, including in vitro and in vivo studies, is needed to validate these results and explore IMI's clinical potential as a chemosensitizing agent in leukemia treatment. This research highlights the potential of drug repurposing in leukemia therapy.

Keywords: Acute Promyelocytic Leukemia, Arsenic Trioxide, Imipramine, Drug Sensitivity, Computational Biology

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OH-6

Abstract Type: Original Research (OH6-G1120)

The effect of mild hypoxia(5% O2) on Stemness of CD34+ cells isolated from umbilical cord blood cocultured with human bone marrow mesenchymal stem cells

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Abstract

Background and Objectives: Cord blood(CB) is a rich source of Hematopoietic stem cells(HSCs) .Beside the advantage of CB، the main disadvantages of CB are the limited number of stem cells and delayed engraftment. Identifying strategies to enhance expansion and maintain stemness of HSCs can improve transplant efficiency. The goal of this study was to examine different culture conditions on *HOXB4* ،*c-Myc* ،*Nanog* و *SOX2* gene expression of CB-HSCs.

Materials and methods :In this study ،human cord blood CD34+ HSC ،Cultured in the serum-free medium supplemented with cytokines(TPO،FLT3L،SCF) with/without Bone marrow mesenchymal stem cell(MSC) in 21% O2 and 5% O2 for 7 days . In day 7 HOXB4،c-Myc Nanog ، SOX2 expression by Real time PCR were evaluated.. The data analyzed using the ANOVA test and Value < 0.05 were considered statistically significant.

Results: Highest number of HOXB4،c-Myc Nanog ، SOX2 mRNA level were seen in coculture of HSC with bone marrow MSC at 5% O2 . Our findings demonstrated statistically significant increase of expansion and stemness markers in 5% O2 tension versus 20%.

Conclusions: Bone Marrow (BM)-MSC and 5% O2 combination enhanced stemness of HSC and better mimicked the niche microenvironment conditions.

Keywords: Cord blood، Hematopoietic stem cell، Mesenchymal stem cell،Coculture، hypoxia.

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OH-7

Abstract Type: Original Research (OH7-G1124)

Correlation of miR-155-5p, KRAS, and CREB Expression in Patients with Acute Myeloid Leukemia

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is a heterogeneous hematological cancer affecting bone marrow. MiRNAs, small non-coding RNA molecules, regulate gene expression by binding to mRNAs. MiR-155 has a dual function in AML, acting as a tumorigenic factor when highly expressed and as a tumor suppressor when moderately expressed. Changes in KRAS expression have not been studied as much as its mutations in AML. KRAS activates several downstream pathways, including CREB1 via the PI3K/AKT pathway. CREB controls the expression of over 4,000 genes involved in various cellular

activities. This article aims to investigate the correlation between miR-155 expression and KRAS and CREB.

Methods: This study involved 21 AML patients from Taleghani Hospital and 9 healthy controls. AML diagnosis was confirmed through flow cytometry, molecular tests, and pathology. Participants had no prior malignancy history and were untreated with cytotoxic therapies. Mononuclear cells were isolated via density-gradient centrifugation at 800 x g for 5 minutes at 4°C, and total RNA was extracted using Trizol reagent. RNA quality was assessed with agarose gel electrophoresis and the NanoDrop 2000 spectrophotometer. cDNA synthesis was performed using the Fermentas RevertAidTM Premium First Strand cDNA Synthesis Kit with the following protocol: 25°C for 10 minutes, 42°C for 60 minutes, and 70°C for 15 minutes. Real-time PCR was conducted using Rotor-Gene Q based on the SYBR Green relative quantification assay. Primers for KRAS, CREB, and miR-155 were designed and validated. Data analysis was performed using SPSS and GraphPad Prism, employing t-tests and Pearson's correlation, with significance set at $p < 0.05$.

Results: The database https://www.targetscan.org identified over 700 genes as targets of miR-155, including CREB and KRAS. The database http://gepia.cancer-pku.cn showed overexpression of both KRAS and CREB in AML. The mean ages of AML and control groups were 50.48 ± 20.33 and 31.33 ± 2.78 years, respectively. The mean WBC counts were 35.43 ± 41.5 × 10^3/µL in AML patients and 7.3 ± 1.7 × 10^3/µL in controls. MiR-155 expression was 35 times higher in AML patients than in controls ($p < 0.0001$). No significant correlation was found between miR-155 and CREB ($p = 0.922$) or KRAS ($p = 0.147$). CREB expression was 1.92-fold higher in AML patients ($p = 0.034$) and correlated significantly with WBC ($p = 0.001$). KRAS expression showed no significant difference between AML patients and controls ($p = 0.89$).

Conclusion: In conclusion, our study showed that miR-155 has significantly increased expression in AML. Also, the CREB transcription factor is more expressed in patients with AML than in normal samples. KRAS is more expressed in patients than in healthy individuals. However, there was no correlation between the expression of miR-155 with KRAS and CREB. In the end, more studies on the miR-155 network in AML are recommended.

Keywords: Adult Leukemia; CREB; Gene Expression; KRAS; MicroRNA.

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OH-8
Abstract Type: Original Research

The methanolic extract of Shirazi thyme (Zataria Multiflora) and its combination with arsenic trioxide (ATO) changes the expression of onco-miRNAs and TS-miRNAs in acute promyelocytic leukemia cell line (NB4)

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Abstract

Background and Aim: Acute promyelocytic leukemia (APL) is responsible for 10–15% of AML new cases. ATO is commonly used for disease recurrence post-ATRA treatment. While

therapeutically beneficial, ATO can lead to various complications. MicroRNAs (miRNAs), 19 to 25 nucleotide-long RNA molecules, play pivotal roles in various cancers. Zataria Multiflora (Shirazi thyme) is a medicinal plant targeting apoptosis-inducing signaling pathways. This study explores the impact of the methanol extract of thyme and its combination with ATO on the expression of onco-MiRs and TS-MiRs in the NB4 cell line.

Methods: Cell viability and metabolic activity of NB4 cells were assessed via trypan blue dye exclusion test and MTT assay. Cell apoptosis rate was evaluated using flow cytometry, and changes in the expression of miRNAs 19a-3p, 23a-5p, 181b-5p, 3156-5p, and 4498 were analyzed through real-time PCR. Finally, docking was performed using MVD and HDOCK software.

Results: When ATO 0.25 µM was combined with 20 µg/ml methanolic extract of Shirazi thyme, cell viability, metabolic activity, and gene expression (excluding 181b-5p) exhibited a significant decrease. At the same time, apoptosis rates showed a notable increase compared to individual drug doses.

Conclusion: The findings of this study indicate that Zataria Multiflora can act as a synergistic adjuvant with ATO and, in some cases, produce superior effects compared to high doses of ATO alone. Docking results confirmed thymol and carvacrol as the potential compounds in the apoptotic effect of ZME.

Keywords: Zataria Multiflora, arsenic trioxide, microRNA, acute promyelocytic leukemia

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OH9

Navigating Panic Values in Clinical Practice: A Comprehensive Framework

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Background and Aim: Panic values are laboratory results that significantly deviate from normal ranges, often indicating potentially life-threatening conditions. Effective management of these values is crucial for patient safety and quality of care.This article presents a structured framework for healthcare professionals to systematically identify, assess, and respond to panic values in clinical practice.

Methods: The framework includes the following key components: definition and identification of panic values; initial response protocols; assessment of urgency based on severity and symptoms; communication strategies to notify relevant personnel; immediate intervention

techniques; follow-up and reevaluation processes; patient education for prevention; and quality improvement measures through regular review and training.

Results: Implementing this framework enhances the recognition and management of panic values, facilitating timely interventions and improving clinical outcomes. By fostering effective communication and ensuring a thorough assessment, healthcare teams can better address the complexities associated with abnormal laboratory results.

Conclusion: A systematic approach to navigating panic values in clinical practice not only promotes patient safety but also empowers healthcare providers to deliver high-quality care. Ongoing education and refinement of protocols are essential for sustaining effective management strategies in dynamic clinical environments.

Keywords: Panic values, clinical practice, patient safety, laboratory results, healthcare protocols.

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OH10

Panic Value Alerts: Enhancing Patient Safety Through Timely Interventions

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Background and Aim

In clinical settings, the timely identification and response to critical laboratory results—often referred to as panic values—are essential for patient safety and optimal healthcare outcomes. Panic value alerts serve as critical indicators of potentially life-threatening conditions, necessitating immediate medical intervention. This article aims to explore the implementation of panic value alerts within electronic health record (EHR) systems, focusing on their role in improving patient safety through timely clinical decision-making.

Methods

We conducted a review of current literature and case studies regarding the use of automated panic value alert systems in various healthcare settings. Data were collected on the effectiveness of these systems in reducing the time from result acquisition to clinical response. We also analyzed the impact of panic value alerts on mortality and morbidity rates associated with critical conditions. Additionally, we examined challenges such as alert fatigue, clinician education, and the integration of alerts into existing workflows.

Results

The implementation of automated alert systems significantly reduced the time taken for clinicians to respond to critical laboratory results. Studies indicated a measurable decrease in mortality rates and morbidity associated with conditions identified through panic value alerts. However, challenges such as alert fatigue were identified, underscoring the need for clinician education and a thoughtful approach to integrating alerts into daily practices to enhance their utility without overwhelming healthcare providers.

Conclusion

The strategic application of panic value alerts is a vital component of contemporary healthcare systems, contributing to a culture of safety and high-quality care. By fostering an environment that prioritizes rapid responses to critical lab values, healthcare institutions can enhance patient safety and improve clinical outcomes. Continued research and innovation are essential to refine alert systems and ensure they meet the dynamic needs of healthcare providers and patients alike.

Keywords

Panic values, electronic health records, patient safety, laboratory results.

OH-11

Original Research

Flow cytometry-based functional assay is a valuable diagnostic approach for confirmation of Heparin-Induced Thrombocytopenia

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Abstract

Background and Aim: Heparin-induced thrombocytopenia (HIT) is a serious immunological adverse drug reaction that rarely occurs in patients receiving heparin. The heparin-induced platelet activation (HIPA) test, a gold standard assay for HIT, is time-consuming, challenging, and produces qualitative results. This study aimed to compare the performance characteristics of a flow cytometry-based functional assay, for HIT diagnosis with HIPA assay.

Methods: This study was conducted on HIT-suspected patients referred to Iranian Blood Transfusion Organization between 2021 and 2023. After clinical evaluation and 4Ts scores calculation, anti-PF4 screening and HIPA test were conducted. Thirty HIPA-positive and 30 HIPA-negative samples were selected. Subsequently, a flow cytometry-based functional assay, Emo-Test HIT confirm, was performed, and the sensitivity and specificity for HIT diagnosis were measured.

Results: Among the 30 samples with negative HIPA results, one was positive with the Emo-test HIT Confirm® assay, and the remaining were negative. Among 30 positive HIPA samples, the result of one sample was inconclusive, two samples were negative with flowcytometry Emo-test and the others were positive. The sensitivity and specificity of this flow cytometry-based functional assay were 90% (95% CI: 79.3-100) and 96.6% (95% CI:90.2-100). The negative predictive value and positive predictive value were 93.5% and 96.4% respectively.

Conclusion: Flow cytometry-based functional assay has a good sensitivity and specificity for HIT diagnosis confirmation, indicating that it may be a promising approach in the clinical setting.

Keywords: heparin-induced thrombocytopenia (HIT), diagnosis, flow cytometry,

functional assay.

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OH-12
Original Research
"Evaluation of the Combined Effect of Venetoclax and Bcl-2 si-RNA in Leukemia Patients"

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Abstract

Background and Aim:

This study aims to evaluate the combined effect of Venetoclax and si-RNA anti Bcl-2 in patients with leukemia. Venetoclax is a targeted therapy designed to inhibit the Bcl-2 protein, which plays a crucial role in the survival of cancer cells. By assessing the efficacy of this combination treatment, the study seeks to determine whether the simultaneous use of Venetoclax and si-RNA against Bcl-2 can enhance the therapeutic outcomes for leukemia patients . Role of si-RNA Anti Bcl-2 **si-RNA (small interfering RNA)** anti-Bcl-2 plays a critical role in cancer therapy by specifically targeting and silencing the Bcl-2 gene, which encodes the anti-apoptotic protein Bcl-2. This protein is often overexpressed in various cancers, including leukemia, contributing to the survival of malignant cells by inhibiting programmed cell death (apoptosis). The combination of Venetoclax and si-RNA against Bcl-2 is expected to have a significant impact on the treatment of the disease. This synergistic effect may enhance the therapeutic outcomes by promoting apoptosis in cancer cells and reducing the levels of the Bcl-2 protein, which is often overexpressed in leukemia. As a result, this combination therapy could lead to improved efficacy in treating leukemia and potentially overcome drug resistance.

Methods:

1. **Cell Culture**: Leukemia cell lines were cultured in appropriate media supplemented with fetal bovine serum (FBS) and antibiotics under standard conditions (37°C,5% CO2).

2. **si-RNA Transfection**: Cells were transfected with si-RNA against Bcl-2 using a transfection reagent according to the manufacturer's instructions. Optimal concentrations and transfection conditions were determined through preliminary experiments.

3. **Treatment with Venetoclax**: Following transfection, cells were treated with varying concentrations of Venetoclax to assess dose-dependent effects. Treatment duration was standardized (e.g.,24,48, or72 hours).

4. Assessment of Bcl-2 Expression: Bcl-2 protein levels were measured using Western blot analysis.

5. **Apoptosis Assay**: Apoptosis was evaluated using flow cytometry with Annexin V/PI staining. Cells were harvested, stained, and analyzed to quantify early and late apoptotic populations.

6. **Statistical Analysis**: Data were analyzed using appropriate statistical methods (e.g., ANOVA, t-tests) to determine the significance of differences between treatment groups. A p-value of <0.05 was considered statistically significant.

Results:

The results of this study will focus on the combined effects of Venetoclax and si-RNA targeting Bcl-2 in leukemia cells.

1. **Bcl-2 Expression Levels**: The effectiveness of si-RNA in reducing Bcl-2 protein levels will be quantified through Western blot analysis, comparing treated and control groups.

2. **Apoptosis Rates**: Flow cytometry results will illustrate the percentage of apoptotic cells following treatment with Venetoclax alone, si-RNA alone, and the combination of both. This will help determine the synergistic effect of the treatments.

3. **Cell Viability**: Results from cell viability assays (e.g., MTT or trypan blue exclusion) will provide insights into the overall impact of the treatments on leukemia cell survival.

4. **Statistical Significance**: The data will include statistical analyses to confirm the significance of the observed effects, with p-values indicating the strength of the results

Conclusion:

Based on this study and other studies, it is expected that during combined treatments, the treatment effect will increase and the effect of resistance to common chemotherapy will be reduced, it is hoped that by the use of these treatments in the clinical phases, we will witness the progress of the treatment and the recovery of patients.

Keywords: Leukemia;venetoclax; Bcl-2 siRNA

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OH-13
Abstract Type: Original Research

Multiple myeloma cell-derived exosomes promote favorable tumor functional performance by polarizing macrophages toward M2-like cells

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Abstract

Background and Aim:

It has long been hypothesized that leukemic cells are able to modulate the fate of resident cells in the tumor microenvironment (TME) toward either supporting or immunosuppressive cells for the development of tumors. Exosomes can be a potential culprit in imposing tumor desire. There is evidence about the impact of tumor-derived exosomes on different immune cells in different malignancies. However, findings about macrophages are contradictory. Here, we evaluated the potential influence of multiple myeloma (MM)-cell-derived exosomes on the polarization of macrophages by examining hallmarks of M1 and M2 macrophages

Methods:

After treatment of M0 macrophages with isolated exosomes (from U266B1), gene expression (Arg-1, IL-10, TNF-α and IL-6), immunophenotyping markers (CD206), cytokine secretion (IL-10 and IL-6), nitric oxide (NO) production, and redox potentiality of target cells were assessed.

Results:

Our results revealed significantly increased expression of the genes involved in the development of M2-like cells but not M1 cells. The CD 206 marker and IL-10 protein levels were significantly increased at different time points. The expression of IL-6 mRNA and IL-6 protein secretion did not change significantly.

Conclusion:

MM-cell-derived exosomes induced significant changes in NO production and intracellular ROS levels in M0 cells.

Keywords: exosome; macrophage polarization; multiple myeloma.

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OH-14
Original Research

The impact of plasma exosomes from both young and elderly donors on the HIF-1α gene and the P21 protein in cord blood hematopoietic progenitor cells

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Abstract

Background and Aim: Exosomes are essential agents of intercellular signaling and their impact on aging has been observed so far. HIF-1α has a crucial role in the regulation of aging and responding to hypoxia. Furthermore, the expression of P21 as a component of the hypoxia

downstream signaling cascade, is increased with aging. Considering the significance of age-related changes in various diseases and the potential role of exosomes, this research aimed to study the influence of plasma exosomes from young and old individuals on the expression of the HIF-1α gene and P21 protein in hematopoietic stem cells (HSCs).

Methods: Plasma exosomes were isolated from both elderly and young males and then characterized. Subsequently, hematopoietic stem cells were derived from umbilical cord blood samples and treated with exosomes derived from both elderly and young males. The MTT assay was conducted to assess cell viability. The expression of the HIF-1α gene and P21 protein was assessed by qRT-PCR and western blot, respectively.

Results: The expression of the HIF-1α gene was significantly elevated in HSCs treated with 10 µg/ml of exosomes derived from young males (Y10-Exo) in comparison to the untreated group (P=0.002). Furthermore, HIF-1α gene expression was significantly reduced in HSCs treated with 10 µg/ml of exosomes derived from elderly males (O10-Exo) compared to the untreated group (P<0.001). The expression of P21 protein was significantly elevated in HSCs treated with 5 µg/ml of exosomes from elderly males (O5-Exo) and O10-Exo, in comparison to the untreated group (P=0.000 and P=0.002, respectively).

Conclusion: Our results indicated that exosomes derived from younger individuals upregulate HIF1-α, possibly contributing to the postponement of aging in HSCs. Moreover, exosomes derived from elderly individuals may contribute to aging by decreasing HIF1-α levels and increasing P21 levels.

Keywords: Aging, Exosomes, Hematopoietic Stem Cells, HIF-1α, P21, Old individuals

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OH-15
Abstract Type: Original Research

Mechanistic Study of cytotoxicity effect of Combretastatin A4 on HL-60 acute myeloid leukemia (AML) cells

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is a type of leukemia that affects bone marrow cells resulted in out of control of blood cells production. Combretastatin-A4 (CA4) has been reported as a potential therapeutic candidate to treat various types of cancer. The aim of this study was to evaluate the cytotoxicity mechanisms of CA4 on acute leukemia cancer cell model (HL-60).

Methods: HL-60 cell line was treated with a range of concentrations of CA4 (1-100000 pg/ml) for 24 h and 48h. The cytotoxicity effect was evaluated by Alamar blue assay. In addition, the cell apoptosis

was detected by Annexin V Staining and Sub-G1 method. The level of gene expression of Cyclin D1, BAX, BCL-2, AKT, and MCL-1 was measured by real-time PCR. Western blot analysis was carried out to determine the expression changes of mitogen-activated protein kinase (MAPK) protein.

Results: In a dose-dependent manner, CA4 inhibited cell proliferation and induced apoptosis in HL-60 cell line. Moreover, CA4 increased significantly (*P <0.05) the expression levels of a pro-apoptotic gene (Bax) and Cyclin-D1, but it reduced those of an anti-apoptotic gene (Bcl-2) and MCL-1 compared to the control group. Furthermore, the expression level of the AKT gene did not change significantly in any of the groups. The MAPK protein levels were also significantly decreased by CA4.

Conclusion: This study suggests that CA4 can induce apoptosis and inhibit proliferation of HL-60 cell line. Therefore, this natural compound could serve as a potential candidate to treat APL in human models and clinical trials.

Keywords: Apoptosis; Anticancer; Combretastatin-A4; HL-60; Leukemia; Microtubule .)

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OH-16

Abstract Type: Original Research

CDC27 gene expression patterns as a potential biomarker in Acute Leukemia

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Background and Aim: Background Treating Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) is difficult due to high relapse rates and drug resistance. Tumorigenesis is largely dependent on disruption of the cell cycle progression. While the role of Cell Division Cycle 27 (CDC27) in the anaphase-promoting complex/cyclosome is well-known, its significance in the pathophysiology of acute leukemia and its potential as a biomarker are less well understood.

Methods : This case-control study used samples from 100 leukemia patients (50 with ALL and 50 with AML) at Shariati Hospital in Tehran, Iran, along with 50 healthy individuals. The

expression of CDC27 was analyzed using quantitative real-time PCR (RQ-PCR). Statistical analysis was done using the nonparametric Mann-Whitney U test.
Result: The results showed that AML and ALL patients had significantly higher levels of CDC27 expression compared to the control group. Although a weak correlation between CDC27 expression and hematological parameters was found, there was no significant correlation with sample type, demographics, clinical variables or prognosis.
Conclusion: Conclusions This study highlights the potential of CDC27 as an oncogene, as well as a possible prognostic and diagnostic marker in acute leukemias. It suggests that CDC27 could be a valuable biomarker or therapeutic target in the treatment of AML and ALL.

Keywords: Acute lymphoblastic leukemia · Acute myeloid leukemia · CDC27 · APC/C · Gene expression

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OH17

Effect of ferric carboxymaltose in the iron deficiency anemia patients undergoing cardiac surgery: a randomized clinical trial

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Background and Aim: Iron deficiency is frequent in patients undergoing cardiac surgery. Intravenous iron agents have been used for treating patients with iron deficiency anemia. The present study aimed to investigate the efficacy of ferric carboxymaltose (FCM) among the iron deficiency anemia patient candidates for cardiac surgery.

Methods: The present non-blinded, randomized, controlled clinical study was performed among two groups of the iron deficiency anemia patients underwent cardiac surgery. The first of whom was infused with a fixed dose of 1000 mg FCM, 3-5 weeks preoperatively, while the second group received no medicine (control). The changes in hemoglobin concentration and biomarkers of iron metabolism were repeated

before surgery and 3 to 5 days after surgery. Moreover, the average number of consumed packed cells was assessed.

Results: In this study, clinical tests, demographic characteristics, and surgery type were similar in two groups. Regarding hemoglobin (Hb) level, a significant difference was demonstrated between FCM-administered group in the preoperative stage (12.1 g/dl, 11.6-12.9) and the control (11.5 g/dl, 10.9-11.8) (p-value < 0.001). Additionally, the preoperative serum ferritin level of FCM group was determined 580 ng/dl (435-787) which significantly differed from that of the control (57 ng/dl, 32-100) (p-value=0.001).

Conclusion: The use of FCM is ineffective for preoperative anemia correction in the patients undergoing cardiac surgery and fails to decrease transfusion during surgery in spite of improvement in in iron stores.

Keywords: Iron Deficiency Anemia, Cardiac surgery, Ferric carboxymaltose, Transfusion

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OI-1

Alteration of peripheral blood natural killer (NK) cells in women with endometriosis during Assisted Reproductive Technology (ART) cycle

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim:

Endometriosis as an estrogen-dependent disease. It is a common cause of infertility in women in reproductive age, often associated with immune system alterations. Peripheral blood NK cells (pNKs) changes are reported in endometriosis.

One of treatments for endometriosis is the use of GnRH agonist/antagonist drugs for about 6 months to a year. Studies have shown that these drugs can affect the activity and number of NK cells in endometriosis.

On the other hand, these drugs are used to ovarian stimulation during ART cycles. The aim of this study is to evaluate the pNKs in women with endometriosis during ART cycles.

Methods:

In this cohort study, 40 infertile women with endometriosis who underwent ovulation stimulation with long gonadotropin-releasing hormone (GnRH) agonist or GnRH antagonist protocols during ART cycles at Royan Institute will be enrolled. Whole blood was collected at two time points: 1) on day2-3 of the menstrual cycle (the start day of the ovulation stimulation cycle 2) day of ovum pickup.

In at each time points 3 cc was collected from women and stained. Comparisons the percentage and cytotoxicity of pNK cell subsets between two time points was done by flow cytometer **(**with specific antibodies PerCP anti-humanCD3 Antibody (T cell marker), APC anti-human CD56 Antibody (NK cell surface marker), FITC anti-human CD16 Antibody (another NK surface marker), PE anti-human CD107a Antibody (NK cell activity marker**)**.

Statistical analysis was performed with Prism statistic version 9. T–test was used for two time points' comparisons. P-value less than 0.05 was considered to be significant.

Results:

Till now 18 women were enrolled (mean of body mass index (BMI): 32.61 Kg/m2 and mean of age: 25.02 years old). Mean percentage of NK cells (CD3-CD56+ cells) in starting day of stimulation cycle is 19.44±15.70 % and in ovum pick up day is 16.67± 15.70 % but this decrease is not significantly different.

On the other hand, the percentage of cytotoxicity markers (CD3-CD16+CD107a+) is 5.76± 7.66 in starting day of stimulation cycle and 5.23± 7.66 in ovum pick up day which its change was not significant.

Conclusion:

Our preliminary data showed that short term use of GnRH drugs could not significantly change the percentage and cytotoxicity of peripheral NK cells. Although completion of study is needed for definite conclusion.

Keywords: Endometriosis, natural killer cells, GnRH agonist, GnRH antagonist, IVF/ICSI

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OI-2

Abstract Type: Original Research

The anti-cancer properties of miR-340 plasmid-chitosan complexes (miR-340 CC) on murine model of breast cancer

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Abstract

MiRNA-340 (miR-340) has been found to have tumor-suppressing effects in breast cancer (BC). However, for clinical use, miRNAs need to be delivered safely and effectively to protect

them from degradation. In our previous study, we used chitosan complexes as a safe carrier with anti-cancer properties to deliver miR-340 plasmid into 4T1 cells. This study explored further information concerning the anti-cancer impacts of both chitosan and miR-340 plasmid in a murine model of BC. Mice bearing 4T1 cells were intra-tumorally administered miR-340 plasmid-chitosan complexes (miR-340 CC). Afterwards, the potential of miR-340 CC in promoting anti-tumor immune responses was evaluated. MiR-340 CC significantly reduced tumor size, inhibited metastasis, and prolonged the survival of mice. MiR-340 CC up-regulates P-27 gene expression related to cancer cell apoptosis, and down-regulates gene expressions involved in angiogenesis and metastasis (breast regression protein-39 (BRP-39)) and CD163 as an anti-inflammatory macrophages (MQs) marker. Furthermore, CD47 expression as a MQs immune check-point was remarkably decreased after miR-340 CC treatment. The level of IL-12 in splenocytes of miR-340 CC treated mice increased, while, the level of IL-10 decreased, indicating anti-cancer immune responses. Our findings display that miR-340 CC can be considered as a promising therapy in BC.

Keywords:
Breast cancer; Chitosan; MiR-340; Murine breast cancer; 4T1 cells

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Comparative Evaluation of Anti-HLA Antibody Detection Methods in Transplant Recipients: Cross-Matching vs. Flow Cytometry

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Abstract

Background and Aim: Since 1960, the cross-match test has been routinely employed to detect specific antibodies against donor lymphocytes in transplant recipients. This diagnostic test, developed by Terasaki using complement-dependent cytotoxicity (CDC), is utilized to identify the presence of IgG antibodies in the recipient's serum, specifically targeting anti-HLA antibodies that contribute to acute transplant rejection. The CDC assay serves as a vital pre-transplantation standard for transplant recipients. In the present study, we compare the use of anti-human globulin (AHG) flow cytometry for detecting lymphocytes bound to antibodies in the serum of transplant recipients with the conventional CDC method.

Methods: The lymphocyte cross-match test was conducted using the complement-dependent cytotoxicity (CDC) method to identify suitable kidney recipients from brain-dead individual donors over a 30-year period at Khurshid University Hospital in Isfahan, Iran. During a one-year period, 95 tests were performed using flow cytometry, and the results were compared with those obtained from the white blood cell (WBC) cross-match method.

Results: In the routine cross-match method, after preparing the cells, antibodies, and complements, microscopic observation of lymphocytes stained with eosin dye is conducted. The percentage of viable cells serves as the basis for calculating and recommending the presence of antibodies in the serum, with >95% viable cells being recommended for transplantation. In contrast, the flow cytometry method involves the binding of the secondary antibody anti-human globulin (AHG) to human IgG on the lymphocytes, which indicates the percentage of cells with specific or non-specific antibodies (<5% of the cell population could be positive in a normal population). The cell population is represented in a separate histogram or in the fourth quadrant of the flow cytometry analysis, which serves as the basis for recognition.

Conclusion: According to previous researches, three different tests are commonly utilized: cytotoxicity assays, enzyme-linked immunosorbent assays (ELISA), and flow cytometry. However, standardization of testing methods for these three assays has not been universally agreed upon by all laboratories. Our investigation recommends the establishment of appropriate equipment and standardized methods governed by the Ministry of Health for implementation across all regions of our country.

Keywords: Transplant; CDC; WBC cross-match; Flow cytometry

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OI-4
Abstract Type: Original Research

Evaluating Nanoparticle-Induced DNA Damage: A Comparative Genotoxicity Study of Sitagliptin Formulations Using Human Lymphocyte Comet Assay

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Abstract

Background and Aim: Diabetes mellitus is a metabolic disorder with high blood glucose levels over a long period of time. Sitagliptin, as a selective and competitive inhibitor of dipeptidyl peptidase-4 (DPP-4) is used for the treatment of type 2 diabetes. Drug delivery system with nanoparticles in general and mucoadhesive nanoparticles in particular offers several advantages by targeting and localizing the dosage form in a specific place. Therefore, the aim of this study is to evaluate the level of genotoxicity and damage potential of sitagliptin and its nanoparticles on DNA and chromosomes of human lymphocyte culture using Comet assay.

Methods: First, after preparation of human lymphocyte cells and passage of the cells to contact the desired drugs in the groups of sitagliptin and its nanoparticles, they are also incubated for 24 and 48 hours. And after contact with Comet test cells was performed.

Results: The results of examining the genotoxicity of human lymphocytes have shown that the amount of genetic damage caused by sitagliptin and sitagliptin nanoparticles in the form of Tail length parameter, Tail moment parameter and %DNA in Tail parameter in a dose of 100 nM of the combination of these two drugs is the highest amount of damage has had.

Conclusion: In general, the results show that due to the nano composition of sitagliptin and its wider and better distribution, it has shown more genotoxic effects. It is very important to examine the drug and ways to reduce it.

Keywords: genotoxicity, sitagliptin, nanoparticles, lymphocyte

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OI-5

Investigation the expression of IL-10 in macrophages after treatment with *Leishmania major*

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Abstract

Background: Cutaneous leishmaniasis is an infectious disease caused by *Leishmania major*. Cytokines such as IL-10 secreted by immune cells including macrophages, play an important role in the wound healing process of cutaneous leishmaniasis. In the present study, the expression level of IL-10 was investigated during treatment of macrophages with *Leishmania major* parasite.

Methods: Peritoneal macrophages were isolated from BALB/c mice, the cells were cultured and treated with the standard strain of *Leishmania major* parasite for 24 and 72 hours. After incubation, macrophage RNA was extracted and IL-10 gene expression was investigated using the real-time PCR method.

Results: The results showed that with increasing treatment time of 72 hours, the expression of IL-10 gene increased in the macrophages treated with *Leishmania major*, but this is not significant($P \leq 0.05$).

Conclusion: An increase in the level of anti-inflammatory cytokines after exposure to the Leishmania parasite is a reason for the non-healing of the cutaneous leishmaniasis.

Keywords: *Leishmania major*, Macrophage, IL-10.

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OI-6

Abstract Type: Original Research

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Higher Circulating Concentration of Interleukin-38 in Patients with Knee Osteoarthritis: Its Association with Disease Severity

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Abstract

Background and Aim: Evidence showed that chronic inflammatory and immunopathological responses play a pivotal role in the development of osteoarthritis (OA). Interleukin-38 (IL-38) as a novel anti-inflammatory cytokine with influential modulatory properties on both innate and adaptive immune responses can be involved in the pathogenesis of OA. Therefore, this study aimed to measure the serum level of IL-38 in OA patients to clarify the positive or negative association with disease and its severity.

Methods: Blood specimens were collected from two groups including 23 newly-diagnosed OA patients and 22 healthy sex and age-matched subjects as a control group. Serum IL-38 quantities were measured using enzyme-linked immunosorbent assay (ELISA).

Results: Significantly higher IL-38 levels were detected in OA patients in comparison with the healthy group (265.78±41.27 pg/mL vs 44.23±6.04 pg/mL, p=0.0001). The IL-38 concentration in OA patients with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores>40 and in OA patients with visual analog scale (VAS) scores >5 were higher than those with WOMAC scores<40, and VAS scores<5 (p=0.026 and p=0.035, respectively). The IL-38 levels in OA patients with body mass index (BMI)<25 were also significantly higher than in patients with BMI>25 (p=0.05).

Conclusion: According to our findings, WOMAC, VAS, and BMI indices may influence the IL-38 serum levels in OA patients and it may be elevated in OA patients to modulate inflammatory responses in a compensatory manner. The patients with OA, especially those with more severe disease express higher serum amounts of IL-38. Accordingly, IL-38 may be considered as a valuable marker for OA.

Keywords: Articular cartilage; IL-38 protein; Inflammation mediators; Joint diseases; Osteoarthritis.

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OI-7

Abstract Type: Original Research

Immunomodulatory Effects of Adjuvants CPG, MPLA, and BCG on the Derp2-Induced Acute Asthma at Early Life in an Animal Model of BALB/c Mice

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Abstract

Background and Aim: The Th1- and Treg cell-related immune responses play key roles in the modulation of Th2 cell-related allergic disorders. The aim was to evaluate the effects of CPG, MPLA, and BCG on the number of Th1-, Th2-, and Treg cell-related parameters in an animal model of asthma.

Methods: BALB/c mice were divided into five groups and immunized subcutaneously (SC) on days 1, 15, and 22 with allergen Derp2. Three groups of mice were pretreated SC on days 0, 14, and 21 with CPG, CPG + MPLA, or CPG + BCG. All mice were then challenged intranasally with Derp2 on days 28–37. Blood samples were collected from the retro-orbital sinus, on days 0, 23, and 40. The serum levels of IL-4, IFN-γ, IgE, and IgG2a were measured using ELISA technique. The blood number of Th1 and Treg cells was determined using flow cytometry.

Results: At the sensitization phase, the number of Th1 and the serum levels of IFN-γ and IgG2a were significantly increased in the Derp2-sensitized group pretreated with CPG plus MPLA, and the number of Treg cells was significantly elevated in Derp2-sensitized mice pretreated with CPG or CPG plus MPLA as compared with that in Derp2-sensitized control mice. At the challenge phase, the number of Th1 was significantly elevated in Derp2-sensitized mice pretreated with CPG plus MPLA, CPG plus BCG, or CPG; the count of Treg cells was significantly increased in Derp2-sensitized mice pretreated with CPG plus BCG group; and the levels of IFN-γ and IgG2a were significantly enhanced in the Derp2-sensitized group pretreated with CPG plus MPLA in comparison with those in Derp2-sensitized control mice. The scores of inflammation and mucus secretion in the lung were significantly decreased in the Derp2-sensitized group pretreated with CPG, BCG, and CPG plus MPLA in comparison with those in the Derp2-sensitized control group.

Conclusion: These results showed that BCG, MPLA, and CPG modulate Th1-, Th2-, and Treg-related parameters and ameliorate lung inflammatory parameters in a mouse model of asthma.

Keywords: asthma; BCG; MPLA; CPG-ODN; inflammation; mice.

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OI-8

Evaluation of the interaction between tumor growth factor-β and interferon type I pathways in patients with COVID-19: focusing on ages 1 to 90 years

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Abstract

Background and Aim: Evidence revealed that age could affect immune responses in patients with the acute respiratory syndrome of coronavirus 2 (SARS-CoV-2) infection. This study investigated the impact of age on immune responses, especially on the interaction between the tumor growth factor-β (TGF-β) and interferon type-I (IFN-I) axes in the pathogenesis of novel coronavirus disease 2019 (COVID-19).

Methods: This age-matched case–control investigation enrolled 41 COVID-19 patients and 40 healthy controls categorized into four groups, including group 1 (up to 20 years), group 2 (20–40 years), group 3 (40–60 years), and group 4 (over 60 years). Blood samples were collected at the time of admission. The expression of *TGF-βRI*, *TGF-βRII*, *IFNARI*, *IFNARII*, interferon regulatory factor 9 (*IRF9*), and SMAD family member 3 (*SMAD3*) was measured using the real-time PCR technique. In addition, serum levels of TGF-β, IFN-α, and SERPINE1 were measured by the enzyme-linked immunosorbent assay (ELISA) technique. All biomarkers were measured and analyzed in the four age studies groups.

Results: The expression of *TGF-βRI*, *TGF-βRII*, *IFNARI*, *IFNARII*, *IRF9*, and *SMAD3* was markedly upregulated in all age groups of patients compared with the matched control groups. Serum levels of IFN-α and SERPINE1 were significantly higher in patient groups than in control groups. While TGF-β serum levels were only significantly elevated in the 20 to 40 and over 60 years patient group than in matched control groups.

Conclusion: These data showed that the age of patients, at least at the time of admission, may not significantly affect TGF-β- and IFN-I-associated immune responses. However, it is possible that the severity of the disease affects these pathway-mediated responses, and more studies with a larger sample size are needed to verify it.

Keywords: COVID-19, TGF-β, Interferon, Fibrosis, SERPINE1

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OI-9
Abstract Type: Clinical trial

Clinical Outcomes of Lymphocyte Immunotherapy in Recurrent Pregnancy Loss due to antinuclear antibodies

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Abstract

Background and Aim: Two or more clinically confirmed fetal losses before 20 or 22 weeks of gestation, as identified by ultrasonography or histopathologic investigation, are indicative of recurrent pregnancy loss (RPL), a debilitating illness. The prevalence of RPL, which affects around 2-5% of couples of reproductive ages globally, is on the increase and presents patients and couples with serious emotional, mental, and physical difficulties. Antinuclear antibodies (ANAs) are one of the most common autoantibodies linked to RPL, and autoimmune diseases are present in around half of women with RPL. In order to add to the increasing amount of data regarding the therapeutic potential of immunological therapies in the therapy of RPL, this study aimed to clarify the effects of lymphocyte immunotherapy (LIT) on RPL by comparing the clinical effectiveness of LIT in RPL patients with positive ANA to those with ANA-negative RPL.

Methods: In this study, 50 healthy pregnant women, 114 ANA-negative RPL patients, and 84 ANA-positive RPL patients were included. Participants used a 1 ml solution of $2x10^7$ paternal lymphocytes from their spouses' peripheral blood for the LIT method. This solution was then subcutaneously injected in five arm regions in three steps four weeks apart in RPL patients. The vaccine ended before pregnancy. Peripheral blood was drawn before and three months after LIT. Ficoll gradient centrifugation isolated PBMCs from 10 mL. The Th1/Th2 ratio and NK cell frequencies in PBMCs were measured by flowcytometry before and after LIT. ELISA was used to quantify secreted cytokines (IL-4, TGFβ, and IFN-γ) in blood, while real-time PCR analyzed cytokine mRNA levels in PBMCs from RPL patients before and after LIT therapy.

Results: Regardless of ANA status, flow cytometry examination of PBMCs before to LIT showed substantially lower Th1/Th2 ratios and NK cell frequencies in healthy pregnant women as compared to RPL patients. In comparison to RPL patients, healthy pregnant women also showed considerably lower levels of IFN-γ and greater levels of TGF-β and IL-4. Both ANA-negative and -positive groups showed a substantial drop in NK cell frequency after LIT, however only ANA-negative patients showed a significant decrease in the Th1/Th2 ratio.

Conclusion: LIT improves pregnancy outcomes for patients with recurrent pregnancy loss (RPL) by creating a Th2-dominant immune environment with higher levels of anti-inflammatory cytokines and lower numbers of NK cells and pro-inflammatory cytokines. Despite promising results in ANA-positive RPL patients, LIT's effectiveness is still debated. This study found that LIT increased pregnancy outcomes for RPL patients with and without ANA. Further study is needed to clarify LIT efficacy in this patient population.

This clinical trial's Iranian Clinical Trials Registry Code (IRCTs): "IRCT20160422027520N19"

Keywords: Recurrent pregnancy loss; lymphocyte immunotherapy; Antinuclear antibodies

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OI-10

Exosomes-derived from mesenchymal stem cells for treatment of Alzheimer's disease

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Abstract

Background and Aim: Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline and memory loss, with limited treatment options available. Recent advancements in regenerative medicine have revealed the potential of mesenchymal stem cells (MSCs) and their secreted exosomes as promising therapeutic agents. This study explores the neuroprotective effects of MSC-derived exosomes in preclinical models of AD.

Methods: We isolated exosomes from human umbilical cord blood-derived MSCs and characterized their size, morphology, and surface markers using nanoparticle tracking analysis and transmission electron microscopy. The efficiency of exosomes was investigated *in vitro* and *in vivo*, via SH-SY5Y, a human neuroblastoma cell line, and a rat model of AD, respectively.

Results: In in vitro study, we found that these exosomes significantly reduced amyloid-beta (Aβ) aggregation and enhanced neuronal survival under oxidative stress. Additionally, in vivo experiments conducted with a rat model of AD showed that administering MSC-derived exosomes improved cognitive function, decreased neuroinflammation, and increased synaptic plasticity. Mechanistic studies suggest that these therapeutic effects may result from the transfer of bioactive molecules, including microRNAs and proteins, which modulate neuroinflammatory pathways and encourage neuronal repair processes.

Conclusion: Our findings indicate that MSC-derived exosomes are a promising cell-free therapeutic approach for AD, warranting further investigation in clinical settings to assess their safety and efficacy in human subjects.

Keywords: Alzheimer's disease, mesenchymal stem cells, exosomes

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OI-11

Optimizing antigen preparation for oxalyl-CoA decarboxylase enzyme diagnostic kit and ELISA system cutoff determination

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Abstract

Background and Aim: The prevalence of kidney stone disease is increasing globally, with calcium oxalate stones being the most common type. Oxalyl-CoA decarboxylase (OXC), an enzyme produced by the gut bacterium *Oxalobacter formigenes*, plays a crucial role in oxalate metabolism. Deficiencies in OXC activity can lead to the accumulation of oxalate, contributing to kidney stone formation. This study aimed to develop a reliable diagnostic assay for OXC by optimizing antigen production and establishing a cutoff value for an enzyme-linked immunosorbent assay (ELISA)

Methods: We cloned, expressed, and purified recombinant OXC protein in *Escherichia coli* BL21(DE3), and generated specific polyclonal antibodies in rabbits. The ELISA system was optimized and validated using serum samples from 40 healthy individuals and 6 patients with oxalate-related disorders. The cutoff value was determined using the formula (M + 2SD), where (M) is the mean and (SD) is the standard deviation of the healthy sample results.

Results: The calculated cutoff value of 0.656750 effectively distinguished between healthy and affected individuals, with a sensitivity of 97.5% and a specificity of 83.3%.

Conclusion: These findings provide a valuable tool for the early detection and management of oxalate-related disorders, with significant implications for clinical practice.

Keywords: urolithiasis, Oxalyl coA decarboxilase

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OI-12
Abstract Type: Original Research

In Vitro Investigation of a Novel Multiantigen mRNA-LNP-based Vaccine against Cytomegalovirus

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Abstract

Background and Aim: Cytomegalovirus (CMV), a member of the Herpesviridae family, is dormant in human tissues and takes a considerable risk of reactivation in immunocompromised people, including organ transplant recipients and AIDS patients. There is an urgent need for an effective vaccine because CMV remains a significant cause of morbidity and mortality despite current preventive therapies.

Methods AND Results : Pentameric complex (PC) and glycoprotein B (gB) are becoming important targets for vaccine development due to their roles in virus entry into host cells. Furthermore, the pp65 protein is a potential target for adaptive immune responses due to its important role in modulating immune defense.This study utilized a comprehensive bioinformatics and experimental approach to predict antigenic targets for potential cytomegalovirus (CMV) vaccine candidates. Gene systems for expressing these antigens were developed and then synthesized, sequenced and verified. Subsequent experiments included in vitro mRNA transcription, encapsulation in lipid nanoparticles, and transfection into HEK293 cells, followed by assessment of protein expression. Optimal gene constructs were developed to express protein of target antigens. mRNA was encapsulated into lipid nanoparticles via ethanol injection to ensure stability and effective delivery. In HEK293 cells, the vaccine showed acceptable protein expression, indicating great transfection efficiency. The results also highlighted ongoing challenges in the development of mRNA vaccines, particularly the debate over modified versus unmodified nucleotides. In summary, this study provides compelling evidence that the synthesized mRNA-LNP vaccine prototype is a promising candidate to combat cytomegalovirus.

Conclusion: In summary, this study provides compelling evidence that the synthesized mRNA-LNP vaccine prototype holds promise as a candidate for combating cytomegalovirus. By demonstrating successful antigen expression in vitro, the findings suggest that the genetic constructs can effectively translate mRNA into viral proteins, potentially eliciting a robust immune response. However, the transition from in vitro to in vivo efficacy remains a critical next step, necessitating further investigation through comprehensive animal studies and clinical trials to fully validate the vaccine's potential.

Keywords: : Cytomegalovirus, HCMV, mRNA vaccine, lipid nanoparticle, LNP

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OI-13

Prophylactic DNA vaccine targeting Foxp3$^+$ regulatory T cells depletes myeloid-derived suppressor cells and improves anti-melanoma immune responses in a murine model

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Abstract

Background and Aim: Abstract Regulatory T cells (Treg) and myeloid-derived suppressor cells (MDSC) are the two important and interactive immunosuppressive components of the tumor microenvironment that hamper anti-tumor immune responses. Therefore, targeting these two populations together might be beneficial for overcoming immune suppression in the tumor microenvironment. We have recently shown that prophylactic Foxp3 DNA/recombinant protein vaccine (Foxp3 vaccine) promotes immunity against Treg in tumorfree conditions.

Methods: In the present study, we investigated the immune modulatory effects of a prophylactic regimen of the redesigned Foxp3 vaccine in the B16F10 melanoma model.

Results: Our results indicate that Foxp3 vaccination continuously reduces Treg population in both the tumor site and the spleen. Surprisingly, Treg reduction was associated with a significant decrease in the frequency of MDSC, both in the spleen and in the tumor environment. Furthermore, Foxp3 vaccination resulted in a significant reduction of arginase-1(Arg-1)-induced nitric oxide synthase (iNOS), reactive oxygen species (ROS) and suppressed MDSC activity. Moreover, this concurrent depletion restored production of inflammatory cytokine IFN-γ and enhanced tumor-specific CTL response, which subsequently resulted in the reduction of tumor growth and the improved survival rate of vaccinated mice.

Conclusion: In conclusion, our results revealed that Foxp3 vaccine promotes an immune response against tumor by targeting both Treg and MDSC, which could be exploited as a potential immunotherapy approach.

Keywords: Regulatory T cells; Myeloid-derived suppressor cells; Foxp3; Melanoma

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OI-14

Abstract Type: Clinical Trial Research

Efficacy of Vaginal Probiotics and Vitamin D in Preventing Recurrent Implantation Failure in Women: A Randomized Clinical Trial

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Abstract

Background and Aim: Recurrent implantation failure (RIF), which affects around 10% of couples receiving in vitro fertilization (IVF) therapy, is one of the most significant issues in the field of assisted reproductive technology (ART). Researchers have conducted several studies on improving IVF outcomes for women with RIF. Probiotics have demonstrated that they are effective in improving microbial equilibrium and enhancing fertility; however, the impact of vaginal probiotic supplements on implantation rate in women with RIF is still debated. Additionally, vitamin D has been associated with a variety of reproductive activities. The effective functioning of the immune system, the regulation of inflammatory reactions, and maintaining endometrial receptivity all require sufficient amounts of vitamin D. Recent research demonstrates that vitamin D and vaginal probiotic supplementation may enhance pregnancy outcomes. Therefore, in this study, we investigated the effects of these supplements on these patients.

Methods: The studied population comprises 112 women with previous experiences of RIF and exhibiting elevated Th1/Th2 levels who were randomly categorized into four groups: The first group received only vaginal probiotics, the second group was administered vitamin D supplements solely, and the third group was given both supplements, while the fourth group, serving as the control, did not receive any additional interventions. The implantation rate is evaluated by ultrasound and β-hCG. Subsequently, we assessed maternal immunological components, including the Th1/Th2 ratio, NK cell activity, and the expression levels of IL-4, IFN-γ, and TGF-β post-treatment. An evaluation of Th1 and Th2 function was conducted utilizing blood specimens from the study population for measuring CD4+ interleukin-4 (IL-4) and CD4+ interferon-γ (IFN-γ) through flow cytometry technique.

Results: The results demonstrate that the third group, which received a combination of vitamin D and vaginal probiotics, showed the highest delivery rate in comparison to the other groups, despite the fact that there had been no statistically significant difference between our groups prior to treatment. Notably, this group was the sole study group that, following treatment, displayed a significant decrease in the Th1/Th2 ratio and the number of NK cells. Additionally, there were marked increases in serum levels of TGF-β and IL-4, alongside a reduction in the serum concentration of IFN-γ.

Conclusion: Combination of vaginal probiotics with vitamin D supplementation improves the immune response in pregnant women with a history of recurrent implantation failure (RIF).

This alteration in maternal immune response markedly enhances pregnancy outcomes, suggesting this combination as a potential therapeutic approach among RIF patients.

Keywords: Vaginal probiotics; Vitamin D; RIF

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OI-15

Evaluation of Immune Checkpoint Molecules Expression in Peripheral Blood mononuclear Cells of Children with Allergic Asthma

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Background: Asthma is a complex and heterogeneous disease. In order to fully understand the pathogenesis of the disease, it is necessary to identify the factors that contribute to the initiation and exacerbation of the disease or mediate immune responses leading to airway inflammation. The involvement of immune checkpoint (IC) molecules as regulators of immune responses in both the progression and prevention of asthma has been discussed recently.

Aim : In the present study, we investigated the gene expression of ICs including TIM-3, ICOS, PD-1, LAIR-1 and CD200R in peripheral blood leukocytes of children with asthma.

Methods : 30 patients diagnosed with mild to moderate allergic asthma based on immunological and spirometry tests were included in the study. Also, 30 healthy children without any personal or family history of asthma or other atopic diseases were selected as the control group. After collection of blood samples, mononuclear cells were isolated and the expression of ICs was evaluated using Real-Time PCR method.

Results: The mean of relative expression of ICs was not significantly different between the two groups of case and control ($p>0.05$). Among ICs evaluated, the expression of PD-1 was remarkably lower in asthma subjects as compared to control group; however the observed changes did not reach a significant level ($p=0.08$). The correlation of ICs expression with total serum IgE level, blood eosinophil and neutrophil counts was also evaluated and no correlation was observed.

Conclusion: Despite the relatively significant evidence of abnormal expression of ICs or their ligands in hypersensitivity diseases, no statistically significant findings were obtained in the present study, which may have been influenced by various factors including the limited sample volume. Overall, more studies are needed to determine the exact role and relationship of the ICs and their ligands in the pathogenesis of asthma.

Keywords: Allergic Asthma , Real time-PCR, Immune checkpoint

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OI-16

Abstract Type: Original Research

Comparison of serum levels of hsCRP in individuals with different 10-year risks of developing atherosclerotic cardiovascular diseases visiting the Persian Cohort Center of Sabzevar

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Abstract

Background and Aim: High-sensitivity C-reactive protein (hsCRP) is a marker of inflammation and has been associated with the risk of developing atherosclerotic cardiovascular diseases (ASCVD). This study aims to compare serum levels of hsCRP in individuals with varying 10-year risk levels for ASCVD.

Methods: A cross-sectional study was conducted at the Persian Cohort Center of Sabzevar. Participants were stratified into different risk categories (low, borderline, intermediate, and high) based on their 10-year risk of developing ASCVD calculated using ASCVD Risk Calculator of American College of Cardiology. Serum hsCRP levels were measured and compared across these risk categories using ANOVA.

Results: Among 873 participants (61.4% women) with mean age of 55±20 years, the 10-year risk of developing ASCVD was low in 587 (67.2%), borderline in 86 (10%), medium in 172 (19.7%), and high in 28 individuals (3%). We found no significant differences in hsCRP levels between the different risk groups ($P > 0.05$).

Conclusion: Despite the established role of hsCRP as a marker of inflammation and its association with cardiovascular risk, our analysis revealed no significant differences in hsCRP levels across the different risk groups. This suggests that hsCRP may not be a distinguishing factor among individuals with varying degrees of ASCVD risk in this cohort.

Keywords: Atherosclerosis, Cardiovascular risk assessment, hsCRP, PERSIAN cohort

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OI-17

Abstract Type: Original Research

Immunomodulatory Effects of Sulfasalazine on Intramuscularly-treated Adult Male Rats with Influenza Vaccine

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Abstract

Background and aims: Growing documentation highlights immunotherapeutics as any interventions modifying the immune responses with therapeutic intent. According to the results acquired from the administration of the influenza vaccine, T CD4+ and T CD8+ lymphocytes are stimulated, which leads to the abnormal expression of several cytokines and hematologic factors. It seems that modifying immune responses with immunomodulators can be helpful. Hence, in this study, the immunomodulatory effects of sulfasalazine on immunohematological markers of influenza vaccine-treated white blood cells in adult male rats were investigated.

Methods: In this study, firstly, male rats were orally treated with various dosages of sulfasalazine for seven consecutive days. On the last day, one hour after the last gavage of sulfasalazine, rats were intramuscularly treated with the influenza vaccine. After 24 hours, white blood cells were counted, and immunohematological parameters were measured.

Results: Administration of the influenza vaccine increased the amount of IL-1β, IL-6, IL-12, TNF-α, IFN-γ, neutrophils, and lymphocytes but decreased SASP. Also, there was an increase in IL-4 levels after the administration of sulfasalazine.

Conclusion: According to the results of this study, it seems that sulfasalazine is indispensable in the induction of anti-inflammatory cytokines and reducing inflammation caused by influenza vaccines.

Keywords: Cytokine; Hematologic Factors; Immunomodulation; Immune Cells; Sulfasalazine; Influenza Vaccine.

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OI-18

Original Research

Royal Jelly-Derived Exosomes as a Novel Therapeutic Approach for Modulating Pro-Inflammatory Cytokines in Inflammatory Bowel Disease Models

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Abstract

Background and Aim: Inflammatory bowel disease (IBD), encompassing Crohn's disease and ulcerative colitis, is characterized by chronic inflammation and immune dysregulation, largely mediated by pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Current treatment options, though effective, are often associated with some limitations, including side effects and incomplete remission rates. Exosomes, nano-sized extracellular vesicles with immunomodulatory properties according to their sources. Royal jelly (RJ), known for its anti-inflammatory effects, represent novel therapeutic opportunities. However, the properties of RJ-derived exosomes (RJ-Exosomes) have only been partially investigated. This study aimed to investigate the effects of RJ-Exo on cytokine levels in experimental models of IBD.

Methods: RJ-Exosomes were isolated using the precipitation method and characterized by Bradford assay (protein content), transmission electron microscopy (TEM, size/morphology), dynamic light scattering (DLS, size distribution), and flow cytometry (CD63 marker, confirmation the exosomal nature of the isolated vesicles). Experimental models of Crohn's disease and ulcerative colitis were established in female Wistar rats after 24-hour fasting with ad libitum access to water. Crohn's disease was induced via subcutaneous injection of indomethacin (7.5 mg/kg) twice in two days, and ulcerative colitis by intrarectal instillation of 2 mL of 4% acetic acid in saline following light anesthesia with intraperitoneal ketamine (90 mg/kg). Treatment groups received either exosomes (100 µg/kg, intraperitoneally on days 2, 5, and 8) or sulfasalazine (100 mg/kg/day). Control groups received normal saline administered

in the same volume and via the same route. Pro-inflammatory cytokine levels (TNF-α, IL-1β, IL-6) in intestinal tissues were measured using ELISA following euthanasia and tissue collection.

Results: The total protein concentration of the isolated RJ-exosomes was measured at 15 mg/mL using the Bradford assay. Transmission electron microscopy (TEM) analysis confirmed the spherical morphology of the exosomes, while dynamic light scattering (DLS) revealed an average particle size of approximately 110 nm. Flow cytometry analysis demonstrated positive expression of the CD63 marker, verifying the exosomal nature of the isolated vesicles. Pro-inflammatory cytokine levels (TNF-α, IL-1β, IL-6) in intestinal tissues were significantly ($p < 0.05$) reduced in the treatment groups receiving RJ-exosomes or sulfasalazine compared to the untreated control group.

Conclusion: These findings indicate that RJ-exosomes exert a potent anti-inflammatory effect, comparable to the therapeutic effects observed with sulfasalazine, a widely used standard treatment for IBD. These findings position RJ-exosomes as a promising, biologically derived therapeutic candidate, offering a novel approach for managing inflammatory bowel diseases. Moreover, the study highlights the broader potential of royal jelly as a valuable source for the development of innovative, exosome-based therapies, warranting further exploration in future research.

Keywords: Exosomes; Royal Jelly; Immunology; Inflammatory Bowel Disease; Cytokines

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OI-19

Evaluation of CXCL1 level as a biomarker in the serum of patients with inflammatory bowel disease (IBD)

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Abstract

Background and Aim: Diagnosis and prognosis of inflammatory bowel disease (IBD)—a chronic inflammation that affects the gastrointestinal tract of patients—are challenging, as most clinical symptoms are not specific to IBD, and are often seen in other inflammatory diseases, such as intestinal infections, drug-induced colitis, and monogenic diseases. To date, there is no gold-standard test for monitoring IBD. Endoscopy and imaging are essential diagnostic tools that provide information about the disease's state, location, and severity. However, the invasive nature and high cost of endoscopy make it unsuitable for frequent monitoring of disease activity in IBD patients, and even when it is possible to replace endoscopy with imaging, high cost remains a concern. Laboratory testing of blood or feces has the advantage of being non-invasive, rapid, cost-effective, and standardizable.

Currently biomarkers applied in clinic include CRP, ESR, pANCA, ASCA, and fecal calprotectin. However, they are far from ideal. Lots of studies are focused on seeking for ideal biomarker for IBD. Thus, we decided to evaluate CXCL1 as a biomarker in the serum sample of IBD patients.

Methods: This case-control study included 50 patients with IBD peripheral blood samples are collected non-randomly from patients referred to the hospital, and related demographic and pathological information is extracted from the patient files in the hospital.

The amount of serum CXCL1, hs CRP and ASCA IgA, ASCA IgG was determined with the help of the enzyme-linked immunosorbent assay (ELISA) method and the amount of pANCA and ANA was checked with the immunofluorescence assay (IFA) method on the basis of kits' protocols.

Results: In this study results show that the serum levels of CXCL1 in IBD patient have no significant difference in comparison to healthy control ($P > 0.01$). Also, the serum levels of ANA in IBD patient have no significant difference in comparison to healthy control ($P > 0.01$). While ASCA IgA and ASCA IgG biomarkers have higher amount in IBD patients in comparison to healthy control subjects ($P < 0.01$), also hsCRP have higher amount in IBD patients in comparison to healthy control subjects ($P < 0.01$).

Conclusion: This study show that however the serum level of CXCL1 in IBD patients has no significant difference in comparison to healthy control but on the basis of other study CXCL1can be as biomarker for IBD but in our study we have limitation because of population

heterogenicity on the basis of IBD type, grade, type of treatment, age, other unknown inflammatory condition, genetics and other a lot of variables in both population of patient & healthy control thus we should continue study with larger sample number and hemogenic groups of subjects.

Keywords: inflammatory bowel disease, ANCA, ASCA, CRP, CXCL1

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OI-20

Evaluation of TIMP-1 level as a biomarker in the serum of patients

With inflammatory bowel disease (IBD)

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Abstract

Background and Aim: Diagnosis and prognosis of inflammatory bowel disease (IBD)—a chronic inflammation that affects the gastrointestinal tract of patients—are challenging, as most clinical symptoms are not specific to IBD, and are often seen in other inflammatory diseases, such as intestinal infections, drug-induced colitis, and monogenic diseases. To date, there is no gold-standard test for monitoring IBD. Endoscopy and imaging are essential diagnostic tools that provide information about the disease's state, location, and severity. However, the invasive nature and high cost of endoscopy make it unsuitable for frequent monitoring of disease activity in IBD patients, and even when it is possible to replace endoscopy with imaging, high cost remains a concern. Laboratory testing of blood or feces has the advantage of being non-invasive, rapid, cost-effective, and standardizable.

Currently biomarkers applied in clinic include CRP, ESR, pANCA, ASCA, and fecal calprotectin. However, they are far from ideal. Lots of studies are focused on seeking for ideal biomarker for IBD. Thus, we decided to evaluate TIMP-1 as a biomarker in the serum sample of IBD patients.

Methods: This case-control study included 50 patients with IBD peripheral blood samples are collected non-randomly from patients referred to the hospital, and related demographic and pathological information is extracted from the patient files in the hospital.

The amount of serum TIMP-1, hs CRP and ASCA IgA, ASCA IgG was determined with the help of the enzyme-linked immunosorbent assay (ELISA) method and the amount of pANCA and ANA was checked with the immunofluorescence assay (IFA) method on the basis of kits' protocols.

Results: In this study results show that the serum levels of TIMP-1 in IBD patient have no significant difference in comparison to healthy control ($P > 0.01$). Also, the serum levels of ANA in IBD patient have no significant difference in comparison to healthy control ($P > 0.01$). While ASCA IgA and ASCA IgG biomarkers have higher amount in IBD patients in comparison to healthy control subjects ($P < 0.01$), also hsCRP have higher amount in IBD patients in comparison to healthy control subjects ($P < 0.01$).

Conclusion: This study show that however the serum level of TIMP-1 in IBD patients has no significant difference in comparison to healthy control but TIMP 1can be as biomarker for IBD because in our study we have multiple limitations such as population heterogenicity on the

basis of IBD type, grade, type of treatment, age, other unknown inflammatory condition, genetics and other a lot of variables in both population of patient & healthy control thus we should continue study with larger sample number and hemogenic groups of subjects.

Keywords: inflammatory bowel disease, pANCA, ASCA, CRP, TIMP-1

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OI-21

Evaluation of inflammatory parameters as eosinophil to lymphocyte, neutrophil to lymphocyte and platelet to lymphocyte ratio in patients with acute urticarial versus to healthy individuals

Authors:

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Background: So far, no comprehensive research has been done to investigate the diagnostic value and follow-up of these values for acute allergic urticaria; Therefore, this study was conducted with the aim of determining and comparing inflammatory parameters such as the ratio of eosinophil to lymphocyte, platelet to lymphocyte, and neutrophil to lymphocyte in patients with urticaria skin allergy compared to healthy individuals in 2018-2023.

Methods: In this case-control study, 200 Patients and healty individuals (100 patients with urticaria and 100 healthy) were examined based on demographic information and information related to CBC. Finally, the information was analyzed by SPSS version 26 statistical software.

Results: The mean and standard deviation of age in patients with acute urticaria and healthy individuals were 29.24 ± 7.93 years and 31.18 ± 7.89 years, respectively, and the frequency distribution of gender in the group of patients with acute urticaria was as follows: 43 men (43%) and 57 women (57%) and in the group of healthy people there were 36 men (36%) and 64 people (64%). The average ratio of neutrophil to lymphocyte, platelet to lymphocyte and eosinophil to lymphocyte in urticaria group was significantly higher than healthy people. NLR (with a cutoff point of 1.31%, sensitivity of 78% and specificity of 69%), PLR (with a cutoff point of 97.5%, sensitivity of 77.8% and specificity of 73%) and ELR (with a cutoff point of 0.11%, sensitivity of 79% and specificity of 78 percent) is a good indicator for diagnosing acute urticaria.

Conclusions: The results of our study showed that the average ELR, NLR, and PLR in the group of people with acute urticaria was significantly higher than that of healthy people. Therefore, these markers can be used as simple, cheap and It was used with acceptable sensitivity and specificity for diagnosis in acute urticaria patients.

Keywords: Acute urticaria - inflammatory parameters– ELR – NLR – PLR

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OM-1
Abstract Type: Systematic Review

The Mycobiome-Gut-Brain Axis in Parkinson's Disease: Mechanisms, and Therapeutic Prospects

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Abstract

Background and Aim: Parkinson's Disease (PD) is a multifaceted neurodegenerative disorder presenting with both motor symptoms such as tremors and bradykinesia and non-motor symptoms, like early gastrointestinal (GI) dysfunction associated with gut microbiota dysbiosis. Recently, the gut-brain axis's bidirectional link has shifted neurology paradigms, especially in Parkinson's Disease (PD) with prominent gastrointestinal dysfunction. Recent studies highlight the gut microbiome and mycobiome's roles, revealing new biomarkers and therapies.

Methods: We systematically searched PubMed, Google Scholar, and Web of Science databases until May 2024 to uncover observational studies investigating the connection between Parkinson's Disease and gut microbiota. Our emphasis was on exploring the less-studied fungal mycobiome within the gut-brain axis. We incorporated studies exploring the link between Parkinson's Disease and gut microbiota. In this research, two reviewers autonomously compiled summary information from published materials, evaluating methodological quality and bias risk. Any discrepancies concerning the inclusion of studies were reconciled through discussions with the corresponding author. Boolean operators were employed to merge the essential search terms, which encompassed, "Parkinson's Disease (PD)", " Microbiome Gut Brain Axis", "Brain Gut Axis", "Intestinal Microbiota", "Gastrointestinal Microbiome", "Gut Microbiota", "Mycobiome", "Fungal Microbiota", "Fungal dysbiosis", "Intestinal fungi", "Microbial imbalance", and "Microbial Interactions".

Results: From 9,970 potential outcomes, we identified 134 studies that met our criteria, focusing on Parkinson's Disease (PD) patients, gut microbiome dysbiosis, and the microbiome-gut-brain axis's role in PD pathogenesis and progression. Based on our findings, Gut microbiota influence alpha-synuclein misfolding in the gut, initiating PD pathology, possibly propagating to the brain via the vagus nerve. In addition, proinflammatory cytokines and chemokines are elevated in PD patients, correlating with gut microbiota alterations and contributing to neurodegeneration

Conclusion: Our systematic review collectively supports the significant role of the microbiome-gut-brain axis in the pathogenesis and progression of Parkinson's Disease. Gut dysbiosis appears to be a critical factor, potentially initiating the disease process and contributing to systemic and neuroinflammation. Misfolded alpha-synuclein proteins may travel from the gut to the brain, further implicating the gut as a starting point for PD.

Therapeutic strategies targeting the gut microbiota offer promising avenues for treatment and early diagnosis.

Keywords: Parkinson's Disease (PD); Microbiome-Gut-Brain Axis; Gut microbiota; Dysbiosis

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OM-2

In vitro antifungal activity of eucalyptol and its interaction with antifungal drugs against clinical dermatophyte isolates including *Trichophyton indotineae*

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Background: Dermatophytosis, is a prevalent fungal infection with considerable treatment failure. It represents a global health challenge and economic burden, urging exploration of alternative therapeutic strategies. Hence, this study was conducted to examine eucalyptol's in vitro activity and its interaction with antifungal agents against dermatophyte isolates.

Materials and Methods: This study was conducted from June 2021 to August 2021 on a total of 489 patients clinically suspected of dermatophytosis referred to the Dermatology Clinic at Razi Hospital, Tehran, Iran. For definitive diagnosis of the diseases, the patients were subjected to mycological investigations including direct microscopic examination and culture. The dermatophyte isolates including *Trichophyton indotinea* were identified by specific primers and sequence analysis of ITS-rDNA region. Furthermore, antifungal activity of eucalyptol, itraconazole, terbinafine and griseofulvin was evaluated according to the guideline of the Clinical and Laboratory Standards Institute (CLSI M38 ed3). The interaction between eucalyptol and the aforementioned antifungals was determined using a checkerboard method.

Results: Dermatophytosis was confirmed in 30 out of 489 (6.13%) patients, with a female-to-male ratio of 3:2 and an age range of 8–67 years. The most commonly observed clinical manifestation was tinea corporis (34.21%), and *Trichophyton indotineae* (n = 14, 46%) was the most common causative agent. Antifungal susceptibility testing revealed that eucalyptol exhibited antidermatophyte properties with minimum inhibitory concentrations (MIC) ranging from 0.78 to 25 mg/mL. Itraconazole demonstrated the lowest geometric mean (GM) value (MIC range: 0.0019–0.25 µg/mL, GM: 0.015 µg/mL), while griseofulvin exhibited the highest GM value (MIC range: 0.125–8 µg/mL, GM: 2.37 µg/mL). The in vitro interaction of eucalyptol with antifungal drugs, except for its combination with terbinafine against two *Trichophyton tonsurans* isolates resulting in

synergistic effects, showed indifference (n = 70, 77.77%) and antagonistic types (n = 18, 20%)

Conclusion: The findings of the present study revealed a significant increase in the frequency of *Trichophyton indotineae* with low susceptibility to terbinafine. Furthermore, in the evaluation of antifungal susceptibility, itraconazole was the most effective antifungal agent against dermatophyte isolates, while eucalyptol alone exhibited a more pronounced effect than when combined with antifungal agents.

Keywords: Dermatophytosis, *Trichophyton indotinea*, Drug interactions, Eucalyptol

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OM-3

Original Research

Platelet-Derived Biomaterials Controls Aspergillus Fumigatus Keratitis by decreasing Fungal Burden: An in Vivo Study

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Abstract

Background and Aim: Fungal keratitis is a severe corneal infection characterized by suppurative and ulcerative lesions. Aspergillus fumigatus is a common cause of fungal keratitis. Antifungal drugs, such as natamycin, are currently the first-line treatment for fungal keratitis, but their ineffectiveness leads to blindness and perforation. Additionally, the development of fungal resistance makes treating fungal keratitis significantly more challenging. The present study used platelet-derived biomaterial (PDB) to manage A. fumigatus keratitis in the animal model.

Method: Freezing and thawing processes were used to prepare PDB, and then A. fumigatus keratitis was induced in the mice. Topical administration of PDB, natamycin, and plasma was performed; quantitative real-time PCR (qPCR) and histopathologic examination (HE) were used to assess the inhibitory effect of the mentioned compounds against fungal keratitis.

Results: The qPCR results showed that PDB significantly decreased the count of A. fumigatus compared to the control group (P-value ≤ 5). Natamycin also remarkably reduced the count of fungi in com¬parison to the untreated animal, but its inhibitory effect was not better than PDB (P-value > 5). The findings of HE also demonstrated that treatment with PDB and natamycin

decreased the fungal loads in the corneal tissue. However, plasma did not show a significant inhibitory effect against A. fumigatus.

Conclusion: PDB is intrinsically safe and free of any infections or allergic responses; additionally, this compound has a potential role in decreasing the burden of A. fumigatus and treating fungal keratitis. Therefore, scientists should consider PDB an applicable approach to managing fungal keratitis and an alternative to conventional antifungal agents.

Keywords: Platelets-derived biomaterials · Aspergillus Fumigatus · Fungal keratitis · New treatment

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OM-4

Abstract Type: Original Research

Molecular Docking and Simulation of Eucalyptol and Linalool: Potential Inhibitors of Chitin Synthase of *Aspergillus* species

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Background and aim: Chitin synthase (CHS) is a crucial enzyme responsible for the biosynthesis of chitin; a polysaccharide serves as a fundamental structural component in the cell walls of fungi, including *Aspergillus spp*. Finding the components that inhibit CHS is vital for developing novel therapeutic strategies against fungal infections. Eucalyptol and Linalool are bioactive compounds of *Myrtus communis* L that have shown potential as inhibitors of fungal growth. In this study we aimed to employing molecular docking studies to simulate the binding interactions between Eucalyptol and Linalool and the CHS, for the identification of optimal binding poses and estimation of binding affinities.

Methods: The CHS protein sequence of Aspergillus was obtained from the NCBI database (an attempt was made to select a sequence that is present in most species). The selected sequence was modeled by AlphaFold v1.5.3 program. The model with the highest score was selected as the receptor for docking. The structures of Eucalyptol and Linalool were obtained from the PubChem database. Finally, docking was done with the help of Molegro offline software v6.0.1. The results were compared with the one-way ANOVA test and using SPSS software. A significance level was considered 0<5.

Results: The docking results exhibits docking score -72.7kcal/mol and -51.3kcal/mol for Linalool and Eucalyptol respectively. Eucalyptol forms one hydrogen bond with a distance of 3.4 Å, and Linalool establishes three hydrogen bonds with varying distances of 3.2 Å, 3.1 Å, and 2.5 Å.

Conclusion: The docking results indicate that Linalool exhibits a significantly lower docking score of -72.7 kcal/mol compared to Eucalyptol's -5.2 kcal/mol (P<0.5). This suggests that Linalool has a stronger binding affinity for the target protein, which may correlate with its potential efficacy as an inhibitor of CHS in *Aspergillus* spp. Eucalyptol forms one hydrogen bond while Linalool establishes three hydrogen bonds with varying distances. The presence of

multiple hydrogen bonds in the case of Linalool indicates a more stable interaction with the target protein, enhancing its potential as an effective inhibitor.

Key words: *Aspergillus* spp, Chitin synthase, Linalool, Eucalyptol

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OM-5

Abstract Type: Original Research

Evaluation of Antifungal Susceptibility in Aspergillus oryzae Isolates

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Abstract

Background and Aim: The treatment of invasive aspergillosis is complicated due to the limited number of controlled clinical trials available and the need for thorough evaluations of various treatment methods' efficacy and safety. The lack of comprehensive studies on the antifungal susceptibility of Aspergillus oryzae isolates, which have been increasingly recognized as significant agents in invasive aspergillosis cases, underscores the importance of this research.

Methods: The in vitro effectiveness of 24 antifungal agents—including various triazoles, imidazoles, allylamines, polyenes, echinocandins, thiocarbamates, and benzoxaboroles—was evaluated against 54 clinical and environmental isolates of A. oryzae. The testing was performed following the Clinical and Laboratory Standards Institute (CLSI) guideline M38-A3.

Results: This study assessed the in vitro antifungal efficacy of 24 different agents against 54 clinical and environmental isolates of Aspergillus oryzae. The tests adhered to CLSI standard M38-A3. Findings indicated that A. oryzae isolates exhibited low minimum inhibitory concentration (MIC) values for nine antifungal agents tested: voriconazole, itraconazole, amphotericin B, tavaborole, luliconazole, lanoconazole, efinaconazole, posaconazole, and anidulafungin. Conversely, other agents displayed higher MIC values against both clinical and environmental strains. The lowest geometric mean (GM) MIC values were recorded for luliconazole and lanoconazole (0.001 µg/ml), followed by anidulafungin (0.06 µg/ml), posaconazole (0.15 µg/ml), itraconazole (0.39 µg/ml), voriconazole and efinaconazole (0.5 µg/ml), tavaborole (0.71 µg/ml), and amphotericin B (0.79 µg/ml).

Conclusion: Our findings suggest that among the azole antifungals evaluated, luliconazole, lanoconazole, and anidulafungin exhibited the lowest MIC values.

Keywords: Antifungal, Aspergillus oryzae, *susceptibility*

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OM-6
Abstract Type: Original Research

Designing of walnut (*Juglans regia* L.) green husk extract W/ O/ W nanoemulsion against amphotericin B-resistant *Candida albicans*: characterization and in vitro assessment

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Background and Aim: Candidiasis, caused by *Candida* species like *Candida albicans* (*C. albicans*), is increasingly difficult to manage due to drug-resistant strains and limited antifungal drugs. Water in oil in water (W/ O/ W) nanoemulsions, which are smaller than 100 nanometers, can encapsulate drugs or extracts and shield them from environmental threats, leading to gradual release and targeted delivery for effective treatment. Walnut green husk has anti-*candida* properties from fatty acids, and flavonoids. As there is no data on the impact of nanoemulsion with walnut green husk extract on resistant strains of *C. albicans*, we aimed to explore this topic in our research.

Methods: 250 grams of fresh walnut green husk were mixed with 50% v/v ethanol and distilled water, then rotated in a shaker incubator for 24 hours at 25°C. The solution was solidified using a rotary evaporator and freeze dryer, creating a nanoemulsion through self nano-emulsification. The 500 mg/ mL of extract aqueous phase and oily phase containing oleic acid, tween 80, and ethanol were combined and stirred before being incorporated into a secondary aqueous phase with phosphate buffer saline. Dynamic light scattering (DLS) and transmission electron microscopy (TEM) tests were done to characterize the nanoemulsion, followed by stability tests at extreme temperatures and high-speed centrifugation. A 24-hour release test was conducted using a dialysis bag, and finally, a MIC test was performed as per CLSI-M27-A3 guidelines on reference strain ATCC 10231 and 3 amphotericin B-resistant *C. albicans*.

Results: Using the described protocol, a 6-gram dry extract was obtained. DLS analysis showed size at 64±2.5 nm, zeta potential at -1.27±1.25 mv, and PDI of 0.32. Encapsulation efficiency was measured at 90±3%. TEM images displayed spherical nano-emulsion particles. The nano-emulsion was stable at low temperatures but separated at high temperatures, causing extract sedimentation. Nano-emulsified extract was released slower than non-nano-emulsified extract. According to the tests, the MIC90 of the extract in the reference strain and strain number one was 250 and 500 mg/ mL respectively, while in strain number 2 and 3, it exceeded 500 mg/ mL. In the case of the nano-emulsified extract, ATTCC strain and strains No. 1 and 2 showed an MIC90 of 31.25 mg/ mL, while the MIC90 of strain No. 3 was 62.5 mg/ mL. MIC90 of reference strain and 3 others against amphotericin B was 8 and (resistant)16≤ µg/ mL respectively.

Conclusion: The study discovered that a W/O/W nanoemulsion with walnut green husk extract can effectively inhibit Amphotericin B-resistant *C. albicans* at lower doses than non-emulsified extract. This suggests it could be a potent antifungal treatment option for combating the challenge of drug-resistant *C. albicans* infections.

Keywords: Amphotericin B; Nanoemulsion; *Juglans regia*; *Candida albicans*

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OM-7

Identification of fungal isolates and drug sensitivity testing on fungal species isolated from onychomycosis patients with NLC-terbinafine drug application

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Abstract

Background and Aim: It is believed that nanotechnology can aid in the efficient drugs of onychomycosis. The present study, aimed to employ nanostructured lipid carriers (NLCs) in a formulation for a more effective delivery of terbinafine .

Out of 20 isolated fungal isolates 50% of the species were Candida yeast isolates and 50% were filamentous.

The drug sensitivity test was performed using the guidelines available in CLSI. The results indicated that NLC loaded with terbinafine was more effective than terbinafine in suppressing fungal growth, and the range of MIC in all Fungal isolates decreased.

Methods: In this research, 20 different species of yeast, saprophyte, and dermatophyte fungi isolated from patients who were suffering from onychomycosis were used the fungal isolates grown after sampling and culture from the nails of volunteers participating in this study. The Genomic DNA strands of fungal isolates were extracted. For molecular identification of saprophytic and dermatophytic isolates the TEF1, beta-tubulin, and ITS rDNA gene sequences were amplified. PCR was performed then the PCR product was sent for sequencing. To accurately identify yeast isolates, colony PCR was performed using universal ITS D1/D2 In vitro antifungal susceptibility testing: Minimum Inhibitory Concentrations (MICs) are the lowest concentration of antifungal drugs at which fungal agents cannot grow in that specific concentration. We observed the guidelines and recipes supplied in CLSI M60 , M-38 for yeasts and filamentous isolates The drug concentration range for terbinafine and NLC-terbinafine included 8µg/ml to 0/016µg/ml and 0/5% to 0/001%.

Results: Out of 20 isolated fungal isolates, 50% of the species were Candida yeast isolates and 50% were filamentous.

After identification by molecular methods, the abundance of Candida tropicalis, Candida albicans (20%) and Candida parapsilosis, Asp niger, ASP tereus, and T-mentagrophytes species was 10%, ASP versicolor, ASP sidui and ASP tubengensis Fusarium proliferatum were 5%.

The results of AFST were interpreted based on CLSI guidelines. significant reduction against NLC-TBF compared with terbinafine ($P<0.05$).

MIC50 yeasts about Terbinafine = 16

MIC50 yeasts about NLC-Terbinafine = 5

MIC50 filamentous about Terbinafine=16

MIC50 filamentous about NLC- Terbinafine=0

Conclusion: According to the results obtained in this study, NLC nanoparticles loaded with terbinafine have more power in inhibiting fungal growth than terbinafine, and according to the obtained MICs, we can hope for these results.

It is better to conduct this study in the trial phase to reach definitive answers.

Keywords: onychomycosis- Terbinafine - NLC_terbinafine - AFST

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OM-8

Prevalence of Fungi Infections in Iranian Hospitals: A Systematic Review and Meta-Analysis

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Abstract

Background and Aim: Infections acquired during a hospital stay are referred to as nosocomial infections. Therefore, the aim of conducting this research is to analyze the prevalence of fungal infections in Iranian patients..

Methods: A systematic review was performed to find studies on Fungi infections in Iran hospitals from 2012 to 2021. The review used Medline/PubMed, Scopus, Web of Sciences, and Google Scholar databases. Data analysis was conducted using STATA software. Additionally, Begg's rank correlation test and Egger's asymmetry test were used to assess publication bias in the studies.

Results: In this study, a total of 11 studies conducted between 2012 and 2021 in Iran were examined. The prevalence of fungal infections varied from 0.004 to 0.857. The meta-analysis results indicated that the overall prevalence of fungal infections in Iran is (P=0.361, 95%CI= 0.19, 0.53). Subgroup analysis based on the type of fungus revealed that in three studies measuring Aspergillus contamination, the prevalence of infection with this fungus was (P=0.093, 95%CI= -0.089, 0.247), in eight studies measuring Candida contamination, the prevalence of infection with this fungus was (P=0.319, 95%CI= 0.124, 0.514), and in three studies measuring Mucormycosis contamination, the prevalence of infection with this fungus was (P=0.371, 95% CI= -0.121, 0.863); the cumulative prevalence of fungal infection in the studies was (P=0.283, 95%CI= 0.129, 0.436).

Conclusion: Implementing monitoring measures and utilizing antifungal agents, hand washing, and sterile use of medical instruments can be considered as key points in the treatment of fungal infections.

Keywords: Fungi. Infection, Candidiasis, Aspergillosis, Mucormycosis, Systematic Review, Meta-Analysis

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OP-1
Abstract Type: Original Research

Molecular epidemiology and multilocus genotyping of *Giardia duodenalis* in individuals attending major public hospitals in Shiraz, southwestern Iran: A public health concern

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Abstract

Background and Aim: Giardia duodenalis is one of the most common causes of waterborne disease worldwide, and is often associated with outbreaks of diarrhea in areas with poor sanitation and hygiene. This study aimed to assess the prevalence and genetic diversity of G. duodenalis assemblages in individuals attending major public hospitals in Shiraz, southwestern Iran.
Methods: From August 2022 to May 2023, a total of 614 stool samples from individuals were collected and initially examined for G. duodenalis cysts using parasitological techniques, sucrose flotation, and microscopy. Microscopy-positive samples were validated by SSU-PCR amplification of the parasite DNA. A multilocus genotyping (MLG) scheme, which focused on the triose phosphate isomerase (tpi) and the glutamate dehydrogenase (gdh) genes, was employed for genotyping purposes.
Results: G. duodenalis cysts were found in 7.5% (46/614) and 8.5% (52/614) of samples through microscopy and SSU-PCR, respectively. Successful amplification and sequencing results were obtained for 77.3% (17/22) and 45.5% (10/22) of the infected samples at the tpi and gdh loci, respectively. MLG data for the two loci were available for only five samples. Out of the 22 samples genotyped at any loci, 54.5% (12/22) were identified as assemblage A, while 45.5% (10/22) were identified as assemblage B. AII was the most predominant sub-assemblage identified [54.5% (12/22)], followed by BIII [27% (6/22)], discordant BIII/BIV [13.6% (3/22)], and BIV [4.5% (1/22)].
Conclusion: In the present study, no assemblages suited for non-human animal hosts (e.g., C–F) were detected. This suggests that the transmission of human giardiasis in Shiraz is primarily anthroponotic. Further molecular-based analyses are necessary to confirm and expand upon these findings. These analyses will also help determine the presence and public health importance of the parasite in environmental samples, such as drinking water.
Keywords: Giardia duodenalis, Prevalence, Assemblage, MLG, Shiraz, Iran

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OP-2

The first microRNA candidate (miRNA like 29a-5p) in *Blastocystis* sp. in irritable bowel syndrome (IBS) patients

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Abstract

Background and aim: MiRNAs are small RNA sequences (18-22 nucleotides) that regulate gene expression. Certain miRNAs are found in the blood and colon biopsies of IBS patients. Research shows that miRNAs play a crucial role in various parasites, like *Giardia lamblia* and *Trypanosoma cruzi*, influencing infection regulation. There are currently no studies on miRNA in *Blastocystis* sp. this research aims to identify potential miRNA candidates by comparing human miRNAs with its genome sequences through bioinformatics and in vitro studies.

Methods: We found (miRNA 29a-5p) in bioinformatics studies and Collected stool samples from 80 individuals across four groups (IBS patients, *Blastocystis* sp. positive individuals, IBS patients with *Blastocystis* sp., and healthy controls) in a Tehran gastroenterology clinic. After these steps, the best miRNA in bioinformatics studies (miRNA 29a-5p) which the initial 14 nucleotides in *Blastocystis* mRNA were completely similar and according to the miRNA fold website can play the role of miRNA was selected and the synthesis and design of miRNA 29a.Then RNA extraction, cDNA synthesis and Real-Time-PCR test were performed and Data analysis by calculating Ct, Fold change, ΔΔCt and T-test statistical analysis to calculate P-value and REST-2009 software was used.

Result: After conducting bioinformatics studies and selecting a miRNA that, in addition to having the largest number of similar nucleotides in *Blastocystis* mRNA, can also perform the function of a miRNA. and performing the Real-time PCR test, in the review and statistical analysis of Real data - Time difference in the first group (patients with IBS) compared to the control group There was a significant difference in the expression level of miRNA-29-5p (P-value < 0.05) and there was also a significant difference in the two groups (positive *Blastocystis* sp. and IBS group) and (positive *Blastocystis* sp.) (P-value < 0.05) . It should be mentioned that in this study, all positive samples of *Blastocystis* sp. were in subtype 1.

The expression level of miRNA29a-5p in the studied groups has increased several times compared to the control group, and the highest fold change was related to (Positive *Blastocystis* sp and positive IBS group) and according to statistical analysis, a significant difference was observed (P- value < 0.05).

Conclusion:

According to the present study, the miRNA sequence identified in the bioinformatics and laboratory studies in *Blastocystis* sp. is miRNA-like-29a-5p and it is introduced as a candidate whose existence proof requires more extensive studies. More studies and research in the field of *Blastocystis* miRNA and checking more sequences in order to identify human-like miRNAs in parasites can help to identify candidates for the cause of some diseases, especially digestive diseases such as IBS.

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OP-3
Abstract Type: Original Research

Evaluation of Pediculosis Prevalence among School Students in Helmand Province, Afghanistan, in 2024

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Abstract

Background and Aim: Head lice (Pediculus humanus capitis) are among the common obligatory hematophagous ectoparasites affecting humans. These parasites cause scalp itching and can lead to psychological issues, especially among children. The purpose of this study is to investigate the prevalence of head lice among school students in Helmand Province, Afghanistan.

Methods: In this study, 500 male students from schools in Gereshk District, Helmand Province, Afghanistan, were examined for head lice infestation and related factors. The questionnaire included demographic information as well as social factors associated with the infestation. Data analysis was performed using SPSS software, applying the chi-square test.

Results: Out of the 500 students, 37 (7%) were found to be infested with head lice, which included both visible lice and nits. There was an inverse relationship between parents' education levels and the prevalence of lice infestation. Additionally, there was a significant association between lice infestation and both family size and hair length.

Conclusion: The findings of this study indicate that the prevalence of head lice infestation among male students in Helmand Province is 7%. Our research demonstrated that parental education level, family size, and hair length are significant factors that may play a key role in the occurrence of lice infestation. The 7% prevalence rate highlights the need for important screening and preventive measures among Afghan students, particularly in warm regions like Helmand.

Keywords: Pediculosis Prevalence; Head Lice Infestation; School Students; Helmand Province; Epidemiology

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OP-4

Diagnosis of Acute and Chronic Cutaneous Leishmaniasis Based on Microscopy, LST and DAT Methods

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Abstract

Background and Aim: Cutaneous Leishmaniasis (CL) is a highly infectious parasitic disease in Iran. Various diagnostic methods exist, but a sensitive and specific approach remains crucial for effective treatment and disease control. Therefore, this study aims to investigate and compare the effectiveness of the microscopic method, DAT test, and LST in diagnosing acute and chronic forms of CL in Iran.

Methods: In our study, we compared the results of conventional methods such as microscopy, the Leishmanin Skin Test (LST), and the Direct Agglutination Test (DAT) across both acute and chronic forms of CL in Iran. Samples (n=50) were obtained from clinically suspected cases of CL, including both acute (healing after one course of treatment) and chronic (non-healing after at least two courses of treatment) patients. Smears were stained with Giemsa 10% for microscopy. For the LST, 1 ml of leishmanin fluid was intradermally injected in all patients, and indurations were measured after 48-72 hours; an induration of 5 mm or more was considered positive. Additionally, serum samples were collected from all 50 patients for the DAT to detect anti-Leishmania infantum antibodies.

Results: The positivity rates for microscopy in acute and chronic forms of CL were 100% (25/25) and 32% (8/25), respectively. For the LST, the positivity rates were 4% in acute and 2% in chronic cases. The DAT showed a positivity rate of 2% in acute cases of CL, with no reported positivity in chronic cases.

Conclusion: The microscopy method appears to be the most sensitive for diagnosing both acute and chronic forms of CL. However, there is a clear need for additional diagnostic methods specifically for the chronic form of the disease.

Keywords: Cutaneous Leishmaniasis; Microscopy test; *Leishmanin* Skin Test; Direct Agglutination Test.

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OP-5
Abstract Type: Original Research

Establishment of Loop-Mediated Isothermal Amplification-Restriction Enzyme assay for the rapid and sensitive detection of *Trichostrongylus* species in human fecal samples

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Abstract

Background and Aim: Gastrointestinal nematodes (GIN) are an important health concern and livestock industries throughout the world Trichostrongylus species as the most significant GIN, remain one of the major health challenges in the tropical and summer rainfall regions worldwide. Identification of *Trichostrongylus* species diagnostic methods is crucial for obtaining a deep understanding about the epidemiology, population biology, anthelmintic treatment efficacy, and drug resistance in order to design effective parasite control strategies. In this study, we developed Loop-mediated Isothermal Amplification-Restriction enzyme or LAMP-RE assay as a simple, rapid and cost-effective method for the detection of *Trichostrongylus* species in human samples from Mazandaran province.

Methods: Eighty fecal samples were processed by salt flotation orWillis method and detected by microscopic examination. DNA was extracted from each stool sample using the AccuPrep Stool DNA Extraction Kit. In our study, LAMP was designed as an isothermal reaction. A set of four primers was designed based on the second internal transcribed spacer of nuclear ribosomal DNA of the genus *Trichostrongylus*; amplification was visualized by eye and addition of fluorescent detection reagent and also confirmed by gel electrophoresis using fecal samples as well as positive/negative controls and blank. Sensitivity was evaluated at serial dilutions in the range of 10 ng, 1 ng, 100 pg, 10 pg, 1pg, 100 fg, 10 fg. The specificity of the LAMP assay for the detection of *Trichostongylus* parasites was evaluated using non-specific DNA templates from *Haemonchus contartus*, *Marshallagia marshali*, *Ostertagia ostertagi*. The LAMP-RE was developed using mRE-LAMP and also *Hinf*I, *Mse*I and *Dra*I restriction enzymes.

Results: An easily visible white precipitate of magnesium pyrophosphate was produced by the 55 samples and positive control. The LAMP reaction mixture, containing amplified fragments, turned green upon addition of the fluorescence dye whereas the blank and negative control retained their original orange color. All the samples were confirmed by gel electrophoresis. There was a 100% agreement in detection of LAMP product between visualize assay and gel electrophoresis. The sensitivity of LAMP assay showed a detection of limit of 10 pg/μl of genomic DNA isolated from a *Trichostrongylus* fecal samples. The specificity experiment showed that LAMP primers successfully amplified *Trichostrongylus* DNA, while no amplification was seen for non-

specific DNA, Blank and negative control. After digestion with *Hinf*I, *Mse*I and *Dra*I restriction enzymes, similar digestion pattern of *T. colubriformis* was obtained from all samples and two different fragments of about 122 and 76 bp were produced after digestion with *Hinf*I restriction enzyme.

Conclusion: Our results showed that *T. colubriformis* is the most common zoonotic species causing human trichostrongylosis in Mazandaran province. The results showed that LAMP assay is a simple, rapid, cost-effective, sensitive and specific tool which can be an alternative to PCR-based assay for detection of *Trichostrongylus* parasite or other pathogens. The LAMP method is suitable for field conditions due to its endpoint detection with fluorescent dyes and other advantages and is useful for diagnostic, epidemiological, ecological studies, and control programs.

Keywords: *Trichostrongylus*; Trichostrongylosis; LAMP-RE.

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OP-6

Antileishmanial Activity of Combined Crocin-Curcumin Treatment: An Experimental Study

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Background: Leishmaniasis is a disease that is transmitted by phlebotomine sand flies and is caused by protozoan parasites of the genus Leishmania as a vector-borne illness. It is endemic in 98 countries and three territories, with an estimated 700,000 to 1 million new cases occurring annually on a global scale. The search for new, effective, and safe alternative treatments against cutaneous leishmanisis (CL) is of the utmost importance, as existing anti-leishmanial treatments have been ineffective for an extended period and are associated with deleterious side effects. The purpose of this study was to examine the leishmaniacidal effects of the combination of Crosin-curcumin in both its separate and mixed forms with Amphotericine B on CL in vivo.

Methods: Crosin and curcumin were extracted from Medicinal plants. The maceration process was employed for plant extraction, and the components were isolated utilizing Mas Chromatography and Spectrophotometry techniques. *Leishmania major* (*L. major*) standard strain promastigotes were purchased from Leishmaniasis research center, Public Health school,

Tehran University of Medical Sciences. This study involved the selection of 36 mice, who were categorized into 6 groups of three individuals each. The initial three groups received dosages of 200, 400, and 800 µg/ml of crosin-curcamin plant extract. Glucantim and Amphotericin B served as positive control groups, while PBS functioned as the negative control group. The cytotoxicity of the compounds on normal human fibroblast cells was assessed using the MTT assay.

Results and conclusions: The findings of this study indicated that Crosin-curcumin demonstrated a satisfactory level of effectiveness, with the highest efficacy observed at a concentration of 800 µg/ml on day 28. The forthcoming decision regarding these compounds requires additional and complementary tests.

Keywords: Anti-leishmaniasis, *Leishmania major*, MTT assay, Crosin, Curcumin

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OP-7

Enhanced clindamycin delivery using chitosan-coated niosomes to prevent *Toxoplasma gondii* strain VEG in pregnant mice: an experimental study

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Abstract

Background and Aim: Congenital toxoplasmosis occurs when a pregnant woman becomes infected with *Toxoplasma gondii* (*T. gondii*) for the first time. Treatment typically involves antimicrobial medications, with spiramycin commonly used to prevent transmission. However, spiramycin's effectiveness is limited due to poor placental penetration. Clindamycin, another antibiotic, can cross the placenta but reaches the fetus at only half the maternal concentration. Encapsulating the drug in Chitosan-Coated niosomes (Cs-Nio) could enhance its effectiveness by targeting specific organs and ensuring sustained release. To address the challenges of using clindamycin, a Niosome-Coated Chitosan system was investigated for treating congenital toxoplasmosis caused by the VEG strain of *T. gondii* in an animal model.

Methods: Pregnant mice were infected with *T. gondii* on the 12th day of pregnancy, followed by treatment with various drugs across six groups. The treatments included Chitosan-Coated Niosomes loaded Clindamycin (Cs-Nio-Cli) and other controls. Parasitological evaluations (microscopic examination and real-time PCR), along with histopathological and immunological assessments, were conducted to assess treatment efficacy. Finally, Statistical

analysis was conducted using GraphPad Prism 8.0 and SPSS 26, comparing test and control groups with T-test and Mann-Whitney test. A p-value ≤ 0.05 was considered statistically significant.

Results: The study found that treatment with Cs-Nio-Cli significantly reduced the number of *T. gondii* cysts in the brain and eyes (97.59% and 92.68%, respectively) compared to the negative control group. It also mitigated inflammatory changes, prevented cell death, and reduced vascular cuffs in the brain. Additionally, Cs-Nio-Cli treatment decreased bleeding, placental thrombosis, and inflammatory cell infiltration in the placenta while improving eye tissue health by reducing retinal folds and bleeds. Immunologically, nanoclindamycin treatment resulted in lower TNF-α cytokine levels and higher IL-10 levels, indicating an enhanced anti-inflammatory response.

Conclusion: Although Cs-Nio-Cli demonstrates promise in reducing the transmission of congenital toxoplasmosis and mitigating the effects of congenital toxoplasmosis, additional research is necessary to determine the optimal treatment regimens for the complete eradication of the parasite in the fetus.

Keywords: *Toxoplasma gondii*, VEG strain, Congenital, Clindamycin, Niosomes-Coated Chitosan

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OP-8

Abstract Type: Original Research

Isolation of free living amoeba from indoor sport water complexes and characterization of their pathogenic endosymbionts

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Abstract

Background and Aim: This study aimed to investigate FLA and their endosymbionts in indoor sport water complexes (ISWCs).

Methods: A total of 90 samples were collected from 15 ISWCs. After morphological and molecular detection, a couple fungi and viral pathogens was investigated in isolated FLA, using real-time PCR.

Results: Totally, 51 (56.7%) were positive for FLA, including *Acanthamoeba* sp., *Vermamoeba* sp., Vahlkampfiidae, and *Thecamoeba* spp., in 33 (36.7%), 20 (22.2%), 24 (26.7%), and 2 (2.2%) of samples. The number of positive samples was 17 in each sauna biofilm, Jacuzzi, and pool water. The genotypes T4, T5, and T11 were characterized in *Acanthamoeba* sp.. All *Vermamoeba* spp. were *V. vermiformis* and Vahlkampfiidae was characterized as *Naegleria* sp.. Each *C. albicans* and *A. flavus* were detected in two samples of pool water and Jacuzzi. The presence of AdV, NoV, and AsV was recorded in two Jacuzzis samples, in which AdV and NoV were detected in a sample at the same time.

Conclusion: Our findings suggest that FLA can resist disinfectant used in ISWCs and high temperature Jacuzzi. In addition, the presence of viral and fungal endosymbionts signifies the important role of FLA in waterborne infections, particularly in places where people are in close contact with them.

Keywords: Free-living amoebae (FLA); Swimming pool; Endosymbionts; Fungi; Viruses.

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OP-9

Rapid diagnosis of cutaneous leishmaniosis using a developed lateral flow test in comparison with molecular and parasitological methods

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Abstract

Background: Cutaneous leishmaniosis with a broad spectrum of clinical manifestations is caused by the *Leishmania* parasites and is transmitted by the bite of sand fly insects. For laboratory diagnosis although, parasitological methods are effective in the early stages of infection but in chronic cases they don't yield enough sensitivity. Molecular methods usually have a high level of sensitivity and specificity but with the need for lab equipment, they are not suitable for field diagnosis. So, it is important to develop a rapid and point-of-care test for diagnose of cutaneous leishmaniosis.

Method: In this work a lateral flow test for diagnosis of cutaneous leishmaniosis has been developed. Thirty-eight patient samples with a clinical suggestion of CL were collected and examined using different lab tests in comparison with the developed lateral flow test.

Results: Results of different tests were compared and considering microscopic results as the gold standard, the sensitivity of %92, was estimated for the developed lateral flow test.

Conclusion: The lateral flow test is a very rapid and easy test for diagnosis of cutaneous leishmaniosis especially in rural areas with fewer lab facilities.

Keywords: cutaneous leishmaniosis, diagnosis, lateral flow

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OP-10

Original research

The therapeutic effect of kojic acid on protoscolices extracted from hydatid cyst, An in vitro study

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Abstract

Background and Aim: Hydatidosis is a zoonotic disease that infects humans worldwide. Due to the side effects caused by common drugs to treat this disease, the use of new methods has been expanded today. The purpose of this study is to investigate the effect of kojic acid on protoscolexes prepared from the livers of infected sheep with hydatid cysts in vitro.

Methods: Hydatid cysts in the liver of sheep were taken from the slaughterhouse. Protoscoleces were collected under sterile conditions from liver hydatid cysts of infected sheep slaughtered in Mashhad slaughterhouse. Protoscolex survival was confirmed after 0.1% eosin staining and kept at 4°C until use. The treatment doses with kojic acid were 100, 200, 400, 800 micrograms/ml. To compare the therapeutic effects of this extract on protoscolex, a group of albendazole therapy (as standard treatment) and a group without adding any active ingredient or standard treatment were considered. The obtained results were analyzed using SPSS v.24 software and using one-way analysis of variance and Tukey's post hoc test. A significant difference was considered with $P<0.05$.

Results: IC50 calculated in 10 minutes was 8393 µg/ml, after 20 minutes IC50 reached 1973 µg/ml and after 60 minutes it was calculated as 265 µg/ml. In 10 minutes, kojic acid with a concentration of 800 acts like bendazole 100 and has no significant difference with it in terms of mortality (P-value=0.59), however, the difference between bendazole 200 with a concentration of 800 is significant (P-value=0.008). In 20 minutes, kojic acid with a concentration of 800 acts like bendazole 100 and has no significant difference with it (P-value=0.99), but it has a significant difference with the concentration of bendazole 200 (P-value=0.002). In 60 minutes, kojic acid 400 has the same mortality effect as bendazole 100 and there is no significant difference with it (P-value=0.9), but it has a significant difference with bendazole 200 (P-value=0.005). At this time, kojic acid with the concentration of 800 acts like bendazole 200 and has no significant difference with it (P-value=0.7).

Conclusion: In general, the results of this study showed that kojic acid has anti-protoscolex effects in hepatic hydatid cyst and the dose of 800 µg/ml was not statistically significantly different from the dose of 100 µg/ml of albendazole, however, further studies are needed to investigate Therapeutic effects and side effects are needed.

Key words: protoscolex, hydatid cyst, kojic acid

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OP-11

Abstract Type: Review

Hydatid Cyst with Negative Serology; Interpretation and Management

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Abstract

Background and Aim: According to the protocols of the World Health Organization, serological tests should be employed to supplement the radiological data in the diagnosis of hydatid cyst; Several serological tests can identify IgG antibodies targeting *E. granulosus*, including complement fixation (CF), indirect hemagglutination assay (IHA), indirect fluorescent antibody (IFA), enzyme-linked immunosorbent assay (ELISA), and western blot (WB). The current gold standard serological test for echinococcosis detects IgG antibodies against native or recombinant antigen B subunits derived from hydatid cyst fluid. Hydatid cysts can be challenging to diagnose, especially when serological tests are negative. This study addressed to the reasons for the negative results of hydatid cyst serological tests, and diagnosis methods management.

Methods: In this study, holistic review of the scientific literature was conducted. Relevant research articles including case reports, clinical studies and review articles were selected from databases such as PubMed, Google Scholar and Scientific Information Database (SID).

Results: Some of serological tests have less than optimal sensitivity in serodiagnosis of human hydatidosis; therefor this point will cause the test results to be falsely negative. In addition, a person with a hydatid cyst with these features may also have a negative serology test:

1. The cyst may be very small and not yet producing enough antigens to trigger an immune response. 2. The cyst may be located in an organ that is not well-perfused with blood, such as the brain or eye. 3. The person may have a weakened immune system, which can make it difficult to produce antibodies.

Conclusion: If a person has a negative serology test but the treating physician still suspects hydatid disease, other methods should be used to confirm the diagnosis, such as imaging tests (sonography, CT scan or MRI) or biopsy of the cyst; Techniques such as Fine-Needle Aspiration (FNA) can be follow with cyst fluid analysis may show elevated levels of eosinophils or specific antigens and can reveal characteristic features like hooklets and scolices. In this situation, imaging techniques like ultrasound, CT scan, and MRI can often provide definitive evidence and requesting serological tests will not have any results except imposing additional costs on the patient.

Keywords: Human hydatidosis; Diagnosis; Serology; Negative Result.

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OV-1

Study of hepatitis C virus infection in patients with RIBA indeterminate results

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Background and Aims:

Anti-HCV and recombinant immunoblot assay (RIBA) are used to diagnose hepatitis C virus infection. Some patients with indeterminate RIBA results may have detectable HCV RNA by RT-PCR

Methods:

This study aimed to determine the prevalence of active hepatitis C virus infection in patients with RIBA indeterminate results. In this study, 3500 patients were enrolled for two years. Samples of serum Anti-HCV were measured by ELISA and recombinant immunoblot assay (RIBA) was used as a confirmatory test. Viral RNA was extracted by High pure viral Nucleic Acid kit (Roche) and then RT-PCR was performed using homemade kits.

Results:

In our study, 4.6% of patients were anti-HCV and RIBA positive. An indeterminate RIBA was found in 41(1.2%) of subjects. HCV-RNA was undetectable in all subjects with RIBA indeterminate results.

Conclusion:

This study showed that HCV-RNA was undetectable in all sera with indeterminate RIBA. It is necessary to evaluate the presence of occult HCV infection in these patients.

Keywords: Hepatitis C, Indeterminate RIBA, RT-PCR, ELISA

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OV-2
Abstract Type: Original Research

Prevalence of human herpesvirus 8 infection in patients undergoing hemodialysis using nested-PCR

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Abstract

Background and Aim: Transmission by blood transfusion is a risk factor for Human herpesvirus (HHV-8) infection. Since hemodialysis (HD) patients require frequent blood transfusions, they are prone to HHV-8 acquisition. To study the prevalence of HHV-8 infection in patients undergoing hemodialysis.

Methods: In this study, blood samples of 89 patients undergoing hemodialysis were collected. DNA was extracted from peripheral blood mononuclear cells and HHV-8 DNA was evaluated by nested-PCR.

Results: Of total 89 patients, 51 (57.3%) were males and 38 (42.7%) were females. The patients' age ranged from 24 to 90 years and the mean age was (57.5±1.4) years. HHV-8 DNA was found in 9 of 89 (10.1%) peripheral blood mononuclear cell samples, 8/51 (15.7%) in males and 1/38 (2.6%) in females (P=0.07). All patients who were positive for HHV8-DNA were more than 50 years old.

Conclusion: This study shows high prevalence of HHV-8. Since hemodialysis patients are candidates for kidney transplantation and due to the possibility of HHV8-reactivation and its serious complications in immunocompromised patients, routine screening for detection of the virus should be implemented for all hemodialysis patients.

Keywords: Human herpesvirus 8; Hemodialysis patients; Nested-PCR

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OV-3
Abstract Type: Original Research

Full genome sequence analysis of the predominant and uncommon G9P[4] rotavirus strains circulating in Tehran, Iran, 2021-2022: evidence for inter and intra- genotype recombination

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Abstract

Background and Aim: Group A rotaviruses (RVAs) are a major cause of acute gastroenteritis in children under 5 years of age worldwide. A whole genome-based classification is presented for RVs using all 11 genomic RNA segments. In this classification system, Gx-P[x]-Ix Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx define the genotype of the VP7-VP4-VP6-VP1-VP2 VP3-NSP1-NSP2-NSP3-NSP4-NSP5/6 genes, respectively.

This study aims to provide a full-genome characterization of three uncommon but prevalent human RVA strains G9P[4] circulating in Iran. The study investigates interspecies transmission and reassortment/recombination events that contribute to the evolution of Iranian human RVA strains, as well as determine if there are genetic linkages between specific RV gene segments.

Methods: The genetic sequences of 11 RNA segments from three uncommon G9P[4] RVA strains found in the stool samples of children under 5 years of age in Tehran, Iran were analyzed using next-generation sequencing (NGS) technology.

Results: The genomic constellations of these three uncommon G9P[4] strains indicated the presence of the double and quadruple reassortants of two G9P[4] strains, containing the VP7/NSP2 and VP7/VP2/NSP2/NSP4 genes on a DS-1-like genetic background, respectively. The genome of one strain indicated a Wa-like genetic backbone in a single-reassortant with the VP4 of the DS1-like human strains. With the exception of VP1, VP2, VP7, NSP2, NSP3, and NSP4 genes, which clustered with RVA of human origins belonging to cognate gene sequences of genogroup 1/2 genotypes/lineages, the remaining five genes (VP8/VP4, VP3, VP6, NSP1, NSP5) displayed direct evidence of recombination.

Conclusion: It is presumed that the presence of uncommon G9P[4] strains in Iran is not linked to vaccination pressure, but rather to the high prevalence of RVA co-infection or the direct import of these uncommon RVA reassortants strains from other countries (especially those that have implemented RV vaccination).

Keywords: Rotavirus; G9P[4]; full genome analysis; recombination; reassortment.

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OV-4

Abstract Type: Original Research

A novel electrochemical DNA biosensor based on hydroxyapatite nanoparticles to detect BK polyomavirus (BK virus) in the urine samples of Bone marrow and renal transplant patients

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Abstract

Immunosuppressive treatment in the renal transplant patients can stimulate the reactivation of BK polyomavirus (BK virus) and consequently cause the polyomavirus- associated nephropathy (PVAN) and hemorrhagic cystitis (HC), which induce the allograft failure. Therefore, the identification of BK virus in the early stage is significantly associated with the improvement of allograft function and patient survival which also prevents the acute rejection of transplantation. Herein, a facil alkoxide-based sol-gel technique was executed to prepare hydroxyapatite nanoparticles (HANPs). The structural properties of HANPs were characterized using Powder X-ray diffractometer (PXRD), Fourier transform infrared spectroscopy (FTIR), Energy Dispersive X-ray Analysis (EDXA), and transmission electron microscopy (TEM). The particle sizes were measured by Scherrer formula and observed using TEM in the amount of 55-65 nm. The results of the current study showed that the electrochemical DNA biosensor based on synthesized HANPs could be used for the rapid detection of BK virus in urine sample. For this goal, a probe ssDNA BK virus was immobilized on the HANPs-modified Glassy Carbon Electrode (GCE), and then the hybridization between the target and probe sequences was studied by measuring the electrochemical response of Methylene Blue (MB) using differential pulse voltammetry (DPV) method. The efficiency of the designed DNA biosensor was investigated by the extracted DNA from the urine samples of transplant patients. The sensitivity and specificity of this biosensor were studied by synthetic sequences including non-complementary, mismatch, and target oligonucleotides. The proposed DNA biosensor indicates a linear response from 50.00×10^{-12} to 1.00×10^{-9} mol/L of DNA target concentrations with a detection limit of 41.08×10^{-12} mol/L.

Background and Aim: Immunosuppressive treatment in the renal transplant patients can stimulate the reactivation of BK Polyomavirus (BK Virus) and Consequently cause the Polyomavirus-associated nephropathy (PVAN) and hemorrhagic Cystitis (HC), which induce the allograft failure. Therefore, the identification of BK virus in the early stage is significantly associated with the improvement of allograft function and patient survival which also prevents the acute rejection of transplantation.

Methods: Herein, a facil alkoxide-based sol-gel technique was executed to prepare hydroxyapatite nanoparticles (HANPs). The structural properties of HANPs were characterized using Powder X-ray diffractometer (PXRD), Fourier transform infrared spectroscopy (FTIR), Energy Dispersive X-ray analysis (EDXA), and transmission electron microscopy (TEM). The particle sizes were measured by Scherrer formula and observed using TEM in the amount of 55-65 nm.

Results: The results of the current study showed that the electrochemical DNA biosensor based on HANPs could be used for the rapid detection of BK virus in urine sample. For the goal, a probe ssDNA BK virus was immobilized on the HANPs- modified Glassy Carbon Electrode (GCE), and then the hybridization between the target and probe sequences was studied by measuring the electrochemical response of Methylene Blue (MB) using differential pulse voltammetry (DPV) Method. The efficiency of designed DNA biosensor was investigated by the extracted DNA from the urine samples of transplant patients. The sensitivity and specificity of the biosensor studied by synthetic Sequences including non- complementary, mismatch, and target oligonucleotides. The proposed DNA biosensor indicates a linear response from $50.00*10^{-12}$ to $1.00*10^{-9}$mol/L of DNA target concentration with detection limit of $41.08*10^{-12}$ mol/L.

Conclusion: In this study, a new laboratory method based on electrochemical biosensor was presented to detect BK virus in urine samples. Our results showed that this designed method can be an alternative to the current detection technique. The performance of this biosensor platform was studied by synthetic sequences and BK DNA from the urine sample. The DNA biosensor can detect the BK virus by immersing the modified- GCE in PBS solution containing BK DNA, however, interestingly, this is contrary to previous studies which used the amplified product of PCR. Therefore, the obtained results indicate that this new free-PCR method is specific to BK virus detection in the early phase of infection.

Keywords: Human Polyomavirus, BK virus, Electrochemical DNA biosensor, Hydroxyapatite nanoparticles.

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OV-5

Abstract Type: Original Research

A Natural Barrier in Healthcare: Investigating the Antiviral Potential of Tannic Acid against Herpes Simplex Virus Type 1

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Abstract

Background and Aim: The attachment of viral surface ligands to cell surface receptors is considered the most critical step in the viral infection process, as it is essential for the virus to enter the host cell and initiate its replicative cycle. Targeting this step with small molecules, such as natural compounds, offers a promising approach for developing novel antivirals. Tannic acid (TA), a plant-derived hydrolyzable polyphenol, is an attractive candidate for biomedical applications due to its natural abundance, cost-effectiveness, remarkable biocompatibility, and high biological activity. This research aimed to investigate the anti-attachment activity of TA against herpes simplex virus type 1 (HSV-1).

Methods: The MTT assay was used to assess the cytotoxic effects of TA on Vero cells (African green monkey kidney cell line). To evaluate the antiviral properties of TA, a pre-treatment assay was performed by incubating Vero cells with sub-toxic concentrations of TA at 37°C for 1 hour, followed by infection with HSV-1. The antiherpetic potency was determined using the 50% tissue culture infectious dose (TCID50) and real-time PCR (qPCR) assays. TCID50 was used to assess the impact of TA on the production of viable virus, while qPCR quantified the copy number of viral genomic DNA.

Results: The MTT assay results indicated that the viability of Vero cells remained above 90% at concentrations up to 25 µg/mL. Pre-exposure of HSV-1 to 25 µg/mL of TA could result in 1.6 log10 TCID50/mL reduction in virus titers, with an inhibition rate of approximately 37% in the copy number of viral genomic DNA (P value < 0.05).

Conclusion: The promising findings of this research highlight the potential of TA as an early-stage antiviral agent. Its ability to inhibit HSV-1 attachment to cellular receptors suggests a broad range of potential applications, including antiviral coatings for medical devices, topical treatments, integration into personal protective equipment (PPE), surface disinfectants, and the enhancement of existing antiviral therapies. Future investigations are essential to validate its safety and effectiveness, paving the way for its incorporation into healthcare settings.

Keywords: HSV-1; Tannic acid; Antiviral; Biocompatible; Topical treatment

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Original Research

OV-6

Prevalence and Genetic Diversity of HTLV-1 Among Blood Donors in Jiroft, Iran: A Comprehensive Study

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Abstract

Background and Aim: This study aimed to investigate the prevalence and phylogenetic characteristics of Human T-cell lymphotropic virus type 1 (HTLV-1) among blood donors in Jiroft Province, southeast Iran, a region previously under-studied regarding this virus.

Methods: A total of 405 blood donor samples were collected from six cities within Jiroft Province. Serum samples were screened for HTLV-1 antibodies using the ELISA method, while peripheral blood mononuclear cells (PBMCs) were analyzed via PCR targeting the long terminal repeat (LTR) and TAX regions of the virus.

Results: The study identified 6 out of 405 blood donors (1.48%) as positive for HTLV-1. Prevalence was higher among females (1.59%) compared to males (1.2%), with the age group of 46-64 years showing the highest positivity rate (4.08%). Phylogenetic analysis revealed that the LTR sequences of HTLV-1 in Jiroft were comparable to those circulating in Mashhad Province, with nine single-nucleotide polymorphisms (SNPs) identified in the LTR region of the isolates.

Conclusion: The findings highlight the necessity for routine HTLV-1 screening among blood donors in Jiroft to ensure blood safety and mitigate the risk of transmission through transfusions. This study provides essential baseline data on HTLV-1 prevalence in Jiroft and contributes to the understanding of its genetic diversity, emphasizing the need for further research in this area.

Keywords: HTLV-1, Blood donors, Prevalence, Phylogenetic analysis, Molecular Virology

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OV-7

Abstract Type: Original Research

Association Between SARS-CoV-2 Upper Respiratory Tract Viral load and *ACE-2* Polymorphisms

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Abstract

Background: The COVID-19 pandemic, triggered by the SARS-CoV-2 virus, has resulted in significant global morbidity and mortality. While several factors contribute to the severity of the disease, both viral and host genetic elements are essential in determining clinical outcomes. This research examines the impact of genetic variations in the *ACE2* gene—namely rs2285666 C>T, rs4646127 T>C, and rs971249 T>C—on the susceptibility to SARS-CoV-2 infection, viral load, and the severity of COVID-19.

Methods: This cross-sectional study analyzed 441 respiratory samples from patients suspected of having COVID-19. After diagnostic testing, participants were categorized into two groups: "cases" (COVID-19 positive) and "controls" (COVID-19 negative). SARS-CoV-2 detection was carried out using real-time reverse transcription PCR (rRT-PCR), focusing on the *E*, *N*, and *RdRp* genes. The viral load of the *E* gene was quantified using a RotorGene Q thermal cycler, with results normalized to the *RNase P* gene. *ACE2* gene polymorphisms (rs2285666 C>T, rs4646127 T>C, rs971249 T>C) were examined via restriction fragment length polymorphism (RFLP).

Results: The study involved 226 COVID-19 positive patients and 215 COVID-19 negative controls. Common comorbidities among patients included diabetes (32.6%), cardiovascular disease (30%), and hypertension (12.9%), with higher rates of diabetes and hypertension in the COVID-19 group. Deceased patients had higher CT values for the *N*, *RdRp*, and *E* genes, suggesting lower viral loads than recovered patients, while hypertensive individuals had higher viral loads. Genetic analysis showed that the T allele of rs971249 C>T was associated with a protective effect against SARS-CoV-2 infection in both males (P = 0.0032) and females (P = 0.0401). The T allele of rs4646127 T>C also provided protection in males (P = 0.0019), but not in females. Additionally, the T allele of rs971249 was linked to higher viral loads of the *E*

gene in COVID-19 patients (P = 0.052). No significant associations were found for the rs2285666 C>T polymorphism.

Conclusion: This study emphasizes the impact of *ACE2* gene polymorphisms on susceptibility to SARS-CoV-2 infection and viral load. The T allele of rs971249 C>T was linked to a protective effect against COVID-19 in both males and females, while the rs4646127 T>C variant showed protection specifically in males. Moreover, hypertensive patients exhibited higher viral loads. These results offer important insights into the genetic factors that influence COVID-19 outcomes and could guide future research into the molecular mechanisms driving the disease.

Keywords: *ACE2*; polymorphism; SARS-CoV-2; viral load

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OV-8

Original Research

Investigation of the frequency of respiratory viral infections in children with acute respiratory symptoms in Tabriz, Northwest of Iran.

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Abstract

Background and aim: Respiratory infections are one of the most common causes of death in pediatrics, and prompt treatment and identification of the causative agent can reduce mortality from these infections. Since viruses are one of the main causes of respiratory infections, which show epidemiological diversity depending on climatic conditions and geographical regions, investigating the prevalence of these viruses helps in rapid identification and effective treatment. Viruses such as rhinoviruses, respiratory syncytial virus (RSV), adenovirus, Boca virus, HCoV-229E, HCoV-NL63, HCoV-OC43, HCoV-HKU1, SARS-CoV-2, metapneumovirus, parainfluenza, influenza A

and B play a role. In the cause of respiratory diseases, since the study of the prevalence of all these viruses worldwide is very limited and comprehensive research has not been conducted in Iran, and in addition to the above, based on the clinical symptoms obtained from hospitalized patients, it was determined that what percentage of hospitalized patients with acute respiratory infection (ARI) have problems in the upper respiratory tract and what percentage of them have problems in the lower respiratory tract, we have done our best in this field. This research aims to address these shortcomings and conduct a comprehensive study.

Methods: Methods: This cross-sectional study was conducted from September 2023 to April 2024 in Tabriz, northwestern Iran. A total of 559 samples were collected from pediatric hospitalized at Zahra Mardani Azar Children's Hospital in Tabriz. After gene extraction, these samples were used for nucleic acid detection using the TaqMan Real-Time PCR method. Finally, the frequency of each virus was evaluated, and it was also determined what percentage of infections were two-infections and what percentage were three-infections.

Results: Findings: According to our results, the most common viral agent involved in respiratory infections is RSV (13.1%), followed by rhinovirus (10.7%), parainfluenza (9.5%), influenza A (۶٫۸%), bocavirus (5.7%), metapneumovirus (3.9%), HCoV-, OC43 (2.9%), HCoV-HKU1 (2.3%), SARS-CoV-2 (2.3%), HCoV-229E(2.3%), influenza B (2.1%), HCoV-NL63 (1.1%). Our research also showed that 41.1% of the infections are lower respiratory tract infections and 58.9% of them are upper respiratory tract infections.

Conclusion: Our research shows that viral respiratory infections are one of the most important causes of respiratory diseases in pediatrics, and attention to and recognition of these viral agents is important and can be effective in treating these respiratory infections and ensuring treatment success.

Keywords: Respiratory virus, pediatric, ARI

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OV-9

Abstract Type: Review Article

The Role and Application of One Health Principles During COVID-19 and Emerging Diseases

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6. Bio Environmental Health Hazards Research Center, Jiroft University of Medical Sciences, Jiroft, Iran

Abstract

Background and Aim: The COVID-19 pandemic has underscored the interconnectedness of human, animal, and environmental health, necessitating a One Health approach for managing emerging infectious diseases. To explore the role of microbiologists within the One Health framework during the COVID-19 pandemic.

Methods: This study utilizes a qualitative literature review, analyzing case studies and reports on One Health initiatives implemented throughout the pandemic. Data sources include peer-reviewed articles and reports from health organizations.

Results: The findings reveal that One Health initiatives significantly improved surveillance and response strategies during the pandemic. Collaborative efforts led by microbiologists enhanced understanding of zoonotic disease transmission and facilitated timely interventions, resulting in effective risk mitigation and positive health outcomes.

Conclusion: The COVID-19 experience highlights the need to integrate One Health principles into public health strategies. The involvement of microbiologists in multidisciplinary teams is crucial for strengthening global health security and resilience against future pandemics. Continued investment in One Health initiatives is essential for the effective management of emerging diseases.

Keywords: One Health; COVID-19; Emerging diseases; Multidisciplinary collaboration; Zoonotic diseases; Public.

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Abstracts of
Poster presentation

PAI-1

Abstract Type: Systematic Review

Investigate effective AI algorithms for analysing clinical and paraclinical data and the early diagnosis of AML patients

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Background and Aim: Acute myeloid leukemia (AML), accounting for 18% of adult leukemia cases and 20% of childhood leukemia cases. AML is a type of blood cancer in which the bone marrow produces a large number of abnormal blood cells. Early diagnosis of AML allows rapid initiation of treatment, prevention of disease progression and reduction of complications. Recently, artificial intelligence (AI) approaches have been used to analyse clinical and paraclinical data to predict and diagnose AML patients early. The aim of this systematic review is to investigate effective AI algorithms for analysing clinical and paraclinical data and the early diagnosis of AML patients.

Methods: The study was conducted based on the PICO criteria, in line with the research objective, and in accordance with the PRISMA checklist. This systematic review included a comprehensive search from 2019 to 2024 in the PubMed, Web of Science, Scopus, Medline, SID, and Google Scholar search engines. The search used MESH keywords including "Artificial Intelligence", "Acute Myeloid Leukemia", "Diagnosis", and Boolean operators. Two independent researchers then screened the retrieved articles based on the study inclusion criteria.

Results: A total of 119 articles were identified through the primary search. After screening the titles and abstracts of the articles, the number of articles was reduced to 9 and finally four articles were included in this research based on the inclusion and exclusion criteria. Most studies have shown that artificial intelligence plays an effective role in early detection of AML. SVM is a machine learning (ML) algorithm used for classification and regression tasks, and by comparing peripheral blood smear images with the ASH image bank, it leads to early diagnosis of AML with 98% accuracy. ANFIS is another ML algorithm that has been used to identify patients and non-patients, as well as to classify different types of leukemia. DNN is a deep learning algorithm based on the combination of two GAN and CNN algorithms, which classifies acute leukemias with more than 99% accuracy using microscopic images.

Conclusion: Artificial intelligence (AI) is a promising tool for early detection of AML. Artificial intelligence can help with early diagnosis of AML with high accuracy, which leads to early initiation of treatment, reduced disease progression and complications, and reduced

treatment costs. However, due to the limitations of the studies conducted in this field, more and more diverse research in this field is recommended.

Keywords: Artificial Intelligence, Acute Myeloid Leukemia, Diagnosis.

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PAI-2

Abstract Type: Systematic Review

The use of Artificial Intelligence in the diagnosis of Sickle Cell Disease: A systematic review

Seyed Mohammadreza Seyedi [1], Farid Mahinizadeh [1,2], Mohammad Ali Jalali Far [3*]

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Background and Aim: Sickle Cell Disease (SCD) is the most common inherited hematologic disease, accounting for approximately 83% of hemoglobin disorders. SCD causes the formation of sickled red blood cells that can block blood vessels. Early diagnosis of SCD can prevent the progression and complications of the disease, provide rapid initiation of treatment, and reduce treatment costs. Recently, Artificial Intelligence (AI) has been used in SCD diagnosis to improve risk stratification and early diagnosis of SCD complications. The aim of this study is to systematically investigate effective AI algorithms in clinical and paraclinical data analysis and early diagnosis of SCD patients.

Methods: This study was conducted based on the PICO criteria and in line with the research objective and following the PRISMA checklist. This systematic review includes a comprehensive search from 2019 to 2024 in PubMed, Web of Science, Scopus, Medline, SID and Google Scholar search engines. MESH keywords such as "Artificial Intelligence", "Sickle Cell Disease", "Diagnosis" and Boolean operators were used in the search. Next, two independent researchers screened the retrieved articles based on the inclusion criteria.

Results: A total of 195 articles were identified through the primary search. After screening the titles and abstracts of the articles, the number of articles was reduced to 21 and finally 7 articles were included in this research based on the inclusion and exclusion criteria. Most studies have shown that AI plays an effective role in early detection of SCD. Artificial Neural Network (ANN) is a Machine Learning (ML) algorithm that is used to classify and predict hemoglobin changes such as hemoglobin S in SCD, and its diagnostic accuracy is 99%. Convolutional Neural Network (CNN) is a Deep Learning (DL) algorithm that analyzes cell morphology in microscopic images with an accuracy of 98.18%. Support Vector Machine (SVM) is an ML algorithm that can detect sickle cells by detecting the overlap of red blood cells in the peripheral blood slide, and its accuracy is 96%.

Conclusion: AI is a promising tool for early diagnosis and management of SCD through various methods, including ML and DL techniques. AI can help in the early diagnosis of SCD with high accuracy, which leads to reduced disease progression and complications, early initiation of treatment, and reduced treatment costs. However, due to the limitations of the studies conducted in this field, it is recommended to conduct more diverse research in this field.

Keywords: Artificial Intelligence, Sickle Cell Disease, Diagnosis.

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PAI-3

Abstract Type: Systematic Review

Revolutionizing Anemia diagnosis: A systemic review on the role of laboratory data and artificial intelligence

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Abstract

Background and Aim:

Anemia is the most prevalent blood disorder globally, affecting approximately 25% of the world's population. Anemia It is characterized by a lower-than-normal number of red blood cells or hemoglobin concentration. Early diagnosis of anemia is crucial, as it allows for prompt treatment and management, ultimately leading to a significant improvement in the quality of life for patients. Artificial intelligence (AI) has been recently employed to analyze laboratory data and achieve early diagnosis and classification of anemias. This systematic review aims to investigate effective AI algorithms for analyzing laboratory data for the early diagnosis and classification of anemias.

Methods:

The study was conducted in accordance with the PICO criteria, aligned with the research objective, and guided by the PRISMA checklist. This systematic review included a comprehensive search from 2019 to January 2024 across the PubMed, SCOPUS, Web of Science, and SID databases, as well as the Google Scholar search engine. The search utilized MESH keywords including "Artificial intelligence", "Anemia" and "Diagnosis". Subsequently, two independent researchers screened the retrieved articles based on inclusion criteria.

Results:

A total of 91 articles were identified during the initial search. After removing duplicates and screening titles and abstracts, the number of articles was reduced to 7. Finally, after considering the inclusion and exclusion criteria and reviewing the full text, five articles were included in this study. Studies indicate that machine learning (ML) algorithms, a subset of AI technologies, effectively analyze laboratory data to aid in the early diagnosis and classification of anemia. Techniques like ELM, ANN, DT, KNN, and SVM have demonstrated significant utility. The ELM algorithm detects complex patterns in CBC data using a fast neural network, while KNN compares patient data with prior cases to predict anemia types. DT constructs a decision tree based on CBC features, leading to diagnosis, and SVM separates different anemia types by defining boundaries. ANN, mimicking brain function, recognizes complex patterns in CBC data for accurate anemia diagnosis.

Conclusion:

The application of AI using laboratory data for diagnosing and classifying anemia shows promise for accurate and timely anemia detection. The integration of artificial intelligence technologies into healthcare practices has the potential to expedite and simplify the diagnostic process, ultimately leading to better management of anemia.

Keywords:

Artificial intelligence; Anemia; Diagnosis

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PAI-4

Abstract Type: Systematic Review

Employing Artificial Intelligence for Early Diagnosis of Acute Myeloid Leukemia: A Systematic Review

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Abstract

Background and Aim:

Acute myeloid leukemia (AML) accounts for approximately 1.2% of all cancers and has an incidence rate of about 4.3 cases per 100,000 people per year. AML is a type of cancer that affects the blood and bone marrow, characterized by the rapid growth of abnormal myeloid cells. Early AML diagnosis enables timely treatment, preventing progression and complications. Lately, artificial intelligence (AI) approaches have been utilized to analyze data to predict and early diagnose AML patients. The purpose of this systematic review is to explore effective AI algorithms for analyzing clinical and paraclinical data for the early diagnosis of AML patients.

Methods:

The study was conducted based on the PICO criteria and aligned with the research objective, adhering to the PRISMA checklist. This systematic review included a comprehensive search from 2019 to 2024 across the PubMed, Scopus, Web of Science, SID, and Medline databases, as well as the Google Scholar search engine. The search utilised MESH keywords including "Artificial intelligence" ،"Acute Myeloid Leukemia" and " Diagnosis". Subsequently, two independent researchers screened the retrieved articles based on inclusion criteria. A total of 148 articles were identified through the initial search. After reviewing the inclusion and

exclusion criteria and critically evaluating the quality of the articles, a total of 4 articles were finally included in the study.

Results:

Studies indicate that machine learning algorithms like XGBoost and deep learning models such as SCEMILA, CNNs, and GNNs are highly effective for AML diagnosis and prognosis.XGBoost has been employed to predict clinical outcomes in AML patients by analyzing their clinical and biological characteristics, showcasing its strong potential in outcome prediction. SCEMILA has shown significant promise in classifying AML subtypes from blood smear images, providing valuable insights for subtype differentiation. Furthermore, CNNs have proven effective in the morphological classification of atypical white blood cells from peripheral blood smear images in AML. A hybrid model combining a deep convolutional autoencoder with CNNs achieved impressive diagnostic results, with an average accuracy of 97%, and sensitivity and precision rates of 97% and 98%, respectively. GNNs have also been explored for predicting patient survival in AML by analyzing longitudinal data from electronic health records. GNNs demonstrated substantial predictive power by efficiently processing complex patient data.

Conclusion:

AI is a promising tool for early AML diagnosis. AI can assist in the early detection of AML, which can lead to prompt treatment initiation, decreased disease progression and complications, and reduced treatment costs. However, due to the limitations of the studies conducted in this field, further and more diverse research in this area is recommended.

Keywords:

AML; Artificial intelligence; Diagnosis

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PAI-5
Abstract Type: Systematic Review

The Role of Artificial Intelligence in Promoting Self-Care in Diabetic Patients: A Systematic Review

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Abstract

Background and Aim:

Diabetes is one of the most common chronic metabolic diseases, with a high global healthcare burden. According to the International Diabetes Federation (IDF), 693 million people will be living with diabetes by 2045. Given the numerous complications and mortality rates associated with this disease, intervention is crucial for both treating and preventing diabetes, as well as for early diagnosis. In this regard, artificial intelligence (AI) has provided comprehensive and secure coverage for diabetic patients, healthcare professionals, and healthcare systems by offering management solutions in the areas of screening, diagnosis, treatment, rehabilitation, and remote education. The aim of this study is to conduct a systematic review of the managerial role of AI in promoting self-care in diabetic patients.

Methods:

The study was conducted based on the PICO criteria and aligned with the research objective, adhering to the PRISMA checklist. This systematic review included a comprehensive search from 2018 to 2024 across the PubMed, Scopus, Web of Science, SID, and Medline databases, as well as the Google Scholar search engine. The search utilised MESH keywords including "Artificial intelligence" ،"Self Care" and "Diabetes". Subsequently, two independent researchers screened the retrieved articles based on inclusion criteria.

Results:

A total of 223 articles were identified through the initial search. After reviewing the inclusion and exclusion criteria and critically evaluating the quality of the articles, a total of 11 articles were finally included in the study. Studies have shown that, with the advent of AI, the diagnosis of diabetes has evolved beyond simply measuring blood glucose levels and glycosylated hemoglobin (HbA1c). Machine learning technology has been proposed to accurately classify diabetes risk and identify diabetic patients based on genetic and metabolic factors. Additionally, support vector regression (SVR) has been developed for preventive intervention in cases where patients have low blood glucose levels. Artificial neural networks (ANNs) have made it possible to diagnose diabetic retinopathy or diabetic macular edema with high

sensitivity. Computer-interpretable guidelines (CIG) are now being utilized for the management and care of gestational diabetes.

Conclusion:

The emergence of AI in delivering services at primary prevention levels, especially considering the number of unscreened patients, can lead to a decrease in chronic diabetic complications. While the use of AI has been somewhat limited thus far, it is recommended that the country's scientific research policies focus on enhancing technological infrastructure and supporting AI-based systems with a multidisciplinary approach in the healthcare field.

Keywords:

Diabetes; Artificial intelligence; Self Care

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PAI-6

The impact of Artificial Intelligence and Technology on Nursing: Challenge and Future implications

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Abstract

Background and Aim: The integration of artificial intelligence (AI) and technology in the healthcare sector has revolutionized patient care and significantly impacted the nursing profession. This systematic review aims to evaluate the challenges faced by nurses due to the implementation of AI and technology and explore the future implications for the nursing workforce.

Method: This systematic review was conducted in March 2024. The databases that were consulted include PubMed-Medline, CINAHL, Scopus and Web of Science. In addition to the electronic database searches, a targeted website search was performed to access relevant gray literature. Abstracts and full-text studies were independently screened by 2 reviewers using prespecified inclusion and exclusion criteria that published from the beginning of 2014 till March 2024. Included articles focused on nursing and technologies that incorporate AI. Data

were charted using the JBI, Critical and Mixed Methods Appraisal Tools. A search strategy was developed with peer review and evidence combining natural and structured language through Medical Subject Headings (MeSH). For example, the search strategy in the PubMed database was ("artificial intelligence"[MeSH terms] or "AI"[title/abstract]) and "technolog*"[title/abstract] and "nurses*"[title/abstract]).

Results: The titles and abstracts of 714 publications and 211 full texts were screened, and 46 publications were included. Emerging AI technologies on nursing discussed in the review included Challenges and Role of AI and technology in Nursing, Future implication for nursing respectively. The results indicated that the challenges of AI and technology in nursing include ethical concerns and accountability issues, data privacy and security risks. Adapting to rapid technological changes, Potential displacement of nurses and job insecurity, creating a balance between technology and human touch in nursing care were other issues. The Role of AI and technology in Nursing included Streamlining workflows and reducing administrative burdens, improving patient monitoring and early detection of health issues, supporting clinical decision-making and predictive analytics, enhancing communication and collaboration among healthcare providers, personalizing patient care and improving patient engagement. Future implication for nursing such as developing new nursing roles and competencies related to technology, integrating AI and technology into nursing education, ensuring ethical AI implementation and usage in healthcare, collaboration with interdisciplinary teams to leverage technology effectively, emphasizing emotional intelligence and empathy in nursing practice.

Conclusion: The integration of AI and technology presents numerous opportunities, such as enhanced efficiency, improved accuracy in diagnostics, predictive analytics, and personalized care. This study emphasizes the importance of addressing these challenges and capitalizing on opportunities to ensure a successful and sustainable future for nursing in the age of AI and technology.

Keywords: Artificial Intelligence, Technology, Nursing, Nursing Workforce, Health Care Sector, Challenge and Future implications

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PAI-7
Narrative review

Application of artificial intelligence in laboratory diagnostics

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Abstract

Artificial intelligence has revolutionized the diagnosis, identification, and management of infectious diseases in clinical laboratory diagnostics. Techniques based on artificial intelligence enable faster, more accurate, and more comprehensive analysis of diverse data sources related to the diagnosis of infectious diseases. Machine learning models can be trained on structured data such as patient symptoms, laboratory test results, and demographic information to aid in disease diagnosis and risk prediction. Deep learning algorithms can analyze unstructured data such as digital microscope images, mass spectra, and genomic sequences to automatically identify pathogens. This article reviews and analyzes the applications of artificial intelligence in laboratory diagnostics, exploring how AI can increase the accuracy and efficiency of laboratory diagnoses and ultimately lead to improved patient outcomes.

Background and Aim: This article discusses the application of artificial intelligence (AI) in laboratory diagnostics, focusing on its transformative impact on the diagnosis and management of infectious diseases. The background highlights the historical evolution of AI in healthcare, tracing its roots back to the 1950s and emphasizing its growing role in enhancing diagnostic accuracy and efficiency. The purpose is to analyze how AI techniques, such as machine learning and deep learning, can analyze both structured and unstructured data, ultimately leading to improved patient outcomes through faster and more accurate disease detection.

Methods: The study design in this document explores how artificial intelligence (AI) enhances laboratory diagnostics, particularly for infectious diseases. It focuses on using machine learning (ML) and deep learning (DL) models to improve diagnostic accuracy, speed, and efficiency. AI systems analyze structured data (e.g., patient symptoms, lab results) and unstructured data (e.g., digital images, genomic sequences) to assist in disease identification and risk prediction. The experimental method involves training AI models on large datasets and comparing their performance to human diagnostics. AI's application includes automated image analysis, pathogen detection, and identification of disease patterns. The study also assesses AI's potential to reduce diagnostic errors, improve disease detection, and optimize personalized treatment plans. Through these methods, the study demonstrates AI’s potential to revolutionize laboratory diagnostics, enhancing precision, efficiency, and healthcare outcomes.

Results: The results of the study demonstrate that artificial intelligence (AI) significantly enhances laboratory diagnostics, particularly in detecting infectious diseases and other complex conditions like cancer and diabetes. AI systems, utilizing machine learning (ML) and deep learning (DL), show improved accuracy and efficiency by analyzing both structured data (e.g., patient symptoms) and unstructured data (e.g., digital images, genomic sequences). The

application of AI reduces diagnostic errors, accelerates disease detection, and aids in developing personalized treatment plans. AI has proven particularly valuable in automating image analysis for pathology, identifying pathogens, and detecting subtle patterns in medical data. The integration of AI in laboratories not only speeds up the diagnostic process but also increases the reliability of diagnoses, ultimately improving patient outcomes. However, the study also points out the need to address data quality, algorithm biases, and ethical concerns for widespread implementation.

Conclusion: The conclusion of this article emphasizes that the integration of artificial intelligence (AI) in laboratory diagnostics significantly enhances the accuracy and efficiency of disease detection and management. AI techniques facilitate rapid analysis of diverse data, allowing for improved identification of infectious diseases through machine learning and deep learning algorithms. This advancement not only streamlines diagnostic processes but also leads to better patient outcomes by enabling earlier detection and personalized treatment approaches. Ultimately, AI is positioned as a transformative force in healthcare, improving diagnostic precision and optimizing resource utilization.

Keywords: Artificial Intelligence (AI)1 ،Laboratory Diagnostics،2 Infectious Diseases، 3 Machine Learning ،4 Deep Learning5

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PAI-8

Abstract Type: Original article

In Silico Identification of Novel ncRNAs involve in pathogenesis and diagnosis of Cervical Cancer

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Abstract:

Background and Aim

Cervical cancer (CC) is one of the most common cancers. Considering that the mortality rate of CC ranks first among the malignant tumors of female in the reproductive system, hence it has become a disease that threatens women's health. Human papillomavirus has identified as a major factor that leads to cervical cancer as well as HPV and cervical cancer have a significant global impact. Although HPV infection alone cannot cause the disease because most infections are could be cleared spontaneously by host immune system and persistent HPV infection, are required decades for progression to cervical cancer. The main types of cervical cancers are squamous cell carcinoma and adenocarcinoma. Most cervical cancers are squamous carcinomas.Majority of the human genome is transcribed to RNAs that do not encode proteins. These non-coding RNAs play crucial roles in regulating the initiation and progression of various cancers. Different types of non-coding RNAs are such as sniRNAs، circRNAs، piRNAs، microRNAs and lncRNAs. Non-coding RNA in gene expression is now widely recognized as a critical component of normal development and cell signaling.

Methods

In this research the effective factors in the pathogenesis of cervical cancer and the data related to non-coding RNAs associated with cervical cancer were retrieved from the databases and then discussion.Also,using bioinfoformatics analyzes and relevant databases,data related to lncRNAs and miRNAs ,two important non-coding RNAs in cervical cancer were extracted.The databases that were examind in this research include: GeneCards ،LncRNADisease ،miRCancer ،MethHC ،EpimiR CCDB ،LncRNAWiki ،YM500،dbDEMC ،LncRNATarD, LncRNA2Target ،OncomiRDB and miRDB.

Results

Also, number of new lncRNAs and microRNAs such as AIRN ،ATXN8OS ،BOKAS1 ، CASC2 ،miR-4724 ،miR-3609 و miR-519c whose is bioinformatically predicted potential role in cervical cancer but they are not still support by experimental studies. Finally, by integrating the results of this research, the possible targets of some non-coding RNAs in the regulation of these pathways have been shown by a biological network.

Conclusion

Considering the importance and prevalence of cervical cancer, drawing this network will help to understand the importance of its role in the development and progression of cervical cancer. Because miRNAs and lncRNAs have high potential as therapeutic agents and innovative biomarkers, they can lead us to promising biological targets about cervical cancer.

Keyword: Cervical cancer ,Long-non-coding RNA, miRNAs

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PAI-9

Spatial modeling and risk mapping of Food borne diseasesin Iran: A GIS-based survey from 2009-2022

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Abstract

Background:

Foodborne diseases are an important cause of morbidity and mortality, The purpose of this study is to determine the incidence, spatial distribution, and hot spots of Foodborne diseases (Fascioliasis and hydatidosis)in Iran using the GIS analyses during 2009 to 2022.

Mthods: The data including Foodborne diseases cases and populations at-risk in different provinces obtained from the Ministry of Health, and Medical Education, Tehran, Iran and other centers from 2009 to 2022. The spatial distribution maps of the Foodborne diseases were generated. Then, the hot spots of the disease in Iran were determined using spatial analysis of ArcGIS10.5 software. Geographically weighted regression (GWR) analysis in ArcGIS10.5 was used to correlate the temperature, relative humidity, normalized different vegetation index (NDVI) and incidence of Foodborne diseases. Data analysis was performed by Linear regression analysis and SPSS 21 software using descriptive statistics test.

Result: The hot spot provinces of were Gilan, Kermanshah, Khorramabad, Zanjan, Khorasan Razavi, North Khorasan, Chaharmahal Bakhtiari, Hamedan, Semnan, and Ardabil .In provinces, the highest correlation between humidity, temperature, vegetation density and the incidence of Foodborne diseases was observed using geographical weighted regression analysis.

Conclusion: Our study revealed that there were significant relationship between the relative humidity, mean annual temperature, NDVI and the incidence of Foodborne diseases in Iran. The Geographical Information System (GIS) can be used to identify risk factors of Foodborne diseases and to assess endemic areas in a specific region.

Keywords: GIS, Risk mapping, Spatial modeling, Foodborne diseases, Iran

PAI-10
Abstract Type: Systematic review

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Machine Learning Models for Malaria Prediction Using Clinical Data: A Systematic Review

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Abstract

Background and Aim: As one of the most essential infectious diseases in tropical and subtropical areas, malaria is still a primary project for global health. Early diagnosis and prediction of this ailment can assist enhance remedy control and decrease mortality. In current years, machine gaining knowledge of fashions have received attention as a brand new technique in predicting sicknesses together with malaria because of their correct and speedy prediction competencies. The goal of this evaluation is to systematically examine current research on the use of system getting to know models to expect malaria the usage of clinical records.

Methods: A systematic review was performed independently by two people based on the PICO criteria and aligned to the research objective and based on the PRISMA checklist and using PubMed, Medline, Cochrane, Sciencedirect, SID databases Google Scholar search engine, and Boolean operators. The time limit between 2019 and 2024 was determined using the MESH keywords " Malaria", " Machine Learning Malaria " and "Prediction". After checking the entry and exit criteria and critically evaluating the quality of the selected articles, a total of 8 articles were included in the study.

Results: inspecting the effects of studies indicates that machine getting to know fashions, particularly algorithms based on deep mastering, have considerable overall performance in as it should be predicting malaria. Extra complicated algorithms, together with deep and reinforcement neural networks, had been able to extract complex capabilities from medical statistics and feature furnished widespread development in prediction accuracy as compared to less complicated models along with decision trees. But, some boundaries, such as the shortage of general statistics and obstacles inside the generalizability of the results to special populations, have nevertheless created demanding situations.

Conclusion: This study suggests the importance of the use of machine getting to know inside the prognosis and prediction of malaria and indicates that destiny research have to develop models that, similarly to excessive accuracy, also can be generalized to exclusive geographic areas and populations. Also, the need for extremely good and standardized scientific information is felt to improve the performance of predictive fashions on a worldwide scale.

Keywords: Malaria ; Machine Learning ; Prediction

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PAI-11

Abstract Type: Systematic Review

Investigating the effect of Artificial Intelligence algorithms in the early diagnosis of Chronic Myeloid Leukemia patients

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Background and Aim: Chronic Myeloid Leukemia (CML) comprises 15% of adult leukemias and accounts for 4% of cancer-related deaths. CML is a clonal myeloproliferative neoplasm characterized by the formation of the BCR-ABL fusion gene and the irregular proliferation of mature granulocytes and their precursors. Early detection of CML allows timely initiation of treatment with tyrosine kinase inhibitors and improves prognosis. Recently, Artificial Intelligence (AI) has been used in CML diagnosis to improve risk stratification and early detection of CML complications. The aim of this study is to systematically investigate effective AI algorithms in the early diagnosis of CML patients.

Methods: This study was conducted based on the PICO criteria and in line with the research objective and following the PRISMA checklist. This systematic review includes a comprehensive search from 2019 to 2024 in PubMed, Web of Science, Scopus, Medline, SID and Google Scholar search engines. MESH keywords such as "Artificial Intelligence", "Chronic Myeloid Leukemia", "Diagnosis" and Boolean operators were used in the search. Next, two independent researchers screened the retrieved articles based on the inclusion criteria.

Results: A total of 215 articles were identified through the primary search. After screening the titles and abstracts of the articles, the number of articles was reduced to 25 and finally 9 articles were included in this research based on the inclusion and exclusion criteria. Most studies have shown that artificial intelligence plays an effective role in early detection of CML. ResNet-34 and DenseNet-121 are deep learning models that are used to automatically identify leukemia subtypes, including CML, and have a diagnostic accuracy of 97.69%. A model based on conditional generative adversarial network (cGAN) called CMLcGAN was designed to distinguish megakaryocytes from myeloid cells in bone marrow biopsy for the diagnosis of CML and has a diagnostic accuracy of 95.1%. The Extreme Gradient Boosting Model (XGBoost) is a machine learning model that analyzes blood cells collected over 5 years in CML patients with a diagnostic accuracy of 92%.

Conclusion: Artificial Intelligence (AI) is a promising tool for early diagnosis and management of CML through various methods, including machine learning and deep learning techniques. AI can help in the early diagnosis of CML with high accuracy, which leads to reduced disease progression and complications, early initiation of treatment, reduced treatment costs, and

improved prognosis. However, due to the limitations of the studies conducted in this field, it is recommended to conduct more diverse research in this field.

Keywords: Artificial Intelligence, Chronic Myeloid Leukemia, Diagnosis.

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PAI-12

Abstract type: review

Application of Artificial intelligence in Diagnoses of Thalassemia: A Review

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Abstract

Background and Aim: Thalassemia is the most common single-gene disorder worldwide and represents a major public health problem due to abnormal ratios of hemoglobin subunits. There are different types of thalassemia characterized by abnormal hemoglobin production. However, all methods for diagnosing hemoglobinopathies are costly and require specialized instrumentation and trained technicians. The use of artificial intelligence in this field can improve the speed and efficiency of diagnoses while simultaneously reducing human errors.

Methods: In this review, research was conducted using Google Scholar and PubMed from 2019 to 2024. The keywords searched were artificial intelligence, thalassemia, diagnosis, and quality of life.

Results: By searching these databases and studying more than 20 articles and research papers on how artificial intelligence works in this important matter, the results show that artificial intelligence has the ability to use the data stored in it and the analyses obtained from patient monitoring, medical imaging, and samples from a broad functional platform to not only diagnose thalassemia but also help specialists in identifying different types of thalassemia. Based on the findings of Chakraborty and her colleagues, it can be said that the use of artificial

intelligence with the MPL (Multilayer Perception) method in the diagnosis of thalassemia produces up to 94.59% specificity, 98.81% sensitivity, and a 98.93% positive predictive value.

Conclusion: New algorithms enable health professionals to identify thalassemia more accurately and quickly, allowing for earlier intervention. More importantly, the new approach not only simplifies diagnostic methods but also creates different forms of care plans for patients. This technique can be used in both clinical and para-clinical settings.

Keywords: artificial intelligence; thalassemia; diagnoses; life quality.

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PAI-13
Abstract Type: Original Research

Evaluation of incidence and spatial distribution of Leukemia in Iran by using of geographical information system (GIS) and quantifying burden of the disease (DALYs) in 2020

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Abstract

Background and Aim: Leukemia is among the diseases that are affected by age, gender, race and environmental factors. Since the prevalence of leukemia and other public health effects can be related to geography, Geographic Information System (GIS) mapping can greatly assist in the management of this disease. In Iran, there is lack of study on the correlation between geographical characteristics of the southwest parts and leukemia prevalence. The present study was conducted to investigate the incidence and spatial distribution of Leukemia in Iran using GIS and disease assessment (DALYs) in 2020.

Methods: Recorded data on Leukemia were collected from the Ministry of Health, the Centers for Disease Control, in the country. Spatial analysis of ArcGIS10.5 software was used to investigate the spatial distribution of Leukemia, to determine the hot spots of the disease in Iran. Finally, for the correlation between temperature, relative humidity, vegetation density and the incidence of Leukemia during 2016 to 2020, geographical weight regression analysis was

used in ArcGIS10.5. The Disability Adjusted Life years index was also used to calculate the disease burden.

Results: The burden for Leukemia was calculated at 22510 years (YLD equals to 18587 years and YLL equals to 4339 years), estimated to be 13205 years for men and 9405 years for women. During the studied years22930 cases of Leukemia were registered in the country. The results of GWR analysis showed that during these years, the highest correlation between humidity, temperature, and NDVI and the incidence of the disease was observed in the provinces of Kurdistan, Golestan,Yazd,fars, Qom ,Esfahan and South Khorasan.

Conclusion: The findings of this study show that the use of maps can provide reliable estimates of the population at risk. Also, the burden of disease has a fundamental and important effect on the economy of our country.

Keywords: Disability Adjusted Life years; Leukemia ; Incidence; Environmental variables; Geographical Information System.

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PAI-14

Abstract Type: Original Research

The Performance of GPT-3.5 and GPT-4 on Genetic Tests at PhD-level: ChatGPT as a Promising Tool for Genomic Medicine and Education

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Abstract

Background and Aim: Natural Language Processing (NLP) in artificial intelligence has significantly advanced language understanding and text generation. Transformer-based models, such as the Generative Pre-trained Transformer (GPT), have shown proficiency in tasks like translation, summarization, and question-answering. This study aims to evaluate GPT-4's performance in comprehending and responding to genetic questions, comparing its effectiveness to that of GPT-3.5.

Methods: GPT-3.5 and GPT-4 were tested on five tasks to assess their knowledge and application of genetics: basic genetic concepts, family pedigree analysis with inheritance pattern identification, genetic mutation notation interpretation, genetic population problems, and a medical genetics Ph.D. entrance exam. Performance metrics included accuracy across multiple-choice (MCQs) and open-ended questions for each task.

Results: GPT-4 achieved a 100% success rate in Tasks 1 and 3, which involved basic genetic concepts and the interpretation of genetic mutations, respectively. For Task 2, focused on pedigree analysis and inheritance pattern identification, GPT-4 correctly answered only 24 of 71 questions, with a high error rate (47 incorrect responses). In Task 4 on genetic population problems, GPT-4 accurately answered 30 of 34 MCQs. For Task 5, involving a genetics Ph.D. entrance exam, GPT-4 answered 58 out of 80 questions correctly but made 19 errors. The model demonstrated higher accuracy with MCQs than open-ended questions.

Conclusion: GPT-4 demonstrates strong performance in fundamental genetic concepts and mutation interpretation but struggles with complex analyses such as family pedigree interpretation and some population genetics tasks. This suggests that developing genetics-specific language models could enhance performance for clinical and educational applications.

Keywords: Natural Language Processing, ChatGPT, GPT-4, GPT-3.5, Genetics

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PAI-15
Abstract Type: Original Research

Risk mapping of human fascioliasis in Iran using a geographical information system from 2013-2022

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Abstract

Background and Aim: *Fasciola hepatica* and *Fasciola gigantica* are the etiologic agents of fascioliasis, an important and emerging infection affecting both humans and animals worldwide. Fascioliasis is considered a major public health problem in many countries. Today, the epidemiologic patterns of *Fasciola* infection have changed to emerging or re-emerging in different regions of the world, and its global prevalence among humans is also increasing. Climate change may alter precipitation patterns and temperatures in different regions, creating new habitats suitable for *Fasciola* parasites and their hosts. Environmental changes may also contribute to the availability of these habitats. These factors may lead to the expansion of endemic areas and an increase in the prevalence of human fascioliasis. Iran, identified by the WHO as a significant endemic area for human *Fasciola* infection in Asia, is one of six countries facing serious problems with Fascioliasis. The aim of our study is to assess the incidence,

spatial distribution, and hotspot regions of *Fasciola* infection in Iran using Geographical Information System (GIS) analysis from 2013 to 2022.

Methods: The data, including *Fasciola* cases and at-risk populations in different provinces, were obtained from the Ministry of Health and Medical Education, Tehran, Iran, and other organizations from 2013 to 2022. The map illustrating the geographical distribution of fascioliasis was created. Spatial analysis of ArcGIS10.5 software was used to determine the hot spot regions of fascioliasis in Iran. Correlation of temperature, relative humidity, normalized difference vegetation index (NDVI) and incidence of fascioliasis (variables affecting the disease) was checked using geographically weighted regression (GWR) in ArcGIS10.5. Data were analyzed using linear regression and SPSS 21 software.

Results: 589 cases of fascioliasis were registered in Iran during the study period. Gilan, Kermanshah and Khorramabad provinces were identified as hot spots of fascioliasis. Using GWR analysis, the high correlation between humidity, temperature, vegetation density and the incidence of *Fasciola* infection was found in Gilan, Kermanshah, Khorramabad, Kurdistan, Semnan and South Khorasan provinces (p-value =0.025).

Conclusion: Our study showed a significant relationship between relative humidity, mean annual temperature, NDVI and the incidence of *Fasciola* infection in Iran. GIS can identify risk factors of fascioliasis and assess endemic areas in a specific region. The data and results of this study can help health policy makers to develop and maintain prevention programs for new cases. GIS is an effective tool and suitable for studying the distribution of effective factors in the health system.

Keywords: *Fasciola* infection**;** Fascioliasis; Geographical Information System (GIS); Risk mapping; Spatial modeling

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PAI-16

Leveraging Bioinformatics in Vaccine Development against Brucellosis: Experiences into SodC and Omp25

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Abstract

Background and Aim: Brucellosis (Malta fever) is a zoonotic infection transmitted to humans from animals like cattle, sheep, and pigs, through contaminated food ingestion, direct contact with infected animals, and inhalation of aerosols. The disease is caused by species of the Brucella spp; gram-negative, aerobic, non-motile, facultative intracellular coccobacilli affecting domestic and farm livestock and a wide range of wild mammals. To date, only a handful of live attenuated vaccines have been produced against brucellosis. However, they are associated with serious side effects and offer insufficient protective efficacy. Hence, in recent years, researchers have turned to designing recombinant vaccines, harboring Brucella immunogenes.

Methods: The objective of this study is to identify multi-epitope vaccine candidates based on the genes SodC and Omp25, encoding periplasmic superoxide dismutase and outer membrane protein 25 in B. melitensis, respectively. Physicochemical properties were investigated by CLC Protein Workbench. Protein 3D structures were predicted by PHYRE2, modeled and compered with their homologues structures reported in Uniprot. Finally, B cell and T cell epitopes were predicted using IEDB, SYFPEITHI, and NetMHCII 2.3 databases, regarding high frequency HLA alleles in Iran.

Results: SodC and Omp25 were composed of 173 amino acids and 213 amino acids, respectively. They were both stable hydrophilic proteins. The instability indices were 37.9 and 23.0, respectively. The hydrophilicity was −0.22 and −0.317, respectively. In the secondary structure of SodC and Omp25 proteins, the α-helix accounted for 16.18% and 23.94%, the β-sheet was 28.90% and 23.47%, the β-turn was 9.25% and 4.23%, and the random coil was 45.66% and 48.36%. Finally, 6 B cell epitopes, 5 Th-cell epitopes and 5 CTL cell epitopes of SodC protein, and 4 B cell epitopes, 3 Th-cell epitopes, and 5 CTL cell epitopes of Omp25 protein were selected as vaccine candidates.

Conclusion: In conclusion, we analyzed physicochemical features of the Brucella melitensis SodC and Omp25 proteins, and also predicted and modeled their 3D structures. Furthermore, we obtained potential B cell and T cell epitopes of the desired proteins. This lays the foundation for the further design of multi-epitope vaccine of Brucella.

Keywords: Bioinformatics; Brucella; SodC; Omp25; Epitope

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PAI-17

Abstract Type: Systematic Review

Using artificial intelligence for accuracy in medical laboratory tests Biosensors: A Systematic Review Article

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Background and Aim: The emergence of artificial intelligence (AI) has brought about many changes in the field of medical and laboratory diagnostics. Biosensors are capable of detecting biological and chemical analytes, which have gained attention in various applications, including diagnostic and research laboratories. This article provides a comprehensive review of how AI algorithms can enhance the accuracy and reliability of laboratory tests by analyzing data obtained from various biosensor technologies.

Method: This systematic review article was performed within articles published at PubMed, Google Scholar, Science Direct until November 2024. The keywords were Artificial Intelligence (AI), Biosensors, Disease Diagnosis and Biochemical Data. By searching this database, 23 articles were found, and 16 were removed by reading titles and abstracts. 7 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: Biosensors, which are analytical devices that convert biological responses into measurable signals, have emerged due to their ability to provide real-time monitoring and rapid diagnosis. These algorithms can detect patterns and abnormalities that may be unobservable to human analysts, thereby improving diagnostic accuracy. Biosensors are capable of detecting biological and chemical analytes, which have gained attention in various applications, including diagnostic and research laboratories. AI-enhanced biosensors, known as AI biosensors, enable early diagnosis of diseases, identify bacteria, and measure hazardous compounds. Integrating AI with biosensors also increases diagnostic accuracy. In addition, integrating AI with biosensors enables personalized medicine approaches. As a result, the combination of AI and biosensor technology holds promise for advancing the accuracy and efficiency of medical laboratory testing. By addressing existing challenges and fostering innovation, this interdisciplinary approach can significantly improve diagnostic capabilities and ultimately enhance healthcare delivery.

Conclusion: It seems that researching in this area is expected to increase in the coming years, with technological advances in sensors and biosensors enabling analysis in various fields, contributing to early disease diagnosis and intervention strategies. The integration of AI with digital health platforms will enable predictive analytics and personalized healthcare, emphasizing the importance of interdisciplinary collaboration across related scientific field.

Keywords: Artificial Intelligence (AI), Biosensors, Disease Diagnosis, Biochemical Data

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PAI-18
review of the literature

Harnessing artificial intelligent for the diagnosis of autoimmune diseases

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Abstract

Autoimmune diseases, characterized by the immune system's attack on the body's own tissues, present significant challenges in diagnosis and treatment. Recent advancements in artificial intelligence (AI) offer promising solutions for improving both aspects of autoimmune disease management. AI-driven technologies, including machine learning (ML), natural language processing (NLP), and deep learning, are being increasingly applied to analyze complex biological data, enhance diagnostic accuracy, and personalize treatment strategies. AI can help identify biomarkers, predict disease progression, and detect autoimmune diseases at earlier stages through pattern recognition in clinical data and imaging. Furthermore, AI models can support precision medicine by analyzing vast datasets to tailor individualized treatment plans, optimizing drug discovery, and predicting patient responses to specific therapies. While AI holds great potential in transforming the landscape of autoimmune disease care, challenges such as data privacy, model interpretability, and integration into clinical workflows must be addressed to ensure effective and ethical deployment. This review explores the current state of AI applications in autoimmune disease diagnosis and treatment, highlighting key innovations, clinical implications, and future directions for research.

Background and Aim

Autoimmune diseases, including conditions such as rheumatoid arthritis, lupus, and multiple sclerosis, arise when the immune system erroneously targets healthy body tissues, leading to chronic inflammation and organ damage. These diseases often present with complex and overlapping symptoms, making early diagnosis and effective treatment a challenge. Traditional diagnostic methods are reliant on clinical evaluation, biomarkers, and imaging, but they can be time-consuming, subjective, and prone to inaccuracies. Additionally, current treatment approaches tend to follow a one-size-fits-all model, which may not always align with the individual patient’s needs or disease progression.

Methods

This study utilized anonymized data from hospitals, and research institutions, including EHRs. keywords in Pubmed, Google Scholar and Scopus from until now were search and all data collected and analyzed. Ethical and data privacy standards were strictly followed throughout the study.

Results:

AI demonstrated significant improvements in both diagnostic accuracy and treatment personalization. In medical imaging, AI models, particularly Convolutional Neural Networks (CNNs), achieved diagnostic accuracy levels comparable to or exceeding human specialists in detecting conditions such as cancer and cardiovascular diseases. Predictive models also enhanced the ability to forecast patient outcomes, guiding earlier interventions for chronic conditions. AI-driven tools enabled personalized treatment plans, especially in oncology, by analyzing genomic data to tailor chemotherapy regimens. Additionally, AI improved clinical workflow efficiency by automating routine tasks and supporting decision-making, leading to better patient care and reduced administrative burdens. However, challenges such as data privacy, algorithm transparency, and model validation remain as areas for ongoing improvement.

Conclusion:

Artificial Intelligence (AI) has demonstrated significant advancements in medical diagnosis and treatment, improving accuracy, efficiency, and personalized care. AI models, such as Convolutional Neural Networks, have achieved diagnostic precision on par with human experts, while predictive tools enable early interventions and better outcomes. Despite challenges in data privacy, model transparency, and integration, AI's potential to revolutionize healthcare remains immense. Continued research, ethical consideration, and validation will be crucial for fully realizing AI's capabilities and ensuring its responsible use in clinical settings.

Keywords

Artificial intelligence, autoimmune disease, treatment and diagnosis

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PAI-19

Abstract Type: Systematic Review

Using Artificial Intelligence in Patient Blood Management

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Abstract

Background and Aim:

Patient blood management (PBM) is a new and crucial aspect of medicine, enabling healthcare professionals to avoid unnecessary blood transfusions by using evidence-based methods and therefore reducing the consumption of blood products. Recent technological developments have led artificial intelligence (AI) to become an important tool in this field that can optimize patient blood-related processes. This study investigates the applications of artificial intelligence in patient blood management and analyzes its impacts on improving healthcare service quality, reducing costs, and increasing patient safety.

Methods:

In this review study, a comprehensive method was employed to examine relevant articles. The keywords "Artificial intelligence," "Transfusion medicine," "Patient blood management," and "Machine learning" were searched in reputable scientific databases including Scopus, Google Scholar, PubMed, and Cochrane, focusing on titles and abstracts. In the first stage, approximately 5,459 articles containing these keywords were identified, published between 2010 and 2024. Following this, 64 selected articles were examined more closely using EndNote software. From these 64 articles, only 20, which were significant in terms of research quality and the latest findings, were chosen for a more in-depth analysis. These articles included clinical studies, review articles, and experimental research that explored the impact of artificial intelligence on blood management processes.

Results:

Artificial intelligence can identify the specific needs of hospitals and optimize blood transfusion processes by analyzing data related to patients. For instance, artificial intelligence can predict the demand for blood and blood products, inventory control, and optimize blood collection from blood donors. AI can use the existing data and consumption patterns to predict upcoming needs and prevent shortages, or oversupply of resources. Additionally, machine learning (ML) algorithms can positively affect blood inventory control and predict the right time and place for blood transfusion. Blood transportation can also be optimized using AI, so that transportation routes can be optimized, and delivery times can be minimized. Monitoring patients, especially patients who are in need of blood transfusion, can be improved through AI technologies. Patient data is collected and analyzed in real-time by using sensors and wearable devices, which assists physicians in making better decisions. AI algorithms can also predict side effects resulting from blood transfusions and can help reduce risks and improve patient safety. AI can predict the probability of side effects and recommend necessary preventive measures.

Conclusion:

AI can serve as an educational tool for healthcare staff and teach necessary skills for managing blood-related crises through simulations. Despite its numerous advantages, AI has created challenges such as data privacy issues and resistance against changes being made among the medical staff. Due to the increasing advancements in AI technology, it is expected that this technology will serve a much more important role in the patient's blood management. Close collaboration of researchers, physicians, and IT professionals is required to achieve the said goals.

Keywords: Patient Blood Management (PBM) 1, Artificial Intelligence (AI) 2, Data Analysis 3, Transfusion Medicine 4, Machine Learning 5

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PAI-20

Abstract Type: Narrative Review

The Application of Artificial Intelligence in the Morphological Diagnosis in Hematology and Clinical Practice: A Review Article

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Background and Aim: Accurate cell morphology diagnosis in hematology is essential for identifying blood disorders like anemia and leukemia, requiring skilled personnel and time due to its complexity. Artificial Intelligence (AI), leveraging advanced algorithms, can automate tasks such as pattern recognition and problem-solving, mimicking human cognitive abilities. With rapid advancements in AI, its application in hematology has become increasingly viable, enabling faster and more precise detection of cell morphology. This study examines the potential of AI technology to enhance the diagnosis of blood disorders by improving the speed and accuracy of cell morphology analysis in hematology laboratories.

Method: We obtained the materials used in our study via PubMed and Google Scholar search from 2020 through 2024. The keywords were “Hematology”, “Artificial Intelligence” AND “Blood Morphology”.

Result: Studies have shown that the ChatGPT-4 model demonstrated 88% accuracy in classifying normal blood cells when compared to a control group of experienced technicians, while its accuracy for abnormal cells was 54%, slightly exceeding the manual method's

accuracy of 49.5%. Additionally, the morphological identification of peripheral leukocytes is a complex and time-consuming process that requires high expertise. Results showed that AI-assisted leukocyte differentiation improved accuracy by 4.79% for normal cells and 15.16% for abnormal cells in novice technologists, and by 7.40% for normal cells and 14.54% for abnormal cells in intermediate technologists. Furthermore, both sensitivity and specificity were significantly enhanced with AI support, and the average time required to classify each smear was reduced by 215 seconds.

Conclusion: It seems that AI applications in hematology, particularly in the automation of cell morphology analysis, hold significant promise in improving diagnostic accuracy and efficiency. While the results of this review highlight the potential of AI, further studies are required to validate these findings, overcome existing challenges, and make AI tools more accessible and interpretable for clinicians**.**

Keywords: Hematology, Artificial Intelligence, Blood Morphology.

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PAI-21

Abstract Type: Original Research

In silico analysis of genes and molecular pathways involved in the pathogenesis of follicular lymphoma

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Abstract

Background and Aim: Follicular lymphoma (FL) is a prevalent subtype of non-Hodgkin lymphoma, characterized by abnormal B-cell proliferation within the germinal center. Although several genetic and molecular pathways have been implicated in FL pathogenesis, the primary mechanisms remain unclear. This study employs a systems biology approach to identify key genes and pathways associated with FL pathogenesis.

Methods: A bioinformatics analysis was conducted using the GSE32018 dataset from the Gene Expression Omnibus (GEO). This dataset includes 36 samples, comprising 23 FL and 13 healthy controls. Differentially expressed genes (DEGs) were identified using thresholds of log fold change >1 and $p<0.05$. Protein-protein interaction (PPI) networks were constructed using

STRING software to elucidate DEG interactions. Key hub genes, transcription factors (TFs), and microRNAs (miRNAs) were analyzed using the miRTarBase and TRUST databases.

Results: A total of 866 DEGs were identified, including 231 upregulated and 635 downregulated genes in FL samples compared to controls. PPI network analysis revealed seven hub genes: RPL37A, MRPS7, RPS14, RPS28, RPL34, RPS20, and RPS3. Among the miRNAs, hsa-miR-191-5p exhibited the highest interactions with the hub genes, while KDM5A was the most significant transcription factor.

Conclusion: This study highlights critical genes and molecular pathways involved in FL pathogenesis, providing potential targets for therapeutic development. These findings offer a foundation for designing strategies to inhibit FL cell proliferation and improve patient outcomes.

Keywords: Follicular Lymphoma; Molecular Genetics; Bioinformatics

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PAI-22

Abstract Type: systematic review

The role of artificial intelligence in predicting distant metastasis of breast cancer: A systematic review

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Background and Aim: Approximately 600,000 annual deaths worldwide are caused by breast cancer, with 90% linked to distant metastases. Breast cancer metastasis (BCM) involves the spread of cancer cells to lymph nodes (local-regional metastasis) or other organs (distant metastasis). The risk of distant metastases depends on factors such as tumor stage, grade, and type. Early detection enables timely intervention, improving survival rates and quality of life. Artificial intelligence (AI), using algorithms for prediction and analysis, plays a crucial role in BCM prediction. AI models help personalize treatment strategies and reduce unnecessary chemotherapy or radiation. This study systematically evaluates practical AI algorithms for BCM prediction.

Methods: This study followed the PICO framework, aligned with the research objective, and adhered to the PRISMA checklist. A systematic review of articles published from 2020 to 2024 was conducted across databases such as PubMed, SCOPUS, Web of Science, SID, Magiran, and Google Scholar, using Boolean operators and MESH keywords like "Breast cancer," "predict," "metastasis," and "Artificial Intelligence". Two independent researchers screened the articles based on inclusion criteria. After a critical assessment, six out of 99 initially identified studies were included in the review.

Results: Most studies emphasize the significant potential of AI algorithms in predicting BCM. The AdaBoost model, using genomic biomarkers and a decision tree algorithm, predicted distant metastasis risk with (92.6%) sensitivity and (95%) specificity. Radiomics-based models using contrast-enhanced computed tomography (CECT) showed strong potential for predicting lymph node metastases with sensitivity (82.4–88.2%) and specificity (88.7–96.3%). Conversely, the convolutional neural network (CNN) deep learning model, analyzing dynamic 3T-MRI images, had limited success in predicting distant metastasis, achieving (52.5%) sensitivity and (80.51%)specificity despite identifying correlations with critical biomarkers. Nevertheless, deep learning models analyzing imaging data reduced invasive procedures and improved diagnostic accuracy.

Conclusion: AI's emergence as a transformative tool in predicting BCM offers the potential to reduce unnecessary invasive procedures, improve the quality of clinical decision-making, personalize treatment, and enhance breast cancer management. Integrating AI into clinical workflows promises early diagnosis, risk stratification, and tailored therapies, reducing mortality and improving quality of life. However, achieving this requires overcoming challenges like model standardization, regulatory approvals, and equitable access to AI technologies across healthcare systems.

Keywords: Breast cancer, Predict, Metastasis, Artificial intelligence

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PAI-23
Abstract Type: Narrative review

Artificial Intelligence in Multiple Myeloma

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Abstract

Background and Aim: Multiple myeloma (MM) is a concerning and debilitating hematologic malignancy characterized by clonal proliferation of plasma cells. Despite significant advancements in treatment, MM remains an incurable cancer. However, there is new insights now days, where artificial intelligence (AI) has emerged as a powerful tool with the potential to revolutionize MM management. This review aimed to explore the current applications of AI in MM, including role in diagnosis, prognosis, treatment selection, and monitoring as well as future prospects.

Methods: A comprehensive literature search was conducted using PubMed and Google Scholar to identify relevant articles published in the past five years. The search terms included "multiple myeloma" "artificial intelligence" "machine learning" "deep learning" "image analysis" and "omics".

Results: AI has demonstrated significant potential in various aspects of MM management. In diagnosis, AI-powered image analysis techniques enhance the accuracy and efficiency of identifying MM, especially in cases with subtle or atypical features. In prognosis, AI algorithms predict patient outcomes by integrating clinical, laboratory, and genomic data, enabling personalized treatment strategies. In treatment selection, AI-driven models can identify patients most likely benefit from specific therapies, optimizing decisions while minimizing adverse effects. Furthermore, AI supports monitoring by analyzing imaging data to track disease progression and treatment response, facilitating early relapse detection and timely treatment adjustments. Additionally, AI accelerates drug discovery by analyzing large-scale genomic and proteomic data to uncover novel therapeutic targets and drug candidates

Conclusion: AI has the potential to significantly improve the diagnosis, prognosis, treatment, and monitoring of MM. By integrating AI into clinical practice, patient outcomes can be enhanced and the overall quality of care for individuals with MM could improve. Future research should focus on developing robust AI models and validating their clinical utility in large-scale studies.

Keywords: multiple myeloma; artificial intelligence; machine learning; deep learning; image analysis; omics

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PAI-24
Abstract Type: Narrative review

Leveraging CD47 Biomarkers and Machine Learning Algorithms for Predicting Graft Rejection

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Abstract

Background and Aim: Graft rejection poses significant challenges in organ transplantation, especially in the early postoperative stages. Current diagnostic methods, predominantly invasive biopsies, are associated with patient discomfort, high costs, and potential delays in intervention. CD47, a key immunoregulatory molecule, has emerged as a pivotal factor influencing graft outcomes through its interactions with immune pathways. This study aims to systematically review the role of CD47 biomarkers and explore the potential of integrating artificial intelligence (AI) to predict graft rejection, thereby reducing dependence on invasive diagnostics.

Methods: A systematic literature review was conducted, focusing on studies examining the role of CD47 in graft rejection and its modulation in transplantation. Databases including PubMed, Scopus, and Web of Science were searched for articles published up to 2024. Relevant data on CD47 expression, its effects on macrophage activity, T-cell responses, and ischemia-reperfusion injury (IRI) were extracted. Machine learning algorithms, including XGBoost, Random Forest, and Support Vector Machines (SVM), were reviewed for their utility in predicting graft rejection. These models incorporated biomarkers such as CD47 levels, eGFR, creatinine, and inflammatory markers, alongside patient demographic and medical history data.

Results: The findings reveal that CD47 modulation plays a dual role in transplantation. While CD47/SIRPα interactions inhibit macrophage-mediated graft rejection, its blockade enhances graft survival in mismatched transplants by reducing inflammation. However, CD47 inhibition may increase T-cell activation, complicating its application. Machine learning algorithms, particularly XGBoost, Random Forest, and SVM, demonstrated high accuracy in predicting graft rejection. These AI models leveraged multimodal data, including biomarkers and clinical variables, and provided explainable outputs using Explainable AI (XAI) tools, which enhanced clinician trust and supported timely decision-making.

Conclusion: CD47 biomarkers represent a critical axis in understanding and mitigating graft rejection. The integration of AI-driven predictive tools, employing advanced machine learning algorithms, offers a transformative approach to transplantation care by enabling early intervention, reducing reliance on biopsies, and supporting personalized treatment strategies. Further research is warranted to optimize CD47 modulation and validate AI models in diverse clinical settings.

Keywords: CD47; graft rejection; transplantation; biomarkers**,** artificial intelligence.

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PAI-25
Abstract Type: A Systematic Review

Revolutionizing Anemia Diagnosis: The Role of Artificial Intelligence in Enhancing Clinical Outcomes

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Abstract

Background and Aim: Anemia is a prevalent blood disorder with significant implications for global health. Effective diagnosis and management of anemia are essential for optimizing patient outcomes. Traditional diagnostic methods often rely on isolated data sources, which can hinder their effectiveness. The integration of artificial intelligence (AI) technologies presents a promising solution to enhance diagnostic accuracy. This systematic review aims to assess the application of AI in the diagnosis of anemia and evaluate its impact on diagnostic efficiency and patient management. The focus is on multifaceted approaches that integrate various data sources, including laboratory results, imaging, and patient history.

Methods: We conducted a comprehensive search of relevant literature across several electronic databases, including PubMed, Scopus, and Web of Science. The review covers studies published between 2013 and 2023. Out of 1500 articles identified in the initial search, 1466 articles were excluded due to lack of relevance to the inclusion criteria. Finally, 34 studies were selected for the final analysis. Both qualitative and quantitative studies were meticulously analyzed to assess the effectiveness of AI-based approaches. This review includes studies evaluating both adult and pediatric populations diagnosed with anemia. The integration of AI technologies, including machine learning algorithms, deep learning for image analysis, and

natural language processing for extracting insights from electronic health records, was evaluated. We compared traditional diagnostic methodologies with those enhanced by AI to determine improvements in diagnostic accuracy and clinical outcomes.

Results: The findings indicate that AI-driven methodologies significantly improve diagnostic accuracy, streamline the identification process of anemia, and support predictive analytics for better personalized treatment strategies. Notably, studies showed a 20-30% increase in diagnostic precision when using AI-assisted tools compared to traditional methods. Furthermore, AI applications demonstrated the ability to analyze complex datasets, reducing the time needed for diagnosis from days to mere minutes, thus enabling timely intervention. In addition, integrating AI technologies into clinical workflows has led to enhanced workflow efficiency, contributing to a more effective anemia management strategy that aligns with individual patient needs.

Conclusion: The integration of AI in the diagnosis of anemia presents transformative potential, facilitating comprehensive assessments through the utilization of diverse data sources. These advancements promote earlier detection, personalized treatment plans, and ultimately improved patient outcomes. Future research should explore the long-term implications of AI implementation in clinical settings and address the challenges related to data integration and algorithm transparency.

Keywords: Anemia Diagnosis, Artificial Intelligence, Machine Learning, Diagnostic Accuracy, Predictive Analytics

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PAI-26

Abstract Type: Systematic Review

Artificial Intelligence A New Approach in Early Diagnosis of Lung Cancer: A Systematic Review Article

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Background and Aim: Lung cancer is one of the most common cancers and the leading cause of cancer-related deaths worldwide. Most lung cancers are diagnosed at intermediate or advanced stages. The overall five-year survival rate of lung cancer is less than 20% and around 2% in advanced stages. This rate is about 70–90% in the early stages of the disease. Therefore, early detection of lung cancer is crucial and can improve the survival rate significantly. Artificial intelligence (AI) has shown remarkable results in early diagnosis of lung cancer. In this study, we examine AI's role in lung cancer diagnosis and its limitations.

Method: This systematic review article was performed using articles published on PubMed, Google Scholar, Science Direct and Clinical Trial until 2024. The keywords were Artificial Intelligence OR AI AND Lung Cancer AND Diagnosis AND Human. By searching these databases, 169 articles were found, and 127 were removed by reading titles and abstracts. 42 articles were selected under the inclusion criteria. All articles were chosen from English articles. Duplicate articles, non-English and ex-vivo articles were excluded.

Results: According to articles, there are many challenges in the early detection of lung cancer through traditional methods. These include the tumor's location, pathological type, complexity of detecting neoplastic changes in pulmonary nodules, the presence of metastasis, and its complications. Previously, cancer diagnosis was primarily performed through tissue biopsy and CT scans, both of which had issues. CT scan images of lung nodules are complex, and accurate diagnosis depends on the radiologist's experience. Manual film reading is difficult and often leads to missed diagnosis or misdiagnosis and Biopsy is an invasive method. Therefore, there was a fundamental need for a new strategy to simplify the data and reduce observational errors. Today, artificial intelligence has emerged as an innovative solution with the potential to improve diagnostic accuracy and interpret existing data through various methods, including machine learning (ML), deep learning (DL), computer vision (CV), neural networks (NN), and natural language processing (NLP**)**

Conclusion: It seems that the emergence of artificial intelligence has led to significant evolution in various sciences, and oncology is no exception. AI has the potential to develop models that can diagnose lung cancer in its early stages and provide personalized treatments both at the time of diagnosis and throughout treatment. However, there are some limitations to AI's widespread application. These include ethical considerations, data security, algorithmic biases, and AI's reliance on public databases.

Therefore, further investigation into the application of AI in lung cancer diagnosis is strongly recommended.

Key Words: Artificial intelligence, Lung cancer, Diagnosis, Early detection

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PAI-27

Systematic Reviw

Artificial Intelligence in breast cancer Diagnosis and Treatment:Advences Challenges,and New perspectives.

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Background and Aim:

Breast cancer is one of the most common types of cancer in women and, despite advancements in treatment, remains one of the leading causes of death. Early detection is crucial, as survival rates are closely linked to the stage at which the cancer is diagnosed. Traditional diagnostic methods, such as mammography, ultrasound, and histopathology, have limitations, including false-positive results and variability in assessments. Artificial intelligence (AI) has emerged as a promising solution to address these challenges. Through machine learning (ML) and deep learning (DL), AI can analyze medical images—such as mammograms and histopathology slides—and detect subtle changes in breast tissue. Additionally, AI contributes to personalizing treatment plans and identifying new drug targets. Advances such as surgical robots and remote monitoring tools also enhance AI's role, improving surgical precision and enabling better patient health monitoring.

Methods:

Relevant articles were collected between April 2024, and August 2024, from databases including Google Scholar and PubMed. A total of seven articles were included in this systematic review.

Results:

The integration of AI in breast cancer diagnosis and treatment holds significant promise. AI enhances the accuracy of early detection, leading to better treatment outcomes and improved survival rates. It also supports personalized treatment plans by analyzing patient data and suggesting tailored therapies. Furthermore, AI aids in monitoring treatment responses and detecting recurrences, enabling timely interventions. However, challenges such as the lack of

standardized data, validation complexities, and the need for large-scale, real-world studies remain significant barriers. Despite these challenges, recent trials, such as MASAI and AITIC, show promising results in breast cancer screening, with AI improving detection rates and screening efficiency. Continued collaboration and investment in infrastructure are essential to

Conclusions:

AI has immense potential to transform breast cancer diagnosis and treatment by enhancing early detection, personalizing care, and improving overall patient outcomes. Technologies such as deep learning algorithms, surgical robots, and remote monitoring systems have already demonstrated their ability to increase diagnostic accuracy and optimize treatment plans. Despite this progress, challenges such as data quality, ethical concerns, and the current limitations of AI in clinical settings remain significant. However, ongoing research and collaboration are gradually addressing these barriers, paving the way for more efficient, accurate, and individualized breast cancer care in the future.

overcome these barriers and fully realize AI's potential in clinical oncology.

Keywords:Breast Cancer.Artificial Intelligence,Diagnosis

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PBa-1
Abstract Type: Systematic Review

Association of infertility and bacterial infections in male and female

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Abstract

Background and Aim: Infertility is a health problem that affects approximately 10% of the world's population. This disease affects one in seven couples and can be caused by female factors, male factors, or both. Infectious diseases such as bacteria, viruses, and fungi can affect a variety of human functions, including reproduction and pregnancy. As previously indicated, infections brought on by infectious agents are widespread worldwide and significantly affect reproductive health. This study is referred to present parameters involved in infertility male and female.

Methods: This study has been explored the published research articles in four databases including PubMed, Web of Sciences, Scopus, Google Scholar by using male infertility, female

infertility, bacteria and *Mycoplasma genitalium* as keywords from February 2019 to September 2024. We examined the agents related to infertility factors and therapeutic methods in obtaining articles.

Results: Many studies have shown that infertility factors such as low sperm count, slow motility, and abnormal spermatogenesis in male and sexually transmitted infections (STDs) caused by *Neisseria gonorrhoeae*, Chlamydia trachomatis, and *Mycoplasma genitalium* and anovulation are common causes of tubal infertility (TFI) in females. For sterile treatment, it is recommended to consider an appropriate method of treating bacterial infections in the first step, since antibiotic resistance has been identified in these bacterial treatments.

Conclusion: The results of this study show that bacterial agents are effective in male and female infertility, so they should be diagnosed in time and appropriate treatment applied.

Keywords: male infertility, female infertility, Mycoplasma genitalium, Neisseria gonorrhoeae, Chlamydia trachomatis.

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PBa-2
Abstract Type: Systematic Review

Novel laboratory diagnostic methods for macrolide resistance in *Mycoplasma genitalium*

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Abstract

Background and Aim: *Mycoplasma genitalium* is seen as a reemerging microorganism and belongs to genital mycoplasmas. It is responsible for sexually transmitted infections in men and women. Macrolide resistance increasingly appears in the worldwide, so detecting methods for samples resistance to macrolide are considered. This study refers to novel laboratory diagnostic methods for macrolide resistance in *Mycoplasma genitalium*.

Methods: The published research articles related to novel laboratory diagnostic methods for macrolide resistance in *Mycoplasma genitalium* were searched in four databases including Web of Sciences, PubMed, Google Scholar and Scopus by using *Mycoplasma genitalium*, macrolide, resistance and diagnose as keywords from February 2019 to September 2024.

Results: Many studies showed that novel laboratory diagnostic methods for macrolide resistance in *Mycoplasma genitalium* are Mg MacrolideR qPCR, Aptima MG (AMG), ResistancePlus MG (RPMG), ResistancePlus, RPMG Flex, MGMR PCR, Macrolide-R/MG

ELITe MGB kit, MgparC-AsyHRM that among them some methods can identify macrolide resistance mutations. The specificity and sensitivity of these methods range from 94-98% and 95-100%, respectively. **Conclusion:** These methods provide high specificity and sensitivity, affordable and can be substituted in the current detection in laboratory. Therefore, using this methods as rapid detection and potent tools can control and therapy patients with macrolide resistance in *Mycoplasma genitalium* infections.

Keywords: *Mycoplasma genitalium*, macrolide resistance, diagnostics.

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PBa-3
Abstract Type: Systematic Review

Novel laboratory diagnostic techniques for brucellosis

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Abstract

Background and Aim: Brucellosis is the most zoonotic infectious disease that transmitted from animals to humans, and caused by the *Brucella* genus as a Gram-negative bacterium. It seems to reemerging in recent years as a public health challenges and many studies have been executed on diagnostic techniques for brucellosis in the laboratory. Also, it is known as an acquired infection through laboratory in the world. To control the disease diagnosis assays are considered. This study presents novel laboratory diagnostic techniques for brucellosis.

Methods: Four databases were used to explore the published research articles correlated to novel laboratory diagnostic techniques for brucellosis including PubMed, Web of Sciences, Scopus, Google Scholar databases using keywords *Brucella*, human brucellosis, diagnosis, serology test, protein, nucleic acid amplification for articles published between February 2019 to September 2024.

Results: Many reports demonstrated some novel laboratory diagnostic techniques including: molecular (URS-PCR, Real-time RPA, DNA aptamer, LAMP assay, PSR assay, PMA-qPCR, RT-LAMP assay, PCR-RFLP and REP-PCR) and serological (Label-free electrochemical immunosensor, RVFT, quantum dot-based immunochromatographic test strip, mAbs, rOmp and LFA). Also, protein immunoassay and bacteriophage-detecting techniques leading to high sensitivity and specificity in comparison with Rose Bengal test (RBT), complement fixation test (CFT). The diagnostic antigen are *Brucella* species lipopolysaccharide (LPS) or outer membrane proteins (OMP) extracted from serum samples.

Conclusion: The results of this study showed that molecular, serological, protein and bacteriophage immunoassays techniques are highly specific and sensitive methods used for

detecting Brucellosis quickly without using complex equipment and grouped as reliable techniques.

Keywords: *Brucella*, human brucellosis, diagnosis, serology test, protein, nucleic acid amplification.

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PBa-4
Original Research

MecA Genes Monitoring in Diabetic Foot Infection in Ardabil City, Iran

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Abstract

Background and Aim: Diabetic Foot infections (DFIs) are one of the frequent complications of patients with diabetes. DFIs are often poly microbial and microbiology of these infections shows that it is rarely static that includes aerobic and anaerobic organisms. Therefore, the aim of this study was to investigate facultative anaerobic and obligate anaerobic bacteria isolated from diabetic foot ulcers of diabetic patients and determine the antibiotic sensitivity pattern and *mecA* gene in *Staphylococcus aureus* isolated from it in Ardabil, Iran.

Methods: 80 Samples were collected from Imam Khomeini hospitals, Ardabil, Iran from March to February 2022 and were cultured using optimal aerobic and anaerobic microbiological techniques. Identification of bacterial isolates was performed through standard microbiological methods and antibiotic susceptibility testing was performed based on administered Clinical and Laboratory Standards Institute (CLSI) guidelines. Combine disk method was used to detect ESBL producing bacteria and the detection of *mecA* gene was performed by PCR assay.

Results: 119 bacterial strains were isolated from 80 samples of diabetic foot ulcers. Predominant aerobic bacteria that were isolated from these infections were S. aureus with 34 isolate and followed by coagulase-negative *Staphylococcus* spp. with 21 isolates and *Enterobacteriaceae* family including *Escherichia coli* with 18, *Citrobacter* spp. with 5, *Enterobacter* spp. with 5, and, *Enterococcus* spp. with 18, *Pseudomonas aeruginosa* with 8 and *Acinetobacter* spp with 5 and *Bacteroides fragilis* with 5 isolates obtained from anaerobic culture. All Gram-positive isolates were susceptible to linezolid while all *Enterobacteriaceae* showed sensitivity to imipenem. According to PCR method from 13 methicillin resistance *S. aureus* that were demonstrated with cefoxitin (30µg) disk, 12 isolates had *MecA* gene.

Conclusion: The high prevalence of MRSA in DFUs represents the high levels of antibiotic usage among patients with diabetes. In this study, resistance to other important clinical antibiotics was detected among MRSA isolates. Predominant bacteria were *S. aureus* and *B. fragilis*. These wounds may require the use of combined antimicrobial therapy as the initial management.

Keywords: Diabetic foot infections, antibiotic susceptibility pattern, anaerobic bacteria, MRSA, PCR

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PBa-5

Abstract Type: Systematic Review

Nanoparticles-based CFP-10 and ESAT-6 genes for *Mycobacterium tuberculosis* detection

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Abstract

Background and Aim: The definitive diagnosis of active Mycobacterium tuberculosis requires bacterial culture through sputum or biopsy, which may take weeks. The diagnosis of *Mycobacterium tuberculosis* is considered for managing disease. The aim of this study was to present diagnostic methods based on nanoparticles for CFP-10 and ESAT-6 genes.

Methods: The published research articles related to effective nanoparticles in the detection of CFP-10 and ESAT-6 genes were explored, which will lead to diagnosis of *Mycobacterium tuberculosis*. By searching in Web of Sciences, Google Scholar, Scopus and PubMed between February 2018 and September 2024, using index words: *mycobacterium tuberculosis*, rapid diagnostic tests, rapid detection, ESAT-6, CFP-10, nanoparticles.

Results: Using AuNP-based-RDTs (gold nanoparticle (AuNP)-based rapid diagnostic tests) can reduce time of LFIA to 15 minutes, which makes it possible to use this method in mobile clinics and field hospitals. The use of MB-AuNP-I-PCR due to having less incubation and washing steps reduces the overall time and increases accuracy by reducing the background signals, which makes it more sensitive than magneto ELISA and GeneXpert assay methods. Also, the direct and quantitative detection of two CFP-10 and ESAT-6 genes antigens in serum

by Nano Disk-MS can increase the speed and accuracy, regardless of the location of the disease or culture status.

Conclusion: The result of this study indicated that diagnosis of *Mycobacterium tuberculosis* using nanoparticles-based CFP-10 and ESAT-6 genes are rapid, highly specific and sensitive and reliable methods.

Keywords: *mycobacterium tuberculosis*, nanoparticles, rapid detection, ESAT-6, CFP-10

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PBa-6

Molecular Typing and biofilm formation analysis of multidrug resistant *Klebsiella pneumoniae* clinical isolates recovered from ICU patients by Enterobacterial Repetitive Intergenic Consensus Polymerase Chain Reaction

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Abstract

Background and Aim: Klebsiella pneumoniae is one of the most important causes of nosocomial infections. Today, prevalence of MDR infections increases dramatically worldwide. These strains are usually a major threat to patients with serious health conditions due to the ineffectiveness of treatments. Enterobacterial repetitive intergenic consensus polymerase chain reaction (ERIC-PCR) technique is a quick, reliable, and cost-effective method for molecular typing of Enterobacteriaceae family members. This study is aimed at assessing the genetic diversity, antimicrobial resistance pattern, and biofilm formation in K. pneumoniae isolates obtained from patients with ventilator-associated pneumonia (VAP) hospitalized in an intensive care unit (ICU) in Iran.

Methods: Seventy *K. pneumoniae* isolates were obtained from patients hospitalized in the ICU. Initial detection of *K. pneumoniae* isolates was done by chemical and conventional microbiological methods. To genotypic confirmation of isolates, DNAs were extracted and the presence of ureD gene was assessed. To detect MDR strains, antimicrobial susceptibility testing was done using the Kirby-Bauer disc diffusion method. The antibiotics discs were as follow: meropenem, piperacillin/tazobactam, tobramycin, ciprofloxacin, gentamicin, and imipenem. Biofilm formation was evaluated through the microtiter plate assay (MTP) Method. Genetic diversity was also analyzed by ERIC-PCR and using the primer ERIC1R (5′-ATG TAA GCT CCT GGG GAT TCAC-3′) and the primer ERIC2 (5′-AAG TAA GTG ACT GGG GTG AGC G-3′). The BioNumerics software was used for band profile analysis. For dendrogram construction, genetic similarity analysis was performed using Unweighted Pair Group Mean Method with Arithmetic mean (UPGMA), Dice similarity coefficient, and 1% band position tolerance.

Results: K. pneumoniae isolates had varying levels of resistance to antibiotics meropenem (80.4%), piperacillin/tazobactam (70%), tobramycin (61.4%), ciprofloxacin (57.7%), gentamicin (55.7%), and imipenem (50%). Around 77.14% of isolates were MDR, and 42.8% of them formed biofilm. Genetic diversity analysis revealed 28 genotypes (E1–E28) and 74.28% of isolates were grouped into ten clusters (i.e., clusters A–J). Clusters were further categorized into three major clusters, i.e., clusters E, H, and J. Antimicrobial resistance to meropenem, tobramycin, gentamicin, and ciprofloxacin in cluster J was significantly higher than cluster H, denoting significant relationship between ERIC clusters and antimicrobial resistance. However, there was no significant difference among major clusters E, H, and J respecting biofilm formation.

Conclusion: *K. pneumoniae* isolates obtained from ICU patients have high antimicrobial resistance and genetic diversity. This diversity causes problems for treatment of infections due to the circulation of diverse *K. pneumoniae* clones, which possibly have different antimicrobial susceptibility patterns. **T**hese findings can help up better predict MDR *K. pneumoniae* outbreaks associated with specific genotyping patterns. Additionally, increased rate of VAP may be associated ventilator contamination. Therefore, establishment of effective infection control system in hospitals could decrease spreading of resistant strains within the hospitals and subsequently transmission of infection to patients.

Keywords: MDR Klebsiella pneumonia; Ventilator-Associated Pneumonia; ERIC-PCR; Genetic Diversity; Biofilm

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PBa-7

Abstract Type: Narrative review

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Chicken immunoglobulin (IgY) as an alternative treatment for bacterial infections, emphasizing advantages, disadvantages and mechanisms

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Abstract

Background and Aim: The overuse of antibiotics has led to an alarming spread of drug-resistant microbial infections, creating an urgent need for new therapeutic technologies. This issue has become a significant concern in recent years due to the increase in mortality rates, especially in hospital infections. One of these technologies that has attracted attention as an alternative or complementary treatment for bacterial and viral infections is chicken immunoglobulin)IgY). A research gap exists regarding the mechanism of action, benefits, and possible side effects of these antibodies so the purpose of this study is to examine these issues.

Methods: In this review, a comprehensive search was conducted using the keywords [Chicken IgY OR immunoglobulin Y OR egg yolk antibody] AND [Bacteria* infect*] across the Pubmed, Pubmed Central (PMC), and Science Direct databases. Additionally, relevant research articles within the fields of immunology and microbiology were identified using the keywords [Chicken IgY OR immunoglobulin Y OR egg yolk antibody] AND [Bacterial infection] specifically within the Science Direct database. This study involved selecting articles from the past ten years, specifically from 2013 to February 2023.

Results: Mechanisms such as inhibiting bacterial attachment, increasing opsonization of pathogens, modulating immunity and finally neutralizing toxins are more prominent. The IgY Advantages include the following: Reducing inflammation, Reduce the transmission of resistance genes, Protective activity for 5 to 10 years at a 4 °C, Non-interaction with host factors such as complement system, rheumatoid factor and FC receptor, Low probability of allergies,

Not cause any complications, More tendency to bind to their target antigens compared to IgG, Its ease, low cost and non-invasiveness, large amounts in egg yolk, Longer shelf life than IgG, Long-term use, especially in sensitive groups, Its high effectiveness, No precipitation in poultry meat. The IgY Disadvantages include the following: Attenuation of its effectiveness by human antibody against IgY, Its breakdown by the digestive system, Its lack of inhibitory properties after toxin binding to the target, Antibody-dependent enhancement (ADE), acute nausea and vomiting in some people.

Conclusion: Antibodies have a natural structure similar to human proteins, making them an effective tool in treating various microbial infections. Recent studies have shown that their side effects or minor disadvantages, such as ADE, can be eliminated with the help of bioinformatics methods and the production of recombinant antigens. However, more research is needed to determine their appropriate dose and route of administration for widespread use in various infections.

Keywords: IgY antibodies; Mechanisms; Benefits; Bacterial infection; Adverse effects

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PBa-8

An evaluation of antibacterial effect of eugenol on *Staphylococcus intermedius* and *Staphylococcus pseudointermedius* bacteria isolated from external ear infections of dogs and comparing it with their antibiotic resistance profile

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Following various failures in the use of different chemical drugs and the emergence of serious resistant strains, mankind has started to produce natural medicinal products with the use of today's knowledge and technology. Eugenol which is one of the most important compounds of clove extract is a phenolic phytochemical substance with many antibacterial and antioxidant properties that has been widely used in pet medicine in recent

decades. This chemical substance acts effectively against a wide range of bacteria and does not cause risks such as drug resistance, therefore the current study was aimed to investigate the antibacterial effects of eugenol on *Staphylococcus intermedius* and *Staphylococcus pseudointermedius* bacteria isolated from ear canals of dogs with external otitis and compare their antibiotic resistance profile results.

Methods: Samples were taken from 20 dog collars whose otitis was confirmed, referred to Faculty of Veterinary Medicine Pet hospital, University of Tehran, and cultured on specific media to isolate *Staphylococcus intermedius* and *Staphylococcus pseudointermedius* species, and finally, MIC and MBC values of eugenol against bacteria were determined based on the microdilution method according to CLSI protocols. The results were analyzed using SPSS software and at 5% levels.

Results: The results showed that 75% of the studied samples were infected with *Staphylococcus intermedius* and *Pseudointermedius* bacteria, and golden retriever dogs were the most susceptible breed, and the highest drug resistance were reported to to clindamycin and penicillin (100 %) and and highest sensitivity to chloramphenicol (86 %) respectively. In addition, MIC and MBC values for eugenol were reported as 1.25 and 2.5 mg/ml. In this study, the diameter of eugenol non-growth halo was reported to be 26.25 mm.

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Conclusion: Based on the findings of this study, it can be stated that eugenol can be potentially used as one of the complementary treatment strategies in otitis in dogs.

Keywords: Eugenol, otitis, antibiotic, staphylococcus.

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PBa-9

Detection of intimin coding gene in *Escherichia coli* isolates obtained from shrimp

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Abstract:

Background and Aim: *E. coli* encompasses several important pathogenic subtypes, One of the pathogenic strains of *Escherichia coli* is enteropathogenic *E. coli* (EPEC), which adheres to the intestinal mucosa, disrupts the normal structure of microvilli, and increases intestinal

permeability, leading to watery to bloody diarrhea in both humans and animals. EPEC includes the virulence gene intimin (*eae*), and this study was conducted with the aim of identifying this virulence gene in *Escherichia coli* isolated from shrimp.

Methodology: In this study, a total of 96 shrimp were collected from supply centers throughout the city of Kerman and transported to the Microbiology Laboratory of Shahid Bahonar University of Kerman within 24 hours, stored on ice. Subsequently, a bag mixer or stomacher was utilized to homogenize the samples, and the resulting suspension was employed for cultivation and isolation in various culture media. In this research, the purified colonies were subjected to DNA extraction using the boiling method. The Touchdown PCR technique was employed to detect the virulence gene *eae* of the Enteropathogenic *Escherichia coli* (EPEC) pathotype. The samples were subsequently analyzed using gel electrophoresis, with observations made under UV light and data collected for analysis.

Results: The results indicated that out of the 96 shrimp samples collected, 76 (79.17%) were confirmed positive for *E. coli* based on biochemical tests. Among these, The prevalence of the intimin gene (*eae*) which encodes EPEC, was observed in 2 samples (2.63%).

Conclusion: Considering that the bacterium *Escherichia coli* is not naturally separated from shrimp and other aquatic organisms, but the results of the present study indicate a significant contamination of the analyzed shrimp with pathogenic strains of this bacterium. This underscores the necessity for further research and actions such as improving sanitary practices, ensuring the production of products with standardized packaging, and enhancing public awareness to achieve health goals and minimize the risks associated with this contamination.

Keywords: *E.coli,* Intimin**,** EPEC**,** shrimp, PCR.

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PBa-10

Abstract Type: Systematic Review

Novel methods for detection of Methicillin-resistant *Staphylococcus aureus* (MRSA)

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Abstract

Background and Aim: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of *Staphylococcus* bacteria that has developed resistance to many common antibiotics. MRSA infections primarily occur in individuals who have been in healthcare settings, such as hospitals, nursing homes, and dialysis centers. Symptoms of Severe MRSA Infections include chest pain, cough or difficulty breathing, fatigue, fever and chills, general malaise, headache, rash, non-healing wounds .The problem is that we need to be able to diagnose this bacteria more cheaply and quickly. This article presents the methods for diagnosing MRSA that are cost-effective and time-efficient.

Methods: We searched for a series of articles in the databases of Google Scholar, Scopus, Web of Science, and PubMed from February 2015 to June 2024. The keywords that we searched are Methicillin-resistant *Staphylococcus aureus*, MRSA, diagnosis, detection, novel, aptamer, CRISPR, *mecA* gene and rapid method.

Results: Recent studies show significant advancements in detecting methicillin-resistant *Staphylococcus aureus* (MRSA): A new method using dual aptamers and CRISPR-Cas12a enhances sensitivity for MRSA detection, a rapid CRISPR-mediated DNA-FISH technique allows for specific detection from cell lysates in 30 minutes, achieving a detection limit of 10 cfu/ml, a clinical study found that 45.8% of *S. aureus* from diabetic foot ulcers were MRSA, with PCR confirming *mecA* gene presence in 41.6%, PMA (Propidium monoazide)-crossing priming amplification (CPA) was optimized for detecting MRSA in the viable but non-culturable state, the cobas vivoDx MRSA assay offers rapid results from nasal swabs in about five hours, significantly faster than traditional culture methods. These innovations improve the speed and accuracy of MRSA detection.

Conclusion: We've come to the conclusion that we can utilize these new techniques for MRSA detection, as they are not only more cost-effective but also faster and more efficient.

Keywords: Methicillin-resistant *Staphylococcus aureus*, MRSA, diagnosis, detect, *mecA* gene and rapid method.

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PBa-11

Abstract Type: Review Article

Recent advances in laboratory detection of Chlamydia trachomatis using gold (Au) nanoparticle-based methods

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Abstract

Background and aim: *Chlamydia trachomatis* infections greatly affect people's quality of life and significantly contribute to the prevalence of sexually transmitted diseases. These infections are especially common in low-income countries and regions, such as the Middle East, Asia, Africa, and South America. The World Health Organization (WHO) acknowledges that *C. trachomatis* is a major global health concern, with a staggering 128.5 million new cases reported among adults in 2020. Consequently, it is vital to establish efficient laboratory diagnostic methods for this infection. However, the existing diagnostic techniques have limitations, emphasizing the necessity for new, rapid diagnostic platforms that can swiftly identify this pathogen with great accuracy, without the need for skilled technicians or significant expenses. One promising approach for addressing these challenges is the utilization of nanotechnology and gold nanoparticle-based methods to rapidly detect *C. trachomatis* infection.

Methods: The study findings were reported following the PRISMA 2020 guidelines. We conducted a systematic search of biomedical databases (PubMed, Scopus, Google Scholar, and Web of Science) to identify all relevant manuscripts published in English from January 2010 to December 2023. The search terms we used were: "*Chlamydia trachomatis* AND Laboratory detection AND Gold OR Au nanoparticle," "Chlamydia trachomatis AND Rapid Detection AND Gold OR Au nanoparticle," "*Chlamydia trachomatis* AND Point-of-care test AND Gold OR Au nanoparticle," "*Chlamydia trachomatis* detection AND Point-of-care test AND nanoparticle," "*Chlamydia trachomatis* AND nanoparticle-based detection," "*Chlamydia trachomatis* detection AND nanoparticle-based biosensor," and "Nanoparticle-based detection of *Chlamydia trachomatis*". In addition, we examined the references cited in these articles in order to discover more relevant articles. Out of the 73 papers, we identified 12 that specifically addressed our objective and were published between 2010 and 2023.

Results: In this section of the study, we focused on the latest advanced methods for detecting *C. trachomatis* infections using Au nanoparticles. Our investigation reviewed 13 studies that suggested various techniques for effectively detecting *C. trachomatis* with the use of nanoparticles. We compared different methods based on their characteristics. The data extraction and analysis process involved categorizing all information about *C. trachomatis* and diagnostic methods worldwide that utilize Au nanoparticles. This information included the method type, nanoparticle type, sample type, turnaround time, limit of detection, purpose of the studies, and application of these methods based on authors' recommendations. Based on the findings, these studies have pointed out the benefits of gold nanoparticles in the efficient and quick detection of *C. trachomatis*.

Conclusion: This review discusses novel methods for detecting *C. trachomatis* infection utilizing gold nanoparticles. The primary goal of these research studies is to introduce new approach that is highly sensitive and specific, cost-effective, rapid, and capable of detecting *Chlamydia* at low concentrations. Additionally, a key aspect highlighted in these studies is the importance of point-of-care capability, which is critical for diagnosis, preventing transmission, and ensuring prompt treatment. Nevertheless, further assessment is necessary to improve the sensitivity and specificity of these methods in vivo and clinical trial studies

Keywords: STDs, *Chlamydia trachomatis*, Gold nanoparticle, STIs, Laboratory diagnosis

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PBa-12
Abstract Type: Systematic Review

Activity of Antimicrobial Peptides against *Pseudomonas aeruginosa* infections

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is a gram-negative bacteria which belongs to *Pseudomonas* genus. It typically targets the respiratory system and show itself with severe coughing. In this study, due to importance of *P. aeruginosa* infections and its increased resistance to common antibiotics, the Antimicrobial peptides (AMPs), have been discussed.

Methods: We searched multiple articles on 4 databases including: Google Scholar, PubMed, Web of Science and Scopus about AMPs and *P. aeruginosa*. The time period, selected on February 2019 to June 2024 and the antimicrobial peptides, antimicrobial resistance, multidrug resistant bacteria and *P. aeruginosa* were searched as keywords.

Results: The results obtained from the studies showed that a novel hybrid AMP for killing *P. aeruginosa* constructed by addition a targeting peptide, OprF porin on *P. aeruginosa*, showed high specificity for *P. aeruginosa* and was significantly greater than that conventional antibiotics in a mouse model. Also, AMPs can be used as inhalation therapy for *P. aeruginosa*. A novel frog AMP called Nigrosi-6VL, reported to be used against *P. aeruginosa* biofilms, which can synergies effectively with cefepime & gentamicin against *P. aeruginosa* biofilms. Trp-containing AMP were found to penetrate the bacterial cell membrane and to bind with genomic DNA of MRR0108. In addition, Trp-containing peptides can reduce the expression of DNA replication initiator genes.

Conclusion: Taken together AMPs hold promise decreasing resistance of cells in *P. aeruginosa* infections and can be for cell or surface infections. Also, by merging them with regular antibiotics, better activities will be shown.

Keywords: antimicrobial peptides, *P. aeruginosa*, antimicrobial resistance, multidrug resistant bacteria and therapeutic.

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Comparative Analysis of Antibacterial Activity of Nickel Oxide Nanoparticle among O-Serotypes of Uropathogenic *Escherichia coli*

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Abstract

Background and Aim: Nanoparticles (NPs) have emerged as a promising therapeutic strategy due to their potential antimicrobial activities. This study aimed to evaluate the antibacterial and anti-biofilm activities of nickel oxide (NiO) nanoparticles against uropathogenic *Escherichia coli* (UPEC) O-serotypes isolated from patients with urinary tract infections (UTIs), based on ERIC-typing.

Methods: A total of 153 UPEC isolates were evaluated for O- serotyping and ERIC-typing by PCR assay. The sol-gel method was used to synthesize the NiO nanoparticle. NiO nanoparticle minimal inhibitory concentration (MIC) was determined by standard broth microdilution. Anti-biofilm activity was assayed by a microtiter-plate screening method.

Results: A Out of 153 UPEC isolates, O2, O4, O6, O8, O15, O16 and O25 were common detected serogroups and O25 was most prevalent serogroup. The results of ERIC-PCR revealed that UPEC isolates were classified into 19 different ERIC-types with 80% similarity including 13 common types and 6 unique types. There was no significant correlation or association between O-serogroups and ERIC-PCR clusters ($p > 0.05$). NiO nanoparticle were exhibited antibacterial effect with MIC at a concentration of 250 to 500 mg/ml against most UPEC isolates and significantly ($P=0.001$) inhibit the biofilm formation at a concentration of 500 to 125 mg/ml.

Conclusion: Our results demonstrated that NiO nanoparticles exhibited promising antibacterial and anti-biofilm activity against biofilm-producing and drug-resistant UPEC strains. Consequently, NiO nanoparticles have the potential to be a valuable therapeutic option as an alternative treatment for bacterial infections.

Keywords: Uropathogenic *Escherichia coli*, Antibacterial, Biofilm, O-Serotype, Urinary tract infection, Nickel oxide nanoparticle, ERIC; Enterobacterial Repetitive Intergenic Consensus,

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PBa-14
Narrative review article

Exploring the gut microbiota as a promising target for breast cancer treatment

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Breast cancer is a heterogeneous disease and highly prevalent malignancy affecting women globally. Breast cancer treatments have been demonstrated to elicit significant and long-lasting effects on various aspects of a patient's life, including physical, emotional, social, and financial, highlighting the need for comprehensive cancer care. Recent research suggests that the composition and activity of the gut microbiota may play a crucial role in anticancer responses. **Methods:** we conducted a comprehensive literature review of databases including PubMed, Google Scholar, Embase and Scopus using the keywords "gut microbiota", " gut microbial population/composition", "cancer treatment", "breast cancer", "breast cancer treatment", "breast cancer prognosis", "gut microbial alteration", "prebiotics", "symbiotics", "postbiotics" and "microbial supplementation" aiming to elucidate the role of gut flora and its alteration in population in determination of BC treatment response and prognosis.

Results: Various compositional features of the gut microbial population have been found to influence both the clinical and biological aspects of breast cancer. Notably, the dominance of specific microbial populations in the human intestine may significantly impact the effectiveness of cancer treatment strategies. Therefore, the manipulation of the microbiota to improve the anticancer effects of conventional tumor treatments represents a promising strategy for enhancing the efficacy of cancer therapy.

Conclusion: Alterations in the gut microbiota composition and activity have the potential to impact breast cancer risk and treatment outcomes

Keywords: Breast cancer, Gut microbiota, Gut flora, Microorganism, Anticancer.

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PBa-15
Abstract Type: Original Research

Potentially Probiotic Bacteria Isolated from Preparation Stages of Kermanshahi Traditional Fat

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Abstract

Background and Aim: Dairy-fermented foods such as yogurt, cheese, fermented milk, buttermilk, curd, butter, and ghee are major diet ingredients in the west of IRAN, such as in Kermanshah province. Ghee (Kermanshahi traditional oil or roughage heiwâni) is traditionally produced from butter milk of yogurt after fermentation. A literature review yielded no study on isolating probiotics from Kermanshahi traditional oil preparation stages. Therefore, the study's purpose was to focus on isolating and identifying lactic acid bacteria in these products using culture and PCR-sequencing methods.

Methods: Fifteen samples of dairy products including yogurt, butter, and Kermanshahi traditional oil were collected in Kermanshah province, Iran. Each sample was diluted, homogenized, and cultured on a selective medium for the growth of lactic acid bacteria. 16SrRNA gene sequence analysis was carried out for the final of these isolates.

Results: After culturing samples on MRS and M17 under aerobic and anaerobic conditions, a total of 78 strains of bacteria were isolated and identified by conventional biochemical tests. The frequency of bacteria in all isolates (78) was 48.71% for Lactobacillus, 33.33% for Streptococcus, 6.41% for Enterococcus, and 6.41% for Bacillus. Lactobacillus, Streptococcus, Enterococcus, and Bacillus genus, were isolated from 84.44%, 57.78%, 11.11%, and 15.56% of all three kinds samples, respectively.

Conclusion: Based on our findings, Lactic acid bacteria and other potentially probiotic microorganisms are present in Kermanshahi traditional oil. Of course, the potential probiotic properties of these isolates and the impact of consumption of Kermanshahi traditional oil containing those on human health need to be analyzed more. By proving the presence of probiotic bacteria in Kermanshahi oil, it may fall into the category of functional foods.

Keywords: Dairy, Kermanshahi traditional oil, Lactic acid bacteria, PCR sequencing, Probiotics

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PBa-16

Abstract Type: Systematic review/ Meta-analysis Research

Global prevalence of mutation in the *mgrB* gene among clinical isolates of colistin-resistant *Klebsiella pneumoniae*: a systematic review and meta-analysis

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Abstract

Background and Aim: Colistin is used as a last resort for managing infections caused by multidrug-resistant bacteria. However, the high emergence of colistin-resistant strains has restricted the clinical use of this antibiotic in the clinical setting. In the present study, we evaluated the global prevalence of the mutation in the *mgrB* gene, one of the most important mechanisms of colistin resistance in *Klebsiella pneumoniae*.

Methods: Several databases, including Scopus, Medline (via PubMed), and Web of Science, were searched (until August 2023) to identify those studies that address the *mgrB* mutation in clinical isolates of *K. pneumoniae*. Using Stata software, the pooled prevalence of *mgrB* mutation and subgroup analyses for the year of publication, country, continent, *mgrB* mutation types, and detection methods of *mgrB* mutation were analyzed.

Results: Out of the 115 studies included in the analysis, the prevalence of *mgrB* mutations in colistin-resistant *K. pneumoniae* isolates was estimated at 65% of isolates, and *mgrB* variations with insertional inactivation had the highest prevalence among the five investigated mutations with 69%. The year subgroup analysis indicated an increase in mutated *mgrB* from 46% in 2014 to 61% in 2022. Europe had the highest prevalence of mutated *mgrB* at 73%, while Africa had the lowest at 54%.

Conclusion: Mutations in the *mgrB* gene are reported as one of the most common mechanisms of colistin resistance in *K. pneumoniae*, and the results of the present study showed that 65% of the reported colistin-resistant *K. pneumoniae* had a mutation in this gene.

Keywords: colistin, *mgrB*, *Klebsiella pneumoniae*, colistin-resistant, global prevalence.

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PBa-17

Abstract Type: Systematic review/ Meta-analysis Research

An overview of case reports and case series of pulmonary actinomycosis mimicking lung cancer: a scoping review

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Abstract

Background and Aim: Pulmonary actinomycosis (PA) is a rare type of *Actinomyces* infection that can be challenging to diagnose since it often mimics lung cancer.

Methods: Published case reports and case series of PA in patients with suspicion of lung cancer were considered, and data were extracted by a structured search through PubMed/Medline.

Results: After analyzing Medline, 31 studies were reviewed, from which 48 cases were extracted. Europe had the highest prevalence of reported cases with 45.1%, followed by Asia (32.2%), America (19.3%), and Africa (3.2%). The average age of patients was 58.9 years, and 75% of all patients were above 50 years old. Male patients (70%) were predominantly affected by PA. The overall mortality rate was 6.25%. In only eight cases, the causative agent was reported, and *Actinomyces odontolyticus* was the most common isolated pathogen with three cases. Based on histopathological examination, 75% of the cases were diagnosed, and the lobectomy was performed in 10 cases, the most common surgical intervention. In 50% of the cases, the selective antibiotics were intravenous and oral penicillin, followed by amoxicillin (29.1%), amoxicillin-clavulanic acid, ampicillin, levofloxacin, and doxycycline.

Conclusion: The non-specific symptoms resemble lung cancer, leading to confusion between PA and cancer in imaging scans. Radiological techniques are helpful but have limitations that can lead to unnecessary surgeries when confusing PA with lung cancer. Therefore, it is important to raise awareness about the signs and symptoms of PA and lung cancer to prevent undesirable complications and ensure appropriate treatment measures are taken.

Keywords: actinomycosis, pulmonary actinomycosis, lung cancer, Actinomyces species, diagnosis

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PBa-18

Abstract type: Meta analysis

Prevalence of Listeria monocytogenes in meat-based products around the world: a meta-analysis

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Background and Aim: The prevalence of Food-borne infections is rising due to a lack of hygiene in the food preparation complexes and resistance of species such as listeria to disinfectants due to excessive use. As a result, epidemiological studies investigating the prevalence of Listeria across different food products can aid healthcare professionals in deploying new and improved public health strategies in the future. In this study, a meta-analysis was conducted on the prevalence of Listeria monocytogenes across different meat products worldwide.

Methods: In this study, PubMed, Web of Science, Scopus, and Google Scholar were systematically searched using the relevant syntax. Initially, a total of 1133 articles were included in the study at first. Finally, a total of 66 articles met our inclusion criteria and were selected for our study.

Results: according to our results**,** the prevalence of total listeria monocytogenes cases was found to be 16.83 % (Cl= 12.326 to 21.887).

Conclusion: the importance of Listeria isolates among food products necessitates the establishment of strict regulations as well as conducting more epidemiological studies with larger samples.

Keywords: Listeria monocytogenes, Prevalence, Meat

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PBa-19

Prevalence of *Brucella* endocarditis, A systematic review and meta-analysis

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Abstract

Objective: Endocarditis caused by *Brucella* infection is one of this infection's complications, including a high mortality rate. However, studies on the prevalence of this complication have been limited to some case reports. This study investigated the prevalence of *Brucella* endocarditis globally using a systematic review and meta-analysis.

Methods: PubMed, Scopus, and web of science databases were searched using appropriate keywords until September 2022. To investigate the pooled prevalence of *Brucella* endocarditis, random model was used in comprehensive meta-analysis (CMA) software.

Results: A total of 25 studies met the inclusion criteria and were included in the systematic review and meta-analysis. The prevalence of *Brucella* endocarditis was 1.3%, and the death rate was 26.5%. The results did not show a significant difference in the prevalence of this complication in different regions.

Conclusion: According to this study's results, the prevalence of *Brucella* endocarditis is low, but it includes a large percentage of the deaths of affected patients. Moreover, the prevalence of *Brucella* endocarditis does not depend on geographical areas. To complete our understanding of this complication and its management, more research should be done to investigate the effect of other factors, such as age and gender.

Keywords: Brucella; endocarditis; CMA; meta-analysis; prevalence

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PBa-20

Prevalence of Antibiotic Resistance in *Salmonella* Typhimurium Isolates Originating from Iran: A Systematic Review and Meta-Analysis

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Abstract

Objective: Antibiotic resistance in *Salmonella* represents a significant global public health concern. Among various serovars, *Salmonella* enterica serovar Typhimurium is prevalent in multiple countries. This study aims to conduct a systematic review and meta-analysis to evaluate the pattern of antibiotic resistance in *S.* Typhimurium isolates from diverse sources in Iran.

Methods: We conducted a comprehensive and systematic search for relevant articles until December 2023 in the following databases: PubMed, Scopus, Web of Science, and SID. The collected data were analyzed using Stata software version 17.

Results: Eighteen studies examined the pattern of antibiotic resistance in *S.* Typhimurium for various antibiotics in Iran. Piperacillin and tetracycline exhibited the highest resistance rates, at 79% and 60% respectively, while cefixime and ceftriaxone had the lowest resistance rates at 0%.

Conclusion: Our findings indicate a high level of antibiotic resistance among the studied antibiotics. This high level of antibiotic resistance raises concerns and underscores the

necessity for monitoring the use of antibiotics. Moreover, resistance to these antibiotics was more prevalent in samples isolated from animals compared to other sources. This highlights the importance of animal screening to detect the presence of drug-resistant isolates, with the ultimate goal of reducing antibiotic resistance and preventing the transmission of resistant strains to humans.

Keywords: *Salmonella* Typhimurium; Antibiotic resistance; Tetracycline; Cefixime; Meta analysis

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PBa-21
Abstract Type: Narrative review

The Possible Pathogenic Mechanisms of Microorganisms in Infertility: A Narrative Review

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Abstract

Background and Aim: Infertility can harm a patient in physical, psychological, spiritual, and medical ways. This illness is unusual because it affects the patient's companion and the patient

individually. Infertility is a multifactorial disease, and various etiological factors like infection are known to develop this disorder.

Methods: Recently published studies were extracted on various pathogens, including *Chlamydia trachomatis*, *Mycoplasma spp*, *Ureaplasma urealyticum*, *Pseudomonas aeruginosa*, Human papillomavirus, Herpes simplex virus, *Candida albicans*, and *Trichomonas vaginalis*.

Results: To this end, the bacteria mentioned can lead to infertility due to immunopathological effects, oxidative stress, and adverse effects on sperm concentration, motility, morphology, and DNA condensation. Among viruses, Human papillomavirus and Herpes simplex virus reduce sperm progressive motility and sperm concentration. Additionally, the viruses can lead to the atrophy of the germinal epithelium and degenerative changes in the testes. *Candida albicans* also harm sperm quality, motility, and chromatin integrity and induce apoptosis in sperm cells. Finally, *Trichomonas vaginalis* leads to distorted heads, broken necks, and acrosomes exocytosis in sperms. Furthermore, this parasite decreases sperm viability and functional integrity. Noteworthy, oxidative stress could have a role in many pathological changes in the reproductive system. Recent findings show that microorganisms can increase ROS concentration inside the host cells, leading to oxidative stress and sperm distress and dysfunction.

Conclusion: This study explores the potential significance of critical pathogens associated with infertility and their pathogenic mechanisms that can affect sperm function and the female reproductive system.

Keywords: infertility, infection, pathogenic mechanisms

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PBa-22
Abstract Type: Original Research

Identification of antibiotic resistance pattern and the presence of Class 4 Integron in clinical isolates of *V. cholerae* NAG

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Abstract

Background and Aim: Antibiotic resistance is one of the major concerns in global health and has been reported in a wide range of bacteria, which has caused the ineffectiveness of existing antibiotics in the treatment of diseases caused by them.

Antibiotic resistance in *V. cholerae* is a very dynamic phenomenon and is susceptible to change and evolution over time due to the different selective pressure of antibiotics. Genetic exchanges of drug resistance genes among bacteria, especially in *V. cholerae*, are carried out with the help of mobile genetic elements (MGEs). Among the mobile genetic elements, Integrons play an important role in acquiring and spreading antibiotic resistance genes.

The pathogenicity of *V. cholerae* non-O1/non-O139 isolates in humans is increasing. The severity of gastrointestinal infections caused by these strains varies from mild to severe. These strains are also scattered in Bushehr province and cause diarrhea every year, especially in hot seasons. The purpose of this study is to identify the pattern of antibiotic resistance and investigate the presence of Class 4 Integron in native samples of Bushehr province.

Methods: In this study, 8 clinical isolates of *V. cholerae* non-O1/non-O139 were collected from diarrheal patients referred to health centers in Bushehr in 2021.

The disk diffusion method (CLSI) detected the antibiotic resistance pattern. Moreover, the presence of the integrase 4 gene was screened in all isolates by PCR.

Results The results showed that in the clinical isolates of this study there was drug resistance to ampicillin, nalidixic acid, aztreonam, nitrofurantoin, amikacin and ofloxacin antibiotics. The highest resistance was to ampicillin (25%), nalidixic acid (25%) and Aztreonam (25%). There was also resistance to nitrofurantoin (12.5%), amikacin (12.5%) and ofloxacin (12.5%). In the case of nalidixic acid antibiotic, drug resistance in the form of semi-sensitive phenotype was observed in one of the isolates. Also, integrase 4 gene was observed in all isolates.

Conclusion: Considering the percentages of drug resistance in these clinical isolates, the results showed that except ampicillin, nalidixic acid, aztreonam, nitrofurantoin, amikacin and ofloxacin, other antibiotics can be effective against *V. cholerae* isolates in this region.

Also, the presence of class 4 Integron in all strains indicates the presence of SuperIntegrons in these strains. Although Class 4 Integron does not carry gene cassettes that encode antibiotic resistance in bacteria, these Integrons play an important role in genomic evolution such as metabolism. DNA changes have adaptive functions and can cause adaptation and survival of *V. cholerae* in its environment.

Keywords: *V. cholerae*, polymerase chain reaction, Integrons, *IntI4*

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PBa-23

Narrative review

Antibiotics-free compounds for managing carbapenem-resistant bacteria; a narrative review

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Abstract

Background and Aim: Carbapenem-resistant (CR) Gram-negative bacteria have become a significant public health problem in the last decade. In recent years, the prevalence of CR bacteria has increased. The resistance to carbapenems could result from different mechanisms such as loss of porin, penicillin-binding protein alteration, carbapenemase, efflux pump, and biofilm community. Additionally, genetic variations like insertion, deletion, mutation, and post-transcriptional modification of corresponding coding genes could decrease the susceptibility of bacteria to carbapenems.

Method: This research reviews ongoing studies and preliminary investigations into different aspects of non-antibiotic approaches for managing and inhibiting the CR bacteria and various methods and procedures used as an alternative for carbapenems against these bacteria.

Result: scientists are looking for new approaches to inhibit CR bacteria. Using bacteriophages, natural products, nanoparticles, disulfiram, N-acetylcysteine, and antimicrobial peptides showed promising inhibitory effects against CR bacteria. Additionally, the mentioned compounds could destroy the biofilm community of CR bacteria.

Conclusion: Using the mentioned antibacterial agent in combination with conventional antibiotics increases the efficacy of antibiotics, decreases their dosage and toxicity, and resensitizes CR bacteria to antibiotics. there is a growing prevalence of bacteria that are becoming increasingly resistant. Hence, it is imperative to employ other strategies to manage

resistant infections, given that antibiotic resistance poses a significant challenge in clinical environments. However, there is a lack of extensive clinical data and in vitro studies in this area. Therefore, further research is needed to determine the most effective non-antibiotic approaches that cause minimal harm to humans, enhance their impact on bacterial pathogens, identify the optimal timing for treatment, and establish the appropriate route and administration dosage. However, non-antibiotic methods could soon be implemented as a viable antibiotic substitute.

Keywords: carbapenems-resistant, natural compounds, bacteriophages, nanoparticle, N-acetylcysteine, antimicrobial peptides

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PBa-24
Abstract Type: Original Research

Frequency of antibiotic resistant EAEC isolates among patients with diarrhea in Bushehr

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Abstract

Background and Aim: Enteroaggregative *Escherichia coli* (EAEC) has been recognized as an emerging foodborne pathogen linked to persistent and acute diarrhea in developed and developing countries. The virulence factors of EAEC are carried on virulence plasmids and pathogenicity islands. *aggR* serves as the primary regulator of virulence factors. Moreover, EAEC can be identified by pCVD432 plasmid encoding autotransporter binding agent. The treatment of *E. coli* infections, has become increasingly complicated by the emergence of resistant strains to most first-line antimicrobial agents. The objective of this study was to determine the prevalence of EAEC strains and antibiotic resistance in patients with diarrhea in Bushehr.

Methods: A total of 147 *E. coli* isolates collected from stool samples of diarrheic patients from November 2021 to April 2022 in Bushehr province. *E. coli* isolates were identified by standard

biochemical tests such as Gram stain, TSI, motility, indole, simmon citrate and urease. Total DNA was extracted by boiling method. *E. coli* was confirmed by detection of *uidA* gene. EAEC isolates were determined by Multiplex PCR for presence of *aggR* and pCVD432 genes. The isolates were analyzed to detection drug resistance through antibiotic susceptibility test according to CLSI recommendations.

Results: Out of these isolates, *EAEC were detected* in 8 (5.4%) samples by PCR, which harbored both *aggR* and pCVD432 genes. Antimicrobial susceptibility testing revealed the highest resistance rate to ampicillin (87.5%), tetracycline (75%) followed by cefotaxime and SXT (50%), ceftazidime, ciprofloxacin, amikacin (12.5%). The most effective antibiotics against EAEC isolates were imipenem, meropenem and gentamycin with 100% susceptibility. Multidrug resistance (MDR) was detected in 50% of EAEC isolates.

Conclusion: The EAEC pathotype is isolated from sporadic cases of diarrhea and outbreaks of gastroenteritis**.** The findings of this study confirm that EAEC was detected in patients with diarrhea and highlight the importance of continuous monitoring for antibiotic resistance in EAEC isolates. The prevalence of MDR isolates emphasizes the urgent need for proper antibiotic stewardship and infection control. Knowledge of antibiotic resistance of EAEC is significant in selecting the suitable therapy in critical diarrheagenic infections and adjusting local antimicrobial guidelines.

Keywords: Enteroaggregative *Escherichia coli*, Diarrhea, PCR, Antibiotic resistance, MDR.

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PBa-25
Abstract Type: Original Research

Investigation of antibiofilm activity of nickel oxide nanoparticles against bacteria implicated in tooth decay

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Abstract

Background and Aim: One of the major concerns in oral health is the formation of biofilms. This event occurs when bacteria on the surface of the teeth form plaque. Streptococcus mutans and Streptococcus sanguinis have important roles in the formation of dental plaque. Inhibiting the growth of these bacteria on the surface of the teeth can prevent tooth decay. Nickel oxide nanoparticles have widespread applications. Nickel oxide nanoparticles act as antibacterial agents against certain bacteria. The aims of this study was to determine the antibacterial effects of nickel oxide nanoparticles against bacteria implicated in tooth decay.

Method: In this study, nickel oxide nanoparticles were synthesized in two molecular weights using the sol-gel method, and the selected bacteria were treated with serial concentrations of these nanoparticles using the microtiter plate assays to assess antibiofilm activity.

Results: The nickel oxide particles were synthesized using the sol-gel method and calcined at two temperatures of 500 and 1000 degrees Celsius. The dimensions of the synthesized nickel oxide particles in the first stage were 8.1 nanometers for particle A and 12nm for particle B. A serial concentration of nanoparticles ranging from 500 to 31 micrograms per milliliter was prepared and tested. The effect of these two particles at a concentration of 31 micrograms per milliliter on the growth and biofilm formation of *S. sanguinis* and *S. mutans* bacteria was significant.

Conclusion: The results of the study indicate that nickel oxide nanoparticles have acceptable antibioflm activity against S. *sanguinis* and *S. mutans*, which can be used in dental materials for preventing the formation of dental plaque.
Keywords: Nanoparticles; Oral diseases, Antibacterial; Nickel oxide; Streptococcus

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PBa-26
Abstract Type: Original Research

Synergism Effects of Vancomycin and Zinc Oxide Nanoparticles on Methicillin Resistance Staphylococcus aureus (MRSA) and lung cancer

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Abstract:

Background: Methicillin-resistant Staphylococcus aureus (MRSA) is an important human pathogen and a historically emerging zoonotic pathogen of public health and veterinary importance and can cause severe chronic infections. The morbidity of MRSA infections has increased worldwide and is of great concern. Nevertheless, a change in treatment strategies, including the use of new antibiotics or combination therapy, is necessary for the treatment of this infection. The research was conducted to investigate the synergistic effects of vancomycin and zinc oxide on methicillin-resistant Staphylococcus aureus and the viability of the lung cancer cell line A549 and the normal cell line BEAS.

Methods: In this study, the minimum inhibitory concentration (MIC) of ZnO NPs and vancomycin was determined using the microdilution method. The Fractional Inhibitory Concentration Index (FICI) was calculated using the checkerboard method to evaluate the synergistic effect of ZnO NPs and vancomycin. The effect of the combination of ZnO NPs and vancomycin on the viability of lung cancer cell line A549 was also tested by MTT assay.

Results: The result of the MIC values showed that all isolates were sensitive to vancomycin, with the exception of one isolate, which had an MIC of ≤2 µg/mL. The synergistic effect of the combination of ZnO NPs and vancomycin was observed in two MRSA isolates and one MSSA strain using the checkerboard method. The combination of vancomycin and ZnO NPs caused less viability in the A549 lung cancer cell line (25.7%) than in BEAS (90%).

Conclusion: The combination of vancomycin and ZnO NPs at appropriate dosage intervals may be beneficial in the treatment of methicillin-resistant Staphylococcus aureus (MRSA). The combination of vancomycin and zinc oxide nanoparticles may also play a dual role in lung cancer patients with evidence of resistance to MRSA by reducing cancer cell survival.

Keywords: Staphylococcus aureus, MRSA, MSSA, synergism, ZnO NPs, vancomycin

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PBa-27

Recovery of filgrastim (anti-cancer drug) from its inclusion bodies expressed in *Escherichia coli* using a new anion exchange chromatography

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Abstract

Background and Aim: High level expression of recombinant proteins in Escherichia coli often forms insoluble and inactive protein aggregates called inclusion body and refolding of these inactive proteins is a crucial step in industry. Protein folding liquid chromatography is a new developed method in recent years for simultaneous refolding and purification of many recombinant proteins.
In this work, we have tried to develop an efficient method for refolding of recombinant human granulocyte colony-stimulating factor (rhG-CSF) with strong anion exchange chromatography.

Methods: A HiTrap Q resin was employed for refolding of filgrastim. Inclusion bodies were solubilized in urea 2 M with pH: 12.5 for 30 mins in refrigerator temperature on roll mixer and then denatured/reduced rhG-CSF refolded into its native form by strong anion exchange chromatography in 2 hrs. Several factors such as time, concentration of redox couple, mobile phases and pH were tested.

Results: Analysis with reversed-phase chromatography indicated that our method can refold rhG-CSF successfully with 78% recovery and 10% oxide form of filgrastim and 3.6% of deamide form but our method did not have reproducibility for greater than ten thousand times and usable for several years.

Conclusion: This approach can refold filgrastim inclusion bodies and this may serve as a promising trend for using protein folding liquid chromatography methods in industry; however, we should just develop a method that can be reproducible greater than ten thousand times.

Key words: Chromatography, G-CSF, Protein Refolding, Cancer, Antineoplastic agents

PBa-28

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Abstract Type: Original Research

Investigation of the Prevalence of Bacterial Hospital Infections and Antibiotic Resistance Patterns of Isolated Bacteria from Patients Admitted to Imam Khomeini Hospital in Sari (2019-2020)

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Abstract

Background and Aim: Continuous monitoring of hospital-acquired infections across different geographical regions, along with their antibiotic resistance patterns, can assist physicians in prescribing more rational antibiotics. Therefore, a retrospective study was conducted over the past two years to evaluate the prevalence of bacterial hospital infections and their antibiotic resistance patterns at Imam Khomeini Hospital in Sari.

Methods: This descriptive-cross-sectional and retrospective study was performed on the medical records of all patients admitted to Imam Khomeini Hospital during the years 1399-1400 (2020-2021).

Results: A total of 500 patient records with hospital-acquired infections were analyzed for the years 1399 and 1400. The average age of the patients was 53/01±19/95 years, and the mean duration of hospitalization was 20/94±13/10 days. Tetracycline(%63) was found to be the most effective antibiotic against Gram-negative bacteria, while oxacillin(%88/3) and vancomycin(%88/2) were most effective against Gram-positive bacteria.

Conclusion: The most common microorganisms associated with hospital-acquired infections in this study were Stenotrophomonas maltophilia, followed by Staphylococcus epidermidis and Escherichia coli. Therefore, targeting these organisms is essential for controlling hospital-acquired infections in this hospital to enhance treatment efficacy and prevention strategies.

Keywords: Bacteria, Hospital-Acquired Infection, Antibiotic Resistance

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PBa-29

Evaluation of bacterial infections in patients with severe Covide-19 admitted to ICU by Multiplex-PCR

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Abstract

Background and Aim: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has killed more than 6.3 million people worldwide. Bacterial co-infections or superinfections are important risk factors related to the mortality of severe Covid-19 patients. The aim of the present study was to determine the frequency of bacterial co-infections including Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii, Haemophilus influenzae and pneumococcus in the respiratory aspirate samples of severe covid-19 patients admitted to the ICU of Valiasr hospital in Zanjan using the Multiplex PCR method.

Methods: All patients diagnosed with severe covid-19 hospitalized in the ICU department of Waliasr hospital in Zanjan from April 2022 to March 2023 were included in the study. 40 severe covid 19 patients were selected by total sampling method. All the demographic and clinical information of the patients were recorded in the information form. A respiratory aspirate sample was collected from each patient in a sterile falcon and immediately transferred to the microbiology laboratory of the Faculty of Medicine. Respiratory samples were kept in a freezer at -20°C until DNA extraction. Genomic DNA extraction was done directly from all respiratory samples and by specific primers, the specific genes of each of the investigated bacteria were amplified by Multiplex PCR. After agarose gel electrophoresis and checking PCR products, data analysis was done using SPSS version 18 software.

Results: Out of 40 hospitalized patients, Real-time PCR test was positive in 40% of patients and negative in 60%. Out of 40 respiratory aspirate samples, 18 cases (45%) were positive in the PCR test for bacterial co-infection including S. aureus, P. aeruginosa, K. pneumoniae, A. baumannii and pneumococcus. H. influenzae was not detected in any of the respiratory samples. Also, in 6 samples (15%), the presence of 2 or 3 bacteria was detected simultaneously in a respiratory sample (mixed bacterial infection). The most common identified bacterial agents were A. baumannii (15%) and (12.5%). A significant relationship was observed between the frequency of some of the investigated bacteria and the variables of age, sex, antibiotic use, underlying disease and laboratory findings ($P<0.05$).

Conclusion: In the present study, the respiratory aspirate samples of 45% of severe Covid-19 patients admitted to the ICU were positive for at least one of the studied bacteria. Considering the relatively high frequency of secondary bacterial infection in patients, it is recommended to take appropriate health measures to control and reduce opportunistic and antibiotic-resistant bacteria from the hospital environment and care and prevention of high-risk patients.

Keywords: Gram-positive cocci; Gram-negative bacilli ; Severe Covid-19; Multiplex PCR;ICU;

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PBa-30

The complex relationship between the Gut Microbiome and HIV: Focus on Mechanisms, Predisposing Factors, and Fecal microbiome transplantation

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Abstract

Human immunodeficiency virus (HIV) is a retroviral infection that causes deterioration of the immune system and vulnerability to infections and opportunistic cancers. Since HIV causes a decrease in CD4 + T cells, and the majority of this decrease occurs in the intestinal tissue, which is a large source of these cells, there is the possibility of a relationship between the intestinal microbiome and this virus, potentially affecting immunity. Some mechanisms show that the change in the abundance of gut bacteria in people with HIV is not coincidental. Several factors, such as sexual orientation, drug use, pharmacological interventions, underlying diseases, depression, and vitamin B deficiency, influence the interaction between HIV and the gut microbiome and can modulate the gut microbiota and exacerbate HIV-related complications. Faecal microbiome transplantation has demonstrated promise as a treatment that can improve the microbial balance of the microbiome, increase microbial diversity, and alleviate many of the gastrointestinal complications caused by HIV disease. Therefore, gaining a deeper understanding of the additional factors and mechanisms and introducing new treatments that enhance the interaction between the gut microbiome and HIV presents a promising avenue for advancing HIV treatment and improving overall health outcomes.

Conclusion: The intestinal microbiome of HIV patients undergoes changes that may affect immune processes, increase inflammation, and change the immune system response and progress of the disease. However, this hypothesis needs more studies to be confirmed. Further investigation is needed to fully understand the complex relationship between gut microbiota and the immune system during HIV infection, as changes in gut flora have been consistently linked to disease progression. Studies have consistently shown a decrease in gut bacterial diversity in HIV-infected individuals compared to uninfected controls, with specific alterations in microbial composition.

FMT has shown great potential as a treatment for restoring equilibrium in the gut microbiome and enhancing gastrointestinal symptoms in people with HIV. FMT can successfully modify the composition of the gut microbiome, enhancing the abundance of beneficial bacteria and substantially enhancing total microbial diversity. It is important to mention that FMT has a positive safety record, with no significant negative effects observed. Nevertheless, additional investigation is required to comprehensively comprehend the enduring consequences of FMT on various HIV patient populations and to enhance its application as a therapeutic intervention in this particular scenario. According to the mechanisms involved in the cycle of this virus, intestinal microbiome, and immune mechanisms that include SCFA and tryptophan metabolism, we can better understand this critical relationship. Later, through these metabolisms, scientists and researchers may be able to find solutions to control this virus through the intestinal microbiome and mechanistic pathways.

Noteworthy, MSM and drug users experience similar changes in their gut microbiome as those seen in individuals with HIV. Certain medications, such as sevelamer and prophylactic antibiotics, can help reduce immune activation caused by the interaction between the gut microbiome and HIV. Underlying diseases, such as diabetes and liver disease, can worsen gut microbiota dysbiosis in HIV patients. Depression in HIV-positive individuals has also been linked to gut dysbiosis and increased inflammation. Additionally, vitamin B deficiency, which is common in HIV patients, can contribute to heightened proinflammatory reactions. According to the mentioned content, the relationship between HIV and the gut microbiome is a dynamic and multifaceted area of research that has the potential to reshape our understanding of the virus and offer new therapeutic possibilities. More research and clinical trials are necessary to validate these promising approaches and thoroughly explore the complex dynamics of this relationship, leading to innovative therapeutic interventions..

Keywords: HIV, gut microbiome, CD4 + T cell, chronic inflammation, retroviral infection, Fecal microbiome transplantation

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PBa-31

Abstract Type: Original Research

Side Effects in Patients Treated with Anti-Tuberculosis Drugs in Kermanshah from 2013 to 2019

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Abstract

Background and Aim: Tuberculosis (TB) remains a significant public health challenge, particularly in developing countries, with 9.9 million cases reported globally in 2020. This study evaluates the clinical outcomes and adverse drug reactions associated with anti-tuberculosis treatments at Imam Reza Hospital in Kermanshah.

Methods: This descriptive cross-sectional study reviewed records of pulmonary tuberculosis cases at Imam Reza Hospital between 2013 and 2019. Data were analyzed using SPSS version 16.

Results: The study included 305 patients (121 women, 39.6%, and 184 men, 60.3%), with a majority over 66 years old. Among them, 153 (50.2%) were smear-positive. Liver toxicity was the most common side effect of anti-TB drugs. Treatment outcomes showed 51.2% achieved complete remission, 20% mortality, 3% treatment failure, 20.6% multidrug-resistant TB (MDR-TB), and 5.2% remained untreated.

Conclusion: Effective TB control requires active engagement from healthcare providers. Early detection and appropriate treatment, alongside a comprehensive understanding of the epidemiological landscape, are essential for managing tuberculosis in the community.

Keywords: Tuberculosis, Anti-Tuberculosis Treatment, Adverse Drug Reactions, Liver Toxicity, Multidrug-Resistant Tuberculosis

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PBa-32

Abstract Type: Original Research

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Drug Resistance Pattern of *Mycobacterium Tuberculosis* in Guilan province, Iran

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Abstract

Background:

Mycobacterium tuberculosis (MTB) is causative agent of tuberculosis (TB), which still remains one of the most common infectious diseases in developing countries. In the recent years, emergence and spread of multidrug-resistant (MDR) TB pointed as public health problem worldwide. This study aimed to determine the rate of drug resistance to first-line anti-TB drugs in Guilan province.

Methods:

MTB isolates were collected from March 2016 to July 2018. Drug susceptibility testing to rifampicin, isoniazid, ethambutol, and streptomycin was performed on Löwenstein-Jensen medium using proportion method.

Results:

A total of 138 MTB isolates were included to this study. The mean age of patients was 47.41, ranged from 17-84 years and 104 (84.1%) patients were male. A set of 128 (92.8%, 95% CI = 87.2%-96%) isolates were pan-susceptible and 10 (7.2%, 95% CI = 4%-12.8%) were resistant to at least one drug. Five isolates (3.6%, 95% CI = 1.6%-8.2%) were resistant to streptomycin, 6 isolates (4.3%, 95% CI = 2%-9.2%) were resistant to isoniazid, 3 isolates (2.2%, 95% CI = 0.7%-6.2%) were resistant to rifampicin, one isolate (0.7%, 95% CI = 0.1%-4%) was resistant to ethambutol. In this study three isolates (2.2%, 95% CI = 0.7%-6.2%) showed resistance to rifampicin and isoniazid then identified as MDR.

Conclusions:

The prevalence of drug resistant isolates in this study area point to the necessity for further enforcement of TB treatment and disease control management. Drug susceptibility testing for all TB cases and continuous monitoring of drug resistance are recommended to prevention and control of drug-resistant TB.

Keywords:

Mycobacterium tuberculosis, Tuberculosis, Multidrug-resistant.

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PBa-33

The relationship between Gut Microbiome and human diseases: Mechanisms, Predisposing Factors and potential intervention

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Abstract

The complex interrelation of gut microbiota with human health underlines the profound influence this microbial ecosystem has on mechanisms of disease and wellness. The gut microbiome profoundly impacts various human diseases, encompassing gastrointestinal disorders, metabolic disorders, neurological disorders, and immune-related diseases. Gastrointestinal disorders are closely linked to microbial imbalances in the gut. Metabolic disorders, including obesity and type 2 diabetes, are influenced by the gut microbiota's role in energy regulation and glucose metabolism. Furthermore, the gut-brain axis highlights the correlation between gut microbiota and neurological conditions such as Alzheimer's and Parkinson's. Moreover, the gut microbiome assumes a pivotal function in regulating the immune system, whereby dysbiosis is implicated in developing immunological-related ailments, including allergies and autoimmune disorders. Predisposing factors, including diet, medicines, lifestyle, and environmental influences, are described as having an important role in the composition of the gut microbiome. By understanding these factors, we can get valuable insights into how to intervene to reduce the chances of a disease. Current interventions, including probiotics, prebiotics, fecal microbiota transplants, and lifestyle modification, show promise, but there are still challenges and unanswered questions in this evolving field that may lead to improvements. This review interrelates the complicated gut microbiome with various human diseases, mechanisms, predisposing factors, and potential interventions.

Conclusion: The gut microbiome plays a critical role in the modulation of immune responses and the maintenance of immune tolerance, which directly or indirectly points out the

importance of gut microbiota in the pathogenesis of various diseases. Predisposing factors, including diet, medicines, lifestyle, and environmental influences, are described as having an essential role in the composition of the gut microbiome. It can be said that the effects of these factors are specifically stated as some of the principal determinants of the gut microbiome. A diet low in fiber provides a less diverse population to the gut microbiota, and poor dietary choices such as high sugar and fat may cause microbial imbalance and dysbiosis. On the other hand, physical activity supports the diversity and stability of the microbiome community, while the sedentary lifestyle influences the reduced diversity of the microbiome. Overwhelming stress decreases gut microbiome stability, causing a change in gut motility and permeability in a way that activates dysbiosis. Medications also significantly influence the composition of the gut microbiome. Antibiotics are uniquely powerful because they kill harmful and beneficial bacteria, reducing microbe diversity and potentially even causing dysbiosis outright. Nonetheless, probiotics could help restore the microbial imbalance by reintroducing beneficial microorganisms. Pollution exposes the microbiome to toxins and pollutants. This process leads to the disruption of the microbial communities by favoring the growth of pathogenic bacteria. Therefore, different agents and conditions can lead to changes in the gut microbiome, which can be related to the pathogenesis of various diseases. By understanding these factors, we can get valuable insights into how to intervene to reduce the chances of a disease. However, data about the exact interactions of microbiome changes and disease progression is limited. To this end, further research and clinical trials are needed to unveil how the gut microbiome participates in health and disease. [i]

Future efforts should focus on optimizing microbiome-based therapies and integrating them into personalized medicine approaches to promote human health and more effectively manage disease. Research should be targeted to understand the metabolisms in the gut microbiome change. Through more research, effective interventions can be made in mechanisms involved in the gut microbiome for the treatment of related diseases or modification in the composition of bacteria living in the gut. Also, future research on the gut microbiome promises transformative insights into its role in human health and disease. Advances in microbiome sequencing and personalized medicine could lead to tailored probiotic and prebiotic therapies, optimizing individual health outcomes. Furthermore, interdisciplinary approaches integrating genomics, metabolomics, and immunology will drive innovative interventions.

Keywords:microbiome; Gastrointestinal disorders; dysbiosis; metabolic disorders; neurological disorders; and immune-related diseases

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PBa-34

Abstract Type: Original Research

The Inhibitory Effect of Thymoquinone on Exo-enzyme T in Pseudomonas aeruginosa through Molecular Docking and Molecular Dynamics Simulation

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Abstract

Background and Aim: Pseudomonas aeruginosa, a gram-negative opportunistic bacterium, is a major cause of hospital-acquired infections, particularly among immunocompromised patients. This pathogen utilizes various virulence factors, including Exo-enzyme T (Exo T), to disrupt host cellular functions, damage cell structures, and evade immune defenses. Conversely, thymoquinone, a bioactive compound found in Nigella sativa seeds, has shown notable antimicrobial and anti-inflammatory properties, making it a potential therapeutic candidate. To investigate the inhibitory potential of thymoquinone on Exo-enzyme T of Pseudomonas aeruginosa with the goal of reducing the bacterium's virulence and infection severity through computational and molecular simulation methods.

Methods: Molecular Docking: Molecular docking was performed to predict and evaluate the interactions between thymoquinone and the active site of Exo T.

Molecular Dynamics Simulation: The stability of the thymoquinone-Exo T complex under various conditions was assessed using molecular dynamics simulations.

Results: Docking Analysis: Thymoquinone demonstrated strong binding interactions and high affinity for the active site of Exo T, suggesting its inhibitory potential on enzyme activity.

Complex Stability: Molecular dynamics simulations confirmed the stability of the thymoquinone-Exo T complex over the simulation time, indicating sustained inhibitory capacity of thymoquinone on Exo T.

Conclusion: Thymoquinone emerges as an effective inhibitor of Exo T, potentially reducing the virulence of Pseudomonas aeruginosa and the severity of associated infections. These findings support the use of natural compounds as viable agents against drug-resistant pathogens, laying the groundwork for future research on thymoquinone derivatives for clinical applications.

Keywords: Pseudomonas aeruginosa, Exo-enzyme T, Thymoquinone, Molecular Docking, Molecular Dynamics Simulation

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PBa-35

Abstract Type: Narrative Review

Roseburia and *Bluatia* in human health

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Background and Aim:

Roseburia and *Bluatia* are significant genera in phylum Firmicutes, one of the fundamental phyla of the intestinal microbiota of humans and other vertebrates. *Roseburia intestinalis*, an obligatory gram-positive anaerobic bacterium, is the most prevalent butyrate-producing bacterium in human colon, account for inhibition of intestinal inflammation, and preservation of energy homeostasis by producing metabolites. *Roseburia*'s metabolite butyrate and presence of flagella, as well as additional unidentified supernatant components, affect immune cell activity and cytokine production. Additionally, *Blautia*, a major genus of gut microbiota, has demonstrated a number of possible probiotic qualities and has involvement in biotransformation, inflammatory illnesses, and metabolic disorders. *Blautia* plays a part in the host's metabolic control and is linked to obesity, which is an inflammatory disease.

Methods: We searched PubMed, Scopus, Google Scholar and Medline databases with the keywords: “Roseburia AND human health”, “Blautia AND human health”, “Blautia AND probiotic”, “Roseburia AND metabolism”.

Results: The data collected revealed that presence of both microorganisms have positive effects in the intestine and thereby on human health, describing their use as probiotic supplements. *Roseburia* and other butyrate-producing organisms, as well as short chain fatty acids (SCFAs), increased with intake of high-fiber diet. An imbalance in the *Roseburia* population, which produces SCFAs in human feces, has been linked to a number of illnesses, including allergies, obesity, Type 2 diabetes, nervous system disorders, neuro-inflammation, and irritable bowel syndrome. *Blautia* species are documented to have an impact in managing obesity and preserving a metabolically healthy phenotype.

Conclusion: Given their capacity to produce butyrate, *Roseburia* species may also be used as probiotics to restore beneficial flora or as biomarkers for symptomatic diseases (such as gallstone production). It is still unknown how prebiotics, including certain oligosaccharides, can be used as substrates to encourage *Blautia* growth and clarify its probiotic properties. In a variety of illnesses linked to microbial dysbiosis, these two bacteria have been targeted and shown possessing a noteworthy therapeutic effect.

Keywords: Roseburia; Bluatia; Human health; Probiotic, Dysbiosis

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PBa-36

Functional annotation of A0A0H3H0G5 protein in *Klebsiella pneumoniae*: In silico study

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Abstract

Background and Aim:

Klebsiella pneumoniae is known to cause several nosocomial infections in immunocompromised patients. There is a wide range of antibiotic resistant strains, resulting in high mortality rates in patients, and it has been declared an urgent threat (1). It's been found that hypervirulent and multidrug-resistant (MDR) bacteria have large accessory genomes made up of plasmids and chromosomal genes (2,3).However, the molecular function of more than 30% of *K. pneumoniae* proteins is not known. In this study, we intended to use computational tools to find potential functions of A0A0H3H0G5 hypothetically regarded as lipoprotein.

MATERIALS AND METHODS:

Uniprot and String databases were used to discover proteins that interact with A0A0H3H0G5 and functional protein association networks analysis. Finally, the I-TASSER and Swiss model server was utilized to predict the functions of the target protein according to its similar proteins.

RESULTS:

we identified the uncharacterized protein A0A0H3H0G5 as interacting with ten bacterial proteins. The interacting proteins predominantly include translocases, a putative H+/gluconate

symporter, a cell division protein, prophage endolysin, and a putative filamentous hemagglutinin. These proteins play a significant role in regulating secretion via the type IV secretion system and in the biosynthesis of siderophore group nonribosomal peptides. Type IV secretion systems (T4SSs) are capable of delivering effector proteins into host cells, thus contributing to the pathogenesis of various infections that affect humans; (4).

The biosynthesis of siderophores in bacterial organisms involves non-ribosomal peptide synthetases (NRPS), which help bacteria extract iron from their environment and are critical for their pathogenic capabilities. (5).

Our findings further indicated that certain motifs within this protein exhibited similarity to the hydrolase inhibitor protein from Salmonella enterica. The hydrolase inhibitor functions by trapping external proteases via a covalent interaction with an activated thioester (6).

Conclusion:

Consequently, it appears that this protein contributes to various bacterial growth and virulence pathways, playing a crucial role in the pathogenesis of *Klebsiella pneumoniae*. As a result, it may be posited as an excellent therapeutic target for future research endeavors.

Keywords: Klebsiella pneumoniae , Functional prediction , **Lipoprotein , A0A0H3H0G5**

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PBa-37

Abstract Type:

10 years study on botulism

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Demography, risk factors, symptoms, complications and prognosis of the patients with botulism - 10 years study

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Abstract

Background and Aim: Botulism is a medical emergency. Rapid diagnosis and timely treatment are very important to reduce the risk of death. This study was conducted with the aim of investigating the demographic characteristics, risk factors, symptoms, complications and prognosis of botulism patients during a period of 10 years (2012 -2022) in Zanjan.

Methods: In this cross-sectional study, all patients with botulism hospitalized in Valiasr Hospital, Zanjan during the years 2012-2022 were studied. The data collection tool was a checklist including demographic variables, risk factors of infection, recent history of botulism in close relatives, clinical manifestations, paraclinical changes and prognosis, which was extracted from the medical records of the patients.

Results: A total of 54 patients with botulism were investigated, including 59.3% of male patients. The mean (± standard deviation) age of patients was 40.66 (± 16.8736) and botulism test was negative in 27.6%. The most common symptoms were ptosis (61.1%) and blurred vision (50%). A statistically significant relationship was observed between the variables of patient age, average length of hospitalization, history of infection in the family, botulism test result, consumed food source, imaging test results and EMG results with the prognosis of botulism ($P<0.05$). However, no statistically significant relationship was observed between the prognosis of botulism and gender ($P>0.05$).

Conclusion: Suspicious food was the most common risk factor and local dairy was the most common food source consumed. If measures such as public health education, using sufficient heat during consumption, not consuming non-pasteurized dairy products can be effective in preventing the occurrence of this dangerous food poisoning.

Keywords: Botulism, risk factor, food poisoning, clinical complications, laboratory complications

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PBa-38
Abstract Type:
Bacterial infections in sepsis by blood culture and Multiplex-PCR

bacterial agents in blood samples of patients with sepsis by culture and Multiplex-PCR

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Abstract

Background and Aim: Sepsis is a life-threatening clinical syndrome with a wide range of physiological and biochemical disorders. Rapid detection and identification of sepsis-causing organisms are important to reduce mortality and treatment costs. The aim of this study was to determine the frequency of common bacterial agents of sepsis including Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Klebsiella, Pseudomonas aeruginosa in blood samples of patients using culture and Multiplex PCR methods.

Methods: In this cross-sectional descriptive study, all patients with sepsis hospitalized in infectious ward of Valiasr Hospital in Zanjan from March 2021 to February 2022. All demographic and clinical information of patients were recorded. Two blood samples were collected under the supervision of a physician and samples were immediately sent to the Microbiology Laboratory of the Medical School. Detection and identification of sepsis-causing microorganisms were done by culturing samples in selected media. Also, genomic DNA was extracted directly from all blood samples. Using specific primers, amplification of bacterial genes was performed using Multiplex PCR. After agarose gel electrophoresis, data analysis was performed using SPSS software version 18.

Results: : Out of 100 blood samples, 13 were positive in culture and 32 were positive in Multiplex PCR. S. epidermidis and P. aeruginosa with a frequency of 8%, S. aureus and Klebsiella with a frequency of 6% and E. coli with a frequency of 4% were identified by Multiplex PCR. There was a significant relationship between the frequency of the studied bacteria and the variables of age, underlying disease, clinical symptoms, imaging findings (pulmonary findings observed in lung X-ray and CT scan) and disease prognosis ($P < 0.05$).

Conclusion: In the present study, blood samples from about one-third of patients with sepsis were positive for at least one of the studied bacteria. Due to the relatively high frequency of bacterial sepsis in patients, it is recommended to take appropriate hygienic measures to control and reduce the opportunistic and antibiotic-resistant bacteria from the hospital environment and to care for and prevent high-risk patients.

Keywords: Staphylococcus, Escherichia coli, Klebsiella, Pseudomonas aeruginosa, blood Culture, multiplex PCR.

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PBa-39
Abstract Type: Narrative review

An overall comparison between different therapeutic strategies of Stargardt disease

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Abstract

Stargardt disease, STGD1, is the most common inherited early-onset retinal disease emanating from ABCA4 gene mutations, leading to lipofuscin deposition within RPE and progressive impairment of central vision. The subsequent review of literature discusses current therapeutic strategies in improving quality of life among patients with STGD1. A comprehensive search on PubMed and Google Scholar was performed with the keywords "Stargardt disease," "gene therapy," and "clinical trials in Stargardt disease." Studies report on the following range of promising treatments: gene therapy approaches, including dual AAV vectors [e.g., ABO-504, VG-801] and AAV5-hRORA; pharmaceutical interventions, such as ALK-001, Emixustat, RBP4 antagonists, and metformin; replacement therapies with stem cells; and genome editing methods, including CRISPR-Cas9. Personalized medicine, especially by genome profiling, holds great promise for targeted treatment. While most of these promising approaches still require further investigation into cost and efficiency, some have shown notable success with pluripotent stem cells, CRISPR-Cas9 for gene editing, and AONs for personalized treatment. Future studies need to take care of these limitations for improvement in therapeutic outcome in patients with STGD1.

Background and Aim: Stargardt disease(STGD1) is one of the most common early-onset inherited retinal diseases (IRDs) caused by a homologous mutation in the ABCA4 gene. This condition leads to the build of "Lipofuscin", a kind of trans-bi-product on retinal pigment epithelium(RPE) with central vision loss. These days, the challenge of improving the quality of vision in these patients is ongoing to make safer, efficacy and stable treatments to increase the quality of their lives. These strategies include; Gene Therapy(GT), Stem cell therapy,

pharmacological therapy, Gene editing and Personalized medicine among them, efforts to enhance gene therapy methods are being developed.

Methods: This work is a literature review that is conducted by searching articles in "Pub Med" and "Google Scholar" with the words "Stargardt disease", "gene therapy", "different therapeutic strategies" and "clinical trials in Stargardt disease".

Results: According to existing techniques for treating wide range of IRDs like dual adeno-associated virus(AAV) vector(ABO-504/VG-801), AAV5-hRORA, Luxturna(in the cure of RPE65 variants) related to gene therapy and several types of drugs such as; ALK-001(deuterated vitamin A), Emixustat (inhibits of producing trans retinoic compounds), RBP4 antagonism(reduces A2E), avacincaptad pegol(inhibition of C5 complement), metformin hydrochloride (stimulating of RPE macroautophagy) and Omega-3 fatty acids(DHA & EPA compounds) in pharmacological trails. Replacing of RPE with Embryonic, Mesenchymal, Bone marrow and plural potent stem cells around Stem cell therapy and CRISPR-Cas9, RNA editing(AONs design),prime-editing for Genome/RNA editing. Finally, Personalized medicine based on an individual's genome profiling is an innovative method.

Conclusion: Despite all these technologies, some of them include; GT vectors and delivery tools, they are cost-consuming. A more effective case of stem cell therapy is Pluripotent stem cell, for gene editing CRISPR-Cas9 technology and about personalized medicine, is Antisense Oligonucleotide (AON), according to the variants obtained from next-generation sequencing(MGS) results of a 10 -year old girl.

They are more successful in clinical trials, but the rest of them are needed to be investigated.

Keywords: Stargardt, gene therapy, stem cell therapy, gene editing, personalized medicine

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PBa-40

Nanoencapsulation for controlled gastrointestinal delivery of probiotics

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Abstract

Background and Aim: Probiotics, those beneficial microorganisms that support our gut health, face several challenges through the human digestive system. The harsh acidic environment of the stomach can decimate their numbers before they even reach the intestines. Nanoencapsulation is an innovative approach revolutionizing the method of administering

probiotics. Indeed, nano based drug delivery system protects probiotics from stomach acid, enzymes, and bile salts, ensuring they reach their destination and ready to colonize. Nanoencapsulation dramatically increases the survival rate of probiotics through the upper gastrointestinal tract. Moreover, these nano-carriers can be designed in a way that release their payload at specific sites in the intestines, thus providing many health benefits for humans.

Methods: Various techniques have been employed for nanoencapsulation of probiotics. The most common encapsulation methods for probiotics are solidify drying, shower drying, ionic gelation, complex coacervation, electrospraying, and electrospinning. Nanoencapsulation of probiotics is regularly accomplished with different biopolymers such as marine extricates, plant extrudates, proteins, dietary filaments, animal and microbial polysaccharide.

Results: The results of other studies indicated that the integration of nanotechnology with microencapsulation techniques can improve the controlled delivery of viable probiotic bacteria to the gut.

Conclusion: The real importance of nanoencapsulation lies in its ability to control the time and place of probiotics release. It is possible to design nanocarriers that respond to specific stimuli in the gastrointestinal tract. Encapsulated probiotics have a longer shelf life and can withstand a broader range of storage conditions. Nanoencapsulation allows us to protect diverse probiotic strains in a single formulation, enhancing the synergistic effects.

Keywords: Nanoencapsulation, probiotic, drug delivery

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PBa-41
Abstract Type: Systematic Review

Prevalence of Methicillin-Resistant *Staphylococcus Aureus* among Nurses in Hospitals of Iran: A Systematic Review

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Abstract

Background and Aim: Methicillin-Resistant *Staphylococcus Aureus* (MRSA) is one of the main causes of hospital infections. Hospital staff, especially nurses, is known as an important source of MRSA infection and because of their close contact with patients, they can transmit this infection to patients. MRSA can cause purulent infections and lead to death in people with immunocompromised. Therefore, the purpose of this systematic review is to investigate the prevalence of MRSA among nurses in Iranian hospitals.

Methods: (Nurse OR Nurses OR Nursing OR "healthcare staff" OR "healthcare personnel" OR "healthcare workers" OR "health personnel" OR "clinical staff" OR hospital OR "Health Center") AND Iran AND ("Methicillin-Resistant Staphylococcus aureus" OR MRSA) keywords selected from MeSH were merged using AND and OR operators and searched in Scopus, PubMed and Web of Science databases and Google Scholar scientific search engine. The search was conducted without time limit on October 19, 2024. Observational studies that investigated the prevalence of staphylococcus among nurses in hospitals of Iran were selected, and studies in which the data of nurses could not be separated from other hospital staff were excluded from the study.

Results: After searching, 754 studies were obtained, after removing duplicate articles, screening the title and abstract, finding the full text and screening the full text using the inclusion and exclusion criteria, 14 articles were included in the study. The selected studies have investigated hospitals in the cities of Tehran, Bam, Kermanshah, Qaem Shahr, Gorgan, Urmia, Dezful, Yasouj, Yazd, Ardabil, Ilam and Babol. A total of 1,354 (100%) nurses participated in these studies, of which 315 (23.3%) nurses were carriers of *Staphylococcus aureus*, and among 315 nurses, 100 (7.4%) of them were carriers of MRSA. In 11 studies, sampling was done only from the nostrils, in 2 studies from the skin of the hands and nostrils, and in one study only from the skin of the nurses' hands. In all studies, at least one nurse was infected with MRSA.

Conclusion: Due to the fact that in all the studies, nurses infected with MRSA were found, in order to prevent further spread of this infection in patients, it is necessary to constantly screen nurses and treat them in case of infection.

Keywords: Methicillin-Resistant *Staphylococcus aureus*; MRSA; Iran; Nurses; Prevalence

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PBa-42

Niosome encapsulated crocin: synthesis, characterization and antimicrobial evaluation of its free and encapsulated form against *Staphylococcus aureus, Escherichia coli* and *Bacillus cereus*

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Abstract

Background and Aim: Increasing awareness of the impact of diet on human health has prompted the scientific community and the food industry to search for effective alternatives to chemical antimicrobial compounds to assure microbial food safety. Microbial contamination of food by food-borne pathogen is a serious concern for consumers worldwide. Crocin, the main apocarotenoid of saffron, is considered the strongest antibacterial agent in the plant's composition. Niosome have been considered as a promising drug delivery system for encapsulation of bioactive compounds and enhancing the antimicrobial effects of natural compounds. Therefore, the aim of this study is to synthesize niosome containing crocin and evaluate its antibacterial effect on food pathogens (*Staphylococcus aureus, Escherichia coli and Bacillus cereus*).

Methods: Various formulations of niosome encapsulated crocin were prepared using different ratios of cholesterol, span, and crocin. Following that, the physical properties and loading percentage of crocin in the nanoparticles were examined using a spectrophotometer, scanning electron microscopy (SEM), zeta potential, Fourier transform infrared spectroscopy (FTIR) and DLS. Finally, the antibacterial effects of crocin in both free and encapsulated forms by nanoparticles at different concentrations were analyzed against the target microorganisms using MIC and MBC methods.

Results: The optimal formulation of niosome had a size of 139 nm and an encapsulation efficiency of 72% in this study. Its structure was spherical based on electron microscope images. The release study indicated that the release rate of crocin in its free form was faster than in the niosome form. Furthermore, Antimicrobial tests demonstrated that the crocin loaded in niosome had higher significantly antimicrobial effects compared to crocin alone against the studied bacteria.

Conclusion: The results of this study indicated niosome encapsulating crocin showed significant antimicrobial effects on three pathogens, Continuous and controlled release of crocin from the niosome, along with reduced the growth of *E. coli, S. aureus* and *bacillus cereus* suggesting their potential as a suitable drug delivery system

Keywords: Niosome, crocin, antimicrobial effects, foodborne pathogens

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PBa-43

A Study on the Prevalence of Coagulase-positive *Staphylococcus aureus* and *Bacillus Cereus* from Cream Sweets Available in Confectioneries in the Southern Regions of Karaj

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Abstract

Background and Aim: Confectionery products, due to their ingredients and nutrients such as milk and egg products, provide a suitable environment for the growth of food pathogens and can quickly become spoiled and inedible if storage conditions are not properly maintained. The aim of this descriptive-cross-sectional study is to investigate the prevalence of coagulase-positive *Staphylococcus aureus* and *Bacillus Cereus* in cream pastries available in confectioneries in the southern region of Karaj.

Methods: In this study, 178 cream pastries of various types were randomly sampled from 25 confectioneries in the southern areas of Karaj, following sampling standards 20834 and 2836. To identify and isolate *Staphylococcus aureus*, the study initially used Giolitti-Cantoni broth (GC) as an enrichment medium, and Baird-Parker agar was used for microorganism culturing. Finally, rabbit citrate plasma was utilized for the coagulase test to confirm the presence of coagulase-positive *Staphylococcus aureus*. To identify *Bacillus cereus*, MYP culture medium was used in the first stage, and then blood agar culture was utilized to confirm the grown colonies and perform hemolysis tests in the second stage.

Results: The results of this study showed that 53 samples (29.8%) of the sweets samples, were contaminated with *Staphylococcus aureus*, and 20 samples (11.24 %) with Bacillus cereus. The highest contamination occurred in summer with *Staphylococcus aureus* (29.8%).

Conclusion: Our study indicates, the high rate of microbial contamination in the Cream Sweets; therefore; more attention and monitoring measures is needed to cream sweets quality and safety in the processing and distribution of these products.

Keywords: Cream Sweets, *Staphylococcus aureus*, *Bacillus cereus*, Bacterial contamination

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PBa-44

Title: Genotyping of Klebsiella pneumoniae isolates recovered from patients admitted to Mousavi and Valiasr hospitals by (GTG)5-PCR method

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Background: *Klebsiella pneumoniae* is not only a major hospital-acquired pathogen but also an important food-borne pathogen that can cause septicaemia, liver abscesses, and diarrhea in

humans. The present study was aimed to determine the capability of (GTG) 5-PCR assay for molecular typing of *K. pneumonia* strains isolated from patients with urinary tract infections.

Materials and Methods: In this descriptive-sectional study, K. pneumoniae strains were collected from hospitalized patients with urinary tract infection in Mousavi and Valiasr Hospital, zanjan, Iran. Isolates were identified by conventional microbiological tests. Bacterial DNA was extracted using boiling method and (GTG) 5-PCR assay was used for subtyping of the isolates. For clustering of isolates, dendrogram was generated according to the unweighted pair group method with arithmetic (UPGMA).

Results: Overall, 105 *K. pneumoniae* isolates were isolated and subjected to the molecular typing study. The (GTG) 5–PCR assay was able to differentiate the *K. pneumoniae* strains into 28 clusters with The 80% similarity level.

Conclusion The (GTG) 5-PCR assay enabled rapid molecular typing of *K. pneumoniae* strains. The strains of *K. pneumoniae* typed in this study would belong to different clones.

Keywords: ***Klebsiella pneumoniae*, Genotyping, (GTG)5-PCR**

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PBa-45

The presence of plasmid mediated quinolone resistance determinants *aac(6')-Ib-cr* gene in Escherichia coli clinical isolates collected from Tabriz hospitals

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Background and Aims

Escherichia coli is one of the important clinical pathogens and responsible for some nosocomial infections; especially urinary tract infection (UTI) pneumonia, septicemia. Fluoroquinolones are broad-spectrum antimicrobial activity group of antibiotics, with many advantageous pharmacokinetic properties including high oral bioavailability, large volume of distribution. Antimicrobial resistance to fluoroquinolones has grown Multiple drug resistance among *Escherichia coli* isolates is one of the most important challenges for treating of such infections worldwide.

This study was conducted with the aim of determining the antibiotic resistance against fluoroquinolone antibiotics and the presence of *aac(6')-Ib-cr* resistance gene in *Escherichia coli* isolates collected from Tabriz hospitals .

Methods

In this study, 150 gram-negative bacterial isolates, obtained from urinary tract infections in Madani and Al-Zahra hospitals in Tabriz were studied. The selective culture media and biochemical test were used for the identification of *Escherichia coli* isolates. Antibacterial susceptibility of isolates was defined to Commonly used antibiotics in the treatment of infections caused by gram-negative bacteria using disk diffusion (Kirby – Bauer) method. The presence of resistance *aac(6')-Ib-cr* gene was checked by PCR using specific primers

Results

80 *Escherichia coli* isolates were identified by biochemical tests. The highest antibiotic resistance of Escherichia coli isolates to Ampicillin with 100% and the lowest resistance with 23% to Gentamycin was observed. Resistance to Nalidixicacid and Ciprofloxacin was observed in 50 and 35%, respectively. *aac(6')-Ib-cr* gene was observed in 14% OF isolates.

Conclusion

High resistance to most of the studied antibiotics, especially fluoroquinolones, in the studied isolates should be consider as a must rigorously take into account. Antibiogram and selection of appropriate antibiotic is recommended before starting treatment.

Key words

Antibiotic resistance pattern; *Escherichia coli; aac(6)-lb-cr*

PBa-46
Abstract Type: Narrative Review

Review on the antibacterial dental implants: emerging strategies in reducing side effects

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Abstract

Background and Aim: Dental implant has siezed great attention in recent years and bacterial infections are the most common side effects associated with them. In this regards, using specific biomaterials in implant composition may reduce oral cavity infections besides increasing implants stability. It was aimed to review on the biomaterials used in different studies to decrease the potential bacterial infections in various types of dental implants.

Methods: We explored the internet in Google Scholar, Pubmed, Pubmed Central and Bing search engines using main key words including dental implant, stability and bacterial infection. All the manuscripts after 2018 were included in the present review.

Results: Si3N4 or Silicon nitride based dental implants follwed by silver-doped hydroxyapatite have demonstrated promising effects in antibacterial charactristics of dental implants. In addition, Si3N4 based implants have shown great biocompatibility and biomechanical flexibility compraed to other studied biomaterials.

Conclusion: Silicon nitride based dental implants maybe the best alternative to traditional biomaterials used in the composition of dental implants. Further studies are warranted to determine the long-term antibacterial effects and implant stability in different individuals with various background disease and oral cavity chemical composition.

Keywords: Dental implant, stability, Bacterial infection, biomaterials

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PBa-47

Molecular survey of plasmid-mediated colistin resistance gene (*mcr-1*) in carbapenem-resistant *Klebsiella pneumoniae* isolated from clinical sources

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Abstract:

Introduction: The most significant challenge in the treatment of *Klebsiella pneumoniae* is the increasing prevalence of resistance to a wide range of antibiotics. This bacterium, with its capacity to develop resistance markers, has rendered antibiotic treatments a significant challenge. Colistin is deliberated the last-resort antibiotic to treat infections caused by multidrug resistant (MDR) Gram-

negative bacteria. The recent increase in the use of colistin in clinical practice, accompanied by its unbridled use in agriculture, have contributed to the rapid dissemination of resistance. The objective of the present study was to investigate the prevalence of the *mcr-1* gene in carbapenem resistant *K. pneumoniae* (CRKP) collected from hospitalized patients in educational hospitals of Mazandaran University of Medical Sciences.

Materials and Methods: A total of 100 isolates of *K. pneumoniae* were collected from a variety of clinical samples over the course of one year. These isolates underwent confirmatory microbiological testing and biochemical analysis. CRKP strains were determined by the disk agar diffusion method, as prescribed by the Clinical Laboratory Standards Institute (CSLI, 2018). Also, colistin susceptibility test was done for CRKP strains by minimum inhibitory concentration (MIC) using broth microdilution method. Finally, colistin resistant strains were assessed for plasmid-mediated mcr-1 gene via polymerase chain reaction (PCR). The statistical analysis of the obtained data was conducted using SPSS 16.0 and Excel software, and the frequency and relative distribution of the variables were evaluated using these software.

Results: The majority of the samples were urine samples. A total of 45 of the 100 *K. pneumoniae* isolates identified were resistant to carbapenems. Among these, 28 were recognized as colistin-resistant base on MIC assay. Although, no plasmid-mediated colistin resistance gene mcr-1 was detected in these isolates.

Conclusion: Overall, the prevalence of colistin-resistance is alarmingly increasing among *K. pneumoniae* strains. Nevertheless, the results indicate that the mcr-1 gene has less important role in resistance to colistin among tested strains in our region. So, other mechanisms such as overexpression of efflux pumps and chromosomal mutations in genes involved in lipopolysaccharide synthesis may be contribute to the resistance to colistin.

Key words: *Klebsiella pneumoniae*, carbapenem, colistin, *mcr-1*

PBa-48
Systematic review

AI-Driven Antimicrobial agents Against Resistant *A. baumannii*

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Abstract

Background and Aim: *Acinetobacter baumannii* is a Gram-negative coccobacillus that poses a significant threat in healthcare settings. Its ability to acquire and accumulate resistance

determinants caused to the emergence of MDR[2] strains. These MDR strains exhibit resistance to a wide range of antibiotics, resulting in treatment failures, prolonged hospital stays, and increased mortality rates. Therefore, the identification of novel antimicrobial agents is imperative. This study aims to leverage the power of AI[3] to accelerate the discovery of effective and non-toxic compounds targeting *A. baumannii*. By analyzing extensive datasets, AI algorithms can efficiently identify and optimize potential drug candidates, thereby reducing time and costs.

Methods: A systematic review adhered to PICO and PRISMA guidelines to identify studies published between 2018 and 2024. A comprehensive search was performed across PubMed, Scopus, Web of Science, SID, Magiran, and Google Scholar using relevant MESH terms, including "Acinetobacter baumannii," "Anti-Bacterial Agent," and "Artificial Intelligence." Two independent reviewers screened the retrieved articles based on established inclusion criteria.

Results: A total of 18 articles yielded from relevant databases. After removing duplicates and irrelevant studies, six articles remained. These six articles described the use of four computational algorithms to identify novel antimicrobial agents and two techniques to design innovative AMPs[4] targeting *A. baumannii*. QSAR[5] analysis identified demethoxycurcumin as a potential therapeutic agent against colistin-resistant *A. baumannii* (MIC[6]: 64 mg/L). PTMLIF[7] model, in conjunction with a virtual screening of compounds derived from *C. incisa*, uncovered two terpene compounds, phytol, and α-amyrin, as effective inhibitors of carbapenem-resistant *A. baumannii* with a MIC of 100 µg/mL. Neural molecular reports identified halicin as a potent broad-spectrum antimicrobial agent capable of eradicating pan-resistant *A. baumannii* at a MIC of 1 µg/mL. MPNNs[8] were leveraged to identify abaucin, a compound demonstrating potent inhibitory activity against MDR-AB[9]. AI techniques were instrumental in developing AMPs such as Yi12, FK13, and SRP-2, which exhibited potent antimicrobial activity against MDR-AB.

Conclusion: These findings underscore the potential of AI to revolutionize antimicrobial drug discovery, offering a promising future in the fight against drug-resistant *A. baumannii*. The discovery of these novel antibacterial agents has the potential to reduce healthcare costs and alleviate the burden of disease. However, further research is needed to address knowledge gaps in this emerging field.

Keywords: Acinetobacter baumannii; Anti-Bacterial Agents; Artificial Intelligence; Drug Resistance; Machine Learning.

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[2] Multidrug-resistant
[3] Artificial Intelligence
[4] Antimicrobial Peptides
[5] Quantitative Structure-Activity Relationship
[6] Minimal inhibitory concentration
[7] The Pharmacophore-based Machine Learning Integrated Fragment-based Ligand Interaction Fingerprint
[8] Message Passing Neural Networks
[9] Multidrug-resistant A. baumannii

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PBa-49

Abstract Type: Systematic Review

Irritable Bowel Syndrome (IBS) and Gut microbiota: A Systematic Review Article

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Background and Aim: Irritable Bowel Syndrome (IBS) is a prevalent functional gastrointestinal disorder, particularly among women under 50 years of age. It affects approximately 10-20% of adults in Western countries, with similar prevalence observed in Asia. Recent microbiological research underscores the complex interplay between humans and their associated microbial communities, which serve as a crucial barrier against external pathogens by modulating the immune response. This study aims to explore the relationship between IBS and gut microbiota.

Method: This review synthesizes studies published on PubMed, Science Direct, and Google Scholar up to November 2024. The keywords were Irritable Bowel Syndrome, Gut Microbiota, Microbial Communities and Dysbiosis. By searching this database, 83 articles were found, and 72 were removed by reading titles and abstracts. 11 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: The equilibrium of the intestinal microbial ecosystem, known as eubiosis, is crucial for gut health, while dysbiosis indicates a disruption of this balance. A notable consequence of dysbiosis is Small Intestinal Bacterial Overgrowth (SIBO), which has been linked to Irritable Bowel Syndrome (IBS). SIBO and other forms of gut microbiome dysbiosis can exacerbate specific symptoms in certain IBS patients, such as bloating and discomfort. Probiotics, particularly strains like Bifidobacteria and Lactobacilli, show promise in preventing colon inflammation and promoting a stable intestinal microecology, potentially alleviating IBS symptoms. Conversely, opportunistic bacteria, including Clostridiales (Firmicutes), Bacteroides, and Escherichia coli (Proteobacteria), can produce harmful toxins that provoke intestinal inflammation, leading to abdominal pain and diarrhea. Understanding these dynamics underscores the importance of maintaining microbial balance and suggests that targeted probiotic therapies may offer a beneficial approach to managing IBS, ultimately improving overall gut health and enhancing the quality of life for affected individuals.

Conclusion: It seems that the relationship between Irritable Bowel Syndrome (IBS) and gut microbiota is complex. The interplay between dysbiosis and eubiosis likely affects IBS symptom severity, suggesting that restoring microbial balance could provide therapeutic benefits. Diet also plays a crucial role in influencing gut microbiota and IBS symptoms, highlighting the need for personalized dietary approaches. Further research is warranted to clarify these relationships and their treatment implications. A deeper understanding of the gut-brain axis may lead to innovative therapies that improve the quality of life for those with IBS.

Keywords: Irritable Bowel Syndrome, Gut Microbiota, Microbial Communities, Dysbiosis

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PBa-50

Investigation of intra-herd and inter-herd prevalence of brucellosis in rural and nomadic cattle population of Kerman province

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Abstract

Background and Aim: Brucellosis also known as "undulant fever" or "Malta fever" is a zoonotic bacterial disease caused by bacteria of the genus Brucella. It is almost transmitted by direct or indirect contact with infected animals, inhalation of infectious particles, and unpasteurized dairy products like raw milk or fresh cheese. In humans, brucellosis manifests with flu-like symptoms such as fever, weakness, malaise, and weight loss. In animals, brucellosis is characterized by abortion, infertility, and reduced milk production. This study was designed to identify the prevalence of Brucella infection in cattle of rural and semi-industrial areas of Kerman province.

Methods: In this study, a total of 495 blood samples were collected from cattle on rural and semi-industrial farms from 6 cities in northern Kerman province. A preliminary screening using the Rose Bengal test was performed, followed by Real-Time PCR analysis. Specific primers targeting IS711 gene of Brucella genus were employed for molecular detection.

Results: Out of 495 samples, 8 (1.6%) were positive by the Rose Bengal test, and 5 (1%) were positive by real-time PCR using Brucella genus-specific primers.

Conclusion: Therefore, Brucellosis infection is present in rural and nomadic livestock in northern Kerman province, identifying them as potential reservoirs for disease transmission. Unfortunately, there is no effective treatment for brucellosis in livestock. So the most effective prevention strategy is to cull infected animals. However, vaccination can be a valuable tool in the prevention of brucellosis within these areas. Prevention of human infection is primarily based on raising awareness, food-safety measures, occupational hygiene, laboratory safety, and pasteurization of milk and cheese to prevent transmission of infection from animals to humans.

Keywords: Brucellosis; Rose Bengal; Real-Time PCR; Kerman

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PBa-51

Abstract Type: Narrative Review

Role of microbiota in developing Parkinson's disease

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Abstract

Background and aim: Parkinson's disease (PD) is a progressive neurodegenerative disorder with rapidly increasing global prevalence and mortality rates, as highlighted by the Global Burden of Disease study. Clinically, PD is characterized by motor symptoms such as stiffness, bradykinesia, and resting tremor. Pathologically, it involves the degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc) and the accumulation of α-Synuclein (α-Syn) in Lewy bodies and Lewy neurites. Recently, the gut microbiota (GM) has been implicated in PD's pathogenesis. This review aims to explore the connection between gut dysbiosis, intestinal inflammation, and PD, emphasizing potential mechanisms and therapeutic interventions.

Methods: We searched PubMed, Scopus, Google Scholar, and Medline databases using the keywords: "microbiota AND Parkinson's disease", "gut microbiota AND neurodegenerative disorders", "Parkinson's disease AND gut-brain axis", and "microbiome AND Parkinson's pathogenesis".

Results: Recent studies indicate that PD patients exhibit increased intestinal permeability and inflammation. Enhanced oxidative stress caused by gut dysbiosis can stimulate intestinal neurons and glial cells, leading to α-Syn folding and accumulation. Furthermore, microglia may uptake α-Syn as it moves from the enteric nervous system (ENS) to the central nervous system (CNS), causing further deposition of α-Syn in the CNS. Activated microglia release IL-1, IL-6, and TNF, leading to neuroinflammation, oxidative stress, and α-Syn aggregation and dissemination, potentially resulting in neuron apoptosis. Persistent enteric inflammation and increased intestinal permeability can cause systemic inflammation, exacerbating blood-brain barrier (BBB) deterioration and microglia activation.

Conclusion: This narrative review highlights the significant role of gut microbiota in the pathogenesis of Parkinson's disease. The findings suggest that gut dysbiosis and intestinal inflammation contribute to the neurodegenerative process in PD through multiple mechanisms, including oxidative stress, microglial activation, and α-Syn aggregation. Further research is needed to explore potential therapeutic interventions targeting the gut-brain axis to mitigate PD progression.

Keywords: Parkinson's disease, Microbiome, Dysbiosis, Neurological disorders

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PBa-52

Abstract Type: Systematic Review

Antimicrobial Activity of Honey: A Systematic Review Article

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Background and Aim: Due to the widespread prevalence of drug-resistant bacterial strains, there is a need to search for antimicrobial substances, and honey with its antimicrobial properties is a very promising substance with a wide range of effects. Various components contribute to the antibacterial effect of honey. These components work synergistically and allow honey to be strong against all types of microorganisms, including multi-drug resistant bacteria, and to moderate their resistance to antimicrobial agents. This study examines the antimicrobial activity of honey.

Method: This systematic review article was performed within articles published at PubMed, Google Scholar, Science Direct until July 2024. The keywords were Honey, Antimicrobial Activity, Inflammation and Antibiotics. By searching this database, 21 articles were found, and 16 were removed by reading titles and abstracts. 5 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: The use of antibiotics with honey has the potential of anti It brought better microbial and synergistic effects against biofilms were observed. In medicine, honey is used in the treatment of superficial wounds, burns and inflammations, and if antibiotics are used, the effectiveness of honey increases. In addition, it has antiseptic effects and disinfects the wound site and produces vascular endothelial growth factor. stimulates Using honey cleans wounds or burn areas from free radicals and reduces scars. The anti-inflammatory and antibacterial property of honey prevents the destruction and fibrosis of the damaged area. Honey can heal scars quickly. Phenolic acid in honey is one of the most important groups of compounds with antimicrobial properties. Compounds in honey, such as lysozyme and phenolic acids, played a key role in the beneficial properties of the honeys tested in our study.

Conclusion: It seems that honey into medical treatments presents significant advantages, including reduced economic burdens and improved patient outcomes. By decreasing reliance on conventional antibiotics, honey not only lowers direct healthcare costs but also accelerates recovery times and minimizes hospitalization rates. Its multifaceted antibacterial and anti-inflammatory properties make it a valuable adjunct in wound care and infection management. More studies are still needed about the antimicrobial activity of honey.

Keywords: Honey, Antimicrobial Activity, Inflammation, Antibiotics.

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PBa-53

Original Research

Analysis of resistance genes in *Streptococcus agalactiae* isolated from pregnant women

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Abstract

Background and Aim:

Streptococcus agalactiae (*S. agalactiae*) is a commensal bacterium found in the human digestive and genitourinary tracts and is globally associated with severe diseases in neonates. Prevention strategies for *S. agalactiae* are challenged by antibiotic resistance, making the analysis of antibiotic-resistance genes critical for selecting suitable antibiotics for known carriers. The antimicrobial resistance profile of Group B Streptococcus (GBS) can differ significantly across geographic regions.

This study aimed to determine the patterns of antibiotic resistance genes in GBS isolates from pregnant women at Kosar Hospital, a teaching hospital in Urmia, Iran.

Methods:

Thirty-one isolates of *S. agalactiae* were obtained from rectal and high vaginal swabs of pregnant women. These isolates were tested for the presence of four resistance genes (*mef*A, *erm*B, *erm*TR, and *lin*B) using the polymerase chain reaction (PCR) method.

Results:

The only resistance gene detected in this study was *erm*(B), which encodes 23S rRNA methylases and contributes to macrolide resistance by modifying the antibiotic target site. Among the 31 isolates examined, four (12.90%) were found to carry this gene.

Conclusion:

The findings indicate the presence of the *erm*(B) gene in *S. agalactiae* isolates from women attending the gynecological clinic at Kosar Hospital in Urmia, Iran. The detection of this gene, which is linked to macrolide resistance, underscores the need for continued monitoring of antibiotic resistance patterns in clinical isolates of GBS. This information is essential for guiding effective antibiotic prophylaxis and treatment strategies to manage infections and prevent neonatal complications associated with S. agalactiae. Further research involving a larger sample size and additional resistance genes is recommended to obtain a more comprehensive understanding of the antibiotic resistance landscape in this region.

Keywords:

Streptococcus agalactia, Drug Resistance, Polymerase Chain Reaction, Macrolides

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PBa-54
Original Research

Capsular serotypes determination of *Streptococcus agalactiae* isolated from pregnant women in Urmia, Iran

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Abstract

Background and Aim:

Group B Streptococcus (GBS) is a bacterium that can cause life threatening infections such as sepsis, meningitis, and pneumonia in neonates. This bacterium is often carried in the vaginal tract of women and can be transmitted to infants during childbirth. There are ten capsular types of GBS, and their distribution varies globally. Vaccines based on capsular epitopes offer an effective approach to prevent neonatal infections, but the prevalent serotypes in Iran, particularly in Urmia, remain inadequately characterized. Therefore, the present study aimed to identify the capsular polysaccharide types of GBS isolated from pregnant women in Urmia, Iran.

Methods:

This experimental study analyzed 31 GBS strains collected from pregnant women between 35 and 37 weeks of gestation. The capsular serotypes of these GBS isolates were identified using the conventional polymerase chain reaction (PCR) method with specific primers, to assess the prevalence of GBS types in Urmia, Iran.

Results:

All 31 GBS isolates were successfully typed. Four capsular types—Ia, II, III, and V—were detected, while other serotypes were not observed. The distribution of these serotypes was as follows: type II (38.7%), type V (38.7%), type Ia (19.3%), and type III (3.2%).

Conclusion:

In conclusion, this study highlights that the predominant capsular types of Group B Streptococcus (GBS) in pregnant women in Urmia, Iran, are types II and V, followed by type Ia, with type III being relatively rare. The identification of these serotypes provides crucial

information for public health strategies and potential vaccine development tailored to the local epidemiological profile. These results underscore the need for further surveillance and study to support the formulation of preventive measures against neonatal GBS infections in the region.

Keywords:

Streptococcus agalactia, Serotyping, Polymerase Chain Reaction (PCR), Capsule, Women

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PBa-55

Carbapenem resistant in *Klebsiella pneumoniae* ST258

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Abstract

Klebsiella pneumoniae is an opportunistic pathogen and a hospital-acquired pathogen that poses a global health threat, causing chronic infections of the urinary tract and soft tissues, pneumonia and sepsis particularly in individuals with compromised immune systems. Transmission occurs through human contact. The ST258 strain of *Klebsiella pneumoniae* is a human pathogen responsible for nosocomial infections. This strain consists of two distinct genetic clades: clade I and clade II, which have different capsular polysaccharide gene regions. Clade II is derived from the ST11 and ST442 clones, while clade I has differentiated from clade II by the addition of ST42, based on homologous recombination of the capsular polysaccharide gene region. The formation of biofilms and iron acquisition contribute to the persistence of this strain.

Carbapenems are the last line of defense against multidrug-resistant gram-negative pathogens, such as *Klebsiella pneumoniae* strain ST258. Carbapenemase and metallo-β-lactamase are the primary mechanisms of carbapenem resistance in *Klebsiella pneumoniae*. The presence of replicative plasmids in this bacterium contributes to its resistance to carbapenems. Antibiotic resistance genes on plasmids are evolving over time through genetic changes.

The plasmid content in ST258 includes two subgroups, I and II. Subgroup I has greater diversity, and lncFII, the most common plasmid type associated with carbapenem resistance, belongs to this subgroup.

Background and Aim: *Klebsiella pneumoniae* is a gram-negative bacterium from the *Enterobacteriaceae* family. This bacterium is an opportunistic pathogen that coexists in the gastrointestinal tract and nasal passages of healthy individuals without causing disease. However, in people with immune deficiencies, this bacterium can cause illness due to its opportunistic nature.

Concerns have arisen worldwide regarding its resistance to carbapenems. Plasmids are the main agents responsible for the transmission of carbapenem resistance in *Klebsiella pneumoniae* ST258. The sharing of these plasmids raises significant concerns about human health globally. Identifying the resistance genes is crucial for preventing the spread of this bacterium.

Methods: Article for this review were identified using google scholar.

Results: *Klebsiella pneumoniae* ST258, which is resistant to carbapenems and multiple other antibiotics, as well as new medications, can be effectively treated using immunotherapy, specifically monoclonal antibodies and antibiotics that target the bacterial polysaccharide capsule. These antibodies help eliminate the ST258 strain through both intracellular and extracellular processes, preventing the spread of infection.

Capsules and surface lipopolysaccharides are developed strategies to combat carbapenem-resistant strains, including ST258. Monoclonal antibodies can be used in cases where antibiotic failure occurs in the face of infection. Vaccines also help reduce antibiotic resistance and limit the emergence of resistant strains.

Conclusion: The high prevalence of carbapenem resistance in *Klebsiella pneumoniae* strain ST258 in hospitals is concerning. Identifying carbapenem resistance genes through molecular typing provides important information about the global transmission of these resistance genes in ST258. Genomic analyses based on whole genome sequencing are effective for identifying genomic markers, but they are associated with high costs. The identification of carbapenem resistance genes in *Klebsiella pneumoniae* should be continuously updated to utilize the most appropriate new antimicrobials and to prevent their spread.

Keywords: *Klebsiella pneumoniae*, ST258, carbapenem resistance, plasmid, opportunistic pathogen

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PBa-56

Article Type: Original

Detection of mupirocin, gentamicin and erythromycin resistance genes in methicillin resistant *Staphylococcus aureus* clinical isolates

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Background and Aims:

For early diagnosis and detection of nosocomial infections, markers and antibiotic-resistant genes (ARG) serve as an important route in any hospital setting. *Staphylococcus aureus* is one of the etiological agents involved in many nosocomial infections. The emergence of methicillin resistant *Staphylococcus aureus* (MRSA) has alter the therapeutic regimen of this organism. In the present study we developed a multiplex PCR for the detection of *S.aureus* and resistant to methicillin, aminoglycosides, macrolide, mupirocin genes.

Methods

A total of 1389 clinical samples from patients admitted to the University based hospital and developed nosocomial infection after 72 hours of admission were enrolled in the study. The specimens were send to Division of Microbiology, Sina Hospital where they were processed for any bacterial growth. The *S.aureus* isolated from these specimens were subjected to antibiotic susceptibility test by disk diffusion assay. PCR was later performed on *S.aureus* isolates which were found methicillin-resistant by cefoxitin disk (as per CLSI criteria) and then E-test was performed for oxacillin, gentamicin and mupirocin.

Results

Among 89 MRSA isolates, all isolates were found to harbor *mecA* gene. Resistance towards aminoglycosides by possession of genes (*aph(3)-IIIa, aac(6)-Ie-aph(2)-Ia, ant (4)-Ia)* was observed in 28.4% ,31%, and 38.5% isolates respectively. The first mentioned gene was isolated from wound infections and next two genes were observed in *S.aureus* isolated from body fluids. Twenty two strains were found clindamycin resistant and *ermA* and *ermC* genes were observed in isolates cultured from endotracheal aspiration. Mupirocin gene was prevalent among isolates obtained from abscesses. Multiplex PCR took less time to observe simultaneously the presence of MRSA along with ARGs.

Conclusion

Classical method of detection of MRSA and the antibiotic resistance is a time consuming taking 72 hours. However, if a diagnostic laboratory develops multiplex PCR for the detection and presence of ARG, it will help in reporting in less time paving way for the earliest treatment with appropriate antibiotic.

Key Words

Staphylococcus aureus, MRSA, Aminoglycosides, Mupirocin, Erythromycin, Antibiotic resistant genes

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PBa-57
Abstract Type: Original Research

Three years study of bacterial etiology of surgical site infections in the North of Iran

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Abstract

Background and Aim: Surgical site infections (SSIs) are a serious and common complication that can occur after surgical procedures. SSIs are caused by bacteria introduced into the surgical wound during the operation, either through contaminated instruments, healthcare personnel, or implants. Prompt recognition and management of these infections are crucial in preventing further complications and ensuring positive patient outcomes. The present study aimed to determine the prevalence and bacterial etiology of SSIs in the North of Iran.

Method: This cross-sectional study was conducted over a three-year period from March 2021 to 2024 on all cases of SSIs hospitalized at the Poursina hospital in the North of Iran. Standard microbiological tests were followed for bacterial isolation and identification. IR.GUMS.REC.1403.283

Results: Among the 276 patients studied, the frequency of isolated bacteria from surgical wound infections included 83 cases (30.1%) of *Enterobacter* spp., 60 cases (21.7%) of *Klebsiella* spp., 45 cases (16.3%) of *Escherichia coli*, 37 cases (13.4%) of Staphylococci, 29 cases (10.5%) of *Pseudomonas* spp., and 22 cases (8%) of *Acinetobacter* spp. The average age of the studied patients was 48.45 ± 18.65 years. Of the patients, 201 (72.8%) were male and 75 (27.2%) were female. The average length of hospitalization for the patients was 33.40 ± 10.24 days. Totally, 219 patients (79.3%) were discharged and 57 patients (20.7%) died.

Conclusion: The findings of regional assessments, provide good epidemiological background for comparing our situation with other regions. The results also indicate that there should be more focus on controlling and preventing hospital-acquired infections in patients. Ultimately, to improve the quality of healthcare services and reduce mortality from hospital-acquired infections, greater cooperation between healthcare and research centers is essential.

Keywords: Surgical site infections; Bacterial infection, Hospital-acquired infections

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PBa-58

Evaluation of Prevalence and Antibiotic Susceptibility Pattern of Bacterial meningitis in hospitalized and outpatients Children in Ahvaz Abuzar Hospital in

2020-2021

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Background and Aim:

Meningitis is a considerable neurologic emergency that opportune diagnosis and treatment can reduce disease burden. Identification of bacterial meningitis is essential to determining the frequency of bacterial meningitis and its pattern of antibiotic susceptibility in children.

Methods:

the present study was conducted on records of 302 suspected bacterial meningitis patients from March 2020 till March 2021 in Abuzar Children Educational-Health Care Center Ahvaz, Iran. The patients' microbiological records with suspicion of meningitis were collected using hospital database files. Cerebrospinal fluid samples of suspected patients were inoculated on both blood and chocolate agar culture medium then isolated for 24 hours in an anaerobic jar. Gram stain tests were also performed to help with bacterial identification. Causative agents were determinded by disk defusion assay. Eventually, obtained data were analyzed by IBM statistic SPSS 26. A P-value of ≤0.05 was considered statistically significant

Results:

. This study comprised 15 positive bacterial cultures out of 302 suspected meningitis samples. 40% of the patients were male, and all of them were younger than two years of age. Among 15 children with positive culture according to gram stain test results, 47% of positive bacteria, and the rest of them were gram-negative bacteria. *Streptococcus agalactiae* (n=3; 20%) and *Staphylococcus epidermidis* (n=2; 13.3%) were detected as the most common gram-positive bacteria while the most common isolated gran-negative bacteria were *Entrobacter* (n=3; 20%) and *E.coli* (n=2; 13.3%). Antibiogram test results indicated the susceptibility of *Streptococcus agalactiae* and *Staphylococcus epidermidis* to vancomycin and ciprofloxacin; however, both

have shown high resistance to β-lactam antibiotics like penicillin and ampicillin. Besides, gram-negative bacteria such as *Entrobacter* and *E.coli* were resistant to most of the antibiotics used in this study.

Conclusion:

The initial findings affirmed that gram-positive bacteria, particularly *Streptococcus agalactiae* and *Staphylococcus epidermidis*, are the leading causes of bacterial meningitis in children. Because antibiotic resistance is one of the most serious global health threats and how antibiotics' effects became harmful in bacterial meningitis or efficient in treating it, timely and careful diagnosis is crucial.

Keywords: antibiotic resistance, bacterial meningitis, hospitalized children

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PBa-59
Abstract Type: Review Article

Beyond Antibiotics: Harnessing Microbial Cell Death Mechanisms for Disease Control

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Abstract

Background and Aim: As antimicrobial resistance (AMR) continues to grow, traditional antibiotics face significant challenges in treating infections. Recent research has turned to microbial cell death pathways as a promising alternative strategy to control pathogens. These mechanisms, including apoptosis-like cell death, autolysis, and programmed cell death in

bacteria, provide an innovative approach to combat infections without relying on conventional antibiotics.

Methods: This review examines studies published in the last decade that focus on microbial cell death mechanisms and their potential applications in disease control. A comprehensive search was conducted across PubMed, Scopus, and Web of Science databases using keywords such as "microbial cell death," "antimicrobial resistance," and "alternative therapies." Inclusion criteria were original research articles and reviews that specifically explored microbial self-destruction pathways and therapeutic applications. Data extraction focused on methodologies, results, and outcomes relevant to each type of cell death mechanism.

Results: : A total of 45 studies were included, categorizing findings into apoptosis-like cell death, autolysis, and necrosis in bacterial and fungal pathogens. Apoptosis-like death mechanisms, observed in *Escherichia coli* and *Mycobacterium tuberculosis*, were found to be inducible by environmental stresses, potentially limiting pathogenic survival. Autolysis, particularly in biofilm-forming bacteria, showed potential for weakening biofilms and enhancing immune clearance. Studies on necrosis-like pathways highlighted the potential of genetic manipulation to initiate self-destruction in pathogens, reducing infectivity and transmission rates.

Conclusion: The review highlights microbial cell death mechanisms as an underexplored field with substantial promise in antimicrobial therapy. Utilizing these pathways may help in controlling AMR, particularly in biofilm-associated infections and persistent infections where traditional antibiotics are ineffective. However, further studies are needed to understand the regulatory factors and potential side effects of manipulating these pathways. This review supports microbial cell death mechanisms as a viable, innovative alternative to conventional antibiotics, providing a foundation for future research in microbial self-destruction therapies.

Keywords: Microbial cell death, Antimicrobial resistance, Alternative therapies.

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PBa-60
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Emergence of Colistin resistance among clinical isolates of *Enterobacteriaceae*

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Abstract

Background and Aim: Antibiotic resistance has emerged as a critical global health issue. The *Enterobacteriaceae* family is responsible for numerous infections and fatalities worldwide, primarily due to their ability to acquire resistance to nearly all available antibiotics. The alarming increase in multidrug-resistant (MDR) strains has compelled healthcare professionals to resort to colistin as a treatment alternative. Regrettably, resistance to colistin has also escalated in recent years. This study was conducted to identify clinical isolates of E. coli and Klebsiella spp. that exhibit resistance to colistin in northwestern Iran.

Methods: In this investigation, isolates of E. coli and Klebsiella spp. were obtained from various clinical specimens collected from patients at seven hospitals in northwestern Iran. Following the completion of sample collection, the isolates were assessed for colistin resistance using a microdilution method with cation-adjusted Muller Hinton broth (CAMHB) at concentrations of 2 µg/mL and 4 µg/mL of colistin. According to CLSI guidelines, a minimum inhibitory concentration (MIC) of ≤ 2 mg/mL was classified as colistin susceptible, while an MIC of ≥ 4 mg/mL was deemed resistant. Subsequently, the precise MIC for each colistin-resistant strain was determined.

Results: During the study period, a total of 500 bacterial isolates were evaluated for colistin resistance. Among these, 19 isolates (3.97%) demonstrated phenotypic resistance to colistin, as indicated by the microdilution assay. The MIC values for the resistant isolates ranged from 32 to 512 µg/mL.

Conclusion: The results of this study suggest that the prevalence of colistin resistance is relatively low; however, this finding serves as a cautionary note for treatment practices, as the dissemination of these resistant strains may increase with continued prescription by healthcare providers.

Keywords: Colistin resistance; Enterobacteriaceae; Klebsiella; E. coli, Clinical specimens

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PBa-61
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Antibiotic Susceptibility Patterns of Multidrug-Resistant *Pseudomonas aeruginosa*: Evaluating Colistin-Based Combination Therapies in Laboratory Conditions

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is a notable multidrug-resistant (MDR) pathogen frequently responsible for severe infections in hospitalized patients, particularly in intensive care units (ICUs). The increasing prevalence of antibiotic resistance among strains of *P. aeruginosa* necessitates urgent research into effective treatment regimens. This study aims to evaluate the antibiotic susceptibility patterns of MDR *P. aeruginosa* isolates to colistin-based regimens in laboratory conditions, focusing on the combination effects of colistin with amikacin and meropenem.

Methods: In this study (Approval ID: IR.DUMS.REC.1401.099), clinical isolates of *P. aeruginosa* were collected from patients at Ganjavian Hospital. Antibiotic susceptibility testing was performed using the disk diffusion method (Kirby-Bauer) following CLSI 2023 guidelines. The Minimum Inhibitory Concentration (MIC) for colistin, meropenem, and amikacin was determined using micro broth dilution techniques. Additionally, the checkerboard assay was employed to assess the synergistic effects between colistin/amikacin and colistin/meropenem combinations, with the Fractional Inhibitory Concentration (FIC) index calculated to interpret the results.

Results: A total of 38 *P. aeruginosa* isolates from patients at Ganjavian Hospital were examined. Of the patients, 46% were male and 54% were female, with a mean age of 42.48 years. The highest antibiotic resistance was observed against levofloxacin (57.9%), aztreonam (52.6%), and ciprofloxacin (52.6%), while the highest sensitivity was found for colistin (65.8%), piperacillin/tazobactam (60.5%), and ceftazidime (60.5%). Of the isolates, 58% were multidrug-resistant (MDR) and 26% were extensively drug-resistant (XDR). The chi-square test revealed a significant relationship between gender and resistance ($p = 0.008$), but no significant association was found between resistance and other factors such as immune system status ($p = 0.686$), heart failure ($p = 0.698$), diabetes ($p = 0.829$), and catheter use ($p > 0.05$). The checkerboard assay results confirmed no antagonistic effects for colistin/amikacin and colistin/meropenem combinations, suggesting that these combinations may be effective therapeutic options against MDR strains of *P. aeruginosa*.

Conclusion: The findings underscore that *P. aeruginosa maintains* significant resistance against several antibiotics while remaining susceptible to colistin, piperacillin/tazobactam, and ceftazidime. The lack of antagonism in combination therapies involving colistin suggests that these regimens may serve as effective strategies against MDR infections. Given the rising

challenge of antibiotic resistance, these results highlight the necessity for ongoing surveillance and innovative therapeutic approaches to combat infections caused by resistant bacterial strains.

Keywords: *Pseudomonas aeruginosa*; Drug Resistance; Colistin.

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PBa-62
Abstract Type: Original Research

Prevalence and Antibiotic Resistance Patterns of *Klebsiella* spp. in Nosocomial Infections: Insights from a Seven-Year Surveillance in Ilam Province, Iran

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Abstract

Background and Aim: *Klebsiella* spp., especially *Klebsiella pneumoniae*, is a major nosocomial pathogen linked to severe healthcare-associated infections (HAIs), including pneumonia, bloodstream infections (BSI), and urinary tract infections (UTI). Its multidrug resistance, particularly in extended-spectrum beta-lactamase (ESBL) and carbapenemase-producing strains, poses significant therapeutic challenges. This study aimed to evaluate the prevalence, distribution, and antibiotic resistance trends of *Klebsiella* spp. in nosocomial infections over seven years in Ilam Province, Iran, to inform local infection control and treatment strategies.

Methods: This descriptive-analytical study utilized data collected from the National Nosocomial Infection Surveillance System over seven years (March 2017 to March 2024) from 13 hospitals in Ilam Province. HAIs were defined according to national protocols, requiring infections to occur at least 48 to 72 hours post-admission, with no prior evidence of infection at admission. Infection sites were categorized into instrument-associated infections (e.g., ventilator-associated pneumonia [VAP], catheter-associated urinary tract infections [CA-UTI],

catheter-associated bloodstream infections [CA-BSI]) and primary infection groups (e.g., pneumonia [PNEU], BSI, UTI, surgical site infections [SSI]). Antibiotic resistance data were analyzed for key antimicrobials, focusing on ESBL and carbapenemase-producing strains. Statistical analyses were conducted using SPSS version 27 to assess prevalence, resistance trends, and their clinical implications.

Results: *Klebsiella* spp. contributed to 164 instrument-associated infections (12.31%), including 64 VAP, 28 CA-UTI, 6 CA-BSI, and 66 other infections. Among primary infection groups, it caused 275 cases (7.43%), predominantly ventilator-associated events (VAE, 115 cases), followed by PNEU (52), UTI (48), BSI (25), SSI (27), and other categories (8).

Resistance data highlighted *Klebsiella* spp. as a major multidrug-resistant pathogen. ESBL production, indicated by resistance to 3rd/4th generation cephalosporins, averaged 79.68%, peaking at 85.18% in 2020 and decreasing to 75.18% in 2023. Fluoroquinolone resistance averaged 68.55%, gradually declining from 80% in 2017 to 67.5% in 2023. Carbapenem resistance, indicative of KPC production, averaged 58.46%, with fluctuations, peaking at 80% in 2020 and rising to 73.46% in 2023 after a dip in 2021 (47.91%). These trends underscore persistent resistance despite interventions, requiring focused action.

Conclusion: *Klebsiella* spp. continues to be a formidable challenge in nosocomial settings, with high prevalence and significant resistance to critical antibiotics. The study underscored the widespread prevalence of ESBL and KPC-producing strains, particularly against cephalosporins and carbapenems, highlighting gaps in current infection control strategies. The fluctuating trends in resistance suggest partial effectiveness of interventions but also emphasize the need for consistent, tailored antibiotic stewardship and infection control measures.

Keywords: *Klebsiella*; nosocomial infections; antibiotic resistance; infection control; healthcare-associated infections

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PBa-63

Global landscape of vancomycin-resistant enterococci in hematopoietic stem-cell transplantation patients: a systematic review and meta-analysis

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Abstract

Background and Aim:

One of the main risks of infection after hematopoietic stem cell transplantation (HSCT) is infection by gram-positive bacteria, including vancomycin-resistant enterococci (VRE). Based on the format of a global review and meta-analysis study, this study aims to investigate the incidence of VRE bloodstream infection (BSI) after HSCT in colonized individuals.

Methods: The keywords of the systematic search included vancomycin-resistant enterococci and HSCT. These words were searched in Google Scholar, PubMed/Medline, Scopus, and Web of Science databases from January 1, 2000, to March 1, 2024. Studies that reported the prevalence of vancomycin-resistant enterococci in patients undergoing HSCT were included. The random effects model was used for the meta-analyses. Investigations were conducted according to PRISMA guidelines, and the protocol was registered in PROSPERO: CRD42024543491.

Results:

Out of 1100 screened papers, 28 were eligible. The random effects model was established to analyze the incidence of VRE BSI after HSCT. The pooled prevalence of co-infection for Allo-HSCT recipients was 3.023 (95% CI, Z-value = -3.5, p-value < 0.0001), and this value for Auto-HSCT recipients was 11.89 (95% CI, Z-value = -2.923, p-value < 0.001). These results showed that the rate of BSI due to vancomycin-resistant enterococcus in Auto-HSCT recipients is higher than Allo-HSCT.

Conclusion:

The prevalence of vancomycin-resistant *enterococci* in Auto-HSCT recipients is higher than that of Allo-HSCT, possibly due to colonization of the intestines of these people with vancomycin-resistant *enterococci* before transplantation. VRE Colonization before transplantation increases the likelihood of post-transplant VRE BSI and other bacterial infections, including Gram-negative. The strains should be analyzed by sequencing before and after HSCT for a more detailed investigation.

Keywords: Vancomycin-resistant enterococci , Hematopoietic stem-cell transplantation , Bloodstream infections , Meta analysis

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PBa-64

The Effect of Climate Changes on Human Bacterial Infectious Diseases

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Abstract

Background and Aim: Climate change poses a significant challenge to global health, particularly through its influence on the emergence and spread of bacterial infectious diseases. Rising temperatures, altered precipitation patterns, and increased frequency of extreme weather events are reshaping the ecological landscape in which these pathogens thrive. This review aims to synthesize current research on how climate change affects human bacterial infectious diseases, focusing on the mechanisms of disease emergence, geographic distribution changes, and implications for public health

Methods: A comprehensive literature review was conducted, analyzing peer-reviewed studies that examine the relationship between climate variables and the incidence of bacterial infections. The review encompasses epidemiological data, climate modeling studies, and ecological assessments to provide a multidisciplinary perspective on this pressing issue

Results: Findings indicate that climate change has significantly expanded the geographical range of various bacterial pathogens, particularly those associated with waterborne and vector-borne diseases. Increased temperatures have been linked to higher incidences of infections such as cholera and salmonella, while extreme weather events facilitate outbreaks by disrupting sanitation and health infrastructure. Additionally, climate-induced human migration exacerbates the transmission dynamics of these diseases.

Conclusion: The interplay between climate change and bacterial infectious diseases underscores the urgent need for integrated public health strategies that consider environmental factors. Proactive measures are essential to mitigate the impacts of climate change on infectious disease patterns, including improved surveillance systems and enhanced healthcare infrastructure to cope with emerging threats.

Keywords: Climate change, bacterial infectious diseases, public health, epidemiology, environmental

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PBa-65
Abstract Type: Original Research

Evaluation of pathogenic microorganisms in body fluids

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Abstract

Background and Aim: In hospital wards, infections are one of the most common complications that need to be managed both prophylactically and personally. This study was conducted to evaluate the culture for the diagnosis of infection and evaluate the clinical and laboratory characteristics of the disease on body fluids.

Methods: In this study, patients hospitalized in one of Zahedan's hospitals over 36 months were examined. A total of 192 samples were collected and cultured at 37ºC for 48 hours. If there was no growth on the plates, they were examined daily for 3-7 days. We included and analyzed 192 samples collected over 3 years (2020-2023). These clinical samples (abdominal fluid, pleural fluid, pleural fluid, synovial fluid, ascites fluid, peritoneal fluid, and cerebrospinal fluid (CSF)) were examined for positive bacterial cultures and isolated pathogens.

Results: Plural fluid (38.54%, n=74), CSF (35.41%, n=68), Ascites fluid (10.41%, n=20), Pleural fluid (6.25%, n=12), Abdominal fluid (5.20%, n=10), Synovial fluid (4.16%, n=8) and peritoneal fluid (0%, n=0) were the clinical samples. Of the 192 samples collected at admission, 24 were positive, with 8 bacterial strains and 2 fungi isolated. Gram-negative cocci predominated at 66.6%. The most frequent were Acinetobacter species (37.5% of Gram-negative / 25% of total isolated strains), Klebsiella species (20.8%), Escherichia coli (E. coli) (12.5%), and Pseudomonas aeruginosa species (8.3%). Additionally, the frequency of Enterococcus species was 12.5%, Staphylococcus epidermidis 8.3%, and Staphylococcus aureus 4.1%.

Conclusion: Increasing awareness of these data may help guide future treatment outcomes. The new concept is that pathogenic microorganisms present in the community's microbial environment increasingly affect the hospital's microbial environment.

Keywords: Body fluids, Microorganisms, Culture, Infection

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PBa-66

Investigation of antimicrobial susceptibility of *Salmonella* serotypes among children in Iran

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Abstract

Background and Aim: Salmonella gastroenteritis causes significant morbidity among pediatric patients, mainly in developing world, such as the Middle East and North Africa (MENA) region. Concurrently, data from MENA countries like Iran, regarding prevalence of Salmonella serotypes, antimicrobial susceptibility, and biofilm production is scarce.

Methods: To determine the serogroup of 140 Salmonella isolates recovered from 4477 stool specimens collected from children with gastroenteritis, slide agglutination was used, and isolates were serotyped by PCR assay. The antimicrobial susceptibility of isolates was assessed by disk diffusion assay using CLSI guidelines**.**

Results: Nearly 94% of *Salmonella* isolates were recovered from ≤5-year-old patients, and 99% of isolates were non-typhoidal. *Salmonella* Enteritidis (41%) was the most common serotype that showed the highest antimicrobial susceptibility rate (>96%). Also the highest resistance with 48% being resistant to ≥1 test antimicrobial was shown among 35% of isolates that were not-typed (NT).

Conclusion: The most effective measure that may control pediatric salmonellosis outbreaks is raising awareness of parents of preschoolers about food safety. Majority of serotypes were sensitive to first-line antimicrobials.

Keywords: *Salmonella* serogroups, Serotypes, Antimicrobial susceptibility

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PBa-67

Review Article

The Gut-Brain Axis: Understanding the Influence of Gut Microbiota on Multiple Sclerosis

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Abstract

Background: Multiple sclerosis (MS) is a complex neuroinflammatory disorder characterized by the immune-mediated destruction of myelin in the central nervous system (CNS). Recent research has highlighted the significant role of the gut microbiota in modulating immune responses and its potential influence on the pathogenesis of MS through the gut-brain axis. This review aims to synthesize current knowledge regarding the interactions between gut microbiota and MS, exploring mechanisms of dysbiosis, immune modulation, and potential therapeutic strategies.

Methods: This study review synthesizes current literature on the relationship between gut microbiota and MS. We examined studies investigating microbial diversity, specific bacterial taxa associated with MS, mechanisms of immune modulation, and therapeutic strategies targeting the gut-brain axis.

Results: Evidence indicates that MS patients exhibit reduced microbial diversity and alterations in specific gut bacteria compared to healthy controls. Dysbiosis may lead to increased intestinal permeability, systemic inflammation, and altered immune responses that contribute to neuroinflammation. Mechanistic insights reveal that gut microbiota can influence T cell differentiation and neuroinflammatory processes through various pathways, including the vagus nerve.

Conclusion: The interplay between gut microbiota and MS underscores the potential of the gut-brain axis as a therapeutic target. Strategies such as probiotics, dietary modifications, and fecal microbiota transplantation may offer new avenues for MS treatment. Further research is needed to elucidate the precise mechanisms involved and to evaluate the efficacy of these interventions in clinical settings.

Ketwords: Gut Microbiota; Multiple Sclerosis; Gut-Brain Axis; Dysbiosis; Immune Modulation

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PBa-68

Quercetin: A promising phytochemical for methicillin-resistant *Staphylococcus aureus*

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Background and Aim: Quercetin, a phytochemical belongs to the flavonoid group of polyphenols and is found in fruits, vegetables, and various beverages, as well as in flowers, leaves, and seeds. The most abundant source of quercetin is onion (Allium cepa) and its other sources include tea, red wine, kale, and apples. The drug is effective against gram-positive and gram-negative organisms. Its effectivity on *S. aureus* and *Escherichia coli* has attracted many scientists and evidences show its potentiality against methicillin resistant *S.aureus* (MRSA).

Methods: Databases such as PubMed, Google scholar, and Medline were searched by key words "Quercetin", "Gram-Positive Bacteria", "Antibacterial", "pharmacological properties", "structure", *Staphylococcus aureus*" and "Methicillin resistant *S.aureus*" for this review.

Results: Quercetin has been shown to significantly inhibit *S. aureus* biofilm formation. In addition, quercetin can accelerate the wound-healing process by increasing fibroblast proliferation. Considering its antibacterial properties, at least 20 µg/mL of quercetin is sufficient to inhibit *S. aureus* and *Pseudomonas aeruginosa*. Quercetin showed marked antibacterial activity against hypersensitive MRSA strains at a concentration of 50 micro-m. Quercetin markedly inhibited the growth of hypersensitive MRSA strains in a dose-dependent manner. Further experiments showed that quercetin and tannic acid inhibited the formation of biofilms formed by three *S. aureus* strains in a dose-dependent manner. In particular, quercetin (1 µg ml1) inhibited biofilm of MRSA by >80% and MSSA (ATCC 6538 and ATCC 25923) by >50% (7). 7-*O*-pivaloxymethyl quercetin has also revealed an enhancement in the bactericidal activity of various antibiotics (EtBr, tetracycline, ciprofloxacin).

Conclusion: Quercetin as a phytochemical that belongs to the flavonoid group of polyphenols has many beneficial antibacterial effects, and as an antibacterial drug providing a new perspective for developing antibacterial drugs. These properties must be considered utmost of importance.

Keywords: Quercetin; Gram-Positive Bacteria; Antibacterial effects; *Staphylococcus aureus*;

MRSA

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PBa-69
Abstract Type: Systematic Review

The Potential of Polyclonal and Monoclonal Antibodies as Therapeutic Agents for Sepsis: A Systematic Review

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Abstract

Background and Aim: Despite ongoing challenges in addressing sepsis-related mortality, research has yielded inconsistent findings regarding the efficacy of monoclonal and polyclonal antibodies in treating septic patients. This study aims to update the existing literature by reviewing clinical randomized trials published up to March 2024.

Methods: The primary objective is to evaluate the impact of monoclonal and polyclonal antibodies on mortality rates and hospitalization outcomes in patients with sepsis. Comprehensive searches were conducted across Scopus, Web of Science, EMBASE, PubMed, and Cochrane databases, focusing on randomized controlled trials involving patients with septic shock or bacterial sepsis. Two independent reviewers evaluated the eligibility of identified trials based on predefined criteria and subsequently performed data collection and analysis.

Results: The results indicate that both monoclonal and polyclonal antibodies are generally safe, with mild to moderate adverse effects reported. However, most studies did not demonstrate statistically significant differences in inter- and intra-group comparisons ($p > 0.05$).

Conclusion: Further research is warranted; nonetheless, the findings suggest potential benefits such as increased survival rates, greater numbers of ventilator-free and ICU-free days, resolution of organ dysfunction, and modulation of inflammation-related cytokines.

Keywords: Monoclonal antibody; Sepsis; Septic shock; Septicemia; Randomized clinical trial

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PBa-70

Abstract Type: Original

Prevalence of nosocomial infections in burn patients in Velayat hospital, Rasht, Iran

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Abstract

Background and Aim: Burn patients are at high risk of developing nosocomial infection because of their injured skin barrier and suppressed immune system. This study aims to determine the frequency of nosocomial infections in burn patients.

Methods: This study was a cross-sectional study conducted at Velayat Hospital in northern Iran from 2017 to 2022. Demographic and clinical characteristics of the patients such as age, gender, percentage of burns, hospitalization department, duration of hospitalization, use of invasive methods, and type of hospital infection were collected and entered into SPSS software version 22, and statistical analysis was carried out.

Results: Out of 24,558 burn patients referred during the study period, the prevalence of nosocomial infection was 3.98%. Of which 843 cases had skin and soft tissue infections, 58 cases bloodstream infection, 53 cases ventilator-associated pneumonia, 18 cases urinary tract infection, 4 cases pneumonia, and 2 cases surgical site infection. The average age of the patients was 39.39 ± 20.62 years, and 705 (72.08%) were male, and 273 (27.91%) were female. The average burn percentage of the patients was 37.16 ± 23.59%. Also, 473 cases (56.1%) were hospitalized in the internal wards and 370 cases (43.9%) were hospitalized in the intensive care units. The average length of hospitalization of the patients and hospitalization to infection was 21.4 ± 58.7 days and 5.1 ± 20.6 days, respectively.

Conclusion: Our findings emphasize the need for careful disinfection and more strict infection control procedures in areas that serve immunosupressed individuals, such as burn patients. It is essential to conduct periodical and epidemiological studies of nosocomial diseases.

Keywords: Nosocomial infection; burns; epidemiology.

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PBa-71
Abstract Type: Original Research

Molecular Typing and Profile Analysis of Efflux Pumps, Outer Membrane Porins and Virulence-Associated Genes in *Klebsiella pneumoniae* Strains Recovered from Hospitalized Patients

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Abstract

Background and Aim: *Klebsiella pneumoniae* (*K. pneumoniae*) is a significant pathogen responsible for a range of healthcare-associated infections. The spread of hypervirulent and multidrug-resistant *Klebsiella pneumoniae* (hvKp) strains among hospitalized patients is a growing concern. These strains not only pose treatment challenges due to their resistance to multiple antibiotics but also contribute to increased morbidity and mortality. Understanding the genetic basis of resistance and virulence, including the role of efflux pumps and outer membrane porins, as well as the clonal relatedness of these strains, is crucial for developing targeted strategies to control their dissemination. In this study, we evaluate the antibiotic susceptibility, pathogenicity factors, and genetic diversity of *K. pneumoniae* strains isolated from hospitalized patients in Mazandaran province, North Iran.

Methods: A total of 95 *K. pneumoniae* isolates were collected from patients admitted to four teaching hospitals in Mazandaran, Iran. The isolates were confirmed using routine microbiological and/or biochemical diagnostics tests. Antibiotic susceptibility testing was screened using the disk diffusion method, and the presence of resistance and virulence genes was assessed through PCR-based technique. Genetic diversity of all clinical isolates of *K.*

pneumoniae was evaluated using the Enterobacterial Repetitive Intergenic Consensus (ERIC-PCR) method.

Results: The resistance patterns of the *K. pneumoniae* isolates varied significantly. The highest resistance rates were observed for ampicillin/sulbactam (95.8%), followed by ceftriaxone (88.4%), and ceftazidime (83.2%). Conversely, the lowest resistance was observed for Fosfomycin (3.2%). Interestingly, two isolates were non-MDR, remaining susceptible to all antibiotics tested. A wide range of virulence-associated genes were detected, including *mrkD* (90.5%), *fimH-1* (80%), *entB* (92.6%), *iutA* (25.3%), and *ybtS* (68.4%). Genes encoding efflux pumps and outer membrane porins, such as *AcrAB* (98.9%), *tolC* (95.8%), *mdtK* (83.2%), *OmpK35 (*95.8%), and *OmpK36* (92.6%), were also prevalent. The high frequency of these genes highlights the potential for these isolates to evade antibiotic treatment and contribute to virulence. Genetic typing using ERIC-PCR revealed that the strains clustered into 17 distinct groups with a similarity coefficient of 90%. While the majority of isolates displayed similar profiles, 11 isolates were identified as singletons, suggesting the presence of genetically diverse strains in the hospital setting.

Conclusion: This work underscores the widespread frequency of MDR *K. pneumoniae* strains in hospitalized patients, with high diversity of virulence factors and the occurrence of genes linked to antibiotic resistance. The genetic diversity of these strains, as evidenced by ERIC-PCR analysis, indicates the potential for clonal spread within healthcare settings. These findings highlight the urgent need for comprehensive infection control measures, surveillance, and the development of novel therapeutic strategies to combat the rising threat of *K. pneumoniae* infections, particularly those caused by MDR and virulent strains.

Keywords: *K. pneumoniae*, MDR, virulence factor, ERIC-PCR.

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PBA-72
Abstract Type: Review Article

Microbial Imbalance and Fecal Microbiota Transplantation in Neurological Diseases

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Abstract

Background and Aim: Dysbiosis, an imbalance in the gut microbiota, has been implicated in the pathogenesis of various neurological disorders such as Parkinson's disease, multiple sclerosis, and autism. Fecal microbiota transplantation (FMT) is emerging as a therapeutic intervention to restore gut microbial balance, potentially offering neurological benefits.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Fecal microbiota transplantation, Microbiome, Neurological Diseases, 78 articles related to inclusion criteria were extracted and then analyzed.

Results: Research highlights a significant connection between gut-brain axis dysfunction and neurological diseases. Studies show that FMT can alter gut microbiota composition, reduce inflammation, and improve neurological symptoms. However, clinical trials are still in early stages, and results are variable depending on the disorder.

Conclusion: While FMT shows promise, particularly in disorders like Parkinson's and autism, its efficacy and safety are still under investigation. Mechanistic pathways through which gut microbiota influence the central nervous system need further exploration. FMT could complement current treatments but requires standardization in protocols for optimal outcomes. In conclusion, FMT represents a novel therapeutic approach for neurological disorders linked to dysbiosis. However, more research is necessary to validate its long-term safety and efficacy.

Keywords: Fecal microbiota transplantation, Microbiome, Neurological Diseases.

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PBa-73

Prevalence of Extended Spectrum β-Lactamase *Escherichia coli*, Klebsiella spp., and Proteus spp. in urine samples by disk diffusion and molecular methods in ,Urmia, Iran

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Background and Aim: Resistance to a wide range of common antimicrobials has made the proliferation of extended-spectrum beta-lactamase (ESBL)--producing strains a serious global health concern, complicating therapeutic strategies. The high proportion of ESBL producers among Enterobacteriaceae and the complex molecular epidemiology with different types of ESBL genes are of concern. ESBLs are plasmid-mediated groups of enzymes that hydrolyze penicillins, extended-spectrum cephalosporins, and aztreonam. This study was conducted to identify ESBL production in different Gram-negative bacilli isolated and further identify ESBL producers among Escherichia coli and Klebsiella bacteria by PCR method in Urmia city.

Methods: A total of 1500 isolates of gram-negative bacilli were isolated by examining more than 10000 urine culture samples. Then, all the isolated bacteria were identified by microbiology diagnostic methods such as differential media and diagnostic discs. The presence of ESBL positivity was detected using a double disc synergy test (DDST). The discs used in this experiment were ceftazidime and ceftazidime clavulanate. After antibiogram analysis, PCR for beta-lactamase (bla) genes of SHV, TEM, and CTX-M family was also performed using primers designed in 25 ESBL isolates of each Escherichia coli, Klebsiella, and Proteus species.

Results: Among 1500 Gram-negative bacilli isolated, 760 (39.69%) were ESBL producers. The main source of ESBL production was urine samples, with the highest ESBL production in Klebsiella sp. (60.12 %). Resistance to multiple classes of antibiotics was observed among ESBL producers. Among the bacteria that can have EBLS resistance, Proteus was the least of all. Among ESBL-producing genes, the prevalence of bla-CTX-M (68.3%) was the highest, followed by bla-TEM (41.2%) and bla-SHV (52.3%) in the present study. The frequency of ESBL-producing strains among clinical isolates is steadily increasing. Monitoring advanced drug resistance and molecular characteristics of ESBL isolates is essential to guide the appropriate and judicious use of antibiotics.

Conclusion: Multidrug-resistant Gram-negative bacilli have been increasingly responsible for life-threatening illnesses all over the world. Multiple risk factors were associated with ESBL infections both in the community and hospital setting It must be given importance. Prediction tools are needed to improve the protocol of appropriate empiric antibiotic selection while preserving antimicrobial stewardship recommendations.

Keywords: Extended-spectrum β-lactamase (ESBL), bronchoalveolar lavage, Antibiogram, PCR, urinary tract samples

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PBa-74

Molecular typing of Escherichia coli isolated from blood cultures of leukemia patients using ERIC-PCR

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Background

Leukemia is a type of cancer that affects the blood and bone marrow, causing an increase in white blood cells in these areas that affects the production of blood cells. Bloodstream infection (BSI) occurs when a pathogen such as bacteria or fungi is found in the blood from a sample taken. "Individuals diagnosed with blood cancer frequently experience bloodstream infections, with reported rates between 11 to 50%, and mortality rates between 10 to 35.3%. New research indicates that infections caused by gram-negative bacteria are more frequent compared to those caused by gram-positive bacteria. ERIC-PCR(Enterobacterial repetitive intergenic consensus)is a molecular typing technique that is employed to distinguish between bacterial strains by examining differences in both the length and sequence of intergenic regions found between conserved ERIC DNA sequences.

Methods

From June 2021 to December 2022, a research was carried out in Iran where 67 *E. coli* strains were identified from leukemia patients with bloodstream infections in hospitals located in two distinct regions. The genetic similarity of these E. coli isolates was investigated using the ERIC-PCR method. This procedure was performed using the primers as described previously program . The ERIC-PCR patterns of bands on agarose gel was compared by Gel Compar® II v.4.1 software (Applied Maths BVBA, Sint–Martens–Latem, Belgium).

Results

The results of ERIC-PCR analysis indicated that *E. coli* isolates had a similarity of ≥80–100%. Among 67 isolates by detecting 47 different ERIC profiles with a similarity cutoff of ≥95%. In total, 47 different ERIC profiles, including 8 common types and 39 single types (including one isolate) was detected among 67 isolates. Out of these eight common types, seven common types included two strains and one common type included 14 different strains.

Conclusion

Our research utilizing ERIC-PCR revealed the genetic variety and clonal relationships of E. coli strains that result in bloodstream infections in patients with leukemia or hematologic malignancies. The findings from our study, as well as others, suggest there is genetic diversity present among the *E. coli* strains identified in bloodstream infections.

Keywords *Escherichia coli*, Blood stream Infections (BSIs), Leukemia, ERIC-PCR, Molecular typing

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PBa-75

Comparison of the frequency of broad-spectrum beta-lactamases in gram-negative bacilli isolated from inpatients and outpatients with urinary tract infections

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Background and Aim: Broad-spectrum β-lactamases (ESBLs) are types of β-lactamase that can hydrolyze third-generation cephalosporins and are resistant to inhibitors. Some gram-negative bacilli, including *Klebsiella pneumoniae* and *Escherichia coli*, produce ESBLs; These bacteria are among the opportunistic pathogens that cause hospital infections Antibiotic resistance in ESBLS-producing strains has recently been raised as one of the emerging healthcare problems in the world. This study aims to compare the frequency of broad-spectrum beta-lactamases in gram-negative bacilli isolated from hospitalized and outpatient patients with urinary tract infections.

Methods: This is a laboratory study and was carried out in 1403 in the medical diagnosis laboratories of Urmia city. After collecting the samples, they were cultivated in general and selective cultivation environments. Out of 800 cultured samples, 91 samples were positive and were differentiated using differential culture media and diagnostic tests. It was also done for diagnosis and screening in two stages. The screening test was done by disk diffusion method and the confirmation step was done by a combination method with ceftazidime clavulanic acid and cefotaxime clavulanic acid disks.

Results: Of the 91 examined samples, the frequency of Escherichia coli and *Klebsiella pneumoniae* strains was 6.84 and 4.15, respectively, out of 77 strains: *Escherichia coli* 76.6

from outpatient samples and 4.23 from hospitalized samples, and from 14 strains of *Klebsiella pneumoniae* /57/ 1 of the outpatient samples and 9.42 of the inpatient samples were assigned to themselves. Was 16.35 in this way the frequency of ESBLS in *Escherichia coli* strains was 35.06 (22.72% of inpatients, 73.73% of outpatients), and *Klebsiella pneumoniae* was 71.35% (33.83% of inpatients, 0% of outpatients) has been.

Conclusion: The results indicate antibiotic resistance and a higher prevalence of ESBLS in samples isolated from hospitalized patients, which was due to their weak physical strength and immunity. Health control in hospitals is the most important factor in infection control in hospitals. Also, health control and use of equipment One-time use is necessary in hospital environments by personnel.

Keywords: Comparison, spectrum beta-lactamases, gram-negative bacilli

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PBa-76

Investigating the pattern of aminoglycoside resistance among uropathogenic *Escherichia coli* isolated from urine

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Background and Aim: Urinary tract infections are one of the most common bacterial diseases in humans, and Escherichia coli is the most common etiological agent, accounting for 80% of these cases. Aminoglycosides are powerful bactericidal agents that inhibit the synthesis of bacterial proteins by binding to the 30S ribosomal subunit. E. coli. It shows multiple resistance to some antibiotics, including aminoglycosides. Enzymatic inactivation of aminoglycoside antibiotics by aminoglycoside-changing enzymes (AMES) is the main mechanism of resistance to these drugs in this bacterium. In the present study, the pattern of aminoglycoside resistance among uropathogenic Escherichia coli isolated from urine was investigated.

Methods: In this research, 300 isolates of Escherichia coli isolated from urinary tract infections of patients referred to medical laboratories were randomly collected after confirming the

identity of the isolates with the usual microbiological tests of the antibiotic sensitivity pattern of the isolates against antibiotics. Gentamicin, tobramycin, kanamycin, amikacin, and netilmycin (MAST Co UK) were determined by the disc diffusion method following the principles of CLSI. To determine the MIC for gentamicin antibiotic, the dilution method in agar was used.

Results: Findings The results showed that 63.24 of Escherichia coli isolates were resistant to tobramycin, 18.23 to kanamycin, 10.01 to gentamicin, 15.6 to netilmicin, and 62.3 to amikacin. In the MIC results, 19.66% of the resistant isolates were resistant. They were resistant to gentamicin in the disc diffusion method.

Conclusion: In this study, the resistance of Escherichia coli isolates to different aminoglycosides was evaluated, which is a significant increase in resistance compared to previous studies. Since the enzymatic inactivation of these antibiotics is one of the main mechanisms of resistance in Escherichia coli and studies have been conducted, the aac (3)-lla gene is the most common gentamicin resistance gene in Escherichia coli isolates, so in the second phase of this research Investigating the genes coding for the modifying enzymes of these antibiotics was done by PCR method.

Keywords: Investigating, aminoglycoside resistance, uropathogenic, *Escherichia coli*

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PBa-77

Prevalence of antibiotic resistance pattern in methicillin-resistant *Staphylococcus aureus* strains from clinical specimens of Laboratory in Urmia

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Background and Aim: *Staphylococcus aureus* is both a commensal bacterium and a human pathogen. Approximately 30% of the human population is colonized with *Staphylococcus aureus*. Simultaneously, it is a leading cause of bacteremia and infective endocarditis (IE) as well as osteoarticular, skin and soft tissue, pleuropulmonary, and device-related infections(1). Methicillin-resistant *Staphylococcus aureus* (MRSA) refers to a group of gram-positive bacteria that are genetically distinct from other strains of *Staphylococcus aureus*. MRSA is

responsible for several difficult-to-treat infections in humans. MRSA is any strain of *Staphylococcus aureus* that has developed, through horizontal gene transfer and natural selection, multiple drug resistance to beta-lactam antibiotics(2).

Methods: This cross-sectional study was performed on 11514 patients from Dr. Nemati's Laboratory during a 9-month period from December 2018 to October 2019.Clinical specimens included urine,sputum,wound discharge, nasal secretions, bronchoalveolar lavage and abscess.Specimens obtained after growth in blood agar medium were subtracted from Streptococci using catalase assay. Then in order to identify *Staphylococcus aureus* from standard microbiological methods such as gram staining,coagulase tests, fermentation of mannitol, DNase, novobiocin sensitivity, and oxidase test were performed. The antimicrobial resistance patterns of the isolates were determined using the KirbyBauer disk-diffusion based on CLSI guidelines.MRSA strains were confirmed using cefoxitin disc. In this study, antibiotic discs of Rosco made in Denmark were used.

Results: Of 11514 cultured samples, 3687 were males and 7827 females (80.95% males and 19.05% females were diagnosed with *Staphylococcus aureus*). It showed methicillin-resistant staphylococci, all of which were female. The highest resistance to penicillin was 100% and the highest sensitivity was to gentamicin and amikacin and trimethoprim-sulfamethoxazole discs. However, resistance to other antibiotics was Ciprofloxacin 60%, nitrofurantoin 37.50%, doxycycline 4.45%, erythromycin 90% and clidamycin 80%, respectively.

Conclusion: This study showed that the prevalence of *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* strains was relatively low in this laboratory.controlling vectors and their treatment could prevent the transmission of this bacterium. Antibiotics gentamicin, amikacin and trimethoprim-sulfamethoxazole have the best activity against Staphylococcus strains.

Keywords: antibiotic resistance, methicillin-resistant, *Staphylococcus aureus*

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PBa-78

Abstract Type: Narrative Review

Exploring the Therapeutic Potential of Different Sources of Mesenchymal stem cells: Novel Approach to Combat Burn Wound Infections

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Abstract

The most prevalent and harmful injuries are burns, which are still a major global health problem. Burn injuries can cause issues because they boost the inflammatory and metabolic response, which can cause organ malfunction and systemic failure. On the other hand, a burn wound infection creates an environment that is conducive to the growth of bacteria and might put the patient at risk for sepsis. Also, scarring is unavoidable, and this results in patients having functional and cosmetic issues. Wound healing is an amazing phenomenon with a complex mechanism that deals with different types of cells and biomolecules. Cell therapy using stem cells is one of the most challenging treatment methods that accelerates the healing of burn wounds. Since 2000, the use of mesenchymal stem cells (MSCs) in regenerative medicine and wound healing has increased. They can be extracted from various tissues, such as bone marrow, fat, the umbilical cord, and the amniotic membrane. According to studies, stem cell therapy for burn wounds increases angiogenesis, has anti-inflammatory properties, slows the progression of fibrosis, and has an excellent ability to differentiate and regenerate damaged tissue. Figuring out the main preclinical and clinical problems that stop people from using MSCs and then suggesting the right ways to improve therapy could help show the benefits of MSCs and move stem cell-based therapy forward. This review's objective is to assess mesenchymal stem cell therapy's contribution to the promotion of burn wound healing.

Keywords: Mesenchymal Stem Cell (MSCs); Burn injury; Infection; Stem cells-based therapy; Wound healing

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PBa-79
Abstract Type: Systematic Review

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Gut-thyroid axis as a therapeutic target in Hashimoto thyroiditis management: A Systematic Review

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Abstract

Background and Aim: Hashimoto thyroiditis (HT) is one of the most common autoimmune thyroid disorders worldwide, which is characterized by chronic thyroid inflammation and autoantibodies against thyroid peroxidase (TPO) and thyroglobulin (Tg). The gut microbiota has a vital role in maintaining health benefits to its host, especially in autoimmune disorders. This study aims to review the therapeutic potential of gut-thyroid axis in HT management.

Methods: This review article was performed within articles published on PubMed, Science Direct, Google Scholar, and Web of Science until November 2024. The keywords were Hashimoto thyroiditis, gut microbiota, and dysbiosis. By searching this database, 33 articles were found, about 12 of them by reading titles and abstracts were removed, and 21 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: A review of 21 articles showed that microbiota-gut-thyroid axis linked HT to the gut microbiota. Immune responses were triggered by structural similarities in thyroid antigens, such as TPO and Tg and bacterial wall antigens. TLR-4 was activated by lipopolysaccharides, resulting in contributing thyroiditis. HT patients often had increased intestinal permeability, as indicated by elevated levels of zonulin. Moderate levels of butyrate producers like *Clostridia_UCG-014* and Desulfovibrionales and increased levels of pro-inflammatory bacteria, such as *Bacteroides fragilis*, resulted in microbiota dysbiosis with aggravated inflammation. By affecting iodine uptake and metabolism, microbiota influenced thyroid hormone regulation. Increased iodine intake was associated with higher HT risk. Short-chain fatty acids showed anti-inflammatory effects by suppressing cytokine production, like a microbial product. *Akkermansia* and *Bifidobacterium* were common in HT, influenced by environmental and hormonal factors, while *Lachnoclostridium* and *Klebsiella* were enriched in healthy controls.

Conclusion: In the future, HT treatment will focus on the gut-thyroid axis, for slowing disease progression and alleviating symptoms by restoring gut microbial balance. Intestinal permeability issues suggest early interventions to repair the gut barrier and prevent immune cell migration. However, further clinical data and in vivo research are needed on this topic.

Keywords: Hashimoto thyroiditis, gut microbiota, autoimmune thyroid disease

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PBa-80

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Investigating the infections resulting from urine culture of children in the medical diagnosis laboratories of Urmia city

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Background and Aim: Urinary tract infection or UTI in children is of great importance due to its complications such as kidney damage, kidney failure, urosepsis, and urinary system problems. In children, UTI is the second most common cause of infection after respiratory infections due to antibiotic resistance. Urine culture test, while being simple, provides a lot of information in the diagnosis of various diseases, and considering that There are many errors before the test in children's urine cultures By implementing a quality control program, it is possible to prevent the occurrence of false positive cases.

Methods: In this study, 200 urine culture samples of children under 5 years of age were tested after cultivation in general and selective culture media and diagnosis through differential culture media and diagnostic tests, by implementing all quality control procedures, and the results of these tests were in agreement with the results of the years It was compared before the quality assurance program was implemented.

Results: The results of this research showed that most errors of urine culture testing in children are related to the stage before the implementation of quality control based on the standards of the health reference laboratory. Also, 40% of the errors are related to not informing the children's parents about the correct method of urine sampling and not providing sample instructions. It was obtained by the relevant laboratory. 30% of errors are related to contamination of children's urine with feces or other pollutants, especially in children whose samples were taken from a urine bag. It should be noted that 20% of errors are related to not properly storing urine samples in the laboratory. Or failure to perform the test on time. Finally, 10% of the errors are related to contaminated sampling containers.

Conclusion: after the implementation of the quality control program, the number of errors decreased by 85%, and in repeating the tests, the false positive results were changed to negative results.Performing regular quality control based on the standards of the health reference laboratory in urine culture testing is as important as other clinical tests, and urine culture testing in children provides accurate and useful information in the diagnosis and follow-up of treatment and prevention of various diseases, including kidney, liver, metabolic, and blood diseases.

Keywords: Investigating, infections, urine, diagnosis

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PBa-81

Abstract Type: Narrative Review

A Sight into the Combination of CRISPR/Cas9 System and Nanoparticles in the Management and Treatment of Antibiotic-resistant Infections Associated with Biofilms

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Abstract

The increasing concern of antibiotic resistance is a critical global health challenge, significantly hindering the effective treatment of bacterial infections. As pathogens rapidly develop resistance to conventional antibiotics, innovative solutions are urgently needed.

Biofilms are complex structures in which bacteria adhere to a surface and are surrounded by polymeric materials highly resistant to antibiotics. Bacteria in biofilms show increased antibiotics resistance due to genetic exchange and environmental changes.

CRISPR/Cas9 technology is used to target and delete antibiotic resistance genes in bacterial biofilm. CRISPR/Cas systems which are adaptive immune mechanisms in prokaryotes, offer a promising approach to this problem. These systems include variants such as Cas9, Cas12, Cas13, and Cas14 that enable precise targeting and editing of nucleic acids, providing new ways to combat antimicrobial resistance (AMR).

CRISPR/Cas systems can detect and reverse bacterial resistance, thereby resensitizing bacteria to existing antibiotics. They also have the potential for modulating virulence factors and disrupting biofilm formation, which are crucial in managing chronic and recurrent infections. The integration of nanotechnology enhances the potential of CRISPR-Cas systems. Nanoparticles can improve the delivery and efficacy of CRISPR components, ensuring targeted and efficient treatment of multidrug-resistant (MDR) bacterial infections.

CRISPR/Cas9 specifically identifies and targets genes responsible for antibiotic resistance. These genes are usually located on bacterial plasmids or chromosomes. Using guide RNA (gRNA), the CRISPR/Cas9 system binds to these genes and cuts them, resulting in the inactivation of the resistance genes. To deliver the CRISPR/Cas9 system into bacterial biofilms, nanoparticles are used.

Nanoparticles are used as drug carriers that can penetrate deeply into biofilms and deliver drugs or gene editing systems of bacteria. Nanoparticles can deliver CRISPR/Cas9 molecules precisely to target cells, which increases efficiency and reduces side effects. Nanoparticles can protect CRISPR/Cas9 molecules from enzymatic degradation, increase stability, and provide controlled expression of CRISPR/Cas9 molecules. These nanoparticles can be chemically modified to improve the stability and efficiency of the CRISPR/Cas9 system, including lipid, polymer, and gold nanoparticles. Lipid nanoparticles are widely used for CRISPR delivery due to their amphiphilic properties. Also, polymer nanoparticles are widely used for CRISPR delivery due to their high safety and biocompatibility. Gold nanoparticles (AuNPs) are suitable for delivery of the CRISPR RNP complex due to controllable properties and relative safety.

By targeting and inactivating resistance genes, the biofilm structure will be weakened. This makes the bacteria more susceptible to antibiotics and the biofilm gradually degrades. This system can target and inactivate genes associated with biofilm formation, preventing new biofilm production.

This combination of advanced technologies can effectively combat antibiotic-resistant infections and biofilms, offering new hope in medical science and infectious disease treatment.

Despite these advancements, several challenges remain, including the efficient in vivo delivery of CRISPR components and minimizing off-target effects. Ongoing research and development are essential to address these issues and fully harness the potential of CRISPR/Cas systems in justifying the global antibiotic resistance crisis.

Keywords: antibiotic resistance; biofilm; CRISPR/Cas9 System; nanoparticles.

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PBa-82

Isolation and identification of pathogenic mycobacteria isolated from patients with immune system defects in Urmia City in 1401

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Background and Aim: According to the reports of the World Health Organization, children account for 10-20 of the total TB statistics, and the majority of these numbers are seen in countries where the prevalence of AIDS is high. After the outbreak of the deadly AIDS disease in the late 80s, the number of tuberculosis increased in most parts of the world in a short period, tuberculosis led to illness and death of people in most parts of the world.

Methods: In this study, sputum samples were obtained from all AIDS patients referred to Urmia City Pulmonary Tuberculosis Center, two of these patients were smear positive, and as a result, their samples were cultured on Lowenstein's medium containing pyruvate and glycerin. DNA extraction was performed according to the standard Van Solingen protocol. Then to determine the molecular identity of the extracted DNA of the strains according to the results obtained from the biochemical tests of niacin and catalase, IS6110 primer was used and to determine the exact molecular identity, RD typing technique was applied.

Results: In this research, after determining the molecular identity, it was determined that both isolates belonged to the Mycobacterium tuberculosis complex, and the result of RD typing confirmed that they were Mycobacterium tuberculosis. It should be noted that children, the elderly, AIDS patients, and people whose level of CD4 type T lymphocytes is low, often show unusual forms of tuberculosis, but in this research, after determining the molecular identity, it was determined that both isolates were Mycobacterium tuberculosis. Given that the above infections are recurrences of old infections. According to the current state of tuberculosis statistics in Iran, as well as AIDS-related MDR-TB, which is an alarm to reduce the tuberculosis program in the world, research should be increased on patients infected with the AIDS virus.

Conclusion: Refers to In addition, since the AIDS disease is transmitted from the mother to the fetus and considering that the second cause of death in AIDS patients is caused by infection with mycobacterium, therefore, the isolation and identification of pathogenic mycobacteria species in AIDS patients is an important part of the disease eradication and control program in It is the responsibility of the community to generalize programs based on the identification of pathogenic mycobacteria in AIDS patients, it seems necessary to eradicate tuberculosis.

Keywords: Isolation, identification, mycobacteria, immune system

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PBa-83

Investigating the antibiotic sensitivity of *Klebsiella pneumoniae* isolated from blood, urine, and stool samples to beta-lactam cephalosporin, quinolones, and aminoglycoside antibiotics in 1402 in Urmia city

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Background and Aim: *Klebsiella pneumoniae*, which is also called bacillus Friedlander, in addition to causing lung infections, can also cause infections in other parts of the body, including the urinary tract, blood circulation, and meninges. This bacterium also causes hospital infections. This bacterium is more resistant to antimicrobial agents such as antibiotics and antiseptics than all bacilli. The majority of Klebsiella samples are sensitive to aminoglycoside antibiotics, cephalosporins, chloramphenicol, and tetracycline, but recently resistant types have also been reported. The purpose of this study is to investigate the antibiotic sensitivity of *Klebsiella pneumoniae* to β-lactam cephalosporin, quinolones, and aminoglycoside antibiotics.

Methods: This descriptive-cross-sectional and prospective study was conducted on 300 strains of Klebsiella isolated from samples of patients referred to hospitals and medical diagnostic laboratories in Urmia city in 1402 to isolate Klebsiella from stool samples of patients with diarrhea. Directly on mechanical agar culture medium and for separation from urine, samples were used on E.M.B agar culture medium, and blood agar was used for separation from blood after enrichment in blood culture medium.

Results: Out of 100 Klebsiella strains isolated from urine culture, positive for the highest drug sensitivity, respectively, to ceftriaxone 90%, ciprofloxacin 90%, tobramycin 88%, ceftazidime 87%, amikacin 86%, ceftizoxime 86%, gentamicin 84%, nalidixic acid 82%, cephalothin 76%, and cefazolin. Was 72%; Among the 100 strains of Klebsiella isolated from the positive stool culture sample, the most drug sensitivity was, in order, to Cefipim (91), Zoxime (90), Ceftazidime (87), Ceftriaxone (86), Ciprofloxacin (85), Nalidixic acid (82), Tobramycin (81), Gentamicin (81%), Cephalothin (77%), and Cefazolin (76%). From the number of 100 Klebsiella strains isolated from the positive blood culture sample, the highest drug sensitivity was to Ceftriaxone 86, Ceftazidime 81, Zoxime 79, Tobramycin 76, Amikacin 65, Ciprofloxacin 62, Nalidixic Acid 62, and Nalidixic Acid 48. Gentamicin was 46%, cephalothin was 46% and cefazolin was 30%

Conclusion: The results of this study showed that cefepime, ceftriaxone, and ceftazidime are more suitable for treatment. Therefore, the use of 4th and 3rd generation cephalosporins can be effective in controlling and reducing infection, but it should be noted that the indiscriminate use of these antibiotics can cause antibiotic resistance in society, so the treatment must be based on Valid laboratory results should be adopted.

Keywords: *Klebsiella pneumoniae*, antibiotic sensitivity, beta-lactam cephalosporin, quinolones, aminoglycoside

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PBa-84

Investigating the pattern of aminoglycoside resistance among uropathogenic *Escherichia coli* isolated from urine

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Background and Aim: Urinary tract infections are one of the most common bacterial diseases in humans, and Escherichia coli is the most common etiological agent, accounting for 80% of these cases. Aminoglycosides are powerful bactericidal agents that inhibit the synthesis of bacterial proteins by binding to the 30S ribosomal subunit. E. coli. It shows multiple resistance to some antibiotics, including aminoglycosides. Enzymatic inactivation of aminoglycoside antibiotics by aminoglycoside-changing enzymes (AMES) is the main mechanism of resistance to these drugs in this bacterium. In the present study, the pattern of aminoglycoside resistance among uropathogenic Escherichia coli isolated from urine was investigated.

Methods: In this research, 300 isolates of Escherichia coli isolated from urinary tract infections of patients referred to medical laboratories were randomly collected after confirming the identity of the isolates with the usual microbiological tests of the antibiotic sensitivity pattern of the isolates against antibiotics. Gentamicin, tobramycin, kanamycin, amikacin, and netilmycin (MAST Co UK) were determined by the disc diffusion method following the principles of CLSI. To determine the MIC for gentamicin antibiotic, the dilution method in agar was used.

Results: Findings The results showed that 63.24 of Escherichia coli isolates were resistant to tobramycin, 18.23 to kanamycin, 10.01 to gentamicin, 15.6 to netilmicin, and 62.3 to amikacin. In the MIC results, 19.66% of the resistant isolates were resistant. They were resistant to gentamicin in the disc diffusion method.

Conclusion: In this study, the resistance of Escherichia coli isolates to different aminoglycosides was evaluated, which is a significant increase in resistance compared to previous studies. Since the enzymatic inactivation of these antibiotics is one of the main mechanisms of resistance in Escherichia coli and studies have been conducted, the aac (3)-lla gene is the most common gentamicin resistance gene in Escherichia coli isolates, so in the second phase of this research Investigating the genes coding for the modifying enzymes of these antibiotics was done by PCR method.

Keywords: Investigating, aminoglycoside resistance, uropathogenic, *Escherichia coli*

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PBa-85

Abstract Type: Systematic Review

Detection of *Chlamydia trachomatis* using loop-mediated isothermal amplification: A Systematic Review

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Abstract

Background and Aim: *Chlamydia trachomatis* is one of the most common pathogens responsible for sexually transmitted infections (STIs), which is a severe public health concern, especially in underdeveloped regions. Also, it can cause serious complications if untreated. Therefore, developing rapid and sensitive point-of-care (POC) tests for screening *C. trachomatis* is crucial for early treatment and preventing transmission.

Various diagnostic methods have been developed over the years, including cell cultivation and PCR, in comparison to which, LAMP assays present several advantages such as simplicity, speed, specificity at constant temperature, and ease of interpretation. As a result, we have provided an overview of these aspects.

Methods: In order to perform a systematic review, Several databases such as Pubmed, Google Scholar, Scopus, Web of Science, etc. were searched using the terms "*Chlamydia trachomatis*" and "LAMP".

Results: High sensitivity and specificity of the LAMP method have been observed in several studies. Some even reported a specificity of 100%. By using the *OmpA* target gene for detecting *C. trachomatis* in 870 clinical samples of endocervical swabs, vaginal swabs, and genital secretion, sensitivity and specificity ranging from 91-93.65% and 95-100% were achieved. Another target gene, the cryptic plasmid, was used for 115 clinical samples, including vaginal swabs, urine, and cervical swabs, resulting in a sensitivity and specificity of 73% and 100%. The *GyrA* target gene was used in one study with 103 clinical samples. LAMP products were detected using turbidity, gel electrophoresis, colorimetry, and fluorescence. All mentioned studies used PCR-based methods as the reference.

Conclusion: infection with *C. trachomatis* is usually asymptomatic at the early stages, leading to delayed medical treatment. Hence, early and sensitive diagnosis is crucial for timely treatment. The results of reviewed studies demonstrated that LAMP assay enables rapid and sensitive detection of C. trachomatis with no need for DNA extraction or purification steps before DNA amplification. Therefore, expensive equipment would not be required. As a result, the LAMP assay could be applied as a point-of-care diagnostic method. Nevertheless, the clinical use of the mentioned methods requires further investigation.

Keywords: *Chlamydia trachomatis*; loop-mediated isothermal amplification (LAMP); point of care.

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PBa-86

Systematic Review

The importance of making and producing vaccines against *Staphylococcus aureus* resistant to treatment

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Abstract

Background and Aim

Invasive gram-positive *Staphylococcus aureus* is a major cause of global illness and death (1-3). This microorganism can induce various diseases, ranging from moderately severe dermatological infections to life-threatening conditions such as pneumonia and sepsis (1). Treating *S. aureus* infections is increasingly challenging due to the rise of antibiotic resistance (1, 3, 4). The rise of MRSA and vancomycin-resistant strains limits treatment options and highlights the need for new approaches, like vaccines (2). Many vaccine candidates showed promise in preclinical studies, but none have succeeded in clinical trials (2, 5). This review emphasizes that three vaccine candidates, V710, StaphVAX, and SA4Ag, underwent assessment in advanced clinical trials (4, 5).

Methods

SA4Ag comprises four antigens, including CP5 and CP8, each conjugated to the nontoxic mutant form of diphtheria toxin, from *Staphylococcus aureus* that is presented on the surface and specifically targets three virulence mechanisms that are activated during the initial stages of infection (4). A third antigen consists of a recombinant variant of clumping factor A (ClfA) that features a single amino acid alteration (Y338A), inhibiting its ability to interact with its natural ligand, fibrinogen (4). The fourth antigen is identified as a recombinant, non-lipidated variant of the *S. aureus* manganese transporter C (MntC) protein, designated as rP305A (4). V710 focuses on the iron scavenger protein IsdB, and StaphVAX targets polysaccharide capsules CP5 and CP8 (5). StaphVAX was tested in dialysis patients, showing some reduction in bacteremia but ultimately failing in later trials (5).

Results

V710, in particular, was associated with increased mortality in patients who developed postoperative *S. aureus* infections, raising concerns about its safety and effectiveness (5). The analysis of immunological responses in vaccine recipients revealed that low pre-vaccination IL-2 levels combined with vaccination and subsequent infections were linked to increased mortality rates following cardiothoracic surgery (5). Findings from the finalized Phase 1/Phase 2a clinical trials carried out with healthy volunteers in the United States demonstrated that a single administration of SA4Ag prompted a swift and substantial generation of functional antibodies targeting the four vaccine antigens (CP5-CRM197, CP8-CRM197, ClfA, and MntC). The vaccine exhibited an acceptable safety profile among healthy individuals aged 18 to 85 (4).

Conclusion

In this summary, we conclude that there is an urgent need for effective vaccines against multi-drug-resistant *Staphylococcus aureus*, due to the high incidence of infections and mortality rates, especially in vulnerable groups like neonates and immunocompromised individuals (5). *S. aureus* vaccines should be prioritized within the broader AMR research agenda to ensure vaccine R&D perspectives are fully integrated (5). The demonstrated safety and efficacy of SA4Ag within the STRIVE (STaphylococcus aureus suRgical Inpatient Vaccine Efficacy) population is anticipated to reflect the vaccine's safety and effectiveness in other elective orthopedic surgical groups (4).

Keywords

Staphylococcus aureus, Vaccine, Antimicrobial Resistance (AMR), Immunology, Antigen

PBa-87

Abstract Type: Original Research

Seeking Effective Strategies to Control *Bacillus anthracis* through Anthrax Toxin Inhibition: Insights from Molecular Docking

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Abstract

Background and Aim:

Anthrax, a disease caused by *Bacillus anthracis*, poses a significant threat to both human and animal health. Prompt and comprehensive treatment is essential due to its easy and various modes of dissemination and its ability to cause substantial morbidity and mortality. The increased occurrence of antibiotic-resistant strains and absence of effective treatments for anthrax emphasizes the critical need for innovative pharmacological approaches to combat illnesses linked to the toxin. Given that the primary virulence factor of anthrax is its toxin, the objective of this study was to identify the most potent ligand capable of inhibiting toxin through molecular docking analysis.

Methods: The 3D structure of Bacillus anthracis toxin (PDB ID: 1J7N) was obtained from the RCSB PDB database. CGS-27023, also known as N-Hydroxy-2(R)-[[(4-methoxyphenyl)sulfonyl](3-picolyl)amino]-3-methylbutanamide (CID446504) and twenty of its analogs were selected as inhibitors from the PubChem database in SDF format. After preparing the protein and ligands, molecular docking was performed by the Molegro Virtual Docker version 6.0. The interactions were analyzed to identify the best binding with the lowest energy by the Molegro Molecular Viewer software. Finally, the pharmacokinetic properties were evaluated by the SwissADME server.

Results: Among all the inhibitory analogs, the most effective analog for Bacillus anthracis toxin was “2-[benzyl-(4-methoxyphenyl)sulfonylamino]-N-(pyridin-3-ylmethyl)acetamide”

with CID1072907. This compound has a molecular weight of 425.5 g/mol and a binding energy of -158/285 kcal/mol. "2-[benzyl-(4-methoxyphenyl)sulfonylamino]-N-(pyridin-3-ylmethyl)acetamide" creates five steric interactions with the anthrax toxin residues of Tyr542(B), Pro492(B), Lys500(B), Gln537(B), and Ser538(B), and two hydrogen bonds with Lys500(B), and Gln537(B) residues , and no electrostatic interaction. The ADME analysis revealed that "2-[benzyl-(4-methoxyphenyl)sulfonylamino]-N-(pyridin-3-ylmethyl)acetamide" has a logS (water solubility) score of -3.72, a lipophilicity (XLogP3) of 2.55, a polarity (TPSA) of 96.98Å², and one hydrogen bond donor and six hydrogen bond acceptors.

Conclusion: These results indicate that "2-[benzyl-(4-methoxyphenyl)sulfonylamino]-N-(pyridin-3-ylmethyl)acetamide" is a promising candidate for inhibiting *Bacillus anthracis* infection. Further in vitro and in vivo studies are required to confirm it as a therapeutic agent.

Keywords: *Bacillus anthracis*; Molecular docking; CGS-27023; 2-[benzyl-(4-methoxyphenyl)sulfonylamino]-N-(pyridin-3-ylmethyl)acetamide; Anthrax toxin.

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PBa-88
Abstract Type: Original Research

Targeting Type IV Pilin for Antibacterial Therapy: A Molecular Docking Analysis of *Neisseria gonorrhoeae*

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Abstract

Background and Aim: *Neisseria gonorrhoeae*, is a gram-negative pathogen that is involved in sexually transmitted infections. *Neisseria's* pili is an essential virulence factor which causes the bacteria to attach to the epithelial cell surface .Previous studies have shown that *N. gonorrhoeae* has a remarkable ability to develop and maintain high antibiotic resistance rates. These concerns have risen because cephalosporins are currently the last-line treatment for gonorrhea. Therefore, current research approaches involve the use of small-molecule inhibitors or substrate analogs to combat this bacterium. In this study, we aimed to determine the most potent pili inhibitor through molecular docking analysis.

Methods: The 3D structure of the native *Neisseria gonorrhoeae* Type IV pilin (PDB ID 2HI2) was obtained from the RCSB PDB database. The structures of the type IV pilin's inhibitory

ligand, 10-[3-(4-methylpiperazin-1-yl)propyl]-2-(trifluoromethyl)phenothiazine (trifluoperazine) with PubChemCID 5566, and 40 of its analogs were retrieved from the PubChem database in SDF format. The protein and inhibitory ligands were prepared for docking using Molegro Virtual Docker version 6.0. After docking, the best interaction with the lowest energy binding was analyzed through Molegro Molecular Viewer v.7 software. Finally, the pharmacokinetic properties of the ligands were evaluated using the SwissADME server.

Results: Through all inhibitory ligands for Type IV pilin, the best ligand was 1-[2-[(4-Methyl-5-phenyl-1,2,4-triazol-3-yl)sulfanyl]acetyl]pyrrolidin-2-one (PubchemCID:2633356) with a molecular weight of 316.1 g/mol and binding energy of -99.424 kcal/mol. This ligand created three steric interactions with the Pilin protein residues Asp 143, Thr 144, and Cys 151, and one hydrogen bond with Thr 144 residues, and no electrostatic interaction. The ADME results showed that this ligand has a water solubility score (logS) of -3.039, a hydrophilic score (LogP) of 1.140, a polarity score (TPSA) of 68.09, and lastly, hydrogen bond donors of 6 and hydrogen bond acceptors of 0.

Conclusion: These results indicate that 1-[2-[(4-Methyl-5-phenyl-1,2,4-triazol-3-yl)sulfanyl]acetyl]pyrrolidin-2-one is a promising candidate for inhibiting *Neisseria gonorrhoeae* infection. Further in vitro and in vivo studies are required to confirm their potential as therapeutic agents.

Keywords: Molecular Docking; *Neisseria gonorrhoeae*; Type IV pilin; ADME.

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PBa-89
Abstract Type: Original Research

Molecular Docking Study of Oseltamivir Acid and Its Analogues as *Klebsiella aerogenes* Inhibitors: A Novel Therapeutic Strategy

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Abstract

Background and Aim: *Klebsiella aerogenes* causes antibiotic-resistant nosocomial infections. These infections pose a global healthcare threat due to rapid spread, ineffective treatments, and

high mortality rates, highlighting the urgent need for improved interventions. N-acetylneuraminate lyase (NanA) of *Klebsiella aerogenes* plays a key role in the pathogenicity of this bacterium by catalyzing reversible aldol cleavage of N-acetylneuraminic acid (sialic acid). Therefore, new efforts to combat multi-drug resistance of *Klebsiella* may be involved in virulence factor-targeted therapeutic studies. Understanding the role of NanA in its pathogenicity offers potential for targeted therapies. This study explores inhibiting NanA through molecular docking to develop a promising drug candidate.

Methods: The 3D structure of N-acetylneuraminate lyase (NanA) of *Klebsiella aerogenes* (PDB ID: 8u93) was obtained from the RCSB PDB database in PDB format. The structures of oseltamivir acid (DrugBank ID: DB02600) and its 30 analogs were obtained in SDF 3D format from the PubChem database. After preparing protein and ligands by removing water molecules and ligand from the protein structure and energy minimization, molecular docking was performed using the Molegro Virtual Docker v. 6. Only the top 1 pose of each ligand was selected in Molegro Virtual Viewer v. 7, and the best ligand with the lowest energy binding was evaluated. Finally, the pharmacokinetic properties of ligand were estimated using the SwissADME database.

Results: The best ligand for N-acetylneuraminate lyase (NanA) of *Klebsiella aerogenes* was ethyl (3R,4R,5S)-4-acetamido-5-azido-3-[(3R)-hex-5-en-3-yl]oxycyclohexene-1-carboxylate (PubChem CID: 10569862), with a molecular weight of 350.4 g/mol and the most negative ΔGbind (-130.797 kcal/mol). This ligand formed three hydrogen bonds with the NanA residues, Tyr137, Ser47, and Thr48, and 10 steric interactions involving the NanA residues Leu142, Ile139, Tyr190, Ser47, Tyr137, Gly46, Thr48, Ile206, Gly189, and Thr167. Moreover, the ADME results indicated that this ligand had a water solubility score of (Log*S*) -3.26, seven hydrogen bond acceptors, one hydrogen bond donor, a lipophilicity score of (XLOGP3) 3.33, and a polarity score (TPSA) of 114.38.

Conclusion: Based on the obtained results, ethyl (3R,4R,5S)-4-acetamido-5-azido-3-[(3R)-hex-5-en-3-yl]oxycyclohexene-1-carboxylate (PubChem CID: 10569862) ligand may serve as an inhibitor candidate drug for N-acetylneuraminate lyase (NanA) of *Klebsiella aerogenes*, although further testing is necessary.

Keywords: Molecular docking; *Klebsiella aerogenes*; N-acetylneuraminate lyase; NanA.

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PBa-90

Abstract Type: Original Research

The adeH and adeS efflux pump genes in imipenem and colistin-resistant Acinetobacter baumannii clinical isolates

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Abstract

Background and Aim: Acinetobacter baumannii is one of the most important causes of nosocomial infections. In this bacteria, several mechanisms contribute to resistance against antimicrobial agents. The present study investigated the prevalence of adeS and adeH genes and the role of efflux pumps in imipenem and colistin-resistant A. baumannii clinical isolates.

Methods: This study included 70 A. baumannii isolates collected from medical centers affiliated with the Qom Medical Science University, Qom, Iran (Kamkar Arabnia Hospital and Shahid Beheshti Hospital) from January 2023 to October 2024. The antibiotic susceptibility pattern was examined using the broth microdilution MIC method according to clinical and laboratory standards institute (CLSI) guidelines. Also, the adeS and adeH genes were amplified by PCR

Resaults: The isolates were 100% imipenem-resistant and 83.8% colistin-resistant. The adeH and adeS genes were detected in 94% and 83% of the isolates.

Conclusion: The high frequency of adeS and adeH efflux pump genes and the high drug resistance in A. baumannii clinical isolates indicated that adeS and adeH efflux pump genes play an important role in emerging antibiotic resistance in this species. Therefore, our results provide essential information about high drug resistance in A. baumannii clinical isolates that can help limit the horizontal and vertical transmission of efflux pump genes in antibiotic-resistant A. baumannii isolates that causes nosocomial infections in susceptible strains.

Keywords: Acinetobacter baumannii; Efflux pump; adeS gene; adeH gene

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PBa-91
Abstract Type: Original Research

Identification and serotyping profile of enterohemorrhagic *Escherichia coli* isolates from Babol city

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Abstract

Background and Aim: The enterohemorrhagic *Escherichia coli* (EHEC) is recognized as human pathogens that can cause food-borne infections and potentially fatal illnesses in humans, such as hemorrhagic colitis (HC) and hemolytic uremic syndrome (HUS). The aim of this study was to molecularly investigate the presence of these important pathogens and to study the prevalence of the serotypic profile of these bacteria in Babol city.

Methods: A total of 250 samples collected from two hospitals in the Babol city were utilized in this study and identified using standard methods based on their biochemical characteristics. The enterohemorrhagic *Escherichia coli* isolates were confirmed through polymerase chain reaction (PCR) via assessment of presence of shiga-like toxin genes of 1 and 2 (*stx1* and *stx2*) and also subjected to serotyping tests.

Results: Out of 250 patient samples, 90.8% (n = 227) of *E. coli* were isolated through culture and biochemical testing. Among the 227 *E. coli* isolates, 5.28% (n = 12) were identified as EHEC using PCR methods (*stx1* and/or *stx2* positive isolates). Serotyping of the EHEC isolates revealed that 6 (50.0%) belonged to serotype O21, 2 (16.66%) to serotype O26, another 2 (16.66%) to serotype O145, 1 (8.33%) to serotype O24 and finally 1 (8.33%) to serotype O111.

Conclusion: According to the results of this investigation the enterohaemorrhagic *Escherichia coli* prevalence has not increased compared to older studies, and these results are consistent with other assessments. However, serological tests show the prevalence of serotype O21, which does not confirm the results of other studies. The results of this study will help strengthen epidemiological information.

Keywords: Enterohemorrhagic *Escherichia coli* (EHEC), serotyping, Shiga-like toxin.

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PBa-92
Abstract Type: Original Research

Antibacterial activity of biogenic arsenic oxide nanoparticles against Clinical carbapenem-resistant *Klebsiella pneumoniae*

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Abstract

Background and Aim: The prevalence of Carbapenem-resistant *Klebsiella pneumoniae* is currently increasing worldwide, prompting WHO to classify it as an urgent public health threat. Due to the limited therapeutic options available for treating infections caused by Carbapenem-resistant *Klebsiella pneumoniae*, there is an urgent need to explore novel treatment strategies. Investigating the antibacterial effects of biogenic arsenic oxide nanoparticles (AsO NPs) might provide a hopeful approach to finding alternative solutions for combating multidrug-resistant pathogens.

Methods: Nanoparticles were biosynthesized using an aqueous extract of *Rosa damascena*, and microwave irradiation was employed to facilitate the synthesis process. The physicochemical properties of AsO NPs were characterized by various techniques, including FESEM, XRD, EDX, FTIR, DLS, and UV-Vis spectroscopy. Additionally, the antibacterial activity of these nanoparticles was evaluated against one standard strain of *Klebsiella pneumoniae* and three carbapenem-resistant clinical strains of *Klebsiella pneumoniae* using the microdilution method.

Results: FESEM imaging revealed that the AsO NPs were spherical with an average size of 21 nm. FTIR analysis identified characteristic vibrations associated with protein amides, hydroxyl groups (O-H), and arsenic ions. DLS analysis showed a single peak corresponding to biosynthesized AsO NPs with a size of 22 nm. XRD analysis confirmed the crystalline structure of the arsenic oxide phase. The antibacterial evaluation demonstrated that the minimum inhibitory concentration (MIC) of AsO NPs were 1600 µg/ml, 800 µg/ml, 800 µg/ml, and 400 µg/ml for three carbapenem-resistant clinical strains and one standard strain of *Klebsiella pneumoniae*, respectively.

Conclusion: The significant antibacterial activity of the biogenic nanoparticles suggests that these nanoparticles have considerable potential as antimicrobial agents. These findings pave the way for further exploration of AsO NPs in medical applications, particularly in the fight against resistant bacterial infections.

Keywords: Arsenic nanoparticles; Antibacterial activity; Biosynthesis; Carbapenem-resistant *Klebsiella pneumoniae*.

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PBa-93
Abstract Type: Narrative Review

Engineered phage, engineered and recombinant endolysin Against Carbapenem-Resistant Gram-negative Bacteria

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Abstract

Background and Aim: We are currently confronted with a significant challenge in clinical settings due to bacterial infections that have developed resistance to antibiotics. This resistance extends not only to commonly used antibiotics but also to last-resort options like carbapenems and colistin. As a result, healthcare professionals and researchers are compelled to devise new strategies to tackle these antibiotic-resistant Gram-negative bacteria (GNB), with phages emerging as one of the most promising solutions. Nevertheless, specific mechanisms have been identified in these bacteria that enable them to resist phage treatment. While phage resistance remains relatively limited, the issues of biofilm formation and the constraints of natural phages have led to the exploration of engineered phage (EP), engineered endolysin (EE), and recombinant endolysin (RE) as potential alternatives.
Methods: This narrative review article was conducted by examining articles indexed in multiple databases, including Web of Science, PubMed, Scopus, and Google Scholar, without any time restrictions. The following keywords were utilized for this study: "carbapenem-resistant infections," "engineered phage," "engineered endolysin," "recombinant endolysin," and "antibiotic-resistant Gram-negative bacteria." The search was restricted to original full-text articles published in English.
Results: Research has demonstrated that EP, EE, and RE can be more precisely targeted and effective than natural phages and endolysins in combating antibiotic-resistant GNB. By modifying phages and endolysins, scientists can enhance their specificity, thereby improving their antimicrobial effectiveness, temperature resistance, and permeability. Studies indicate that EP, EE, and RE significantly impact carbapenem-resistant bacteria.
Conclusion: These advanced targeted therapies demonstrate a significant effect on Gram-negative carbapenem-resistant bacteria, suggesting their potential for future use in combating infections. However, further clinical studies are necessary to explore their effectiveness.
Keywords: carbapenem-resistant infections, engineered phage, engineered endolysin, recombinant endolysin
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PBa-94
Abstract Type: Systematic Review

The interplay between gut microbiota and levothyroxine metabolism in patients with hypothyroidism: A Systematic Review

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Abstract

Background and Aim: Hypothyroidism is classified as a chronic condition that requires long-term treatment. It is usually treated by taking daily hormone replacement tablets called levothyroxine, which is one of the most commonly prescribed drugs globally. Gut microbiota may affect levothyroxine uptake and influence its action. The aim of this study is to review the interplay between gut microbiota and levothyroxine metabolism in patients with hypothyroidism.

Methods: This review article included studies published on PubMed, ScienceDirect, Google Scholar, and SID until November 2024. The keywords were levothyroxine, gut microbiota, and hypothyroidism. By searching these databases, 23 articles were found. About 12 of them were removed by reading titles and abstracts, and 11 articles were selected under the inclusion criteria.

Results: A review of 11 articles showed that levothyroxine therapy had the potential to impact the intestinal microbiota composition and thus also affected its function. Gut microbiota modification increased levothyroxine availability and stabilized thyroid function. With an increased dosage of levothyroxine for hypothyroidism treatment, the bacterial genera Odoribacter and Enterococcus showed significant growth, suggesting that levothyroxine might have impacted gut microbiota composition. The composition of the gut microbiome could influence both the pharmacokinetics and pharmacodynamics of levothyroxine, regardless of whether the medication was taken for a limited or extended period. Alistipes and Ruminococcus are equipped with β-glucuronidase activity, which can synthesize both glucuronidase and sulfatase enzymes. These enzymes enable the bacteria to hydrolyze thyroxine conjugates, thereby promoting their reabsorption from the gastrointestinal tract and contributing to enterohepatic cycling. Consequently, elevated expression of these enzymes enhanced the responsiveness to thyroxine and the efficacy of levothyroxine treatment.

Conclusion: It seems that levothyroxine, as a medication prescribed to individuals with hypothyroidism based on weight and age, interacts dynamically with the gut microbiota. This suggests a need for personalized treatment approaches that consider the individual's unique microbial profile. However, more research is required on this topic.

Keywords: Gut Microbiota, Levothyroxine, Hypothyroidism

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PBa-95

Abstract Type: Narrative Review

Phage and endolysin therapy against antibiotics resistant bacterial otitis and rhinosinusitis; a narrative review on in vivo and in vitro applications

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Abstract

Background and Aim: Chronic otitis media (OM) and chronic rhinosinusitis (CRS) are prevalent inflammatory diseases that impact a large number of individuals globally. These conditions are believed to arise from a multifactorial disease process involving bacterial infections that lead to inflammation. Factors contributing to treatment failures in OM and CRS include bacterial infections, biofilm formation, obstructed ventilation, and the inflammatory response. The rise of antibiotic resistance, particularly among multidrug-resistant (MDR) strains and biofilms, has rendered many antibiotics ineffective in preventing infections related to OM and CRS. Consequently, there has been significant interest among researchers in exploring alternative treatments, such as phage therapy.

Methods: This narrative review article was carried out by analyzing articles indexed in various databases, including Scopus, Google Scholar, PubMed, and Web of Science, without any temporal limitations. The study employed the following keywords: "chronic otitis," "chronic rhinosinusitis," "phage therapy," "biofilm," and "antibiotic resistance." The search was limited to original full-text articles published in English.

Results: In the studies reviewed, phages were recognized as biological agents possessing antibacterial and anti-biofilm properties, making them promising candidates for managing persistent infections associated with chronic otitis media (OM) and chronic rhinosinusitis (CRS). Growing evidence from research examining the effects of phages on OM and CRS—conducted in vitro, in vivo, in animal models, and in human patients—indicates that phages significantly contribute to the elimination of various bacterial infections related to these conditions. As such, they could serve as effective therapeutic agents to address the key challenges posed by these infectious diseases and their associated biofilms.

Conclusion: Considering the promising effects of phages in treating CRS and OM infections, there is a need for higher-quality human trials involving a broader range of participants. These studies should adhere to good clinical practice guidelines and explore the potential synergistic effects of bacteriophages in combination with antibiotics and other antimicrobial agents.

Key words: chronic otitis, chronic rhinosinusitis, phage therapy, biofilm, antibiotics resistance

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PBa-96
Abstract Type: Original Research

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Comparative Molecular Docking Analysis of Propofol and 2,3',4,5'-Tetrahydroxystilbene as Potential Anti-Staphylococcal Agents: A Preliminary Study

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Abstract

Background and Aim:

Staphylococcus aureus is a pathogen responsible for a diverse range of infections, from mild skin conditions to life-threatening diseases. Over the past decade, the prevalence and severity of diseases caused by *Staphylococcus aureus* have escalated, largely attributed to the rise of antibiotic-resistant strains, rendering traditional treatments less effective. Aureolysin is a very important virulence factor in this bacterium. By examining this protein and inhibiting it, we can play a significant role in designing candidate drugs and helping to inhibit this bacterium. In this study, we compared the potential of two inhibitory components against aureolysin using molecular docking analysis.

Methods: The 3D structure of aureolysin (PDB ID: 7skl) was retrieved in PDB format from the RCSB PDB database. Propofol (CID 4943) and 2,3',4,5'-Tetrahydroxystilbene (CID 73197) ligand structures were obtained from the PubChem database in SDF format. Afterward, using Molegro Virtual Docker 6.0, we exposed the desired protein and these two ligands together after preparing the protein and its ligands. Interactions between them were assessed using the Molegro Molecular Viewer program. Finally, using the SwissADME site, we investigated pharmacokinetic properties.

Results: 2,3',4,5'-Tetrahydroxystilbene exhibited a more favorable profile for drug development. Specifically, this ligand with a molecular weight of 244.24g/mol demonstrated higher binding energy (-107.777 kcal/mol) compared to propofol (-69.4599 kcal/mol) with a molecular weight of 178.27g/mol. Furthermore, the analysis of molecular interactions revealed that 2,3',4,5'-Tetrahydroxystilbene formed a greater number of steric interactions (four) and hydrogen bonds (five) with aureolysin residues, including Asp318, Asp61, Gln317, Ile54, Asn56, Asn319, Asn60, and Asp61. In contrast, propofol formed only one steric interaction with His356 and two hydrogen bonds with Asn375 and Leu365. In terms of ADME properties, 2,3',4,5'-Tetrahydroxystilbene had better water solubility (-3.46 vs. -3.54), lower lipophilicity (2.77 vs. 3.79), and higher polarity compared to propofol (80.92 vs. 20.23), indicating improved bioavailability and reduced toxic effects. Finally, the number of hydrogen bond donors and acceptors in 2,3',4,5'-Tetrahydroxystilbene (four each) was higher than that in propofol (one each), which may facilitate its interactions with biological targets.

Conclusion: Our docking analysis revealed that 2,3',4,5'-Tetrahydroxystilbene was a more promising candidate for inhibiting aureolysin in *Staphylococcus aureus* than propoful. Further

in vitro and in vivo studies are required to confirm their efficacy and potential as therapeutic agents.

Keywords: *Staphylococcus aureus*; Aureolysin; Propofol; 2,3',4,5'-Tetrahydroxystilbene; Molecular Docking.

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PBa-97
Abstract Type: Original Research

Computational Screening of Inhibitors Targeting Chlamydia Protease-Like Activity Factor (CPAF) in *Chlamydia trachomatis*: A Molecular Docking Approach

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Abstract

Background and Aim: Urogenital *Chlamydia trachomatis* infection is one of the most common types of sexually transmitted illnesses worldwide. A highly conserved virulence factor of *Chlamydia trachomatis*, Chlamydial protease-like activating factor (CPAF), mediates the evasion of the innate immune response, inhibites the complement activation pathway, and degrades the antimicrobial peptides with its anti-chlamydial activity. Recent studies emphasize the importance of developing specific CPAF inhibitors to reduce its activity and attenuate bacterial virulence, offering a promising strategy for effective clinical management. Therefore, this study aimed to identify the most potent CPAF inhibitor through molecular docking analysis.

Methods: The 3D structure of CPAF (PDB ID: 3DPM) was obtained from the PCSB PDB database. The structure of Lactacystin as an inhibitory ligand (PubChemCID: 6610292) and a total of 20 of its analogs were retrieved from the PubChem database in SDF format. After preparing the protein and ligands, molecular docking was performed using Virtual Docker Molegro.6.0. Subsequently, the best interaction with the lowest energy binding was analyzed using Molegro Viewer software. Finally, pharmacokinetic properties such as the distribution, absorption, metabolism, and excretion of the ligand were investigated using the SwissADME server.

Results: Among all ligands, the best ligand for CPAF was identified as 2-acetamido-3-[3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxopyrrolidine-2-carbonyl] sulfanyl

propanoic acid (PubChem ID: 10407181) with a molecular weight of 376.43 g/mol and binding energy of -136.889 kcal/mol. This ligand formed 8 hydrogen bonds with the CPAF residues Glu406, Lys53, Asn530, Asn535, Thr403, lle539, Lys540, and Phe533, as well as 12 steric interactions with the residues Glu406, Phe529, Asn530, Lys53, Pro534, Asp405, Phe533, lle539, Lys540, Phe111, Thr403, and Asn535. Moreover, the ADME results indicated that this ligand had a water solubility score (logS) of -1.41, a lipophilicity score (XLOGP3) of -0.27, a polarity score (TPSA) of 178.33 Å², and hydrogen bond donors and acceptors of 5 and 7, respectively.

Conclusion: Consequently, after further in vitro and in vivo analysis, 2-acetamido-3-[3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxopyrrolidine-2-carbonyl] sulfanylpropanoic acid (PubChem ID: 10407181) may be considered a candidate for inhibiting *Chlamydia trachomatis's* CPAF.

Keywords: *Chlamydia trachomatis;* Molecular Docking; CPAF factor.

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PBa-98

Frequency of methicillin resistant *Staphylococcus aureus* strains isolated from hospitalized patients in Sanandaj, Iran

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Abstract

Background and Aim: Methicillin-resistant *Staphylococcus aureus* (MRSA) poses a significant public health challenge worldwide, particularly in hospital settings. This study aims to evaluate the prevalence of MRSA strains isolated from clinical samples in Sanandaj, Iran, and to assess their antimicrobial resistance patterns.

Methods: A cross-sectional study was conducted, collecting a total of 65 *Staphylococcus aureus* (*S. aureus*) isolates from clinical specimens at two teaching hospitals in Sanandaj. Identification of isolates was performed using standard biochemical tests. Methicillin resistance was evaluated through three methods: polymerase chain reaction (PCR) for the *mecA*

gene, agar dilution for determining oxacillin minimum inhibitory concentration (MIC), and disk diffusion tests for detecting resistance to methicillin and oxacillin. Antimicrobial susceptibility patterns were assessed using the disk diffusion method.

Results: Among the clinical specimens, the highest prevalence of *S. aureus* was found in urine samples (36.23%). Notably, 56.92% of MRSA strains were isolated from patients in the Intensive Care Unit (ICU). According to phenotypic methods, 43 out of 65 isolates (63.15%) were identified as MRSA. Antimicrobial susceptibility testing revealed that 64 isolates (98.46%) were susceptible to vancomycin, and all isolates (100%) were susceptible to mupirocin. Conversely, all isolates (100%) exhibited resistance to ceftriaxone, penicillin, and clindamycin. Additionally, 54 isolates were classified as multidrug-resistant (MDR). PCR analysis confirmed the presence of the *mecA* gene in all isolates that were phenotypically identified as methicillin-resistant (63.15%).

Conclusion: The high prevalence of MRSA among *S. aureus* isolates, particularly in ICU patients, underscores the urgent need for effective infection control measures in healthcare settings. The resistance pattern observed, with all isolates resistant to several commonly used antibiotics but susceptible to vancomycin and mupirocin, highlights the importance of continuous surveillance and appropriate antibiotic stewardship to manage MRSA-related infections effectively. Further studies are warranted to explore the molecular epidemiology of MRSA in this region and its implications for public health.

Keywords: Methicillin-resistant *Staphylococcus aureus*; MRSA; Antimicrobial resistance; *mecA* gene; Multidrug-resistant

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PBa-99

Artificial Intelligence in Drug Discovery and Development Against Antimicrobial Resistance

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Abstract

Background and Aim: Antimicrobial resistance (AMR) poses a significant global health threat, undermining the effectiveness of existing antibiotics and endangering public health. The rising incidence of AMR necessitates innovative strategies. However, the conventional drug discovery process aimed at tackling AMR is characterized by high costs, extended timelines, frequent failures, and various developmental challenges. **Objectives:** This study investigates the potential of artificial intelligence (AI) in combating AMR through drug discovery and development. It evaluates the current landscape of AMR, critiques the shortcomings of traditional drug discovery approaches, and highlights the opportunities and advancements that AI can provide.

Methods: Data for this study were gathered from reputable databases such as Scopus, PubMed, and Google Scholar.

Results: The review explores multiple applications of AI, including machine learning, deep learning, and language models, for discovering new antimicrobial agents, enhancing drug design, and predicting mechanisms of AMR. It also discusses how AI can be integrated with high-throughput screening, genomics, and proteomics to accelerate the identification and development of novel antimicrobial compounds.

Conclusion: The study concludes by addressing the challenges and ethical implications associated with the use of AI in AMR research, stressing the need for collaborative efforts among scientists, policymakers, and healthcare professionals to effectively address AMR.

Keywords: Artificial Intelligence, Drug Discovery, Drug Development, Antimicrobial resistance, Machine Learning, Deep Learning

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PBa-100

Evaluating the Antimicrobial Potential of Novel Sulfonohydrazide Compounds Against Sulfonamide-Resistant Escherichia coli

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Abstract

Background and Aim: One way to control the spread of drug resistance is to investigate the antibacterial effect of non-toxic chemical compounds. Sulfonohydrazide compounds are sulfonamide compounds that can be used in the treatment of bacterial infections. The aim of this study was to investigate the antimicrobial effect of five sulfonohydrazide-derived chemicals on *Escherichia coli* strains of standard and resistant to sulfonamide.

Methods: Five sulfonohydrazide-derived chemicals including chlorobihexylsulfonohydrazide, biphenylsulfonohydrazide, 4-methyltoluenesulphonohydrazide, 4-nitrobenzenesulfonohydrazide, and 4-bromobenzenesulfonohydrazide were designed and manufactured. Antibacterial effect of these compounds on the standard strain of *E. coli* (ATCC-25922) and the Hospital isolates of sulfonamide-resistant *E. coli* was evaluated by disk diffusion and minimum inhibitory concentration (MIC) methods.

Results: The purity of the synthesized compounds was variable from 82%-94%. The mean MIC of chlorobihexylsulfonohydrazide on the standard strain of E. coli (ATCC-25922) and sulfonamide-resistant *E. coli* was 0.27 mg/ml and 0.62 mg/ml, respectively. In contrast, biphenylsulfonohydrazide, 4-methyltoluenesulphonohydrazide, 4-nitrobenzenesulfonohydrazide, and 4-bromobenzenesulfonohydrazide had no antibacterial effect on *E. coli* strains. The mean MIC was different between chlorobihexylsulfonohydrazide and sulfamethoxazole-trimethoprim ($p = 0.208$). The mean MIC was statistically significant between sulfonamide-resistant E. coli and the standard strain of *E. coli* ($p = 0.031$).

Conclusion: This study identified that one of the made compounds from sulfonohydrazide may partially inhibit the growth of sulfonamide-resistant *E. coli*. These compounds can be suitable for the preparation of antibacterial drugs. In larger studies, non-antibiotic drugs derived from sulfonohydrazide and other non-toxic chemicals with low side effects may have more antimicrobial effects.

Keywords: Antibacterial agents, Antibiotic resistance, MIC, Sulfonamide, Sulfonyl hydrazide

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PBa-101

Investigating the Association Between Gut Microbiota Composition and Type 2 Diabetes

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Abstract

Background and Aim: Emerging evidence indicates a potential connection between alterations in gut microbiota composition and metabolic disorders, including type 2 diabetes (T2D). This study aims to assess the compositional changes in intestinal microbiota in T2D patients compared to healthy non-diabetic people.

Methods: A case-control study was conducted involving 18 T2D patients and 18 healthy controls. Gut microbiota profiles were determined by extracting bacterial DNA from fecal samples and analyzing it using quantitative real-time polymerase chain reaction (qPCR).

Results: The study revealed that T2D patients had significantly higher frequencies of the genus Bacteroides and the phylum Bacteroidetes compared to controls ($P=0.03$ and $P<0.001$, respectively). In contrast, the phyla Actinobacteria and Firmicutes were significantly more abundant in the controls ($P=0.01$ for both). No significant differences were observed in the fecal populations of the genus Enterococcus, Clostridium clusters IV and XIVa, phylum Proteobacteria, and total bacterial count between the groups ($P=0.88$, $P=0.56$, $P=0.8$, $P=0.99$, and $P=0.7$, respectively).

Conclusion: The findings suggest that T2D is associated with fluctuations in gut microbiota composition. These insights may be instrumental in developing strategies to manage or treat T2D by restoring intestinal microbiota through targeted administration of specific probiotics/prebiotics and lifestyle/dietary modifications.

Keywords: Type 2 diabetes; Gut microbiota; Metabolic disorder; Bacteroidetes; Firmicutes; Actinobacteria; Real-time qPCR.

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PBa-102

Molecular Identification and Analysis of Multi-Drug Resistant (MDR) Bacteria in Renal Failure Patients

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Abstract

Background and Aim: Multi-Drug Resistant (MDR) have emerged as a significant concern for patients with kidney failure, elevate their susceptibility to infections. Ineffective infection control measures have contributed to increased antibiotic resistance, leading to higher healthcare costs and elevated mortality rates. This study aims to isolate and identify these resistant bacteria in patients with kidney failure to enhance understanding and improve management strategies.

Methods: In this cross-sectional study, which was conducted in 2022, urine samples were collected from 100 hospitalized patients. The patients were included 50 male and 50 female with kidney failure at Ziyaei Hospital in Ardakan, Yazd, Iran. After culturing the samples, the isolates were identified through biochemical methods, and their antibiotic susceptibility was assessed using the disk diffusion technique. Subsequently, DNA was extracted from the isolates, and polymerase chain reaction (PCR) was employed for 16S rRNA sequencing, as well as for the examination of resistance genes, including *tetA*, *mecA*, *aadA1*, *CITM*, and *CMA1*.

Results: Of the total isolates, 85% were Gram-negative with *E. coli* (55%) in female, and 15% were Gram- positive, with *Sthaphylococcus aureus* (8%) in male and female. The results indicated the presence of specific antibiotic resistance genes in various bacterial isolates. In *Escherichia coli* isolates, the genes *CITM* and *tetA* were detected, indicating resistance mechanisms against certain antibiotics. *Klebsiella pneumoniae* isolates contained the *CITM* gene, contributing to their resistance profile. In *Staphylococcus aureus*, both *tetA* and *mecA* genes were identified, signifying their capability to resist multiple antibiotics, including methicillin. Furthermore, *Pseudomonas aeruginosa* isolates exhibited a combination of *tetA*, *mecA*, and *CMA1* genes, making them highly resistant to several antibiotic classes. In *Enterobacter* isolates, the *tetA* gene was also confirmed, further expanding their resistance

capabilities. Additionally, the *aadA1* gene was exclusively found in *Proteus* isolates. A significant correlation was observed in the antimicrobial resistance of *Escherichia coli* and *Staphylococcus aureus* ($p< 0.05$) in this study.

Conclusion: The study identifies specific antibiotic resistance genes in bacterial isolates from renal failure patients, including *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Enterobacter*. The presence of resistance genes such as *CITM*, *tetA*, *mecA*, and *CMA1* highlights the diverse mechanisms these bacteria use to resist antibiotics. This underscores the need for effective infection control measures and targeted antibiotic therapies to improve patient outcomes and reduce healthcare costs associated with Multi-Drug Resistant infections.

Keywords: Multi-Drug Resistance, renal failure, polymerase chain reaction, antibiotic resistance genes, urine sample

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PBa-103
Abstract Type: Original Research

Discovery of Novel Hyaluronan Lyase Inhibitors: A Molecular Docking Analysis of *Streptococcus pneumoniae*

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Abstract

Background and Aim:

Streptococcus pneumoniae, a formidable pathogen, relies heavily on its hyaluronate lyase (spnHL) as a critical virulence factor to facilitate infection and dissemination. Whit the increased occurrence of antibiotic-resistant strains and absence of effective treatments for pneumococcus infections, in this study, we aimed to identify a suitable ligand to inhibit spnHL, with the ultimate goal of developing a potential therapeutic agent to combat *Streptococcus pneumoniae* infections. To achieve this, we employed molecular docking techniques to systematically evaluate the binding affinity and specificity of various ligands for spnHL and identify the most promising candidates for further development.

Methods: The 3D structures of hyaluronate lyase (PDB ID: 1EGU) and its inhibitor (ascorbic acid) (Pubchem CID: 54670067), along with of 60 its available analogs, were retrieved from

the RCSB PDB and PubChem databases, respectively. After preparing the protein and ligands by lowering the energy level, removing the ligand and water molecules from the protein, and adding electric charges and hydrogen atoms, molecular docking was performed using Molegro Virtual Docker v. 6, and the best interaction with the lowest energy binding was analyzed using Molegro Molecular Viewer software. Using the SwissADME database, the pharmacokinetic properties of ligands (ADME) were evaluated.

Results: Among all ligands studied, magnesium ascorbate hydrate (PubChem CID: 54690252) with a molecular weight of 200.43 g/mol, exhibited the most negative ΔGbind (-116.504 Kcal/mol). This ligand formed seven hydrogen bonds with the hyaluronate lyase residues Trp292, Asn349, Asp352, Ser463, Arg466, Glu477, and Asn410, and 13 steric interactions involving the hyaluronate lyase residues Trp292, Asp352, Val411, Asn349, Arg460, Tyr404, Ser463, Arg462, Arg466, Gly406, Glu477, Ala407, and Asn410. Moreover, the ADME results indicated that this ligand had a water solubility score (LogS) of 0.08, lipophilicity (XLoGP3) of -1.64, polarity (TPSA) of 107.22, and hydrogen bond donors and acceptors of 4 and 6, respectively.

Conclusion: Our findings provide a basis for future experimental validation and potential drug development efforts aimed at reducing *Streptococcus pneumoniae* infections through targeted inhibition of hyaluronate lyase. Further analysis is required to confirm this finding.

Keywords: *Streptococcus pneumoniae*; Magnesium ascorbate hydrate; Molecular Docking.

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PBa-104
Abstract Type: Original Research

Exploring New Therapeutic Avenues: Molecular Docking Study of Streptococcal pyrogenic exotoxin B (SpeB) Inhibitors

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Abstract

Background and Aim: *Streptococcus pyogenes* causes a wide range of diseases, from mild infections such as pharyngitis to dangerously invasive conditions like necrotizing fasciitis and streptococcal toxic shock syndrome. One of the most important virulence factors of *S. pyogenes* is streptococcal pyrogenic exotoxin B (SpeB) which is responsible for toxic shock syndrome

and plays a crucial role in *pyogenes's* pathogenesis. With the emergence of antibiotic-resistant strains and increasing concerns regarding the treatment of diseases caused by this bacterium, it is essential to explore new alternatives. In this study, our main purpose is to identify the most potent SpeB inhibitor through molecular docking analysis.

Methods: The 3D structure of the streptococcal pyrogenic exotoxin B (SpeB) (PDB ID: 1PVJ) was obtained from the RCSB PDB database. The structures of the SpeB inhibitory ligand, (3R)-3-{[(BENZYLOXY)CARBONYL]AMINO}-2-OXO-4-PHENYLBUTANE-1-DIAZONIUM, with PubChemCID 17754225 and 30 of its analogs were retrieved from the PubChem database in SDF format. The protein and inhibitory ligands were prepared for docking using Molegro Virtual Docker version 6.0. After docking, the best interaction with the lowest energy binding was analyzed through Molegro Molecular Viewer v.7 software. Finally, the pharmacokinetic properties of the ligands were evaluated using the SwissADME server.

Results: Through all inhibitory ligands for Streptococcal pyrogenic exotoxin B (SpeB), the best ligand was benzyl N-[1-amino-1,4-dioxo-6-(phenylmethoxycarbonylamino)hexan-2-yl]carbamate (PubchemCID:564108) with a molecular weight of 427.45 g/mol and binding energy of -135.956 kcal/mol. This ligand created six steric interactions with the SpeB protein residues Lys229(A), Gly174(A), Val172 (A), Lys229 (D), Leu169 (D), and Ile270 (D), and two hydrogen bonds with Val172 (D) and Lys229 (D) residues, and no electrostatic interaction. The ADME results showed that this ligand has a water solubility score (logS) of -2.56, a hydrophilic score (LogP) of 2.37, a polarity score (TPSA) of 136.82 and lastly, hydrogen bond donors of 3 and hydrogen bond acceptors of 6.

Conclusion: These results indicated benzyl N-[1-amino-1,4-dioxo-6-(phenylmethoxycarbonylamino)hexan-2-yl]carbamate is a good candidate for inhibiting streptococcal pyrogenic exotoxin B (SpeB). Further in vitro and in vivo studies are required to confirm their potential as therapeutic agents.

Keywords: Molecular Docking, *Streptococcus pyogenes*, Streptococcal pyrogenic exotoxin B (SpeB), ADME.

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PBa-105

Abstract Type: Original Research

Molecular Docking Study of N~2~,N~2~-DIMETHYL-N~1~-(6-OXO-5,6-DIHYDROPHENANTHRIDIN-2-YL)GLYCINAMIDE and Its Analogues as *Pseudomonas*

aeruginosa's Exotoxin A Inhibitors: A Novel Therapeutic Strategy

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is an opportunistic bacterium that causes serious systemic infections, especially in immunocompromised patients. The pathogenic potential of *Pseudomonas aeruginosa* is largely attributed to presence of Exotoxin A, a potent virulence factor that precipitates a cascade of systemic complications, including hematological disturbances, metabolic dysregulation, cardiovascular instability, and multifocal organ damage. New efforts to combat multi-drug resistance of *Pseudomonas* may be involved in virulence factor-targeted therapeutic studies. Understanding the role of Exotoxin A in pathogenicity offers potential for targeted therapies. This study explores Exotoxin A inhibitors through molecular docking to develop a promising drug candidate.

Methods: We retrieved the three-dimensional structure of the *Pseudomonas aeruginosa* Exotoxin A protein with PDB ID of 1XK9 from the PDB databases. The structure of PJ34 inhibitor (N~2~,N~2~-DIMETHYL-N~1~-(6-OXO-5,6-DIHYDROPHENANTHRIDIN-2-YL)GLYCINAMIDE) with PubChemCID of 4858 and a total of 20 of its analogs were obtained from PubChem database in SDF format. After preparation of protein and inhibitory ligands, molecular docking was conducted using Molegro Virtual Docker v. 6. The best ligand with the lowest energy binding was evaluated by Molegro Virtual Viewer v. 7, and finally, the pharmacokinetic properties of the ligand were estimated using the SwissADME database.

Results: The best ligand for Exotoxin A protein with the lowest energy binding was 5-(2-Fluorobenzamido)-2-methyl-1,2,3,4-tetrahydroisoquinoline (PubChemCID: 39866), with a molecular weight of 284.33 g/mol and the most negative ΔGbind (-96.12 kcal/mol). This ligand formed one hydrogen bond with the Exotoxin A residue Asp403 and six steric interactions involving the residues Thr418(A), Pro521(B), Trp466(B), Ile465(B), Asp403(A), and Gly404(A). Furthermore, the ADME results demonstrated that this ligand had a water solubility score of (Log*S*) -3.55, three hydrogen bond acceptors, one hydrogen bond donor, a lipophilicity score of (XLOGP3) 2.79, and a polarity score (TPSA) of 32.34.

Conclusion: Our results demonstrated that 5-(2-Fluorobenzamido)-2-methyl-1,2,3,4-tetrahydroisoquinoline (PubChemCID: 39866) ligand may be considered as an inhibitor candidate drug for inhibiting *Pseudomonas aeruginosa's* Exotoxin A, although further in vitro and in vivo analysis are necessary.

Keywords: *Pseudomonas aeruginosa*; Molecular Docking; 1XK9; Exotoxin A.

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PBa-106

Virulence Factors and Risk Factors of *Staphylococcus aureus* in Infective Endocarditis: Pathogenesis and Clinical Implications

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Abstract

Staphylococcus aureus, a prominent pathogen in human infections, is closely associated with infective endocarditis (IE), a serious condition involving inflammation of the heart valves. This review article examines the relationship between *S. aureus* and IE, focusing on key virulence factors that facilitate bacterial colonization, immune evasion, and persistence within cardiac tissues. Notably, *S. aureus* utilizes surface adhesion molecules such as clumping factor A (ClfA) and fibronectin-binding proteins (FnBPs) to adhere to host endothelium, forming the initial basis for endocardial infection. Additionally, secreted toxins like alpha-toxin and Panton-Valentine leukocidin (PVL) contribute to host cell lysis and tissue invasion, further aggravating infection severity. The formation of biofilms provides an additional layer of immune evasion by resisting phagocytosis and limiting antibiotic efficacy, particularly in cases involving prosthetic valves. This review also analyzes critical risk factors, including underlying cardiac conditions, prosthetic heart valves, intravenous drug use, and invasive medical procedures, that significantly predispose patients to *S. aureus* endocarditis. The role of methicillin-resistant *S. aureus* (MRSA) is emphasized, as it complicates treatment protocols and is linked to worse clinical outcomes. Emerging diagnostic and therapeutic strategies aimed at improving patient outcomes are discussed, as are prevention measures targeting high-risk populations. Overall, this article underscores the importance of understanding the pathogenic mechanisms of *S. aureus* in endocarditis and the need for targeted interventions to reduce the impact of this complex infection.

Keywords: Staphylococcus aureus, infective endocarditis, risk factors, virulence factors, antibiotic resistance

PBa-107
Abstract Type: Original Research

Microbiological profile and antibiotic resistance of bacteria isolated from patients with wound infection hospitalized in Allameh-Bohloul Gonabadi hospital in 2023

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Abstract

Background and Aim: Wound infection is considered as a common hospital infection and an important factor in patient mortality. The present study was designed and carried out with the aim of investigating the microbiological profile and antibiotic resistance of bacteria isolated from patients with wound infection hospitalized in Allameh-Bohloul Gonabadi hospital in 2023.

Methods: The current descriptive cross-sectional study investigated 121 patients with wound infection hospitalized in Allameh Bahloul Gonabadi Hospital in 2023, who were selected by census method. The files of the patients with the entry criteria were reviewed and the required information was entered in the data registration checklist. The data was analyzed using SPSS version 26 software by determining the mean and standard deviation indicators for quantitative variables and determining the frequency and percentage for qualitative variables.

Results: The average age of the studied patients was 59.46 ± 21.68 years and most of them were women. The most common wound infections observed in patients admitted to Allameh Bahloul Gonabadi Hospital were surgical site infection (19.8%), soft tissue infection (19%) and diabetic foot ulcer (14.2%), and most of them were caused by staphylococcal bacteria.

aureus (23.1%), Escherichia coli (20.7%), Klebsiella (14%) and coagulase-negative Staphylococcus (14%). The highest rate of multidrug resistance was related to Proteus mirabilis bacteria (100%), Micrococcus (100%) and Acinetobacter (77.8%), and the result of hospitalization in 16.5% of the studied patients was death.

Conclusion: The results of this study showed that most of the wound infections observed in hospitalized patients were surgical site infections and most of them were caused by Staphylococcus aureus. Also, the highest rate of multidrug resistance was observed in Proteus mirabilis and Acinetobacter.

Keywords: Microbiological Profile, Antibiotic Resistance, Wound Infection

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PBa-108
Abstract Type: Original Research

Investigating the Impact of Laboratory and Clinical Factors on the Prognosis of Sepsis Patients Admitted to Ganjavian Hospital, Dezful

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Abstract

Background and Aim: Sepsis, a life-threatening condition caused by dysregulated immune responses to infection, remains one of the leading causes of hospital mortality worldwide. Characterized by a progression from localized infection to systemic inflammation, severe sepsis, and septic shock, this condition poses significant challenges in both diagnosis and treatment. Despite advancements in medical therapies, mortality rates associated with sepsis remain alarmingly high. Early identification of prognostic factors is crucial to improving outcomes and optimizing care for these patients. This study evaluated laboratory and clinical

factors significantly influencing the prognosis of sepsis patients admitted to Ganjavian Hospital, Dezful.

Methods: This cross-sectional observational study (Approval ID: IR.DUMS.REC.1402.019) involved 189 hospitalized sepsis patients. Comprehensive data were collected, including demographic details, laboratory parameters (bilirubin, ALT, AST, LDH, INR), and clinical indicators (oxygen saturation Sato2, Glasgow Coma Scale GCS, respiratory rate RR, and comorbidities such as diabetes, pulmonary, and cardiac diseases). Statistical analyses were conducted to determine the associations between these variables and patient outcomes, specifically mortality or discharge status. Additionally, the impact of treatment timing and therapeutic interventions on prognosis was assessed.

Results: The study revealed a significant correlation between elevated laboratory biomarkers, particularly ALT, AST, LDH, INR, and bilirubin, and higher mortality rates ($P<0.05$). Deceased patients also exhibited markedly reduced oxygen saturation (Sato2) and lower GCS scores than discharged patients. Increased respiratory rate (RR) was significantly associated with mortality ($P=0.012$), highlighting its potential as an early indicator of disease severity. Chronic conditions such as pulmonary and cardiac disorders were identified as major risk factors. Moreover, delays in initiating appropriate antibiotic therapy were linked to disease progression and poorer outcomes. Patients with multiple comorbidities experienced higher mortality, emphasizing the need for integrated management strategies.

Conclusion: The findings of this study underscore the importance of comprehensive monitoring of laboratory and clinical indicators in sepsis patients. Early detection and intervention based on these parameters can significantly improve prognosis and reduce mortality rates. Establishing structured diagnostic and therapeutic protocols, combined with training healthcare providers to recognize early warning signs, can enhance the overall management of sepsis. These results advocate for the implementation of standardized care pathways to mitigate the burden of this life-threatening condition.

Keywords: Sepsis; Laboratory factors; Clinical factors; Prognosis; Mortality.)

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PBa-109
Abstract Type: Original Research

Production of low-cost and alternative culture media using legumes

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Abstract

Background and Aim: Most of the culture media used in bacterial growth are composed of complex compounds that increase the value of the product. This makes the practical search of microbiology more difficult. Therefore, the development of an alternative culture medium with a simple and low-cost composition becomes necessary

Methods: This work was carried out with the aim of using plant sources and legumes such as white beans, lentils, chickpeas, soybeans, dry bread, beans, green peas to make a low-cost and alternative culture medium that allows the growth of a variety of bacteria. The target bacteria, including *Pseudomonas spp.*, *Bacillus spp.*, *Escherichia coli*, were used for cultivation on the prepared media. After incubation, it was observed that they grew well on the media containing these items. The tested microorganisms were of two groups, gram positive and gram negative, and were initially cultured on nutrient agar control media and then compared with the production media.

Results: This work shows that it is possible to use easy and low-cost culture media. Compared to conventional media, alternative culture media often provide satisfactory results in terms of microbial growth efficiency and production cost.

Conclusion: In this study, we present recent studies involving alternative culture media formulated with products of plant origin. Therefore, the aim is to serve as a scientific basis for the development and use of these inexpensive culture media in laboratory studies and research. It was observed that Gram-positive bacteria grew better on the prepared culture media than Gram-negative bacteria, and no pigment production was observed in any of the constructed media.

Keywords: Recycling, Differential Media, Cheap Culture Media

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PBa-110

Human gut microbiota and its possible relationship with obesity and diabetes

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Abstract

Aim: Obesity and diabetes are public health problems that are leading causes of death in the world. Recent surveys suggest that there is a relationship between diabetes and bacterial residents of the gastrointestinal tract. This case-control study was designed to evaluate the composition of the gut microbiota in patients with type 2 diabetes (T2DM) and obesity compared to the healthy people.

Method: A total of 91 adult subjects (25 patients diagnosed with T2DM, 48 obese patients, and 18 healthy individuals) were included in the study. The gut microbiota composition was investigated by quantitative real-time polymerase chain reaction (qPCR) method using bacterial 16S rRNA gene.

Results: The frequency of all bacterial species in the obese group compared to the control group have significantly changed ($p < 0.05$) except Bacteroides fragilis, whereas the level of bacterial composition was not changed significantly ($p > 0.05$) in the diabetic patients versus the control ones, except for Bacteroides phylum and Lactobacillus spp. Moreover, the mean body mass index (BMI) in control, T2DM, and obese groups were 24.28 ± 3.00, 26.83 ± 3.29, and 44.65 ± 3.73, respectively. Our analysis showed a positive correlation between diabetic patients plus obese ones and the number of bacteria ($p < 0.05$).

Conclusion: To sum up, these findings show that specific changes in microbial community composition are associated with T2DM and obesity. More extensive, our survey suggests that modulation of the microbiome warrants further investigation as a potential therapeutic strategy for metabolic diseases.

Keywords: Obesity; diabetes; microbiota

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PBa-111
Abstract Type: Original Research

Efficacy of Ethyl Acetate Extract from Teucrium polium in Inhibiting *Helicobacter pylori*: An In Vitro Study

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Abstract

Background and Aim: Untreated *Helicobacter pylori* infection can lead to gastric cancer. This bacterium exhibits significant resistance, and the spectrum of associated disorders is expected to become more apparent over time, highlighting the need to develop more effective treatments. Phytomedicine, or herbal medicine, involves the use of whole plants or their extracts for medicinal purposes. This study aimed to investigate the in vitro effects of ethyl acetate extract of Teucrium polium on *Helicobacter pylori*.

Methods: Ethyl acetate extracts of Teucrium polium were initially prepared. Subsequently, *H. pylori* strains were isolated from patient stomach biopsies and standardized suspensions were prepared at two distinct concentrations. The minimum inhibitory concentration (MIC) of ethyl acetate extract from Teucrium polium was determined using the agar dilution method. Briefly, the bacterial suspensions were inoculated into Brucella agar medium containing serial dilutions of the extracts, ranging from 1024 µg/mL to 8 µg/mL. Following incubation, bacterial growth was assessed.

Results: The ethyl acetate extract of Teucrium polium, at a concentration of 1024 µg/mL, showed significant antibacterial activity and effectively inhibited bacterial growth up to a dilution of 32 µg/mL. Consequently, the minimum inhibitory concentration (MIC) for this extract was determined to be 32 µg/mL.

Conclusion: The results of this study indicate that the ethyl acetate extract of Teucrium polium possesses significant in vitro antibacterial activity against *H. pylori*, suggesting its potential for further investigation as a therapeutic agent.

Keywords: *Helicobacter pylori*, Herbal extract, anti-*Helicobacter pylori* activity,

Teucrium polium

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PBa-112
Abstract Type: Systematic review

Study of the transmission of *Pseudomonas aeruginosa* from wildlife to humans with emphasis on the role of food

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Abstract

Background and Aim: *Pseudomonas aeruginosa* is a Gram-negative, opportunistic bacterium known for its high adaptability to various environments, including water, soil, and the host body. It is naturally found in the environment and can colonize wild animals. Studies have shown that wild animals can act as important reservoirs for pathogens and can be transmitted to humans through contaminated food (such as meat, fish, or dairy products), increasing the risk of zoonotic transmission and the emergence of multidrug-resistant strains in natural ecosystems and wildlife. The importance of Pseudomonas aeruginosa has been recognized due to its widespread antibiotic resistance and ability to cause severe infections in humans, especially in immunocompromised individuals.

Methods: A comprehensive search was conducted via databases such as PubMed, Scopus, Web of Science and Google Scholar to identify the relevant titles and abstracts using specific terms regarding *Pseudomonas aeruginosa*, zoonotic diseases, wildlife, food safety, foodborne pathogens.

Results: Food chain contamination is caused by poor hygiene practices in hunting, processing, and storing food products originating from wildlife. The results of the study show that *Pseudomonas aeruginosa* lives as an opportunistic bacterium in natural environments such as soil, water, and the bodies of wild animals and can be transmitted to humans through contaminated food. Wild animals act as the main reservoirs of this bacterium and can transmit it to humans through meat, fish, and dairy products. This bacterium poses significant health risks due to its high antibiotic resistance and ability to cause severe infections, especially in people with weak immune systems. The findings indicate that hygiene measures in food processing and consumption are essential to prevent contamination with *Pseudomonas aeruginosa* and reduce health risks.

Conclusion: *Pseudomonas aeruginosa* is not only a potential threat to public health, but also poses serious challenges in treating infections caused by it due to its widespread drug resistance. The study recommends that more careful monitoring of the food chain, improved hygiene standards, and effective infection control methods be implemented. Combining new diagnostic technologies with environmental surveillance of wildlife can help to better understand the transmission pathways of *Pseudomonas*. In addition to improving public health outcomes, this approach can also help develop conservation strategies to reduce the impacts of antibiotic resistance on ecosystems. Collaboration between the fields of microbiology, ecology, and public health is essential to address this challenge.

Keywords: *Pseudomonas aeruginosa*, zoonotic diseases, wildlife, food safety

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PBa-113
Abstract Type: Original Article

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Prevalence, antimicrobial resistance, and biofilm-formation of Listeria monocytogenes in bulk raw milk in East Azerbaijan province, Iran

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Abstract

Background and Aim: The aims of this study were to determine the prevalence, antimicrobial resistance and the biofilm-forming ability of Listeria spp. in bulk raw milk in East-Azerbaijan province, Iran.

Methods: A total of 192 bulk raw milk samples were collected from six distinct parts of East-Azerbaijan province. Selective enrichment and isolation were done by using United States Department of Agriculture (USDA) method, then isolates were identified by biochemical tests and confirmed by polymerase chain reaction. Susceptibilities of isolates to different antibiotics were determined by using the disk diffusion assay. Two phenotypic methods were used for investigation of biofilm production: Congo red agar (CRA) and microtiter plate (MTP).

Results: The prevalence of *Listeria monocytogenes* and other Listeria spp. were 11.97% and 0%, respectively. The highest prevalence rate was found in one of regions located in the center of province (30.43%) and northeast of province had the lowest prevalence rate (3.12%). All isolates were susceptible to vancomycin, erythromycin, chloramphenicol, kanamycin, gentamicin, tetracycline, streptomycin, amoxicillin-clavulanic acid and rifampicin. Only one isolates had intermediate susceptibility to ciprofloxacin. There was the highest resistance to nalidixic acid (100%), followed by to ampicillin (17.39%), and penicillin (13.04%), and the lowest resistance to clindamycin (8.6%) was observed. Based on MTP, 91.30% of isolates were weak biofilm formers. Biofilm production of L. monocytogenes using CRA plates showed that 34.78% and 52.17% of isolates were positive and intermediate biofilm producers, respectively.

Conclusion: The results indicate that prevalence rate of *L. monocytogenes* is relatively high and there is a potential risk for consumers of raw and unpasteurized milk.

Keywords: *Listeria monocytogenes*; biofilm; infection prevention; treatment regimens, public health

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PBa-114
Abstract Type: Original Research

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Evaluation of the antibacterial efficacy of polydimethylsiloxane-based hydrophobic sponges containing metal organic framework and thymol for use as a self-cleaning surface

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Abstract

Background and Aim: In recent years, the emergence of surface design strategies offers an effective alternative solution to tackle bacterial infections. The design strategies of self-cleaning surface especially to prevent bacterial adhesion have attracted increasing attention. In this study, we evaluated the antibacterial/antiadhesion efficacy of polydimethylsiloxane-based hydrophobic sponges containing metal organic framework and thymol against multi-drug resistant (MDR) *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*.

Methods: Several composite sponges containing CuBDC, ZnBDC and thymol were developed and then characterized based on chemical and surface properties. Then, the antibacterial effect of the prepared sponges was assessed. Also, the long-term antibacterial effect of the most effective sponge was evaluated by performing four antibacterial evaluation cycles. In the next step, the anti-adhesion activity of the most effective sponges was assessed. Meanwhile, antibacterial activity of the best sponges was analyzed using field emission scanning electron microscopy (FESEM).

Results: The prepared nanocomposites containing CuBDC, ZnBDC and thymol showed significant antibacterial activity against all tested strains (> 4 log10 reduction in CFU). PDMS-CuBDC 2.5%-Thymol 2.5% sponge showed the best antibacterial activity against *S. aureus*, *E. coli*, and *P. aeruginosa*. This composite preserved its strong antibacterial activity against all tested strains after four washing cycles. Meanwhile, this sponge showed the best anti-adhesion activity against all tested strains. Also, FESEM images confirmed the potent antibacterial ability of PDMS-CuBDC 2.5%-Thymol 2.5% sponge against tested bacteria.

Conclusion: In summary, the results demonstrated that PDMS-CuBDC 2.5%-Thymol 2.5% sponge has great potential for use as a self-cleaning surface.

Keywords: Polymeric composite; Bioactive compound; Anti-adhesion activity; Self-cleaning coatings

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Evaluation of PEG-ZIF-۸.CIP Nanozymes on Biofilms and Infected Wounds Caused by Ciprofloxacin-Resistant *Pseudomonas aeruginosa*: A Novel Approach to Wound Healing

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Abstract

Objective: This study aimed to evaluate the antibacterial, antibiofilm, and wound-healing effects of ZIF-۸ and PEG-ZIF-۸.CIP nanozymes on infected wounds caused by ciprofloxacin-resistant *Pseudomonas aeruginosa* in a mouse model. Wound infections, especially in burn patients, pose significant therapeutic challenges due to antibiotic resistance and biofilm formation. Biofilms act as physical and chemical barriers, reducing antibiotic efficacy. This study sought to develop an innovative solution to reduce bacterial load, disrupt biofilms, and accelerate wound healing in drug-resistant infections.

Materials and Methods: ZIF-۸ and PEG-ZIF-۸.CIP nanozymes were synthesized via mechanochemical. Their physicochemical properties, particle size, morphology, and superoxide dismutas)SOD(like activity, were characterized through FTIR, SEM and functional SOD activity assays with NBT . *In vitro* studies evaluated the ability of the nanozymes to inhibit bacterial growth and disrupt biofilms formed by ciprofloxacin-resistant *P. aeruginosa*. Infected wounds were generated in BALB/c mice, infected wounds were treated with nanozymes *in vivo*, and histopathological analyses were evaluated.

Results: PEG-ZIF-۸.CIP demonstrated significant antibacterial activity and biofilm disrupting potential compared to ZIF-۸. *In vivo* studies showed that PEG-ZIF-۸.CIP accelerated wound healing, reduced inflammation, and enhanced tissue regeneration. The SOD-like activity of the nanozymes indicated strong antioxidant effects, which contributed to mitigating oxidative -damage and promoting wound repair. The results highlighted PEG-ZIF8. CIP's superior penetration into biofilm matrix, effectively disrupting their structure and enhancing bacterial sensitivity to treatment. This characteristic played a pivotal role in overcoming antibiotic resistance and improving therapeutic outcome.

Conclusion: The findings of this study underscore the potential of PEG-ZIF-۸.CIP as a groundbreaking nanozyme with high efficacy in combating antibiotic resistance, disrupting resistant biofilms, and accelerating the healing of infected wounds. Its multifunctional

properties, including antibiofilm, antibacterial, and wound-healing effects, make it a promising candidate for developing advanced therapeutic approaches for drug-resistant wound infections.

Keywords: PEG-ZIF-8.CIP, Antibiofilm, Antibactrial, Nanozyme, Wound healing.

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PBa-116

Original Research

Epidemiology and Antibiotic Resistance Pattern of Shigella in Children with Diarrhea Referred to Shahid Rahimi Hospital in Khorramabad during 2013-2023

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Abstract

Background and Aim: Diarrhea is one of the most significant causes of child mortality in developing countries.shigellosis is endemic worldwide, this study was designed and conducted to investigate the epidemiology and antibiotic resistance patterns of shigella in children with diarrhea who were referred to Shahid Rahimi hospital in khoramabad during the years 2014_2023.

Methods: this research was a cross-sectional descriptive-analytical and retrospective study.The study population included all children under 14 years old with acute diarrhea who were admitted to the inpatient departments of Shahid Rahimi Hospital in khoramabad from 2014 to 2023.The sampling method was census-based The required information was collected though a checklist.After data collection,the data were entered into SPSS software version 27 and subjected to statistical analysis Finally,a P-value of less than 0.05 was considered statistically significant.

Results: In this study,1842 records of children with diarrhea were examined.Among these,74 cases(4%)were diagnosed with shigella.the average age of shigella onset was 5.3 years;50% were boys,60.8% resided in urban areas,47.3% had shigella flexneri, 43.2% had shigella sonnei, and 1.4% had shigella boydii. The hospitalization duration for 45.9% of the shigella-infected patients was less than 5 days. The highest incidence of shigella was observed in June

of the year 1401. The most prevalent antibiotic resistances were observed for ampicillin, trimethoprim-sulfamethoxazole, tetracycline,cefixime, cefotaxime,and ceftriaxome at 89.3%,87.5%,84.7%,82.5%,82.1%,and 79.5%, respectively.**Conclusion:** Summary of the most important findings and the importance of the study

Conclusion: It can be examined Among can be be concluded that there is a statistically significant difference in antibiotic resistance to trimethoprim-sulfamethoxazole between age groups under and over 5 years, in antibiotic resistance to ampicillin between genders,and in antibiotic resistance to cefepime among shigella strains. However, no statistically significant relationships was observed between antibiotic resistance and urban or rural residence, or the duration of patient hospitalization in the observation ward.It is suggested that future studies of this kind be conducted with larger sample sizes and in various populations.

Keywords: Antibiotic Resistance,shigella, Diarrhea, children

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PBa-117
Abstract Type: Narrative Review

Phage Therapy as a Promising Future Treatment for Invasive Nontuberculous Mycobacterial Infections; A Forward-Looking Perspective on Open Chest Post-Cardiac Surgery Patients

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Abstract

Background and Aim: Invasive nontuberculous mycobacterial (NTM) infections may arise from an overlooked source: heater-cooler devices utilized during cardiac surgeries. Outbreaks of NTM infections represent an ongoing challenge, particularly among patients who have undergone cardiac procedures. These outbreaks often manifest as surgical site infections or infections linked to contaminated medical products, such as prosthetic implants and cardioplegia solutions. Clinically, NTM infections pose significant difficulties due to the prolonged antibiotic treatment regimens, which frequently fail to eradicate the infections and are associated with limited positive outcomes, drug resistance, and adverse side effects. Consequently, bacteriophages have emerged as a potential supplementary treatment option in clinical settings.

Methods: Reputable scientific databases such as Web of Science, PubMed, Scopus, and Google Scholar were utilized to compile this narrative review article without any time constraints. The study employed the following keywords: "phage therapy," "nontuberculous mycobacteria," "post-cardiac surgery infection," "surgical site infections," and "drug resistance." Various inclusion and exclusion criteria were applied, and the search was restricted to full-text articles published in English.

Results: Numerous studies indicate that bacteriophages are an effective tool for combating nontuberculous mycobacterial infections derived from various sources in patients. Phages can significantly impact these infections both independently and in conjunction with antibiotics. Consequently, employing phages as either a primary or supplementary treatment for nontuberculous mycobacterial infections associated with open-chest cardiac surgery may prove beneficial.

Conclusion: The treatment of nontuberculous mycobacterial infections with phages presents significant challenges due to the limited availability of therapeutically effective phages. However, positive clinical outcomes in patients who have no other treatment options reinforce the need for ongoing development of adjunctive phage therapy for certain mycobacterial infections. Therefore, given the impact of phages on nontuberculous mycobacteria, it is advisable to conduct further research focused on infections related to open-chest cardiac surgery caused by these pathogens.

Keywords: phage therapy, nontuberculous mycobacteria, post-cardiac surgery infection, surgical site infections, drug resistance

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PBa-118
Abstract Type: Systematic Review

Applications of Next-Generation Sequencing in the Development of New-Generation Probiotics: A Systematic Review

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Abstract

Background and Aim: Probiotics are beneficial microorganisms that are used to improve health; Also, new generation probiotics (NGPs) seek to provide better treatments using microbial strains. Next-generation sequencing (NGS) techniques hold great promise in identifying microbiome composition, gene function, and microbial interactions to fill this gap. The purpose of this review is to emphasize the opportunities provided by NGS to identify new

strains, determine genetic diversity and provide valuable information in the process of designing probiotics with optimal performance.

Methods: This review article included studies published on PubMed, ScienceDirect, Google Scholar, and SID until November 2024. The keywords were Next-generation sequencing, microbiome, and probiotics. By searching these databases, 31 articles were found. About 15 of them were removed by reading titles and abstracts, and 16 articles were selected under the inclusion criteria.

Results: Finally, 16 studies were reviewed which showed that the use of NGS in the production of next generation probiotics helped to identify and evaluate the positive effects of the gut microbiome on human health. *Akkermansia muciniphila*, *Bacteroides fragilis*, and *Faecalibacterium prausnitzii* were introduced as new generation probiotics with potential therapeutic roles. Observations based on bacterial genome sequencing revealed that probiotics had effects on immune regulation, including increased expression of TGF-β1 and decreased inflammatory cytokines such as TNF-α. Researchers noted improvements in blood sugar control and gut health in clinical trials. One of the challenges in this field was the difficulty in cultivating oxygen-sensitive strains and limitations in clinical validation. Comparative studies showed that new generation probiotics against traditional probiotics identified from bioinformatics and NGS studies targeted certain diseases, and the specific feature of these probiotics was their use as Biotherapy.

Conclusion: Studies have highlighted the role of NGS in improving and expanding next generation probiotics as a promising future against a variety of diseases. However, further research is needed to overcome potential challenges such as the difficulty of cultivating species and oxygen-sensitive limitations in clinical validation.

Keywords: probiotics; next-generation sequencing, genomics, microbiome

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PBa-119

Abstract Type: Original Research

High prevalence of extended-spectrum beta-lactamase-producing Enterobacteriaceae in clinical isolate Referred to Taleghani Hospital Gorgan Iran

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Abstract

Background and Aim: Antibiotic resistance, especially due to Extended-Spectrum Beta-Lactamases (ESBL)-producing Enterobacteriaceae, is a major concern, complicating treatment protocols. This study evaluates the antibiotic resistance patterns of ESBL-producing Enterobacteriaceae isolated from clinical specimens at Taleghani Pediatric Hospital in Gorgan, from December 2022 to December 2023.

Methods: In this descriptive cross-sectional study, 153 ESBL-producing Enterobacteriaceae isolates were examined. Identification of ESBL-producing strains was conducted using CLSI guidelines via the Combination Disk method. Antibiotic susceptibility was assessed with the disk diffusion method across 15 antibiotics. SPSS version 22 was employed for data analysis.

Results: Among 27,630 cultures performed, 513 (1.86%) were Enterobacteriaceae, of which 153 (29.82%) were ESBL producers, comprising 0.55% of total cultures. The majority of patients were female (67.3%), with 47.1% aged 0–5 years. Urine samples were the most common (60.8%), followed by tracheal (9.2%), throat (8.5%), and blood (7.2%) samples. Escherichia coli was the most frequent ESBL-producing isolate (65.4%), followed by Enterobacter (16.3%), Klebsiella pneumoniae (9.8%), Citrobacter (3.9%), and less frequent isolates such as Proteus vulgaris, Serratia, and Hafnia alvei (each <3%). Among the ESBL-producing isolates, 64.7% were classified as multidrug-resistant (MDR). The highest sensitivity was observed for meropenem (91.5%), while resistance was highest for ceftriaxone (76.5%).

Conclusion: The high prevalence of ESBL-producing E. coli and K. pneumoniae isolates in pediatric patients highlights the urgent need for effective antimicrobial stewardship. Nitrofurantoin and gentamicin have proven to be effective empirical treatments for these pathogens in children. However, the significant rates of multidrug resistance and ESBL production emphasize the importance of routine surveillance and early detection strategies to effectively manage these infections and prevent further resistance development.

Keywords: ESBL, Children UTI, E. coli, Klebsiella

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PBa-120
Abstract Type: Original Research

Assessing Molecular Docking of Inhibitors against Anthrax Lethal Factor

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Abstract

Background and Aim: Global warming could greatly affect several infectious agents, including anthrax, a zoonotic disease caused by the bacterium *Bacillus anthracis*. The lethal toxin (LT) produced by anthrax plays a vital role in its pathogenicity; numerous animal studies indicate that reducing toxin activity significantly decreases morbidity. By increasing the occurrence of antibiotic-resistant strains, current research approaches involve antibodies, small molecule inhibitors, and substrate analogs to combat the toxin. Therefore, this study aimed to identify the most potent ligand capable of inhibiting the lethal factor as a promising drug candidate through molecular docking analysis.

Methods: The 3D structure of the Anthrax lethal Factor was extracted from the RCSB PDB database (PDB ID: 1zxv). The inhibitory ligand of lethal factor, (E)-3-(5((5-(4-CHLOROPHENYL)FURAN-2-YL)METHYLENE)-4-OXO-2-THIOXOTHIAZOLIDIN-3-YL)PROPANOIC ACID (MFM), with PubchemCID 1286536, and a total of 20 analogs were selected from the PubChem database in SDF format. After preparing the protein and its ligands by eliminating the ligand from the protein, lowering the energy level, and adding electric charges and hydrogen atoms, molecular docking was conducted using Virtual Docker Molegro v. 6. Subsequently, the best interaction with the lowest energy binding was analyzed using Molegro Molecular Viewer software. Finally, the pharmacokinetic properties of the ligand were investigated using the SwissADME server.

Results: Among all the ligands studied, the following ligand, 3-[(5Z)-5-[[5-(3,5-dichlorophenyl)furan-2-yl]methylidene]-4-oxo-2-sulfanylidene-1,3-thiazolidin-3-yl]propanoic acid with PubchemCID 6196013 and a molecular weight of 428.31 g/mol, exhibited the most negative ΔGbind (-159.597 Kcal/mol). This ligand formed two Hydrogen bonds with lethal factor residues of Tyr542(B) and Pro492(A) along with 8 steric interactions involving Glu539(A), Ala493(A), Ala493(B), Tyr 542(B), Pro492(A), Ser 538(B), Lys 540(B), and pro 492 (B). In addition, this ligand has a LogS score of -5.31, a LogP score of 3.12, and its hydrogen bond donors and acceptors are 1 and 4, respectively. Furthermore, the polarity index (TPSA) is 128.14.

Conclusion: As a result, compared to other ligands, the AKOS002802288 analog may be used as an important candidate to inhibit the targeting of *Bacillus anthracis's* lethal factor protein. Further in vitro and in vivo studies must confirm it as a therapeutic agent.

Keywords: Anthrax Lethal Factor; Molecular Docking; AKOS002802288.

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PBa-121
Evaluation of the inhibitory effect of *Carthamus tinctorius* plant extract on silencing the quorum sensing system of *Pectobacterium carotovorum*

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Abstract

Background and Aim: Quorum Sensing (QS) is a process by which intracellular signaling molecules are produced, released, and responded to by other bacterial cells. The regulation of pathogenic gene expression in most bacteria is carried out by the QS process, disruption of which leads to the lack of gene expression and ultimately the control of the disease. This process is carried out by signaling molecules called AHLs. The pathogen *Pectobacterium carotovorum* also uses AHLs in the quorum sensing process. In this study, the anti-QS effect of a plant extract *Carthamus tinctorius* on the soft rot disease caused by Pectobacterium was evaluated.

Methods: In this study, two bacterial strains, *Pectobacterium carotorum* and *Chromobacterium violaceum* CV026 (biosensor) were used. External signal (AHL) C12-HSL: N-(3-Oxooctanoyl)-L-homoserine lactone was used. *Carthamus tinctorius* was collected from different areas of Fars province and extracted with a soxhlet apparatus. Evaluation of the growth inhibitory effect of strain CV026 and *Pectobacterium carotorum* against several antibiotic groups and *Carthamus tinctorius* plant extract was performed by disk diffusion method (CLSI 2024). In order to measure the anti-population activity, B agar-STA double-layer culture medium was used. To investigate the effect of the extract on the activity of *Pectobacterium carotorum*, under sterile conditions, potato tubers were inoculated with 25 µl of bacterial suspension (1×10^{6} CFU ml^{-1}) and 25 µl of extract. Data analysis of the findings was conducted using SPSS version 21, and the significance level was shown at ($p<0.05$).

Results: In addition to the antimicrobial effect of *Carthamus tinctorius* extract (5.5 ± 0.2 mm), the inhibitory effect of violacein production in the CV026 biosensor was also reported in the studied plant (12.6 ± 0.5 mm). In vitro, the compounds in the extract caused a disruption in pathogenicity and reduced the diseases caused by it in potato tubers. This blocking of AHLs in *Carthamus tinctorius* was reported to be 33%. The results showed that *Carthamus tinctorius* extract suppressed the production of violacein pigment in *C. violaceum* CV026 bacteria and caused the formation of bright colonies of reporter bacteria around the well of the extract. *Carthamus tinctorius* extract had a destructive effect on the activity of LuxI and LuxR proteins of the reporter bacteria, and had a significant effect on suppressing the sensory threshold.

Conclusion: Biological control test showed that the extract inhibits the activity of pectinolytic enzyme and, by reducing AHL production in *Pectobacterium*, prevents the progression of plant tissue destruction. This practical approach can be an effective development in the production of compounds with an interference effect on the expression of pathogenic genes, which is important and worth considering. Considering the effect of the extract compounds on AHL degradation and preventing the progression of the disease, this plant can be used to prevent plant contamination by various pathogenic bacteria.

Keywords: Quorum Sensing, anti-QS, *Pectobacterium*, AHL, CV026.

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PBa-122

Abstract Type: A Systematic review

The effect of dietary on guts microbiota :A Systematic review

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Abstract

Background and Aim: The gut microbiome includes millions of microorganisms that live in symbiosis with the human body which plays an important role in maintaining the health of the body. the most important factor that affect this population and their metabolic products, is dietary. The type of nutrition that a person have can affects the composition, diversity and function of gut microbiota. The purpose of this study is to present the effects that diet can have on the microbiome that cause health or disease that is the complications that result from its dysbiosis.

Methods: The data were collected by searching PubMed, Scopus and Google Scholar search engine. The advanced searched keywords were: “gut microbiota”, “microbiome”, “dietary” and “dysbiosis”. Out of the 20 studies identified in the initial search, 13 were included in the analysis. The search was limited to studies in the English language and accessible full texts that published from 2018 to 2024. Review, duplicate, and non-relevant articles were excluded.

Results: According to the findings, the consumption of carboxymethyl cellulose reduces the number of the intestinal microbiome and in some people causes the change of microbiome diversity, which can play an important role in causing chronic inflammatory diseases. Diets rich in fiber promote the diversity of the microbiome and their beneficial metabolites such as short-chain fatty acids. Conversely, diets high in fat or sugar have been shown to be associated with inflammation and dysbiosis. Also, the results show that diets suitable for weight loss, which include foods with moderate and low-fat proteins, can also change the gut microbiota.

that this change can treat intestinal dysbiosis in obese patients with severe metabolic dysfunction and a person with ulcerative colitis. It is interesting that research has shown that by taking inulin supplements, it is possible to increase the diversity of gut microbiota and restore the balance of dysbiosis formed in obese children.

Conclusion: The obtained results emphasize the important role of dietary interventions in modulating the composition and diversity of intestinal microbiota. These findings indicate that in addition to the fact that diet can change the composition of the microbiome and cause dysbiosis and, as a result, various disease states, it has the potential to restore the balance of the intestinal microbiome to a normal state, which results in the improvement of a person's health. Further research is required to explore mechanisms, optimize interventions, and assess long-term effects.

Keywords: gut microbiota ; microbiome ; dietary ; dysbiosis.

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PBa-123
Abstract Type: Systematic review

Investigating the role of *Listeria monocytogenes* in food safety and public health with emphasis on modern laboratory approaches and the role of wildlife

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Abstract

Background and Aim: *Listeria monocytogenes*, the main cause of listeriosis, is a zoonotic pathogenic bacterium that enters the environment and food chain through wildlife. The disease poses a serious threat to vulnerable groups and can be transmitted from wildlife to humans. Wildlife and livestock play a key role in the transmission cycle of this bacterium, as the feces of wild animals can contaminate the environment and lead to the transfer of contamination to livestock, water sources, and agricultural products. In this study, the role of wildlife in the transmission and detection of this microorganism and its impact on food safety are assessed.

Methods: A review of scientific literature has examined the role of wildlife as a major source of *Listeria monocytogenes* contamination, as well as the prevalence, persistence, and antibiotic resistance of this bacterium. Selected studies include the role of wildlife, livestock, and the environment in the transmission of this bacterium into the food chain, and articles related to modern diagnostic and therapeutic methods, including biomolecular-based technologies, nanotechnology, and genomic tools. Research on the ability to survive in harsh environmental conditions and resistance to disinfection methods was also reviewed.

Results: Modern laboratory methods for diagnosing *Listeria monocytogenes* are as follows:

Advanced molecular techniques:

1. Real-time PCR (qPCR): Used for rapid and accurate detection of *Listeria monocytogenes* in food, environment and animal samples.

2. CRISPR-based methods: CRISPR-Cas systems have been used to identify DNA sequences specific to this bacterium and have attracted attention due to their speed and high accuracy.

3. Biosensors: Optical and electrochemical biosensors have been developed for the rapid detection of *Listeria contamination* in food, especially in the meat and dairy supply chain.

4. Genomics and whole genome sequencing (WGS): This method is used to identify outbreak patterns, analyze antibiotic resistance and trace the source of contamination.

Modern methods of treating listeriosis are as follows:

Bacteriophages, Antibacterial nanoparticles, Immunotherapy, Antibacterial peptides, Probiotics

Conclusion: *Listeria monocytogenes* is a serious threat to public health due to its persistence in the environment and its ability to be transmitted from wildlife, livestock and agricultural products to humans through the food chain.

Reducing contact between livestock and wildlife, managing natural resources, and continuous monitoring of wildlife populations are among the measures that can reduce the risk of infection transmission.

Effective diagnosis and treatment of *Listeria monocytogenes* requires the use of new technologies. Further research is needed on the practical applications of these methods in the food chain.

Keywords: Listeria monocytogenes; wildlife; food safety; modern laboratory approaches; public health

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PBa-124
Abstract Type: Systematic Review

New Horizons in Infection Treatment: Assessing the Clinical Potential of Antimicrobial Peptides: A Systematic Review

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Abstract

Background and Aim: Growing antibiotic resistance is a serious public health threat, creating challenges in treating infections by multidrug-resistant (MDR) pathogens. This has emphasized the need for alternative therapies like antimicrobial peptides (AMPs), which are effective against a range of pathogens. However, issues such as toxicity and stability hinder their clinical application. This study investigates the potential of AMPs as antibiotic alternatives, particularly for MDR infections, and assesses their clinical applicability based on recent studies.

Methods: A comprehensive review of articles published from 2020 onwards was conducted using Google Scholar, PubMed, and Web of Science. Fifteen articles were reviewed, evaluating the effectiveness, mechanisms, and challenges of AMPs in clinical applications. The antimicrobial properties of AMPs against a variety of pathogens, such as Gram-positive and Gram-negative bacteria, fungi, and viruses, were investigated. Additionally, the synergy of AMPs with traditional antibiotics and their effects on modulating the host immune response were explored.

Results: The results demonstrated that AMPs exhibit broad antimicrobial activities, particularly against multidrug-resistant pathogens. Studies reported their effectiveness in disrupting microbial membranes, reducing resistance emergence. In preclinical studies, AMPs showed promise in treating biofilm-related infections. Synergistic effects were observed when combined with conventional antibiotics, enhancing therapeutic outcomes. However, challenges like low metabolic stability, potential toxicity, and limited oral bioavailability need addressing. Recent advancements in formulation strategies and chemical synthesis are expected to improve AMPs' clinical use.

Conclusion: Studies suggest AMPs can effectively replace traditional antibiotics for multidrug-resistant infections. However, challenges like toxicity, stability, and oral absorption must be addressed for clinical success. Advances in formulation and combination therapies could expand their clinical use. AMPs could offer a solution to the antibiotic resistance crisis and help combat resistant bacterial infections.

Keywords: Antimicrobial Peptides; Antibiotic Resistance; Multidrug Resistance; Biofilm Infections; Clinical Trials.

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PBa-125

Abstract Type: Original Research

Helicobacter pylori Prevalence in patients referred to Dr. Esmaeilzadeh's laboratory in Urmia,West Azarbaijan, Iran

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Abstract

Background and Aim: *Helicobacter pylori* is a gram-negative bacillus that is motile and belongs to the Helicobacteraceae family. *H. pylori* is a common infectious agent worldwide and is the most prevalent cause of chronic gastritis. In some individuals, it can lead to severe gastrointestinal damage such as gastric and duodenal ulcers, as well as stomach cancer. Infection rate in developed countries is less than developing countries. Diagnosis can be made using serological methods to detect antibodies in blood or antigens in stool, or through tests based on urease activity such as breath tests or molecular tests like PCR .

Methods: A total of 742 samples were collected from October 2022 to October 2024 that referred to Dr. Esmaeilzadeh's laboratory in Urmia. The samples were tested using the Helicobacter pylori Antigen kit in stool from Pishtaz Teb Company via ELISA and cutoff method, with data analyzed using SPSS version 26.

Results: The average age of the participants was 37 years (with a minimum age of 1 year and a maximum age of 84 years), comprising 62.7% females and 37.3% males. Among the 742 samples, 78.2% were negative, 19.5% positive, and 2.3% borderline results were reported.

Conclusion: Analysis using SPSS26 and Mann–Whitney U test showed no significant relationship between gender and infection rates. However, a Spearman analysis indicated a significant correlation between infection rates and the age of participants

Keywords: *Helicobacter pylori* , Antigen , Elisa , Prevalence

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Abstract Type: Original Research (Times New Roman, font size 12)

Antimicrobial Activity of Halophilic Bacteria Isolated from Saline Soil of Shushtar City, Iran

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: The rise of multi-drug-resistant bacteria seriously threatens human health. Some microorganisms can produce new antimicrobials that have effects on multidrug-resistant bacteria. On the other hand, halophilic bacteria show promise in producing novel bioactive antimicrobial compounds that could benefit drug development. This study aims to investigate the antimicrobial properties of halophilic bacteria recently isolated in soil samples from Shushtar City, Khuzestan Province, Iran.

Methods: In this research, saline soil samples were collected from the salty areas around Shushtar City. The soil sample was then cultured in an enriched culture medium, and in order to isolate the halophilic bacteria, they were cultured in a solid medium. The microorganisms were examined for the production of antimicrobial agents using the agar well diffusion method. Subsequently, the halophilic bacteria were identified through molecular analysis of the 16S rRNA method. The phylogenetic tree was constructed using Mega software through the neighbor-joining method.

Results: Twenty-two strains were isolated in this study. Strain E1, identified as *Alkalihalobacillus* sp, displayed antimicrobial activity against Enterococcus faecalis. The MIC and MBC of the *Alkalihalobacillus* extracts against *Enterococcus faecalis* were determined to be 25 µg/mL.

Conclusion: This research highlights the potential therapeutic and preventive advantages of *Alkalihalobacillus* sp. extracts as antibacterial agents. This research report, for the first time, reveals that isolated *Alkalihalobacillus* in Iran has the ability to produce antimicrobial agents. The discovery and isolation of beneficial bacteria from natural sources could have significant implications for future pharmaceutical and industrial applications.

Keywords: *Alkalihalobacillus* sp., antimicrobial activity, Human pathogens, *Enterococcus faecalis*, MIC.

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PBa-127

Abstract Type: Systematic Review

Targeting the Microbiome-TME Axis to Improve Colorectal Cancer Outcomes

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Background and Aim: Colorectal cancer (CRC) represents a prevalent neoplasm characterized by a dismal prognosis, particularly in its metastatic phases. Recent research highlights the critical role of the gut microbiome in influencing the characteristics of the tumor microenvironment (TME) and its subsequent effect on the advancement of cancer. Dysbiosis, conceptualized as a disruption within the gut microbiota ecosystem, has been correlated with the initiation and spread of CRC. This article endeavors to examine the intricate interactions between the microbiome and TME in CRC, with the objective of elucidating therapeutic strategies that target this interaction to enhance treatment outcomes.

Methods: The article integrates findings derived from preclinical models, human investigations, and meta-analyses. It conducts a comprehensive review of microbiome profiling in CRC patients, with a concentrated emphasis on microbial species and metabolites that are implicated in tumor progression. Immunological investigations pertaining to microbiome-TME interactions, encompassing immune cell infiltration and cytokine modulation, are scrutinized. Furthermore, therapeutic interventions such as probiotics, fecal microbiota transplantation (FMT), and microbiome modulation in conjunction with immunotherapy are investigated.

Results: Investigations reveal that specific bacterial species, including Fusobacterium nucleatum and pks+ E. coli, facilitate CRC progression through mechanisms of inflammation induction, immune evasion, and DNA damage. Beneficial microbial taxa, notably Faecalibacterium prausnitzii, are capable of synthesizing short-chain fatty acids (SCFAs), which exhibit inhibitory effects on tumor proliferation. Additionally, microbial metabolites exert influence on immune cell functionality within the TME, thereby augmenting anti-tumor immune responses. Interventions such as probiotics and microbiome restoration have exhibited potential in enhancing therapeutic efficacy.

Conclusion: Targeting the microbiome-TME axis presents a promising strategy to augment treatment outcomes in CRC. Modulation of the gut microbiome through the application of probiotics, prebiotics, or FMT has the potential to restore immune equilibrium and enhance therapeutic responses. Subsequent clinical investigations are necessary to substantiate these strategies, particularly emphasizing the integration of microbiome modulation with conventional therapeutic modalities such as chemotherapy and immunotherapy to improve the survival and quality of life for CRC patients.

Keywords: Colorectal Cancer, Gut Microbiota, TME

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PBa-128

Abstract type: Systematic Review

The Microbiota-Graves' Disease Connection: A Systematic Review

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ABSTRACT

Background and Aim: Graves' disease (GD) is an autoimmune disorder that is considered one of the most important causes of hyperthyroidism. The exact cause of GD is still unknown, and its treatment typically involves anti-thyroid drugs, radioiodine, or surgery, each of which carries its own specific side effects and risks. Recently, studies have been conducted on the relationship between microbiota and GD, indicating a significant correlation between the two. In this study, we examine previous research related to microbiomes and Graves' disease.

Methods: This review article was conducted using articles published in PubMed, Science Direct, Google Scholar, SID, and Web of Science up to October 2024. The keywords used were 'Graves' disease' AND 'microbiome' OR 'microbiota.' By searching these databases, 17 articles were found. Four of them were removed after reading the titles and abstracts. Thirteen articles were selected based on the inclusion criteria. All selected articles were in English and Persian.

Results: A research study that included 65 patients diagnosed with Graves' disease (GD) alongside 35 healthy controls analyzed 12 different bacterial types. The findings revealed significant alterations in the microbiota, supporting the connection between GD and microbial changes. Additionally, another study involving 14 healthy subjects and 15 patients found elevated levels of bacteria such as Lactobacillus, Veillonella, and Streptococcus in the patients compared to the healthy group. Following treatment, notable shifts in bacterial levels occurred. A comparative study indicated that the Actinobacteria family was more prevalent in patients, while Bacteroidetes were less common than in healthy controls. Subsequent investigations showed a reduction in microbial diversity among patients, which approached control levels after treatment. Ultimately, certain bacteria were identified as risk factors for GD, while others were recognized as protective agents.

Conclusion: In conclusion, a significant relationship was identified between gut microbiomes and GD, raising hope for the use of gut microbial markers in the non-invasive diagnosis and treatment of the disease. However, further research in this area is needed

Keywords: microbiota; microbiome; Graves' disease

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PBa-129
Abstract Type: Systematic Review

Bacteriophage Therapy: A Novel Solution to Combat Antibiotic Resistance

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Abstract

Background and Aim: The rise of antibiotic-resistant bacteria is a significant challenge in modern medicine. Overuse and misuse of antibiotics have led to the development of multidrug-resistant (MDR) and extensively drug-resistant (XDR) pathogens, making many treatments ineffective. Bacteriophage therapy, using natural viruses that target bacteria, is gaining attention as an alternative. Phages offer advantages such as high specificity and the ability to penetrate biofilms. This review explores the potential of phage therapy alongside antibiotics, focusing on its mechanisms, clinical applications, and implementation challenges.

Methods: A comprehensive narrative review was conducted by searching peer-reviewed studies published between 2020 and 2023 in databases such as PubMed, Google Scholar, Scopus, and Web of Science. A total of 15 relevant articles, including clinical trials, case reports, and laboratory studies, were analyzed. These studies were selected based on their focus on the application of bacteriophages in treating multidrug-resistant bacteria, mechanisms of phage action, clinical outcomes, and the use of genetically engineered phages. The review also assessed the safety, efficacy, and potential for phage-antibiotic combination therapies.

Results: The review findings suggest that bacteriophage therapy shows promise in treating multidrug-resistant infections. Clinical trials and case reports indicate that phages can effectively target antibiotic-resistant bacterial pathogens, especially those involving biofilm-associated bacteria. Combining phages with antibiotics enhances therapeutic efficacy by breaking resistance mechanisms. Genetically engineered phages have shown effectiveness in preclinical studies, and personalized phage therapy may cater to individual patient needs. However, challenges remain, including phage resistance, regulatory approval, and the need for standardized protocols.

Conclusion: Bacteriophage therapy shows promise as an alternative or supplement to antibiotics for treating multidrug-resistant bacterial infections. It offers a synergistic approach when combined with antibiotics, potentially overcoming current antimicrobial limitations. However, challenges such as standardized protocols, phage resistance, and regulatory hurdles

need to be addressed. Continued research, clinical trials, and advancements in genetic engineering and personalized medicine are essential for its widespread application.

Keywords: Bacteriophage Therapy; Antibiotic Resistance; Phage Engineering; Multidrug-Resistant Bacteria; Phage-Antibiotic Combination.

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PBa-130

Abstract Type: Review

A Comprehensive Insight into New Synergistic Antimicrobial Approaches in the Treatment of Infections Caused by Multidrug-Resistant Pathogens

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Abstract

Background and Aim: The emergence of multidrug-resistant (MDR) pathogens is increasing daily, and the World Health Organization (WHO) has declared it one of the ten threats to public health. Given this crisis, the treatment of many infectious diseases with conventional methods has been challenged, and therefore, the replacement of new therapeutic approaches is essential. One of the cases that has recently attracted the attention of researchers worldwide is the use of synergistic antimicrobial methods. This abstract discusses new strategies to increase the effectiveness and reduce resistance to antimicrobial agents.

Methods: A comprehensive review of studies conducted in recent years on MDR pathogens using different synergistic antimicrobial combinations was conducted. Then, their results were extracted, and presented as new approaches in the treatment of MDR pathogens.

Results: Synergistic antimicrobial methods yield benefits:

Phage-Antibiotic Combinations: It leads to the defeat of MDR pathogens, a lowering in the number of bacteria, and a decrease in antimicrobial resistance. Currently, studies are focused on the creation of phages developed by genetic engineering and CRISPR-Cas methods for making more targeted.

Antibiotic-Nanoparticle Conjugates: These compounds increasing affinity for the antibiotic target, raising permeability and crossing the cell wall, and overcoming resistance mechanisms, including disrupting efflux pumps.

Antimicrobial Peptides (AMPs): These agents can facilitate the entry of antibiotics into the microorganism cell through membrane interaction. Disruption of the formed biofilms is another favorable effect. AMPs can affect bacteria in the latent phase.

Adjuvants Targeting Bacterial Metabolism: These agents are used as inhibitors of beta-lactamases, efflux pumps, amino acid biosynthesis, and folate pathways. The synergy of these agents with antibiotics can significantly affect their MIC, and their ability to disrupt biofilms.

Conclusion: With the increasing resistance to existing antimicrobial agents and the decrease in the production of new antibiotics, it is necessary to pay attention to the new methods for treatment. The results of studies on new approaches to treat infections caused by MDR pathogens are very promising. The use of Synergistic Antimicrobial methods represents a breakthrough in combating them, which can be used in the future by optimizing them for specific pathogens in a completely targeted manner in treatment.

Keywords: Drug Resistance; Drug Synergism; Bacteriophages; Nanoparticles; Peptides.

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PBa-131

Abstract Type: Original Research

OprD Inhibition: A Molecular Docking Approach to Combat Pseudomonas Infections

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Abstract

Abstract

Background and Aim: *Pseudomonas aeruginosa* is the main cause of chronic lung infections and the third-most-common hospital pathogen, which possesses a high intrinsic resistance to antimicrobial agents, including antibiotics and disinfectants. The most significant virulence

factor of *P. aeruginosa* is the outer membrane protein D (OprD), which exhibits low outer membrane permeability and is implicated in the resistance of bacteria to imipenem. Many studies have shown that any change, mutation, or inhibition of OprD porin can affect the antibiotic susceptibility of bacteria, especially to imipenem. Therefore, in this study, we aimed to determine the most potent OprD inhibitor through molecular docking analysis.

Methods: The three-dimensional structure of the OprD protein (PDB ID: 3SY7), OprD inhibitor ligand (Dodecyldimethylamine N-oxide with PubChemCID:15433) and a total of 20 of inhibitor analogs were retrieved from PDB and PubChem databases, respectively. The protein and inhibitory ligands were prepared for docking using Molegro Virtual Docker version 6.0. After docking, the best interaction with the lowest energy binding was analyzed through Molegro Molecular Viewer v.7 software. Finally, the pharmacokinetic properties of the ligand were evaluated using the SwissADME server.

Results: Through all inhibitory ligands for OprD protein, the best ligand was 1-Pentadecanamine, N,N-dimethyl-, N-oxide (PumchemCID: 9860272) with a molecular weight of 271.48g/mol and binding energy of -114.577 kcal/mol. This ligand created three steric interactions with the OprD protein residues Tyr214, Thr121, and Ala127, and one hydrogen bond with Tyr214 residue, and no electrostatic interaction. The ADME results showed that this ligand has a water solubility score (logS) of -1.38, a hydrophilic score (LogP) of 3.49, a polarity score (TPSA) of 29.43, and lastly, hydrogen bond donors of 0 and hydrogen bond acceptors of 1.

Conclusion: These results indicated that 1-Pentadecanamine, N,N-dimethyl-, N-oxide (PumchemCID: 9860272) is a promising candidate for inhibiting *Pseudomonas aeruginosa* infection. Further in vitro and in vivo studies are required to confirm its potential as therapeutic agents.

Keywords: Molecular Docking; *Pseudomonas aeruginosa*; OprD protein.

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PBa-132

Systematic Review

Bacterial Resistance of Nanoparticles Against Antibiotics

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Background;

Multidrug resistant bacteria have caused global mortality in recent decades and antibiotic treatment has increased the number of resistant species the increasing resistance of bacteria and the ineffectiveness of conventional antibiotics led to the adoption of nanotechnology techniques and technology to combat microbial infections.

Nanoparticles have multiple mechanisms and simultaneous effect against microbes the synthesis conditions of nanoparticles and the building blocks of its NPS materials are one of the main factors of this feature.

In general,resistance to antimicrobial agents increased the broad activity of NPS against MDR strains.

Methods:

In this paper we investigate the resistance mechanism the of NPS against microorganisms and compare it with antibiotics.

We collected relevant information from google scholar .a total of five paper were included in this systematic reviw.

Result:

Several new generation nanoparticles with new therapeutic methods have been developed since last decades.

Using new methods,it is used to improve bacterial infections and reduce their resistance.

The use of combination therapy ,the nanoparticle systems are new therapeutic agents.

Conclusion:

Since MDR bacteria have become a global challenge,using nanoparticles instead of current antibiotics to fight MDR bacteria and treat infections caused by these strains is a suitable strategy to reduce antibiotic side effects and death rates.

Therefor ,it is necessary to understand the adaptive mechanisms of microbial resistance against nanoparticles

Nanoparticles will cause innovation due to their unique properties,but it should be noted that its toxic effect on humans is reduced.

Keyword:

Nanoparticles,MDR,antibiotics

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Antibacterial effect of glycolipoprotein (G-90) purified from *Eisenia fetida* earthworm on biofilm production and *pslA* gene expression in Multi Drug Resistant (MDR) strains of *Pseudomonas aeruginosa* isolated from burn wounds.

Introduction: The prevalence of antibiotic resistance of *Pseudomonas aeruginosa* has increased in recent years. Glycolipoprotein G-90 from tissue homogenate of the earthworm, *Eisenia fetida* is a blend of macromolecules with some biological properties including antioxidant, antibacterial, bacteriostatic, antitumor, anti inflammation and hemolytic activity.

Material and Method: Glycolipoprotein G-90 of collected earthworm *Eisenia fetida* was extracted by chloroform-methanol solution. Analysis of crude protein (glycolipoprotein G-90) done by SDS-PAGE method. 25 multi drug resistant (MDR) strains of *Pseudomonas aeruginosa* were isolated and confirmed by biochemical methods. The antibacterial activity was determined by well diffusion method. The biofilm formation assay and anti-adhesion activity were determined by microtiter plate method. Also Minimum inhibitory concentration was determined by macro broth dilution. Finally, decreased *pslA* gene expression was investigated for 4 MDR *Pseudomonas aeruginosa* isolates with strong biofilm via Real Time PCR.

Result: Protein pattern of (glycolipoprotein G-90 from homogenate of *Eisenia fetida*) showed some protein bands in the range of (15-100kDa). evaluation of the antibacterial effect of the glycolipoprotein G-90, which was conducted using the well diffusion method, all isolates at a concentration of 7.65 µg (from the original stock concentration) exhibited an unstable growth inhibition effect, with growth inhibition zone ranging from 20-27 mm. After 24 hours, the concentration of the proteins decrease, Therefore, it has a bacteriostatic effect. Minimum inhibitory concentration (MIC) was 255µg/ml. Glycolipoprotein G-90 significantly ($P<0.05$) exhibited anti-adhesive effects on the studied isolates with strong biofilms. the reductions in adhesion were found to be 66%, 35%, 46.6%, and 27%, respectively. In the analysis of the reduction in *pslA* gene expression in the four isolated strains with strong biofilms, a reduction of 60%, 55%,10%,82% in *pslA* expression was observed in multidrug-resistant strains with strong biofilms, as determined by Real-Time PCR.

Conclusion: The results of this study on the antibacterial effects of the G-90 protein extract indicated that the total crude protein extracted from the earthworm *Eisenia fetida* could have a bacteriostatic effect and inhibit the growth of multidrug-resistant *Pseudomonas aeruginosa* isolated from burn wounds. its effectiveness is unstable.Additionally, this extract significantly reduces adhesion and decreases the expression of the *pslA* gene, which is involved in biofilm formation. With further studies, in combination with antibiotics, it could be used for the control and treatment of multidrug-resistant strains.

Keywords: Antibiotic resistance, *Pseudomonas aeruginosa*, *Eisenia fetida* earthworm, G-90 , Biofilm, Antibacterial activity, *pslA* gene expression

PBa-134

Mutations in QRDRs of gyrA and parC Genes as Key Drivers of Fluoroquinolone Resistance in Pediatric Shigella flexneri Infections

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Abstract

Background and Aim:

Shigella flexneri is a major cause of bacterial dysentery, particularly in children under five years old. The increasing resistance of *Shigella* spp. to fluoroquinolones poses a significant public health challenge. This study aimed to investigate mutations in the quinolone resistance-determining regions (QRDRs) of *gyrA*, *gyrB*, *parC*, and *parE* genes and the presence of plasmid-mediated quinolone resistance (PMQR) genes in *Shigella flexneri* isolates.

Materials and Methods: A total of 132 clinical isolates of *Shigella flexneri* were collected and subjected to antimicrobial susceptibility testing against nalidixic acid and ciprofloxacin. Polymerase chain reaction (PCR) and DNA sequencing were performed to detect mutations in QRDRs of *gyrA*, *gyrB*, *parC*, and *parE* genes. The presence of PMQR genes (qnr) was also assessed.

Results:

Antimicrobial susceptibility testing revealed that 86% of isolates were resistant to nalidixic acid, while 21% were resistant to ciprofloxacin. Sequencing analysis identified mutations in *gyrA* and *parC* in 51% of nalidixic acid-resistant isolates and in 60% of ciprofloxacin-resistant isolates. The most frequent mutations were observed in codons 83 and 87 of *gyrA* and codons 80 and 84 of *parC*. Mutations in *gyrB* and *parE* were not detected. Ciprofloxacin-resistant isolates were predominantly associated with double mutations in *gyrA* and *parC*.

Discussion:

These findings indicate that point mutations in *gyrA* and *parC* are critical contributors to fluoroquinolone resistance in *Shigella flexneri*. The high prevalence of resistance highlights the importance of continuous surveillance and alternative therapeutic strategies to address the rising resistance in pediatric infections.

Keywords: *Shigella flexneri*; Fluoroquinolone Resistance; gyrA; parC; Pediatric Infections; QRDR Mutations; Ciprofloxacin Resistance

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PBa-135

Virulence Gene Profiles and Their Association with Clinical Manifestations in Shigella Isolates

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Abstract

Introduction:
Shigella spp. are significant pathogens causing gastrointestinal infections, with their virulence attributed to the presence of specific genes. This study aimed to analyze the prevalence of virulence genes in *Shigella* isolates and their correlation with clinical symptoms.

Materials and Methods:
Shigella isolates were tested for the presence of virulence genes (ipaH, ipaBCD, virA, stx, ial, sen, sat, set1A, and set1B) using PCR. Statistical analysis was performed to evaluate the association between virulence factors and clinical symptoms, such as bloody diarrhea and hospitalization.

Results:
All isolates tested positive for ipaH, ipaBCD, and virA, while only 1.4% were positive for stx. The prevalence of ial, sen, sat, set1A, and set1B genes was 74.7%, 45.4%, 28%, 24%, and 24%, respectively. Genes set1A, set1B, and sat were exclusively detected in *S. flexneri* isolates. Among *S. sonnei* isolates, 77.5% harbored ipaBCD, ipaH, virA, and ial simultaneously, whereas 19 *S. flexneri* isolates carried ipaBCD, ipaH, virA, ial, and sat. The presence of set1A, set1B, and sat in *S. flexneri* was statistically significant ($p < 0.05$). A strong association was observed between bloody diarrhea, hospitalization, and the presence of sen ($p = 0.001$).

Discussion:
This study highlights the significant role of virulence genes in *Shigella* pathogenicity. The exclusive presence of set1A, set1B, and sat in *S. flexneri* suggests its higher virulence potential. The findings also emphasize the critical link between the sen gene and severe clinical outcomes, such as bloody diarrhea and hospitalization.

Keywords: *Shigella* spp.; Virulence Genes; *S. flexneri*; *S. sonnei*

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PBa-136
Abstract Type: Narrative Review

From Farm to home: Colistin Resistance in Livestock Superbugs and Its Implications for Human Health

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Abstract

Background and Aim: In the era of antibiotic resistance, where multidrug-resistant (MDR), extensively drug resistant (XDR), and pan-drug resistant (PDR) Gram-negative infections are prevalent, identifying the primary sources of antibiotic resistance, understanding resistant mechanisms, and developing strategies to combat these mechanisms are crucial. The emergence of resistance to last-resort antibiotics like colistin has sparked a war between humanity and resistant bacteria, leaving humanity struggling to find effective countermeasures.

Methods: This narrative review article was developed using well-regarded scientific databases, including Web of Science, PubMed, Scopus, and Google Scholar, without any limitations on publication dates. The research focused on specific keywords such as "Colistin resistance," "*mcr* gene," "Livestock," "Animal foods," "Veterinary medicine," and "Multidrug-resistant." A set of inclusion and exclusion criteria was established, and the search was limited to full-text articles available in English.

Results: Although colistin is used as a highly toxic antibiotic in infections that are not treated with routine antibiotics, its widespread use in animal breeding and veterinary medicine has contributed to the spread of colistin-resistant bacteria, plasmid-borne colistin resistance genes (*mcr*), and antibiotic residues in livestock and animal-derived foods. These sources can potentially transmit colistin resistance to humans through various routes.

Conclusion: Therefore, managing the use of colistin in livestock and animal foods, implementing strict monitoring, and establishing guidelines for its proper use are essential to prevent the escalation of colistin resistance.

Keywords: Colistin resistance, *mcr* gene, Livestock, Animal foods, Multidrug-resistant, Veterinary medicine

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Abstract Type: Narrative Review

A Review of the Antimicrobial Properties and Chemical Structure of Glutaraldehyde: Applications and Challenges

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Abstract

Background and Aim:

Glutaraldehyde is a broad-spectrum biocide used broadly in healthcare and medical sectors with strong antimicrobial activity. It is also known to have excellent chemical stability and as a result, is widely used to disinfect medical instruments and sensitive surfaces, and in water purification. The chemical structure, mechanism of action, and antimicrobial properties are reviewed, focusing on those factors that are critical to its effectiveness, such as concentration, pH, contact time, and environmental conditions. Further, this study has looked into its applications, benefits, and challenges, raising concern for the need for other methods because of the risks associated with it.

Methods:

Results based on critical evaluations of a decade of work emanating predominantly from the PubMed data repository, the selected literature represents work on glutaraldehyde's antimicrobial properties. Emphasis would rest on how effective this action might be under laboratory experiments; its potential in medical equipment sterilization and the equipment utilized within a hospital are other aspects for which its workability could be harnessed. Research studies are focused on its effects: temperature, pH, or in general, exposure time.

Results:

The results show that glutaraldehyde is a very potent agent in the destruction of a broad range of microorganisms, including bacteria, viruses, fungi, and spores. Its action is highly dependent on surrounding conditions. For example, studies indicate that at higher temperatures, its action against microbes is enhanced, while too far from optimal pH, it is less effective. Glutaraldehyde has been especially successful in the disinfection of endoscopes, surgical equipment, and dialysis equipment and in water treatment and surface sanitation. However, there is a potential for adverse environmental effects and health hazards associated with glutaraldehyde resulting from improper handling or overexposure.

Conclusion:

Glutaraldehyde remains the cornerstone in infection control and medical sterilization because of its excellent antimicrobial action and versatile uses. However, due to the associated risks with its use, it requires critical application and further research into the development of alternatives. All in all, striking a balance between its strong disinfection action and safety with environmental sustainability is crucial for continued assurance in healthcare and beyond.

Keywords:

Disinfection; Glutaraldehyde; Biocide; Hospital Sterilization; Antimicrobial Resistance

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PBa-138

A comparative study on the synergistic effects of thymol/ceftazidime against *Acinetobacter baumannii* and *Klebsiella pneumoniae*

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Abstract

Introduction: This study aims to compare the synergistic antimicrobial effects of thymo/cefazidime on *Acinetobacter baumannii* and *Klebsiella pneumoniae*.

Material and methods: Antimicrobial effects of thymol/ceftazidime were performed first individually and then combined on *K. pneumoniae* ATCC 100031 and *A. baumannii* ATCC 19906 by the MIC-MBC method. Therefore, the antimicrobial effects of the compounds that had a synergistic impact were performed on ten clinical strains using the MIC-MBC method. The identification of chemical bonds, functional groups, and molecular interactions of the

mentioned compound was investigated using an FTIR device. Checkered method, biofilm inhibition on *K. pneumoniae* ATCC 100031 and *A. baumannii* ATCC 19906, cytotoxicity investigation on red blood cells (RBCs) by hemolysis and human skin fibroblast cells (Ffk) by MTT method were performed. Thymol/ceftazidime and had synergistic effects. Finally, the results of the tests were compared between the two bacteria.

Results: The results of this study showed that the antimicrobial effects of the thymol/ceftazidime (4/1 µg/ml) were on *K. pneumoniae* better than on *A. baumannii* (512/128 µg/ml) in both clinical and ATCC strains. In the examination with the FTIR device, had bonds of OH carbohydrates proteins, polyphenols, C=O Amide I band, C-O-Cpolysaccharide, C-Namide III band, but one band named C=C conjugated, C≡C in compound showed the connection between thymol with ceftazidime. The biofilm inhibition effects of thymol/ceftazidime on *K. pneumoniae* ATCC 100031 (59.54%) were better on *A. baumannii* ATCC 19906 (24.41%). The cytotoxicity of synergistic compounds on RBCs and human Ffk cells was not different and was lower than that of Triton X-100.

Discussion: Considering the antibiotic resistance of ceftazidime in the treatment of diseases caused by *K. pneumoniae* and *A. baumannii*, thymol/ceftazidime showed better antimicrobial and anti-biofilm effects in *K. pneumoniae* than *A. baumannii* in this study. After further studies, this compound can be used as a new drug in patients.

Keywords: *Klebsiella pneumoniae*, *Acinetobacter baumannii*, Thymol, Ceftazidime, Synergistic

PBa-139

Comparative investigation of synergistic effects of thymol/cefotaxime on *Acinetobacter baumannii* and *Klebsiella pneumoniae*

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Abstract

Introduction: The purpose of this study is to compare the synergistic antimicrobial effects of thymol/cefotaxime on *Acinetobacter baumannii* and *Klebsiella pneumoniae*.

Material and methods: Antimicrobial effects of thymol/cefotaxime were performed first individually and then combined on *K. pneumoniae* ATCC 100031 and *A. baumannii* ATCC 19906 by the MIC-MBC method. Therefore, the antimicrobial effects of the compounds that had a synergistic impact were performed on ten clinical strains using the MIC-MBC method. The identification of chemical bonds, functional groups, and molecular interactions of the mentioned compound was investigated using an FTIR device. Checkered method, biofilm inhibition on *K. pneumoniae* ATCC 100031 and *A. baumannii* ATCC 19906, cytotoxicity investigation on red blood cells (RBCs) by hemolysis and human skin fibroblast cells (Ffk) by MTT method were performed. Thymol/cefotaxime and had synergistic effects. Finally, the results of the tests were compared between the two bacteria.

Results: The results of this study showed that the antimicrobial effects of the thymol/cefotaxime (4/1 µg/ml) were on *K. pneumoniae* better than on *A. baumannii* (512/128 µg/ml) in both clinical and ATCC strains. In the examination with the FTIR device, had bonds of OH carbohydrates proteins, polyphenols, C=O Amide I band, C-O-Cpolysaccharide, C-Namide III band, but one band named C=C conjugated, C≡C in compound showed the connection between thymol with cefotaxime. The biofilm inhibition effects of thymol/cefotaxime on *K. pneumoniae* ATCC 100031 (46.36%) were better on A. *baumannii* ATCC 19906 (24.41%). Cytotoxicity of synergistic compound on RBCs and human Ffk cells was not different and was lower than that of Triton X-100.

Discussion: Considering the antibiotic resistance of cefotaxime in the treatment of diseases caused by *K. pneumoniae* and *A. baumannii*, thymol/cefotaxime showed better antimicrobial and anti-biofilm effects in *K. pneumoniae* than *A. baumannii* in this study. After further studies, this compound can be used as a new drug in patients.

Keywords: *Klebsiella pneumoniae*, *Acinetobacter baumannii*, Thymol, cefotaxime, Synergistic

PBi-1

Colorectal Cancer Drug Resistance Induced by Body's Detoxification System

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Colorectal cancer (CRC) is a severe and invasive tumor. It can spread to other tissues at a high rate, often leading to unsuccessful therapy and medication resistance. The overexpression of some ATP-binding cassette (ABC) transporter pumps is a common reason of multidrug resistance (MDR) occurrence. Moreover, another cause of MDR is caused by the body's antioxidant system for drug neutralization. The aim of the present study was to evaluate the expression of ABC-transporter pump and antioxidant system status in CRC drug resistance.

Methods: In the current clinical case-control study, control subjects, CRC patients resistant to oxaliplatin (OXP), and non-resistant patients were recruited. We assessed the expression of certain MDR-associated genes including MDR1/P-gp, MRP1, glutathione peroxidase-1 (GPx-1), and glutathione-S-transferase omega-1 (GSTO-1) at the gene and protein levels by RT-qPCR and western blotting, respectively. Furthermore, the total antioxidant capacity (TAC) was measured across these distinct groups.

Results: The mRNA and protein expression of MDR1/P-gp, MRP1, GPx-1, and GSTO-1 in the OXP-resistant patients was significantly higher than that of non-resistant subjects (p 0.001). Moreover, the TCA assay showed that antioxidant capacity in resistant-CRC patients was significantly higher than that of healthy individuals and non-resistant patients (resistant = 277.21 ± 43 µM; healthy subjects = 117.69 ± 35 µM; non-resistant = 105.88 ± 29 µM; p 0.001 and p = 0.003, respectively).

Conclusion: This investigation explored that overexpression of transporters, which can efflux OXP out of the cells, coupled with detoxification through the body’s antioxidant system, may render OXP ineffective against cancer cells.

Colorectal Neoplasms; ATP-Binding Cassette transporters; Drug Resistance, Antioxidants; Oxaliplatin.

PBi-2

Nanoliposome loaded with 5-fluorouracil and Curcumin reduces tumor growth in a mouse model of colorectal cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The rising incidence of colorectal cancer (CRC) and the limited success of traditional treatments have prompted investigations into new drugs that offer greater efficacy with fewer side effects. Curcumin has demonstrated potential anti-cancer properties. Additionally, 5-fluorouracil (5-FU) is a chemotherapy agent commonly used to treat CRC, and research suggests it is more effective when combined with other compounds. Liposomal nanoparticles can facilitate the co-delivery of these medications. Consequently, this study examines the impact of liposomal nanoparticles containing 5-FU and Curcumin on tumor growth in a mouse model of colorectal cancer.

Methods: BALB/c mice were injected with CT26 mouse tumor cell lines, and after one week, the mice were assigned to various groups. Liposomes were synthesized using the lipid thin-film hydration technique, and their characterization was conducted through TEM, DLS, and HPLC analyses. The inhibition of cell proliferation was assessed using an MTT assay. Both liposomal and free compounds were administered intravenously to the mice four times over a span of three days. Tumor size was monitored every other day, and the expression levels of the genes VEGF, VEGF-R2, VE-Cadherin, VEGF-C, and β-Actin in tumor tissue were analyzed via Real-Time PCR

Results: The synthesized nanoparticles were spherical, uniform in size, measuring approximately 200 ± 10 nanometers. HPLC analysis indicated that about 80% of the compound was effectively loaded into the nanoliposome. The MTT assay revealed that treatment of CT26 cell lines with either free 5-FU + Curcumin or nanoliposome-encapsulated 5-FU + Curcumin (NLP + 5-FU + Cur) significantly inhibited cell proliferation in a dose-dependent manner over a 24-hour period. The group treated with nanoliposomes containing 5-FU and Curcumin (NLP + 5-FU + Cur) exhibited the slowest tumor volume increase and the greatest weight gain. The tumor volume increase was lower in formulations containing liposomal 5-FU and Curcumin compared to their non-liposomal counterparts. Furthermore, the expression levels of VEGF, VEGF-R2, VE-Cadherin, and VEGF-C genes in the tumor microenvironment of the NLP + 5-FU + Cur group were significantly reduced compared to the control group (P 0.0001).

Conclusion: The combination of nanoliposomes loaded with 5-fluorouracil and Curcumin (NLP + 5-FU + Cur) effectively slows colorectal tumor growth in mice and decreases the expression of VEGF, VEGF-R2, VE-Cadherin, and VEGF-C genes.

keywords: Cancer, CRC, Nanoliposomes , Curcumin, 5-fluorouracil

PBi-3

Association of Lnc-RNA HOTAIR and mir-34a expressions in ovarian cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: It has been found that long non-coding RNAs (lnc-RNAs) are very important in tumorigenesis and progression of various cancers. Ovarian cancer (OC) is a multifactorial disease characterized by various molecular pathways, including genetic alterations, aberrant cell signaling, and immune system disorders. LncRNA HOTAIR (a novel lncRNA) and microRNA (miR-34a) play important roles in many cancers. However, the relationship between LncRNA HOTAIR and miR-34a in OC progression remains unknown. Therefore, the present study aimed to investigate the role of LncRNA HOTAIR and miR-34a in OC.

Methods: The gene expression levels of miR-34a and lncRNA HOTAIR in tissue samples of patients with OC and healthy subjects were determined by polymerase chain reaction quantitative method using SYBR green and analyzed by 2-ΔΔC T method. U6 and GAPDH were used as reference genes.

Results: The expression of miR-34a was significantly lower in patients with OC compared to the control group. It also showed a significant negative relationship with LncRNA HOTAIR, which was more expressed in OC subjects compared to control subjects.

Conclusion: The results of the present study showed that increasing the expression of LncRNA HOTAIR inhibited the expression of miR-34a by acting as a sponge and vice versa. lncRNA HOTAIR is upregulated in ovarian cancer and thus plays a role in regulating tumor growth and metastasis. Our results suggest that LncRNA HOTAIR-miR-34a axis may play a pivotal role in OC, and may serve as a potential diagnostic biomarker and a powerful therapeutic target for OC.

keywords: LncRNA HOTAIR-miR-34a-Ovarian cancer

PBi-4

miR-132-3p dysregulation in the pathogenesis of non-alcoholic fatty liver disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Nonalcoholic fatty liver disease (NAFLD) is a common liver disease of unknown etiology. Identifying the molecular mechanisms of non-alcoholic fatty liver disease (NAFLD) as therapeutic and diagnostic targets is very important.

Methods: In general, 30 patients between the ages of 22 and 60 with NAFLD and 15 healthy individuals were included in the study. The level of miR132-3p and SIRT1 gene expression was investigated by real-time PCR method in peripheral blood mononuclear cells (PBMCS). After micro RNA extraction from PBMC samples, the expression of miR-132-3p was measured and the extracted micro RNAs were followed by cDNA synthesis. U6 was used as a reference gene. Real-time PCR was calculated using delta ct with the formula ct (reference gene) ct (target gene) and SYBR green.

Results: The expression of miR-132-3p in NAFLD patients was significantly higher compared to the control group, and the expression of SIRT1 was lower in NAFLD patients than in the control group.

Conclusion: The increased expression of miR-132-3p in patients with NAFLD may contribute to the reduction of SIRT1 levels. Upregulation of miR132-3p by targeting SIRT1 signaling can be a therapeutic strategy for patients with NAFLD.

keywords: non-alcoholic fatty liver disease, NAFLD, miR-132-3p

PBi-5

Assessing the Correlation Between Frequent Colds and Digestive System Disorders

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Digestive system disorders, such as irritable bowel syndrome (IBS), gastroesophageal reflux disease (GERD), and peptic ulcers, are common conditions that significantly affect patients' quality of life. Emerging evidence suggests a potential link between the frequency of common colds and the exacerbation of these digestive disorders. The immune response triggered by recurrent colds may influence gastrointestinal health, potentially leading to or worsening existing digestive conditions. Additionally, using antibiotics to treat colds can disrupt the gut microbiota, further increasing the likelihood of developing digestive disorders by altering the balance of beneficial bacteria in the gut, leading to dysbiosis. This imbalance can compromise

Methods: gut health and contribute to various digestive issues. Understanding these relationships is crucial for developing comprehensive treatment and prevention strategies. This study aims to evaluate the correlation between the frequency of colds and the risk of developing digestive system disorders. Methods: This study included 186 patients diagnosed with digestive system disorders referred for endoscopy at Imam Reza Hospital in Tabriz, and 185 healthy individuals who served as the control group. Ethical approval was obtained from the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1394.505). Both patients and controls completed a questionnaire that included a question about the frequency of colds. The control group comprised individuals without digestive system disorders, and they did not undergo endoscopy.

Results: The study identified a statistically significant difference in the frequency of colds between the healthy control group and the GI patient group. Specifically, 76.4% of individuals in the healthy control group reported a low frequency of colds, compared to 55.4% in the GI patient group (P-value = 0.0001). For moderate cold frequency, the results were similar, with 22.7% of the healthy control group and 22.5% of the GI patient group reporting moderate cold frequency, though this correlation was not statistically significant (P-value = 1.00). Notably, only 2.7% of healthy individuals reported frequent colds, compared to 22.1% of GI patients (P-value = 0.0001). This study, which included 371 participants, demonstrated a strong association between a high frequency of colds and susceptibility to GI disorders.

Conclusion: In conclusion, this study demonstrates a significant link between the frequency of colds and GI disorders. The findings show that GI patients have a higher cold history than healthy individuals. These results suggest that cold frequency could be a valuable indicator of GI health. Further research is

essential to understand the underlying mechanisms and to develop effective preventive and therapeutic strategies for those at higher risk.

keywords: common cold, Digestive System Disorders, antibiotics, dysbiosis

PBi-6

Evaluation of IL-37 level in seminal plasma of couples with unexplained recurrent pregnancy loss

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Recurrent pregnancy loss (RPL) is defined as the repeated losses of two or more pregnancies before the 24th week of pregnancy. Seminal plasma contains several cytokines that regulate maternal immune tolerance and disruption in these molecules, could contribute to RPL. This study examined the levels of Interleukin-37 (IL-37) in the seminal plasma of men whose wives had recurrent pregnancy loss without known causes.

Methods: In this case-control study, 39 men aged between 30 to 45 years, were included in two groups: 20 men in the RPL group without any known causes and 19 fertile men in the control group who referred to Royan infertility clinic for sex selection of future child. After seminal plasma collection, the IL-37 cytokine level was measured using the ELISA method (Human IL-37 ELISA Kit, ZellBio GmbH, Germany). T-test was used for statistical analysis.

Results: The mean age of men was significantly higher in the fertile control group (39 ± 3.8 years) than RPL group (38 ± 3.5 years) (P:0.045). The mean body mass index (BMI) was 27.93± 5.4 Kg/m2 and 26.86 ± 3.4 Kg/m2 in the RPL and control groups, respectively, which was not statistically significant. The concentration of IL-37 was significantly higher in the seminal plasma of the RPL group (32.7 ± 3 ng/ml) than the control group (28.1 ± 2.4 ng/ml) (P0.0001).

Conclusion: This study showed that the seminal plasma level of IL-37 was significantly higher in the unexplained RPL group in comparison to fertile men. As expected, the control men were older than the RPL group because fertile men had at least one child. Considering the role of IL-37 in the balancing between Th1, Th2 and Th17 cells, this change in seminal plasma may maternal immune tolerance towards the fetus leading to RPL. Further research is needed to explore underlying mechanisms.

keywords: Recurrent pregnancy loss (RPL), Cytokine, Interleukin 37, Seminal Plasma

PBi-7

Anti-obesity effect of cysteine in a rat model of metabolic syndrome by increasing antioxidant potential in the liver and adipose tissue, as well as decreasing hepatic NF-κB expression

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Insulin resistance is a key characteristic of metabolic syndrome (MetS). The hepatic nuclear factor- κB (NF-κB) signaling pathway plays a crucial role in insulin resistance and the development of type 2 diabetes. Our study aimed to examine the impact of cysteine (Cys) on various biochemical and histopathological parameters in the liver and kidney, hepatic NF-kβ expression, oxidative stress, inflammation, glycation, carbonyl stress markers, and insulin resistance.

Methods: The study involved four groups of rats, each consisting of seven rats: a control group, a MetS group, and two similar groups receiving Cys treatment. Metabolic syndrome was induced in rats by administering a 40% sucrose solution, while, the treated groups received 50mg/L Cys in their drinking water. Various factors, including body weight, hepatic NF-kβ expression, levels of antioxidants, anti-glycation, oxidative stress, carbonyl stress, inflammatory, anti-glycation, and glycation markers were assessed in blood and tissues. Liver and kidney function parameters and metabolic profiles were measured. Finally, liver tissue was also evaluated by a pathologist

Results: The results showed that Cys reduced hepatic NF-kβ expression, oxidative stress, inflammation, glycation and carbonyl stress markers, as well as liver fatty content, blood sugar levels, insulin resistance, cardiovascular risk index, and body weight. The treatment also mitigated histopathological liver changes and acute hepatitis (p 0.001).

Conclusion: Cysteine had anti-obesity and anti-atherosclerotic effects, as well as improving β-cell function, insulin sensitivity, and lipid metabolism. Moreover, it prevented acute hepatitis and improved liver and kidney functions by correcting the effects on the GSH/GSSG ratio, hepatic NF-kβ signaling, and carbonyl stress.

keywords: Cysteine, Insulin resistance, Nuclear factor-kβ, Carbonyl stress, Metabolic syndrome

PBi-8

Hepatoprotective effect of pyridoxal phosphate against lead poisoning by inhibiting Kupffer cell hyperplasia by raising antioxidant potential

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Hepatic nuclear factor-κB (NF-κB) plays a significant role in cellular responses to external stimuli such as lead (Pb) and elevated hepatic NF-κB signaling contributes to liver diseases. Therefore, this study aimed to investigate the effect of Pyridoxal phosphate (PLP) on NF-kβ expression and glutathione metabolism

Methods: Thirty-six rats were divided into four equal groups: control (C), untreated lead toxicity rat model (Pbt), and treated with PLP at concentrations of 100mg/L and 200 mg/L in drinking water, respectively Pbt (PLP100) and Pbt (PLP200). The treated groups received PLP for one month. Pb poisoning was induced in rats by administering 50 mg/L lead acetate in drinking water for a similar period. Oxidative stress and inflammatory markers in sera and liver homogenates were measured. Additionally, the biochemical parameters of liver function and NF-kβ expression were determined. Finally, the livers of the rats were evaluated through histopathological observation

Results: PLP had a dose dependent protective effect against Pb intoxication in rats. Both lower and higher doses of PLP decreased liver damage by inhibiting Kupffer cell hyperplasia, which was attributed to a reductive effect on the NF-kβ/BACT ratio thereby increasing antioxidant potential. The higher dose of PLP also prevented Pb-stimulated histopathological liver alterations, while also having a more beneficial effect on liver function.

Conclusion: Pyridoxal phosphate demonstrated a dose dependent hepatoprotective effect against lead intoxication in rats by inhibiting Kupffer cell hyperplasia and reducing MPO activity through hepatic NF-kβ induction. PLP decreased the NF-kβ/BACT ratio by raising antioxidant potential. It is suggested that increasing the GSH/GSSG ratio and activating of antioxidant enzymes is a useful strategy against lead poisoning.

keywords: Pyridoxal phosphate; Lead poisoning; Oxidative stress; Inflammation: Hepatotoxicity

PBi-9

Relationship between beta1 integrin expression levels and different stages of colorectal cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Colorectal cancer is one of the most common gastrointestinal cancers and is the third most common cancer among men and women worldwide. The first step in the treatment of colon cancer is surgery. However, the molecular markers are also promising to control disease, diagnosis, and prognosis. Integrin beta1 is one of the most important integrins, which is expressed in tumor tissue cells, and by binding to specific ECM proteins, it can play an important role in the initiation, progression, and metastasis. Therefore this study investigates the diagnostic and prognostic potential of integrin beta1 with the stages of colorectal cancer.

Methods: 67 samples from tumor tissues of colorectal cancer in different stages and 67 samples from normal tissue of the same patients were collected. Real-time PCR technique was used to evaluate the expression of beta-1 integrin at the mRNA level and immunohistochemistry for the expression of protein level.

Results: Results from PCR indicated that the expression of integrin beta1 begins to increase from stage 1 to stage 4. Analyzed pictures of immunohistochemistry related to different stages of disease showed significant differences between stage I and stage II, III, and also stage II with stage III and IV. This differences were not observed in the normal group obtained from different stages.

Conclusion: It seems that integrin beta-1 may play a role in distinguishing between early and advanced stages, but it is not able to accurately determine the stage of the disease

keywords: beta1 integrin, colorectal cancer, Immunohistochemistry, Real time PCR

PBi-10

Association of blood Cystatin C level and Depression: A Systematic Review and Meta-Analysis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Cystatin C (Cys C) is a marker of kidney function that is relevant for the health and monitoring adults, especially the elderly. Also depression is highly prevalent in individuals with advanced kidney disease. Cystatins level are associated with neuronal degeneration and nervous system healing but little is known about the link between psychological factors and Cys C. This systematic review and meta-analysis examine the relationship between Cys C status and the risk of depression.

Methods: This systematic review and meta-analysis adhered to PRISMA guidelines. Databases including PubMed and Scopus, along with Google Scholar search engine, were searched using the keywords "cystatin c" AND "depression" OR "depress*" OR "depressive". Observational studies comparing cystatin level in depress people to healthy controls were included. Reviews, interventional and conference papers, animal studies, and case reports were excluded. Two authors independently screened and extracted data, with discrepancies resolved by a third author. Study quality was assessed using the Newcastle-Ottawa Scale, and heterogeneity was evaluated using I^2 statistics. A random-effects model was employed to calculate weighted mean differences (WMD) and pooled odds ratios (ORs). Analyses were conducted with Stata version 14.2.

Results: From an initial 249 studies, 82 duplicates and 152 irrelevant studies were excluded, leaving 12 studies (5 cross-sectional and 7 cohort) with 525708 people, of whom 78019 had depression. Association of blood Cys C level and depression was significant. [WMD =0.11; 95% CI: 0.02,0.21 ; I^2 = 98; N = 6] Higher Cys C levels were associated with increased odds of depression [Pooled OR = 1.41; 95% CI: 1.11, 1.72; I^2 =74 ; N = 9].

Conclusion: According to these results, considering of Cys C levels as a biomarker is recommended.

keywords: Depression; Depressive; Depress*; Cystatin c; Cys c

PBi-11

Serum neurofilament light chain as a potential diagnostic biomarker for encephalopathy; Systematic review and Meta-analysis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Encephalopathy is characterized by impaired consciousness resulting from brain dysfunction, with various underlying causes. Currently, there are no well-established serum-based lablatory biomarkers to predict confusion or encephalopathy. Serum neurofilament light chain (sNFL) has been identified as a promising biomarker for neuronal damage. This review aims to explore the potential of sNFL as a diagnostic biomarker for patients with encephalopathy.

Methods: This systematic review and meta-analysis followed PRISMA and Cochrane guidelines. A systematic search was conducted across databases such as PubMed, Scopus, and Google Scholar using keywords and MeSH terms related to"NFL" and "encephalopathy." Two investigators independently carried out the searches and data extraction, resolving any discrepancies with a third author. The review included observational studies that evaluated sNFL for diagnosing encephalopathy. Excluded studies were reviews, animal studies, conference papers, book chapters, letters, trials, studies without control groups, and those evaluating cerebrospinal fluid (CSF) NFL. The quality of the included studies was assessed using the Newcastle-Ottawa Scale, and heterogeneity was evaluated with I^2 statistics.Results were presented as weighted mean differences (WMDs) and pooled area under the curve (AUC) with 95% confidence intervals (CIs). Data analyses were performed using Stata 14.2

Results: Out of a total of 102 studies, studies were excluded (duplicate: 64; Irrelevant:31). Ultimately, 7 studies (4 case-control, 2 cohort studies,1 observational) were included in the present meta-analysis. The total sample size comprised n= 574, 301 (52%) patients with encephalopathy and 273 (48%) in the control group. NFL concentrations in patients with encephalopathy were higher compared to control group (WMD= 15.38; 95% CI= 6.01-24.73; I2= 88.4%; Z= 3.22; P:0.001) and AUC was 0.74 (95% CI= 0.68-0.81; I2= 38.1%; p=0.199)

Conclusion: serum NFL levels are specifically associated with encephalopathy, thus sNFL may have the potential to become a useful biomarker for diagnosis of encephalopathy.

keywords: neurofilament light chain, NFL, encephalopathy

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PBi-12

Protective effect of Royal jelly on insulin resistance induced by Dibutyl phthalate in Wistar rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Phthalates, which are synthetic endocrine disruptor chemicals, disrupt the body's endocrine system and have various other toxic effects. Phthalate has been reported to cause adverse effects on insulin sensitivity and glucose homeostasis. Previous data has indicated that oxidative stress is involved in developing insulin resistance induced by phthalates. The extensive use of phthalates and their non-covalent binding with various materials result in the leaching of these substances into the environment, leading to significant human exposure to these compounds. In this study, effects of Royal jelly (RJ) on Dibutyl phthalate (DBP)-induced insulin resistance were assessed.

Methods: A total of 40 Wistar albino rats were randomly divided into eight groups (n = 5): 1- control (corn oil), 2- DBP (500 mg/kg), 3- RJ (200 mg/kg), 4- QCN (50 mg/kg), 5- RJ (100 mg/kg)+ DBP, 6- RJ (200 mg/kg) + DBP, 7- RJ (300 mg/kg) + DBP, 8- QCN (50 mg/kg) + DBP. Quercetin (QCN) was used as positive control agent in this experiment. After 28 days of daily oral gavage treatment, animals were euthanized and their blood samples were collected via direct cardiac puncture and were centrifuged at 1500 ×g for 5 min to separate blood serum for determination of glucose, insulin, insulin resistance index. The serum level of insulin and glucose was measured using commercially available kits according to the manufacturer's procedure.

Results: DBP exposure resulted in higher concentrations of blood insulin and glucose and consequently a higher insulin resistance index (IRI) comparing with control group (P0.05). Comparing with DBP group, RJ-DBP group at medium (200 mg/kg/day) and high (300 mg/kg/day) dose levels and QCN-DBP group showed a significant decrease in glucose and insulin content (P0.05). RJ-DBP and QCN-DBP treated animals considerably reduced the DBP-enhanced IRI values (P0.05).

Conclusion: Our findings indicated that royal jelly mitigates the rise in insulin resistance, glucose and insulin induced by dibutyl phthalate.

keywords: Dibutyl phthalate, Royal jelly, Quercetin, Insulin resistance.

PBi-13

The Effect of the Hydroalcoholic Extract of Quercus infectoria Fruit Hulls (Jaft-E-Baloot) on Formalin-Induced Inflammation and Pain in Male Mice

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Herbal medicines have been used to alleviate inflammation and pain since ancient times, and their use is even on the rise. The Quercus infectoria plant has been commonly used for many years to treat inflammation and pain in alternative medicine. Various species and different parts of this plant have been studied. The present study aimed to investigate the anti-inflammatory and analgesic properties of the extract of the fruit hulls of Q. infectoria to find a plant-based alternative to the available drugs with fewer side effects.

Methods: This study used 60 male NMRI mice with a weight range of 35-40 g. The mice were randomized into a negative control group which only received formalin, a positive control group that received diclofenac 200 µg/kg, and four experimental groups that received 50, 100, 150, and 200 mg/kg of the fruit hulls extraction. Formalin was injected into the paws of the mice to induce inflammation and pain. Then, the paw volume was measured during the first three hours after injection with a digital Plethysmometer. Pain score was also evaluated in three stages at 60-minute intervals.

Results: The results showed that the fruit hulls extract could reduce inflammation at all doses, particularly at 200 mg/kg in comparison with the negative control group (P 0.001). Moreover, the fruit hulls extract relieved pain at different doses in acute and chronic stages.

Conclusion: The fruit hulls extract alleviated the pain and reduced the inflammation in mices' paws depending on the dose. Therefore, it can be considered as a possible alternative to chemical drugs.

keywords: Analgesic, Anti-inflammatory, Quercus infectoria

PBi-14

The Neuroprotective Effect of Sodium Nitrite on Ischemic Stroke-Induced Mitochondrial Dysfunction via Downregulation of Intrinsic Apoptosis Pathway

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Ischemic stroke leads to programmed cell death via intrinsic mitochondrial apoptosis pathways. Nitric oxide donors (NODs) are various kinds of drugs with the ability to produce nitric oxide (NO) as a potential bioregulator of apoptosis. Therefore, we aimed to evaluate the effect of sodium nitrite (SN) on ischemic injury-induced mitochondrial damage.

Methods: A 4-hour oxygen-glucose deprivation (OGD) cellular model was developed to mimic cerebral ischemia injury. Cell viability was determined to demonstrate the efficiency of SN as a NO donor on OGD injured PC12 cells. Immunoblotting was performed to measure the expression of Bcl2, Bax and cleaved caspase 3 proteins. Mito Tracker Green label was used for staining the active mitochondria.

Results: The present study confirmed that nitrite inhibited apoptosis via upregulation of Bcl-2 and downregulation of cleaved caspase-3 in OGD-injured PC12 cells as demonstrated by western blot analyses. In addition, nitrite restored mitochondrial vital activity and cell viability in OGD-injured cells.

Conclusion: Resultant data illustrated the protective effects of nitrite and may suggest the in vivo use of nitrite for further confirmations.

keywords: Oxygen-glucose deprivation, PC12, Nitrite, Bcl2, Bax, Mitochondria

PBi-15

Curcumin alleviates inflammatory effects of ketamine anesthesia in postnatal rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Curcumin has been employed in traditional medicine for over a millennium to treat various ailments, and its global use is now widespread. Chinese medicine relies heavily on curcumin as a primary element and uses it to cure infectious diseases, skin disorders, depression, and stress. It has cardioprotective, neuroprotective, and anti-diabetic properties, as well as pharmacological effects on disorders like type II diabetes, atherosclerosis, and human immunodeficiency virus replication. The anti-cancer activity of curcumin has been studied extensively with notable improvements in gastrointestinal, melanoma, urogenital, breast, and lung malignancies

Methods: We investigated the anti-inflammatory effects of curcumin on expression of tumor necrosis factor (TNF)-α, c-Fos, and interleukin (IL)-6 genes in brain and liver tissue owing to the effects of ketamine anesthesia on postnatal rats. The thalamic and hepatic tissues were collected without anesthesia, immediately after anesthesia, and 4 and 12 hr after anesthesia in control and curcumin treated postnatal rats

Results: . The results showed that glucose, triglyceride, high- and low density lipoprotein levels were lowered with curcumin treatment. We also found that ketamine increased c-Fos and inflammatory cytokines like TNF-α and IL-6, all of which contribute to inflammation. Brain and liver immunohistochemistry studies confirmed the real-time polymerase chain reaction findings.

Conclusion: Curcumin injections alone may be effective in decreasing ketamine induced inflammation in both brain and liver tissues. keywords: Brain; Curcumin; Ketamine; Liver; Real-time polymerase chain reaction

PBi-16

Interplay Between Epigenetic factors with Premature Aterosclerosis and Uric Acid Levels

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Medical Biochemistry, Quality control, Trace elements

Background and aim: This study explores how elevated uric acid (UA) levels and epigenetic changes might contribute to the early stages of atherosclerosis. To do this, we compared three groups of men who do not have typical cardiovascular risk factors: those undergoing premature coronary angiography (CPCA), individuals with high UA (HUA), and a control group of normal subjects (NS). Our aim is to better understand the influence of UA and epigenetic shifts on early atherosclerosis, independent of other common risk factors.

Methods: This study included 53 men, aged 30-45, divided into three groups: those undergoing premature coronary angiography (CPCA, n=18), individuals with high uric acid (HUA, n=15), and a control group of normal subjects (NS, n=20). To qualify for inclusion, participants had to be free from cardiovascular risk factors (CVRFs), defined as not currently smoking or using opium, having untreated blood pressure below 140/90 mm Hg, fasting glucose under 110 mg/dl, total cholesterol below 240 mg/dl, LDL cholesterol below 160 mg/dl, and HDL cholesterol above 30 mg/dl. High UA was defined as having serum levels greater than 6.5 mg/dl. DNMT3A/3B and HDAC3/7 expression in peripheral blood mononuclear cells (PBMCs) was analyzed using Real-Time PCR, while adjusting for potential confounding factors.

Results: In our findings, we observed that the expression levels of DNMT3B and HDAC3/7 were significantly lower in both the CPCA and HUA groups compared to the normal group (p 0.05), with the most notable decrease seen in HDAC3 among the CPCA participants. Interestingly, we found no significant correlation between these markers and uric acid levels (p 0.05). On the other hand, DNMT3A expression was significantly higher in both the CPCA and HUA groups (p 0.05) and showed a negative correlation with its own expression (p ~ 0.044).

Conclusion: Changes in epigenetic factors appear to be independently associated with early atherosclerosis and levels of uric acid (UA). This indicates that epigenetics may influence both hyperuricemia and subclinical atherosclerosis, irrespective of traditional cardiovascular risk factors (CVRFs) like age, male sex, diabetes, hypertension, insulin resistance, hypertriglyceridemia, and metabolic syndrome. Importantly, our analysis showed no statistically significant differences in these risk factors or serum UA levels among the groups we studied.

keywords: CAD: Coronary Artery Disease, UA: uric acid, HDAC: Histone Deacetylase,

PBi-17

Calculation of 10-year risk of developing atherosclerotic cardiovascular disease in individuals referred to the PERSIAN Cohort Center of Sabzevar in 2022 and comparing it with five years ago

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Atherosclerotic cardiovascular disease (ASCVD) is still the first cause of death in the world. Effective preventive strategies require extensive efforts to elucidate ASCVD risk in population. Therefore, this study aimed to identify people at higher risk of ASCVD among Sabzevar Persian Cohort Center in 2022 and to compare their risk with five years ago (2016).

Methods: This cross-sectional study is based on the data (such as age, gender, total cholesterol, blood pressure, LDL, HDL, diabetes status and smoking) of 873 participants referring to Sabzevar Persian Cohort Center in 2022. The 10-year risk of developing ASCVD was calculated using an estimator developed by the American College of Cardiology, and the subjects were divided into four categories accordingly; low risk (less than 5%), borderline (5 to 7.4 percent), medium risk (7.5 to 19.9 percent) and high risk (more than 20 percent). The results obtained were compared with the results of five years ago.

Results: Among the participants (61.4% women), the 10-year risk of developing ASCVD was low in 587 (67.2%), borderline in 86 (10%), medium in 172 (19.7%), and high in 28 individuals (3%). Compared with five years ago, the average 10-year risk of developing ASCVD increased from 3.34% in 2016 to 5.16% in 2022. Eleven of the people called in 2022 had ASCVD events in the previous five years.

Conclusion: The increase in the risk of ASCVD during five years shows the lack of control of the effective factors and the low awareness of the society about the importance of this issue. More serious measures are needed in the field of health and primary prevention in order to reduce mortality and morbidity caused by ASCVD events.

keywords: Atherosclerosis, Cardiovascular risk assessment, Primary prevention, PERSIAN cohort

PBi-18

The importance of education and risk management for improving the quality of laboratory results and patient safety: an experimental study in a medical diagnostic laboratory

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Accurate lab results are crucial for correct diagnoses and effective treatment plans. Achieving this desired goal requires the effective cooperation of all health care personnel, including laboratory staff, who assist physicians in clinical decision-making. However, human errors can affect the accuracy of results and lead to inappropriate diagnosis and treatment. Specialized training of personnel along with the implementation of risk management systems are two key factors in reducing human errors and improving the quality of laboratory results. This study investigates the impact of comprehensive training and risk management systems on reducing errors and improving lab result quality, ultimately enhancing patient

Methods: The Salman Farsi Hospital of Bushehr, a reference medical diagnostic laboratory handling a high volume of samples, consistently faces challenges related to pre-analytical, analytical, and post-analytical errors in biochemistry and hematology testing. Among these errors, pre-analytical errors constitute 70% of the total and are influenced by various factors. These errors result in test repetition, delayed results, and decreased patient and departmental satisfaction. This six-month experimental study, using data recorded in error forms, investigated the effectiveness of an educational intervention and risk management system implementation in reducing laboratory test errors. The intervention included comprehensive training for laboratory and bedside personnel, covering sample collection, labeling, transportation, quality control, and result reporting, as well as implementing a risk management system based on root cause analysis. An independent t-test was used to compare error rates before and after the intervention.

Results: The results of this study demonstrated a significant decrease in the rate of various types of errors affecting test results after the intervention, including pre-analytical errors (p0.005), analytical errors (p0.05), and post-analytical errors (p0.05). Among these, the reduction in pre-analytical errors was the most significant, decreasing from 70% to 15% (p0.005). Additionally, the rate of test repetitions due to pre-analytical errors decreased by 50% (p0.05). The effectiveness of this intervention was further supported by a significant increase in the average satisfaction level among physicians, departments, and patients to %95.

Conclusion: Development of a continuous and extensive training program requires the identification of effective factors in the occurrence of errors, which takes steps with the strategy of standardization of processes and the use of risk management tools in order to improve the quality of laboratory services and increase patient satisfaction. Our findings indicate that investing in education and risk management is a valuable investment in improving the quality of paraclinical services, including laboratory services, ultimately contributing to patient safety through effective diagnosis and treatment.

keywords: pre-analytical errors, laboratory results, risk management, education.

PBi-19

Investigating the Expression of LINC01605 in Esophageal Cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Esophageal cancer is the ninth most common cancer and the sixth cause of cancer-related deaths worldwide. Many studies show that the dysregulation of many genes such as (oncogenes and tumor suppressor genes) play an important role in causing this disease. Long non-coding RNAs (LncRNA) play a pivotal role in the progression of various malignancies. Despite recent identification as an oncogene associated with tumorigenesis, the precise role of LINC01605 in esophageal cancer (EC) remains unclear. Therefore, the aim of this study is to investigate the expression of LINC01605 gene in patients with esophageal cancer.

Methods: Esophageal cancer RNA Sequencing data were obtained from The Cancer Genome Atlas (TCGA) database. Gene expression differences between EC patients and controls were analyzed using "limma" and "Dseq2" in R software. Also in this study, we evaluated LINC01605 mRNA levels in 15 pairs of EC tissues compared with adjacent tissues. Determination of LINC01605 mRNA levels was performed by quantitative real-time PCR (qRT-PCR) method. Receiver operating characteristic (ROC) curves were drawn to evaluate the diagnostic power of the LINC01605 gene.

Results: In the analysis of data related to EC in the TCGA database, the expression level of LINC01605 in EC patients was significantly increased compared to the control group (logFC=2.38 and P-value=0.0055(. By analyzing qRT-PCR data, the expression level of LINC01605 gene in patients with EC was significantly increased compared to the control group (P-value0.05). LINC01605 had not good effectiveness in separation between EC samples and adjacent tissues (AUC = 0.65, P-value0.05).

Conclusion: This study uncovers that LINC01605 promotes EC tumorigenesis.

keywords: EC, ESCA, LINC01605, Long non-coding RNA

PBi-21

Survey the effect of combined and separate aqueous extract stevia and metformin on the expression of GLUT4,SIRT1, TNF-α and INSR genes and some antioxidant parameters in in Letrozole- induced Polycystic Ovary Syndrome in Adult female Wistar rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Polycystic ovary syndrome (PCOS) is the most common endocrine and metabolic disorder in women and the most important cause of infertility due to lack of ovulation. The role of chemical drugs and medicinal plants, such as SAE and Met, in improving polycystic ovary syndrome, is being investigated. The aim of this study was to investigate the combined and separate effects of the aqueous extract of stevia (SAE), metformin (Met), On expression of genes involved in insulin signaling, oxidative stress, hormonal imbalance, insulin resistance, and dyslipidemia in rats with polycystic ovary syndrome.

Methods: The estrous cycle of 50 adult Wistar female rats was investigated by vaginal smear. After 3 days, the rats were divided into 5 groups of 10 Including: control (1 ml of carboxymethyl cellulose for 49 days), induction (letrozole, 1 mg/kg/d, for 21 days), SAE, MET, SAE/MET. Treatment options (SAE, Met) respectively were administered orally by gavage at a dose of 400 and 250 mg/kg/d on day 22 and continued for another 28 consecutive days. Vaginal smears were done. The level of expression of GLUT4, SIRT1, TNF-α, and INSR genes were investigated using the RT-qPCR method, and some antioxidant parameters were determined using the detection kits. Finally, the results of this study were analyzed using SPSS software and the one-way and two-way ANOVA, as well as the Tukey test.

Results: SAE and MET treatment led to the recovery of a regular pattern of the estrous cycle in mice. Also, treatment with SAE and MET in PCOS mice showed improvement in hormonal imbalance, dyslipidemia, and hyperglycemia. Administration of SAE and MET significantly increased the levels of antioxidant enzymes SOD and GPx in ovarian tissue (P0.001). Additionally, the mRNA levels for GLUT4, SIRT1, and INSR significantly increased in ovarian tissue of rats treated with SAE and MET, while TNF-a gene expression was significantly decreased (P0.0001).

Conclusion: The findings of present study suggest that the aqueous extract of SAE and Met had protective effects on PCOS model induced by letrozole in rats by activating gene expression involved in insulin signaling and oxidative stress.

keywords: letrozole, stevia aqueous extract, Insulin resistance, oxidative stress, GLUT4, SIRT1,

PBi-22

The development of a logistic regression model for a dataset aimed at forecasting diabetic foot ulcers in individuals with diabetes revealed that high-density lipoprotein (HDL) cholesterol served as a negative predictor

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The development of a logistic regression model for a dataset aimed at forecasting diabetic foot ulcers in individuals with diabetes revealed that high-density lipoprotein (HDL) cholesterol served as a negative predictor

Methods: This investigation constituted a statistical modeling exercise based on a dataset that had been previously published. Coefficients were derived for application in the logistic function to compute the probability.

Results: The pretest probability associated with the outcome was determined to be 30.83%. It is strongly recommended to maintain high-density lipoprotein (HDL) levels above 50 mg/dl. Logistic regression modeling represents a straightforward and pragmatic approach suitable for clinical application.

Conclusion: This model can be used clinically for consulting the patients. The only negative predictor of the risk is HDL cholesterol. Keeping the HDL level more than 50 (mg/dl) is strongly suggested. Logistic regression modeling is a simple and practical method to be used in the clinic.

keywords: logistic regression model, foot ulcers, diabetes, high-density lipoprotein

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PBi-23

Impact of Human Umbilical Cord Mesenchymal Stem Cell Conditioned Medium on the Secretion Profile of Human Liver Cancer Cell Line HEPG2

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Cell therapy and gene therapy have shown promise in enhancing normal liver function and providing a bridge to organ transplantation. Hepatocellular carcinoma (HCC) has doubled in incidence over the past decade, exacerbating the disease burden. Early detection and monitoring of HCC are crucial due to its rapid progression. Identifying sensitive indicators for early detection of individuals at high risk of developing HCC can reduce mortality and medical costs. This study aimed to investigate the impact of purified media from Wharton's jelly-derived mesenchymal stem cells on the human liver cancer cell line HepG2. The evaluation focused on the biochemical functions .

Methods: Enzyme-linked immunosorbent assay (ELISA) is a common laboratory method for the detection and quantification of proteins, antibodies or small molecules. ELISA test is usually used to detect antigen or antibody. In this way, one of these two substances is fixed in the solid bed and used to track the second one. The concentration of PIVKAII, AFP-L3, AFP in different groups was measured by chemiluminescent magnetic microparticle immunoassay (CMIA) according to the instructions of the protocol kit (Abbott. Laboratories, Sligo, Ireland).

Results: The results of the study demonstrated that conditioned environments exert a significant effect on the secretion of these substances from HepG2 cells. Notably, the secretion of alpha-fetoprotein, inducible protein in the absence of vitamin K, liver enzymes, and bilirubin decreased significantly in the presence of purified media. Conversely, the secretion levels of these proteins increased when exposed to refined environments.

Conclusion: In conclusion, the findings provide critical insights into the impact of human umbilical cord mesenchymal stem cell conditioned medium on the secretion profile of the human liver cancer cell line HEPG2. This research offers a deeper understanding of the potential effects of mesenchymal stem cells on liver cancer cells and underscores the need for further exploration in this promising area of study.

keywords: Hepatocellular carcinoma (HCC) ،ucMSC ،HepG2 ، Liver Enzymes

PBi-24

The PI3K/Akt signaling axis and type 2 diabetes mellitus (T2DM): From mechanistic insights into possible therapeutic targets

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Type 2 diabetes mellitus (T2DM) is an immensely debilitating chronic disease that progressively undermines the well-being of various bodily organs and, indeed, most patients succumb to the disease due to post-T2DM complications. Although there is evidence supporting the activation of the phosphoinositide 3-kinase (PI3K)/Akt signaling pathway by insulin, which is essential in regulating glucose metabolism and insulin resistance, the significance of this pathway in T2DM has only been explored in a few studies. The current review aims to unravel the mechanisms by which different classes of PI3Ks control the metabolism of glucose.

Methods: We have collected original data obtained from international research laboratories on this topic using online search databases. We also provide a general overview of the association of impaired PI3K/Akt signaling pathways in the pathogenesis of the most prevalent diabetes-related complications. The last section provides a special focus on the therapeutic potential of this axis by outlining the latest advances in active compounds that alleviate diabetes via modulation of the PI3K/Akt pathway.

Results: Drugs that affect PI3K/Akt signaling pathway must be highly specific to lessen adverse effects of diabetes. Fortunately, contemporary advancements in the field of medicine have witnessed the emergence of nano-based drug delivery systems and editing techniques like CRISPR/Cas9. These cutting-edge technologies offer the potential to design more effective drugs by harnessing their capabilities. By specifically targeting tissues, these drugs have the potential to minimize adverse effects on other organs.

Conclusion: By considering the results of in vivo and in vitro studies, we believe that modulation of the PI3K/Akt signaling axis may open new avenues for therapeutic intervention in T2DM; however, there are still several unanswered questions about targeting PI3K for treating T2DM patients that must be addressed in the future.

keywords: Insulin resistance, Phosphoinositide 3-kinase, PI3K/Akt signaling pathway, Type 2 diabetes

PBi-25

Increased Follicular Fluid Concentration of Resistin in Infertile Women with Endometriosis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Endometriosis is one of the most frequent chronic diseases of women found in 10 to 20 % of reproductive-aged women. Endometriosis pathophysiology is still ambiguous. However, it is indicated that inflammation has a key impact on endometriosis development. Resistin is an adipokine linked to insulin resistance and obesity. Resistin performs a serious role in inflammation via binding to toll-like receptor 4 and stimulation of pro-inflammatory cytokines production. Hence, the goal of this study was to measure the concentration of resistin in the follicular fluid of endometriosis women, and also explore the relationship of its concentration with the severity of endometriosis.

Methods: Based on inclusion and exclusion criteria, 80 women between 20-40 years who underwent intracytoplasmic sperm injection were enrolled in this case-control study. Follicular fluid samples were taken from participants with and without endometriosis during oocyte retrieval by transvaginal puncture. After collecting of oocyte, follicular fluid was centrifuged and stored in the freezer until final analysis. The resistin concentration was determined using the ELISA kit.

Results: Endometriosis women had a greater follicular fluid concentration of resistin when compared with women without endometriosis (p-value= 0.03). According to the American Society for Reproductive Medicine (ASRM) classification system, 25 endometriosis patients were in stages I-II and 15 endometriosis women were in stages III-IV. Results illustrated a tendency to enhance of follicular fluid concentration of resistin in endometriosis women with stage III-IV than stage I-II; however, this variation was not statistically significant.

Conclusion: Findings of this study demonstrated an increased follicular fluid concentration of resistin in endometriosis women.

keywords: Endometriosis, Resistin, Adipokine

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PBi-26

Comparison of Quality Control Factors (pH, LDH, MTT, PLT, RBC, and WBC Counts) in Platelet Apheresis Products from Fresenius COM.TEC and Haemonetics MCS+ on the First Day of Storage

آزیتا چگینی [1], الهه آشوری کفشگر [2] © Ⓟ

استادیار موسسه آموزشی و پژوهشی طی انتقال خون [1]
موسسه آموزشی و پژوهشی طی انتقال خون [2]

Medical Biochemistry, Quality control, Trace elements

Background and aim: : The critical role of platelet transfusion in treating thrombocytopenic patients has increased interest in platelet products and their production methods. As a result, transfusion medicine specialists have developed various techniques for extracting platelets from whole blood. Platelet apheresis, regarded as the purest platelet product, is collected using different apheresis devices available on the market. Each device yields platelet products with unique quality profiles due to differing separation techniques and features. This study compared the quality control factors (pH, LDH, MTT, PLT, RBC, and WBC counts) of platelet apheresis products obtained from Fresenius COM.TEC and Haemonetics MCS+ on the first

Methods: This experimental study involved 50 platelet apheresis products from male donors at the Tehran Blood Transfusion Center. Twenty-five samples were processed using the Fresenius COM.TEC and 25 with the Haemonetics MCS+. Samples were collected on the first day of storage, and tests for pH, LDH, PLT, RBC, and WBC counts, along with the platelet viability test (MTT), were performed at the Iranian Blood Transfusion Research Center laboratory. Data were analyzed using R software, with a p-value of less than 0.05 deemed statistically significant.

Results: Results indicated that on the first day of storage, the pH of products from the MCS+ device was lower than those from the COM.TEC device (P0.0001). Conversely, LDH levels were higher and MTT test results showed lower viability for MCS+ products. Additionally, RBC and PLT counts were higher in MCS+ products (P0.0001 and P=0.003, respectively), while WBC counts were lower in MCS+ products on the first day of storage (P0.0001).

Conclusion: The study indicated that the MCS+ device yielded a higher platelet count, while the COM.TEC device showed a higher WBC count on day one.

keywords: Apheresis,Platelet,Haemonetic MCS+,Fresenius COM.TEC

PBi-27

Fecal calprotectin: a laboratory test for predicting response to therapy in patients with Inflammatory Bowel Disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Inflammatory bowel disease)IBD) is a chronic gastrointestinal disease. IBD has periods of recurrence and remission and includes two main types: Ulcerative Colitis and Crohn's disease. Currently, this disease does not have a definitive treatment, and current treatments only focus on prolonging remission. However, poor response to treatment and disease recurrence is a serious challenge. In recent years, several reports have been published regarding the utility of fecal calprotectin in predicting the response to certain types of treatment in IBD patients. The aim of this review article is to comprehensively review these reports and collect and interpret the latest findings.

Methods: Articles were searched in Pubmed, Science Direct, and Google Scholar. The abstracts of the articles were read and the related references were entered into EndNote software. Then, the full texts of the articles were studied, and a summary of the results and their concepts were interpreted and discussed. In addition, gaps in current knowledge were identified, and suggestions for future studies were made. All this was organized in the form of a review article

Results: In recent decades, some laboratory markers have been suggested for IBD non-invasive management, among which fecal calprotectin has attracted the most attention. Currently, this marker is used to differentiate IBD from IBS, a functional disorder of the gastrointestinal tract. However, the effectiveness of fecal calprotectin to predict the response to treatment and disease recurrence in patients with IBD is still debated. Despite the fact that the findings reported so far are somewhat contradictory, it seems that fecal calprotectin has an acceptable efficiency for predicting the response to treatment and disease recurrence in IBD patients. Some recent studies have even shown the utility of fecal calprotectin in predicting the need for surgery in patients with severe Ulcerative Colitis.

Conclusion: Fecal calprotectin may be helpful for predicting response to treatment and disease recurrence in IBD patients. However, the sensitivity and specificity reported by some studies are not ideal and there is remarkable controversy regarding the appropriate cut-off values. Therefore, it is necessary to conduct more studies on this laboratory test. keywords: IBD; Fecal Calprotectin; Response to treatment

PBi-28

Magnesium deficiency as a contributing factor to type 2diabetes

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetes is one of the common diseases specially in Iran which a lot of people gets involved it. So, we figure out a lot of mechanism that could have affected by diabetes type 2. Magnesium has vital role in some of the important ones.

Methods: A comprehensive literature review was conducted, examining studies clinical outcome of using magnesium for reducing diabetes type 2.

Results: Insulin resistance is a persistent medical condition that contributes to metabolic syndrome and type 2 diabetes mellitus. Magnesium, an essential cation involved in numerous physiological processes, including insulin metabolism, serves as a cofactor for various enzymes in carbohydrate oxidation and glucose transport mechanisms of the cell membrane. Studies have shown that magnesium deficiency significantly decreased insulin-dependent glucose uptake, supporting the notion that magnesium plays a crucial role in glucose handling and insulin sensitivity.

Conclusion: In conclusion, the evidence presented in this discourse demonstrates the vital role of magnesium deficiency in the development and progression of insulin resistance and type 2 diabetes mellitus. Magnesium, an essential cation involved in numerous physiological processes, including insulin metabolism, serves as a cofactor for various enzymes in carbohydrate oxidation, glucose transport mechanisms of the cell membrane, cell replication, and lipid metabolism. Adequate magnesium intake can be considered for the prevention and treatment of type 2 diabetes and its associated complications.

keywords: Sodium potassium pump, Insulin resistance, Lipid metabolism, Pancreatitis, GLUT4, Genetics

PBi-29

The beneficial combined effect of cisplatin and quercetin on ovarian, breast, and cervical cancers

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Ovarian,breast and cervical cancers are important concerns of women's global health .While cisplatin is a potent chemotherapy drug used to treat these cancers,its effectiveness is often hampered by drug resistance and severe side effects.To address these limitations,various studies have investigated the combination of cisplatin with different compounds,including the natural flavonoid quercetin.Quercetin,known for its antioxidant and anti-inflammatory properties,is promising as an anti-cancer agent.To investigate the potential of this combination therapy,a review of relevant studies on ovarian,breast,and cervical cancers was performed.This study aims to summarize the findings of these articles focusing on the combined effects of cisplatin and quercetin.

Methods: In this study, articles published from 2011 to 2023 in the PubMed and Google Scholar databases were searched using the keywords "synergistic effect", "quercetin", "cisplatin" and the names of three types of cancer (ovarian, cervical uterus and breast) were searched. Among the search results, twenty articles were selected for review

Results: In vitro and in vivo studies have demonstrated a synergistic effect of combining cisplatin and quercetin. This combination has enhanced antitumor activity against ovarian, breast, and cervical cancer cells. Recent research indicates that this therapeutic approach can markedly increase cancer cell death, reduce drug resistance, and potentially minimize side effects compared to cisplatin alone. The synergistic effect is believed to be associated with a reduction in drug resistance and side effects.

Conclusion: The combination of cisplatin and quercetin holds significant promise as a potent therapeutic strategy for ovarian, breast, and cervical cancers. This combination's synergistic effect, involving multiple mechanisms such as increased oxidative stress and disruption of cellular signaling pathways, leads to enhanced efficacy and reduced toxicity. Further research is warranted to optimize treatment regimens and translate these preclinical findings into clinical benefits for patients with these debilitating diseases.

keywords: Cisplatin, Quercetin, Ovarian cancer, Breast cancer, Cervical cancer

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PBi-30

Survey on neutrophil gelatinase-associated lipocalin (NGAL) as emerging biomarker of acute renal failure in patients admitted with sepsis and correlation with plasma creatinin

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Acute kidney injury (AKI) is characterized by a rapid decline in kidney function, leading to the accumulation of nitrogen and other waste substances. It affects approximately 1% of the general population and 3-7% of hospitalized patients. The etiologies of AKI fall into three categories: prerenal, renal, and postrenal causes, with sepsis contributing to more than 20% of cases in ICU settings. Research indicates that the mortality rate for patients experiencing AKI in the ICU increases by 3 to 5 times compared to those without this condition.

Methods: A total of 129 patients were involved in this study, comprising 79 from the control group (hospitalized in the cardiac department) and 50 patients diagnosed with sepsis at Valiasr Hospital. Serum levels of Neutrophil Gelatinase-Associated Lipocalin (NGAL) and creatinine were measured in both groups, with NGAL assessed in sepsis patients within the first 24 hours of hospitalization and creatinine levels monitored over three consecutive days. The study aimed to compare NGAL levels between the control group and sepsis patients, correlating these with the rise in serum creatinine as a marker for acute kidney injury. Data were analyzed using SPSS version 11.5, employing descriptive statistics such as counts, percentages, means, and standard deviations.

Results: : In a study comparing serum NGAL levels, the control group exhibited a mean of 74 ± 35.3, while the patient group showed a higher mean of 90.7 ± 95 (P 0.001). The investigation into the relationship between first-day creatinine levels and subsequent acute kidney injury (AKI) in the patient group revealed that initial creatinine levels did not significantly correlate with AKI development (P 0.19). Conversely, serum NGAL levels were significantly associated with AKI, as patients who developed AKI had notably higher NGAL levels than those who did not (P 0.0001).

Conclusion: The results of this study showed that the level of NGAL was higher in patients with sepsis and can predict the possibility of developing acute kidney failure in the next few days.

keywords: NGAL; AKI; Creatinin; sepsis

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PBi-31

Investigating the effect of artemisinin on enzymes functions in mice

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Artemisinin, a phytochemical derived from the Artemisia genus, constitutes one of the most significant sesquiterpene compounds exhibiting a broad spectrum of pharmacological properties, including anti-cancer, antiviral, antifungal, anti-asthmatic, and anti-allergic activities. Moreover, artemisinin has been associated with the suppression of hyperglycemia and the amelioration of diabetes-related metabolic abnormalities. This investigation sought to assess and compare the influence of artemisinin on the enzymatic activity of acetylcholinesterase, α-glucosidase, catalase, and peroxidase under both in vitro and in vivo conditions.

Methods: Thirty healthy adult male mice, each weighing approximately 25-30 grams, were randomly assigned into three groups, with ten individuals per group. The control cohort received no intervention aside from a standard diet and a mixture of corn oil with DMSO. One treatment group was administered a therapeutic dose of artemisinin (50 mg/kg), solubilized in corn oil and DMSO, while another treatment group received an overdose of artemisinin (250 mg/kg), also dissolved in corn oil and DMSO. Following a week of treatment via oral gavage, the mice were anesthetized, and subsequently, the liver, brain, and intestinal tissues were extracted, washed with normal saline, and homogenized using liquid nitrogen. The homogenate was then centrifuged in 0.1 M phosphate buffer at pH 7.4, with the supernatant utilized as the enzyme source. For the in vitro analysis, the enzymatic activity in the presence of varying concentrations of artemisinin was quantified utilizing spectrophotometric techniques.

Results: The findings from the in vitro experiments revealed that catalase activity in the liver, brain, and intestinal tissues was inhibited in a dose-dependent fashion across a concentration range of 10 to 1000 µg/ml of artemisinin. Additionally, artemisinin exhibited minimal effects on intestinal peroxidase activity at concentrations up to 1000 µg/ml, resulting in only an 8% reduction in peroxidase activity. Furthermore, artemisinin similarly had negligible impact on the enzymatic activities of α-glucosidase (saccharase and maltase) within the same concentration spectrum. Acetylcholinesterase activity was also inhibited in a dose-dependent manner within the 10-250 µg/ml concentration range of artemisinin. In vivo results indicated that catalase activity in liver, brain, and intestinal tissues was significantly (P 0.05) diminished in mice treated with both 50 mg/kg and 250 mg/kg of artemisinin in comparison to the control group. The peroxidase enzyme displayed a notable reduction solely in brain tissue among artemisinin-treated mice relative to the

Conclusion: The findings of this investigation demonstrated that while artemisinin serves as an efficacious pharmaceutical agent in the management of various ailments, it concurrently exhibits inhibition of antioxidant enzymes under both in vitro and in vivo circumstances. This aspect has the potential to elevate the generation of free radicals, such as reactive oxygen species (ROS), thereby exacerbating oxidative stress and, in turn, leading to tissue injury. In light of the absence of alterations

in the activity of intestinal α-glucosidase (including saccharase and maltase) when exposed to artemisinin in both in

keywords: Artemisinin, Diabetes, enzymatic activity, Treatment

PBi-32

Engineering Stable, and Bioactive Variants of Recombinant Human Keratinocyte Growth Factor with Reduced Aggregation Propensity

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Recombinant human keratinocyte growth factor (rhKGF) is a highly aggregation-prone therapeutic protein. The present study aimed to reduce aggregation propensity of rhKGF by engineering the aggregation hotspots.

Methods: Initially, 21 mutants were designed based on the previously-identified aggregation-prone regions (APRs) and then four of them including mutants No. 4 (L91K, I119K), 7 (V13S, L91K), 14 (L91D, I119D), and 21 (A51E) were selected based on molecular dynamics (MD) simulations for further experimental studies. The recombinantly produced rhKGF and mutants were analyzed regarding secondary structure, thermal stability, aggregation propensity, and biological activity.

Results: Far-UV CD spectroscopy showed that the mutants have similar secondary structure with rhKGF. A51E mutant showed enhanced stability and decreased monomer loss under heat stress suggesting its reduced aggregation propensity compared to rhKGF. Mutant No. 14 showed higher stability and less aggregation tendency than mutant No. 4 indicating that only mutations decreasing pI of rhKGF are effective in reducing its aggregation tendency. All of the mutants were at least as potent as rhKGF in stimulating proliferation of MCF-7 epithelial cells.

Conclusion: Our results identified A51E as an equally potent, more stable, and less aggregation-prone analog of rhKGF which could be a promising alternative drug candidate for the commercially available rhKGF (Palifermin).

keywords: keratinocyte growth factor (FGF7), protein Aggregation, Aggregation-prone regions, protein stability

PBi-33

Development of Keratinocyte Growth Factor variants with improved acidic pH stability for application in wound healing

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Keratinocyte Growth Factor (KGF) plays a crucial role in promoting epithelial cell proliferation, making it a valuable candidate for wound healing therapies. However, its instability in acidic environments limits its effectiveness in early-stage wound care. This study addresses the instability of recombinant human Keratinocyte Growth Factor (rhKGF) in acidic environments.

Methods: Using pH molecular dynamics (pH-MD) simulations, we previously investigated the influence of pH on rhKGF stability and identified positively charged residues as contributors to its instability. Building on these findings, we employed a rational design strategy to lower KGF's isoelectric point (pI) by introducing targeted mutations. This led to the development of 15 mutants which of them two mutants, K76E and K126E, were selected based on molecular dynamics simulations, and docking studies. Further experimental evaluations including secondary structure analysis, thermal stability, acidic pH stability, and mitogenic activity were performed on these two mutants.

Results: According to the results, both mutants retained similar structural characteristics and potency, and showed lower thermal stability, but modest acidic pH stability improvements compared to native rhKGF. K126E exhibited enhanced stability over extended periods in acidic environments, indicating its potential as a viable alternative for topical applications.

Conclusion: Our findings highlight the efficacy of targeted mutations in acidic pH stability enhancement and underscore the role of electrostatic interactions in KGF stability. Future research should focus on targeting other hotspots for mutants, further computational analysis, and optimizing formulations that leverage these mutants for enhanced therapeutic efficacy in wound care applications.

keywords: Fibroblast Growth Factor 7, Protein Stability, Wound healing

PBi-34

Inverse Correlation between Inflammatory Markers and Homeostatic Model Assessment for Insulin Resistance in Patients with Metabolic Syndrome

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Metabolic syndrome is a condition associated with an increased risk of type 2 diabetes mellitus (T2DM). In the last decade, various studies have shown the role of inflammation in the pathogenesis of T2DM and suggested that a systemic low-grade inflammation has a detrimental effect on insulin signaling. The aim of this study is to examine the levels of inflammatory markers and the correlation between them and certain biochemical factors in patients with metabolic syndrome.

Methods: In this study, serum levels of TNF-α and CRP were measured in patients with metabolic syndrome, of both genders, and compared with healthy individuals using appropriate statistical tests. The correlation between serum levels of these inflammatory markers and biochemical factors was also analyzed using suitable correlation coefficients in patients with metabolic syndrome.

Results: Serum levels of TNF-α and CRP in patients with metabolic syndrome are significantly higher than in healthy individuals. There is a significant positive correlation between the serum levels of these inflammatory markers and the levels of FBS, HbA1c, and homeostatic model assessment for insulin resistance (HOMA-IR).

Conclusion: In patients with metabolic syndrome, there is an exacerbation of inflammatory status. This inflammatory status may enhance insulin resistance and act in the line of increasing the risk of T2DM development. Measurement of inflammatory markers including CRP and TNF-α may be helpful in monitoring disease progression.

keywords: Metabolic syndrome, inflammatory markers, inflammation, Insulin resistance, HbA1c

PBi-35

The role of nutrition in the prevention of metabolic syndrome and non-alcoholic fatty liver disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Metabolic syndrome is a set of metabolic risk factors that exist in a person. These risk factors include insulin resistance, blood pressure, blood lipid disorders, and increased risk of coagulation. Most patients are overweight and obese, and some of them suffer from fatty liver. This point shows the strong connection between fatty liver and metabolic syndrome. The aim of this study was to review the available information on the epidemiology and pathophysiology of non-alcoholic fatty liver and metabolic syndrome.

Methods: By using keywords and searching in SID, PubMed, and Scholar search engines, related studies conducted from 2020 to 2024 were selected based on the topics discussed in the present study.

Results: The global increase in the prevalence of obesity is associated with an increase in the prevalence of non-alcoholic fatty liver disease and an increased risk of type 2 diabetes. Although there is no specific way to treat non-alcoholic fatty liver disease, diet modification plays a significant role in its treatment. Dietary patterns rich in fruits and vegetables were associated with a lower prevalence of metabolic syndrome. High meat intake was associated with components of metabolic syndrome, especially impaired glucose tolerance.

Conclusion: A program based on gradual weight loss and physical activity is still the gold standard for treating non-alcoholic fatty liver disease. Regular consumption of fruits and vegetables is recommended to reduce the risk of metabolic syndrome.

keywords: metabolic syndrome, fatty liver, epidemiology

PBi-36

Engraftment of bioengineered three-dimensional dermal derived matrix-scaffold loaded with curcumin synergically accelerate diabetic wound healing

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Medical Biochemistry, Quality control, Trace elements

Background and aim: A diabetic wound is the most frequent form of chronic wound. Because diabetic wounds have multiple factors contributing to their development, the best treatments involve using a combination of approaches. Herein we assessed whether bioengineered micro-porous three-dimensional dermal derived matrix scaffold (DDMS) loaded with curcumin could accelerate the wound healing process in diabetic rats.

Methods: Diabetic animals were assigned to the non-treated group, DDMS group, curcumin group, and DDMS+Curcumin group. Tissue samples were collected on days 7, 14, and 21 for further evaluations.

Results: The findings showed that in the treatment groups, there was a notably increase in wound closure rate, total volumes of newly formed tissue, numerical densities of fibroblasts and blood vessels, collagen density, and biomechanical parameters than the non-treated group, with the most noticeable changes seen in the DDMS+Curcumin group. Additionally, there was a notably increase in the transcript of miRNA-21, miRNA-146a, TGF-β, bFGF, and VEGF genes in the treatment groups than the non-treated group, with the highest expression observed in the DDMS+Curcumin group. In the DDMS+Curcumin group, there was a much greater decrease in TNF-α and IL-1β expression, as well as in the number of neutrophils, compared to the other groups.

Conclusion: These results validated that the combination of DDMS and curcumin has a greater effect on improving diabetic wound healing.

keywords: Diabetic Wound, Wound healing, Dermal derived matrix, Three-dimensional scaffold, Curcumin

PBi-37

Investigating the compatibility of biochemical and clinical risks and the factors affecting them in fetal health screening

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The prenatal screening program aimed at detecting chromosomal syndromes such as Down syndrome (trisomy 21), Edwards syndrome (trisomy 18), and Patau syndrome (trisomy 13) through various biochemical marker tests, including PAPP-A, Free βHCG, alpha fetoprotein (AFP), Inhibin A, unconjugated sterol of mother's serum , alongside ultrasound assessments of fetal nuchal translucency. The screenings occur in two stages: between 11-13 weeks and 18-22 weeks of pregnancy, focusing on identifying chromosomal disorders and neural tube defects. The study aims to analyze the prevalence of discrepancies between biochemical risk assessments and clinical risk, as well as to explore the factors influencing these mismatches.

Methods: In this study, the information of 500 patients referred to Fajr Sari laboratory in 1402 was used. The information related to biochemical and clinical risk was extracted and the cases of incompatibility between biochemical and clinical risk were extracted and the factors affecting it were investigated.

Results: MOM index (Multiple of Median), in fact, the ratio between the concentration of the biomarker in the patient's blood and the median (Median) of the same biomarker in the normal population with the same fetal age as measured for each marker and by multiplying the probability ratio of each MOM by the initial risk of the mother, the risk It is sometimes observed that the biochemical risk alone is positive, but after entering the ultrasound and demographic information, the final risk is reported as negative. The results obtained in this study showed that the biochemical risks reported are highly dependent on the MOM of the measured biochemical markers.

Conclusion: At the same time, calculating the MOM of biochemical markers requires updating the community of normal mothers at a specific age and day of pregnancy by increasing the number of screening cases.The cases of mismatch between biochemical risk and final risk, which are reported as high biochemical risk and final normal risk, respectively, are caused by the false error of high biochemical risk, which is resolved by modifying the MOM related to biochemical markers.

keywords: Biochemical risks , Fetal health , MOM

PBi-38

Gold Nanoparticles for Enhanced Biomarker Detection in Liquid Biopsies: A New Era in Cancer Diagnosis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Liquid biopsy has emerged as a promising alternative to traditional tissue biopsy for cancer diagnosis and monitoring, offering a minimally invasive approach to analyze disease biomarkers in biofluids. However, the detection of rare biomarkers such as circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), and exosomes remains challenging due to their low concentrations in complex biological samples. This review aims to evaluate the current advances in optical nanomaterial-based detection methods for enhancing the sensitivity and specificity of liquid biopsy biomarker detection.

Methods: This systematic review analyzed 72 articles published between 2014 and 2024, searched through PubMed, Google Scholar, Scopus, and Web of Science databases. Inclusion criteria encompassed English-language, peer-reviewed articles focusing on optical nanomaterials and nanobiotechnology in liquid biopsy applications, with clearly described methodology and results. Studies lacking experimental validation, conference abstracts, and non-English publications were excluded.

Results: Nanoparticle-based detection methods offer enhanced sensitivity for both ctDNA and CTC analysis in liquid biopsies. For ctDNA detection, gold nanoparticles are functionalized with specific antibodies that selectively bind to tumor-derived DNA fragments, enabling detection through surface plasmon resonance (SPR) and surface-enhanced Raman spectroscopy (SERS). This approach provides significantly improved signal-to-noise ratios in complex blood samples. For CTC isolation and detection, magnetic nanoparticles facilitate rapid separation from blood samples, while quantum dots enable fluorescent labeling for visualization and tracking. The integration of these technologies allows for multiplexed detection, where multiple cancer biomarkers can be simultaneously monitored, significantly improving the diagnostic capabilities of liquid biopsy platforms.

Conclusion: While nanomaterial-based liquid biopsy shows significant potential for transforming cancer diagnostics, several limitations must be addressed before widespread clinical adoption. These include standardization of protocols, reduction of manufacturing costs, and improvement of nanomaterial stability. Nevertheless, continued advancement in this field could enable earlier cancer detection and more personalized treatment strategies.

keywords: Liquid biopsy; Nanomaterials; Biomarkers; Exosomes; Cancer diagnostics

PBi-39

Investigation of New Approaches in the Treatment of Alzheimer's Disease: A Systematic Review Article

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Alzheimer's disease(AD) is the most common neurodegenerative disease without a definitive treatment option. Therefore, from the point of view of pathological factors, personalized medicine is needed for better treatment goals, and the change from the common treatment approach has moved us in this direction to form the best clinical intervention for each patient at a specific point of the disease. However, there are also failures in the field of drug modification(DMTs). In this review, we discuss some effective factors in DMT and personalized medicine method.

Methods: This systematic review article was written in 2024 by searching PubMed and Google Scholar databases using the keywords Personal Medicine, Alzheimer's Disease, Neurological Diseases. In the initial search, 69 articles were found. From these, 2 articles were duplicates, 50 were published before 2020, and 4 were excluded due to lack of specificity. Ultimately, 13 articles were included in the final analysis.

Results: The Aβ42 isoform and its prefibrillar forms (PFs) contribute to the progression of Alzheimer's disease (AD) by causing oxidative stress, membrane damage, and synaptic toxicity. Current treatments primarily focus on alleviating symptoms, while disease-modifying strategies aim to inhibit Aβ-42 production to slow disease progression. Although some phase 3 trials have not succeeded, evidence suggests that the BAN2401 antibody can reduce symptoms and amyloid plaques by about 30% in early AD by specifically targeting Aβ PFs. Additionally, using biomarkers like oxidative stress indicators can aid in the early diagnosis of AD, with studies showing significant differences in plasma superoxide dismutase (SOD) levels between AD patients and controls. Genetic analysis highlights the APOE gene variants, particularly ε4, which significantly increase the risk of developing AD, with individuals carrying one or two ε4 alleles having a risk 3-12 times greater than those without.

Conclusion: One of the major issues in the personal medicine of neurodegenerative diseases is the heterogeneity of the disease. Due to the complex pathological pathways of AD, the treatment of patients is still challenging. The correct selection of the main treatment goal, the appropriate drug doses, the accurate classification of AD stages, especially the preclinical stages, require a new research framework for success in this field.

keywords: Personal Medicine, Alzheimer's Disease, Neurological Diseases

PBi-40

The activation of the G-protein-coupled estrogen receptor promotes the aggressiveness of MDA-MB231 cells by targeting the IRE1α/TXNIP pathway

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Medical Biochemistry, Quality control, Trace elements

Background and aim: This study investigated modulating the G protein-coupled estrogen receptor (GPER) on the IRE1α/TXNIP pathway and its role in drug resistance in MDA-MB231 cells.

Methods: To determine the optimal concentrations of G1 and 4-hydroxytamoxifen (TAM), GPER expression and ERK1/2 phosphorylation were analyzed using qRT-PCR and western blotting, respectively. Cells were treated with individual concentrations of G1 (1000 nM), G15 (1000 nM), and TAM (2000 nM), as well as combinations of these treatments (G1 + G15, TAM + G15, and G1 + TAM) for 24 and 48 h. The expression levels of GPER, IRE1α, miR-17-5p, TXNIP, ABCB1, and ABCC1 genes and TXNIP protein expression were evaluated. Finally, apoptosis and cell migration were examined using flow cytometry and the wound-healing assay, respectively.

Results: Activating GPER with its specific agonist G1 and TAM significantly increased IRE1α levels in MDA-MB231 cells. IRE1α through splicing XBP1 led to unfolded protein response. In addition, decreased TXNIP gene and protein expression reduced apoptosis, increased migration, and upregulated the genes associated with drug resistance.

Conclusion: Our investigation revealed that blocking the GPER/IRE1α/TXNIP pathway in MDA-MB231 cells could enhance treatment efficacy and improve chemotherapy responsiveness. The distinct unfolded protein response observed in MDA-MB231 cells may stem from the unique characteristics of

these cells, which lack receptors for estrogen, progesterone, and HER2/neu hormones, possessing only the GPER receptor (ER-/PR-/HER2-/GPER+). This study introduced a new pathway in TNBC cells, indicating that targeting GPER could be crucial in comprehensive therapeutic strategies in TNBC cells.

keywords: Breast cancer; Drug resistance; G protein-coupled estrogen receptor; miR-17-5P; Thioredoxin.

PBi-41

Zinc as a Key Player in the Antioxidant Defense Network: Insights into Mechanisms and Implications

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Oxidative stress is the consequence of an alteration in the delicate balance between radicals and antioxidants within the cell, and this process acts as the basis for the emergence of a wide range of acute and chronic diseases. Zinc is a fundamental trace element primarily recruited as a coenzyme and immune function regulator. However, accumulating evidence over the years points toward a crucial role of zinc in modulating oxidative stress.

Methods: In this narrative review, we summarized the recent findings regarding the association between zinc and oxidative stress within the cell using differential databases consisting of PubMed, Scopus, and ScienceDirect.

Results: According to the results included in this study, zinc regulates the expression of metallothioneins, which act as radical scavengers. Zinc also participates in exchanging active metals including iron and copper, thus inhibiting local oxidative injury. Additionally, zinc suppresses NF-κB and MAPK signaling, increases glutathione levels and total antioxidant capacity, and increases superoxide dismutase activity.

Conclusion: In conclusion, investigative studies conducted on the basis of exploring the molecular role of zinc in regulating oxidative stress can help develop novel therapeutic approaches against a variety of diseases.

keywords: Zinc, Oxidative stress, Antioxidant

PBi-42

Fabrication of docetaxel-loaded polymeric nanoparticles using microfluidic platform for cancer therapy

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Background and Aim: In the field of nanomedicine, the synthesis of drug-loaded nanoparticles has emerged as a revolutionary approach to enhance therapeutic efficacy. Furthermore, NPs have the potential to significantly enhance the early detection and monitoring of numerous conditions. Nevertheless, in order to fully utilize their abilities, they need to be precisely designed, manufactured, and evaluated in relevant models. Microfluidic systems offer a cost-effective method to mimic dynamic fluid flows, gradients and specific microenvironments, making them a useful tool for both NPs synthesis and screening. Microfluidic technologies enable the production of nanoparticles in a controlled condition, improving batch-to-batch reproducibility. Here,

Methods: Methods: A microfluidic flow focusing method was used for the production of docetaxel loaded PEG-PLGA nanoparticles. The effect of solvent type, solvent and anti-solvent flow rate, drug and polymer concentration were among the variables of this study. The toxicity of the prepared nanoparticles was investigated on MDA-MB231 cell line.

Results: Results: The results of our study have shown that docetaxel nanoparticles produced in continuous flow microfluidic devices exhibit a narrow size distribution, typically ranging from 50-100 nm. This uniformity is crucial for optimizing therapeutic outcomes. Another key parameter we have optimized is the drug loading efficiency. Through careful manipulation of flow rates, solvent compositions, and surface chemistries within our microfluidic devices, we have achieved docetaxel loading efficiencies of up to 85%. Nanoparticles containing docetaxel significantly inhibited the growth of cancer cells compared to the free drug.

Conclusion: Conclusion: The main benefit of using microfluidic technology for NP synthesis is the accurate manipulation of flow rates, mixing times, and ratios to control the physicochemical properties of the resulting NPs. There are various shapes of commercial chips, and they can also be customized to answer specific requirements. In terms of time consumption, sample quality (controlled size and size distribution), and consumption of reagents, these devices offer significantly better performance for NP production compared to traditional bulk methods. Docetaxel loaded polymeric nanoparticles fabricated in microfluidic channels have great potential for

keywords: Keywords: Microfluidic, polymeric nanoparticles, docetaxel, drug delivery

PBi-43

Protective effect of thymoquinone against fluoxetine-induced liver damage through enhancing antioxidant and anti-inflammatory system in male rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Fluoxetine is a drug used to treat depression and has toxic effects on liver cells. Thymoquinone, the most important active ingredient in black seed (Nigella sativa), has several pharmacological effects, including sedation, reduced motor activity, and muscle relaxation. This study aimed to investigate the effect of thymoquinone on reducing the hepatotoxicity effects of fluoxetine.

Methods: A total of forty Wistar rats were treated with fluoxetine, thymoquinone, and silymarin for four weeks. Different techniques, including biochemical analysis, qRT-PCR, and histopathological examination, were performed to investigate the effect of drugs on the oxidant/antioxidant system and inflammatory responses.

Results: Our results revealed that fluoxetine increased lipid peroxidation and protein oxidation and inhibited antioxidant systems in rat hepatocytes. In addition, fluoxetine increased the expression of the proinflammatory cytokine TNF-α and also the migration of lymphocytes to liver cells. In contrast, thymoquinone (10, 20, and 40 mg/kg) significantly decreased MDA, PC, and TNF-α levels. Moreover, thymoquinone enhanced the catalytic activity of antioxidant enzymes, including catalase, superoxide dismutase, glutathione peroxidase, and GSH. Thymoquinone only at a dose of 40 mg/kg can inhibit the infiltration of lymphocytes into the liver.

Conclusion: Thymoquinone exerted liver protective effects against fluoxetine hepatotoxicity by inducing antioxidant and anti-inflammatory activities. This study suggests that thymoquinone, in combination with fluoxetine, can be used to reduce liver damage.

keywords: Fluoxetine, Liver damage, Thymoquinone, Antioxidant, Inflammation

PBi-44

The effects of gallic acid on inflammation and oxidative stress in valproic acid-induced hepatotoxicity in rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Valproic acid (VPA) is one of the most broadly used drugs for epilepsy disorders worldwide. Despite its great effectiveness, this drug causes liver toxicity. In this work, the effects of gallic acid (GA) on hepatic injury caused by VPA were investigated.

Methods: We randomly divided 48 Wistar rats into 6 groups. Group 1 was considered as control. The second group received only valproic acid. The third group was a positive control group which was administrated with VPA and then Silymarin. The fourth, fifth, and sixth groups also received GA after taking valproic acid. Then serum lipid profile, alkaline phosphatase (ALP), aspartate transaminase (AST), alanine aminotransferase (ALT), inflammatory factor interleukin-1beta (IL-1β), and liver biomarkers of oxidative stress were assessed.

Results: VPA caused a substantial increase (p 0.05) in AST, ALP, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), ALT, triglyceride (TG), blood urea nitrogen (BUN), very low-density lipoprotein cholesterol (VLDL-C), creatinine (Cr), urea, protein carbonyl (PC), and malondialdehyde (MDA) levels plus serum inflammatory factor IL-1β. This drug also caused an obvious decrease (p 0.05) in high-density lipoprotein cholesterol (HDL-C), catalase (CAT), ferric-reducing antioxidant power (FRAP), vitamin (Vit) C, and superoxide dismutase (SOD). Exposure to GA not only leads to a considerable improvement (p 0.05) against hepatic damage caused by valproic acid, but also increases the antioxidant system and reduces serum ALP, TC, AST, TG, ALT, BUN, LDL-C, Cr, VLDL-C, urea, PC, and MDA levels.

Conclusion: GA with its antioxidant properties shows a protective effect against hepatotoxicity caused by valproic acid. This antioxidant reduces the toxicity induced by the VPA by reducing oxidative stress and inflammatory effects of IL-1β.

keywords: Antioxidants; Valproic acid; Liver injury; Oxidative biomarkers; Interleukin-1β

PBi-45

The Role of Zeolitic Imidazole Framework-8 Nanoparticles in Cancer Targeted Therapy: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Cancer with several drug treatment challenges such as side effects and chemoresistance is a major global health problem today. Drug delivery systems, have greatly improved focus, controlled drug release as well as resistance lowering. The aim of this study is to investigate Zeolitic-Imidazole Framework-8 (ZIF-8), a zinc-based nanoparticle that is notable because of its pH-responsiveness, low toxicity and ability to induce oxidative stress in tumor cells, which results in inflammation and cell death.

Methods: This review article was performed within articles published at PubMed, Science Direct and Google Scholar until Nov 2024. The Keywords were Zeolitic Imidazole Framework-8 (ZIF-8); Drug Delivery; Targeted Therapy; Cancer Therapy; Cancer Treatment. By searching this databases, 169 articles were found, and 158 were removed by reading titles and abstracts. Under the inclusion criteria, 11 articles were selected. All articles were chosen from English articles.

Results: ZIF-8 nanoparticles which was modified with Surfactant enhanced loading and sustained release of drugs like Doxorubicin with an effective role in targeting breast cancer and neuroblastoma. effective encapsulation of 5-Fluorouracil and Camptothecin were confirmed. efficacy of Baicalin on MCF-7 breast cancer cells was improved by PEG-FA@ZIF-8@BAN delivery system, while AE@ZIF-8 nanoparticles enabled Aloe-emodin to bypass the blood-brain barrier for targeting glioblastoma. Also, CEL@ZIF-8@PEG-BIO improved Celastrol delivery to promote enhanced anti-cancer effects in ovarian cancer.

Conclusion: Finally, ZIF-8 is a promising nanoparticle in cancer drug delivery by controlling drug release, and enhancing selectivity, fewer possibility of treatment resistance with lesser side effects. ZIF-8 turns out to be one of the most exciting nanoparticles in cancer therapy. However, Further studies will be necessary to finely modulate drug release, tumor penetration, specific targeting, and minimizing toxicity. These could be a vital improvement in anti-tumor efficiency and water solubility which is going to be worthwhile in offering views for ZIF-8 future applications.

keywords: Zeolitic Imidazole Framework-8, Drug Delivery, Targeted Therapy, Cancer Treatment

PBi-46

The effect of curcumin on PCOS

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Medical Biochemistry, Quality control, Trace elements

Background and aim: PCOS is a multifactorial heterogeneous syndrome that is one of the most common endocrine disorders and the main cause of infertility. In PCOS, hyperandrogenism, insulin resistance, hyperinsulinemia, and hirsutism are observed. Among the antioxidant and anti-inflammatory agents, curcumin , which is an important biologically active substance, has a phenolic structure in turmeric. This substance can be beneficial with several pharmacological effects affecting hyperandrogenemia and hyperglycemia in PCOS. So this question is raised, is the use of curcumin useful for PCOS or not?

Methods: In this review, we extracted data from articles from the year 2016 to 2022 using Google Scholar and PubMed databases. And our search was based on keywords such as: curcumin, polycystic ovary syndrome, and infertility.

Results: Based on the studies, the use of curcumin in PCOS patients observed a decrease in BMI and obesity, and also improved HbA1C and endoplasmic HOMA-IR, but in other studies it was said that it had no effect on HOMA-IR. It also increased PPAR.γ gene expression, but had no effect on GLUT-1 gene expression. According to the studies, contradictory results were found regarding the effect of curcumin on PCOS. It should be noted that according to the studies, curcumin consumption will lead to a decrease in testosterone levels within the standard range and an increase in estradiol and progesterone levels, and in other studies it was announced that this substance affects the levels of FSH, LH and estrogen in people with PCOS.

Conclusion: According to the obtained results, curcumin has a positive effect on insulin resistance, hyperandrogenism, hyperinsulinemia, BMI, Hb1C, PPAR_Y and hormonal changes. But it had no effect on GLUT1. Also, there were conflicting results on blood fat profile and HOMA_IR.

keywords: curcumin, PCOS,Hormon, infertility

PBi-47

Linalool as a Natural Antioxidant to Alleviate the Oxidative Stress

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Since the dawn of humanity, natural herbs and remedies rich in various bioactive compounds have been used as an essential way of combating inflammation and diseases originating from oxidative stress. Linalool, a naturally occurring monoterpene alcohol, is found in an extensive range of plants and fruits and has demonstrated promising effects against oxidative damage to cells and tissues. In this review, the most recent findings regarding the mechanisms of linalool in mitigating oxidative stress are discussed.

Methods: PubMed, Scopus, and ScienceDirect were searched using the relevant syntax.

Results: According to the results, the molecular mechanism of linalool primarily involves the Nrf2/HO1 and Sirt1/Akt/PPRA-α/AMPK pathways which are key for the regulation of redox homeostasis. Additionally, linalool also ameliorates the antioxidant enzymes including catalase, glutathione peroxidase, and superoxide dismutase, enhances total antioxidant capacity, and reduces the malondialdehyde formation within cells, which is considered an end-point product of lipid oxidation.

Conclusion: In conclusion, linalool can overtake the already existing therapeutic approaches as a natural and safer alternative approach. However, more research is essential to the study of linalool's long-term effects on the body.

keywords: Linalool, Oxidative stress, Antioxidant

PBi-48

NF-kB influences the migration of vascular smooth muscle cells subsequent to treatment with heparin and ibrutinib.

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The migration of vascular smooth muscle cells (VSMCs) is one of the most important events in the remodeling of atherosclerosis plaque. The aim of study was to investigate the role of heparin in the VSMC migration, proliferation and its association to the NF-KB, collagen 1. Moreover, the incorporation of heparin was studied in the VSMC culture including Ibrutinib

Methods: The cell groups (n=8) were cultured and treated with heparin and Ibrutinib in accordance with the viability and toxicity data over 24-hour and 48-hour periods. RT-qPCR and western blotting techniques were employed to quantify the expression levels of genes and proteins. The migration and proliferation of VSMCs were ascertained through a scratch assay.

Results: Heparin (30 IU) significantly increased (P0.05) the NF-KB gene and protein expression levels, as well as the migration and proliferation of VSMCs, during the exposure periods. Conversely, Ibrutinib (2 µM) significantly reduced these parameters (P0.05). Heparin (30 IU) elevated the expression of the collagen 1 gene over a 48-hour period. The expression levels of NF-KB and collagen 1 were enhanced in all periods by the addition of heparin to the culture, which also contained Ibrutinib.

Conclusion: The cell migration and proliferation in VSMCs treated with heparin and Ibrutinib were correlated with the expression levels of NF-KB. According to the NF-KB, collagen 1, and expression levels, the modest heparin doses (5 and 15 IU) were safe for VSMCs.

keywords: VSMCs, Heparin, NF-KB, Collagen1, Ibrutinib

PBi-49

The Effect of Coffee Consumption on Adiponectin Gene Expression in Patients with Type 2 Diabetes: A Systematic Review Article

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Type 2 Diabetes Mellitus (T2DM) is a common metabolic disorder marked by elevated blood glucose levels due to insulin resistance and impaired glucose metabolism. Adiponectin, a key protein and hormone, is critical in glucose metabolism and insulin sensitivity. Certain foods and beverages have been explored in recent years as complementary strategies for managing T2DM and improving glucose metabolism. Among these, coffee due to its active compounds like caffeine and chlorogenic. This study aims to review the evidence regarding the relationship between coffee consumption and adiponectin gene expression in T2DM.

Methods: The techniques followed PRISMA guidelines. This systematic review article, conducted in 2024, was written based on searches in the PubMed and Google Scholar databases using keywords such as adiponectin, Type 2 Diabetes or T2DM, coffee or caffeine and Adiponectin Gene Expression. In the initial search, 3,020 articles were identified, of which only 51 were deemed relevant. From these, 7 articles were duplicates, 11 were published before 2020, 2 focused on animal models, and 7 were excluded due to lack of specificity. Ultimately, 14 studies were included in the final analysis.

Results: : A review of studies on 80 individuals with Type 2 Diabetes, aged 50 to 70 years, found that consuming one cup of coffee daily for 6 weeks resulted in a 15% increase in mean serum adiponectin levels ($p = 0.03$), with no significant change in the control group. Another study showed that after 8 weeks of daily coffee consumption, adiponectin gene expression in adipose tissue increased by 20% (p 0.001). Additionally, a separate study found that consuming one cup of coffee daily led to a 25% increase in adiponectin gene expression in the adipose tissue of diabetic patients (p 0.001). A cohort study also revealed that increasing daily coffee consumption by one cup was linked to a 4% reduction in the risk of Type 2 Diabetes. In conclusion, the review indicated that daily coffee consumption results in a 12-20% increase in adiponectin levels

Conclusion: The analyzed research indicates that coffee consumption significantly raises serum adiponectin levels in Type 2 diabetic patients. The findings indicate that coffee could be an important factor in improving metabolic markers in T2DM. Given the rising prevalence of Type 2 diabetes, coffee

consumption may serve as an effective strategy for controlling and managing the disease. However, due to the presence of some conflicting studies and the heterogeneity of their results, further research is recommended to confirm these findings.

keywords: Adiponectin, Adiponectin Gene Expression, Type 2 Diabetes, Coffee.

PBi-50

The enhancement of OCT4 expression observed in the co-culture system involving neonatal mouse spermatogonial stem cells alongside Sertoli cells, both in the presence and absence of melatonin.

Shadan Navid1, Zahra Saadatian2 [1] © Ⓟ

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Medical Biochemistry, Quality control, Trace elements

Background and aim: We have recently reported that melatonin as antioxidant enhance the efficacy of colonization of spermatogonial stem cells (SSCs). Melatonin as an antioxidant plays a positive role in development of SSCs in vitro. This study aimed to investigate evaluation of sertoli cells and melatonin simultaneously on SSC colonization.

Methods: SSCs and sertoli cells were isolated from the testes of three to six day old male mice. Isolated testicular cells were cultured in αMEM medium in the absence (control group) or presence (experimental group) of sertoli cells and melatonin extract for 2 weeks. Suppression of differentiation and maintenance of spermatogonial stem cells was confirmed by immunocytochemistry using OCT4 antibody.

Results: : Higher viability, proliferation were observed in the presence of Simultaneous sertoli cells and melatonin in vitro. Moreover, immunocytochemistry results showed higher OCT4 expression in this group. The number and diameter of the colonies of SSCs were higher in experimental group relative to control group during the 7the and 14the days of culture.

Conclusion: The results of our study suggest that this new protocol can increase the of these proliferation cells can be useful in treatment of male infertility.

keywords: Melatonin, Spermatogonial stem cell, OCT4, Colonization, Mouse

PBi-51

Serum Albumin Level as a Prognostic Factor for Mortality

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Albumin is a negative phase reactant. Studies investigating the link between first-day albumin levels and mortality risk in hospitalized patients have found that long-term mortality rates were higher among those with lower albumin levels, with rates of 29%, 67%, and 83% for patients with mild, moderate, and severe hypoalbuminemia, respectively. The purpose of this review is to provide a focus on the role of serum albumin in mortality rate.

Methods: We used PubMed for searching related articles. The search strategy was: “albumin” AND “mortality”.

Results: As demonstrated in previous studies, the trend of serum albumin levels, the admission serum albumin, and the lowest serum albumin recorded were all significant independent predictors of mortality. Survival probability decreases by 70.6% with a pronounced downward trend in serum albumin, by 63.4% when admission serum albumin is ≤2.45 g/dL, and by 76.4% when the lowest serum albumin reaches ≤1.45 g/dL. Recent study on critically ill patients found that the decrease in serum albumin levels from day 1 to day 3 and from day 1 to day 5 was statistically significant among non-survivors. Hypoalbuminemia could act as a marker of severity and poor prognosis in sepsis, highlighting the importance of further research and personalized interventions.

Conclusion: According to a 2021 systematic review and meta-analysis, hypoalbuminemia is associated with significantly higher rates of both in-hospital and long-term mortality (especially at 1-year post-discharge), with predictive accuracy comparable to that of serum B-Type Natriuretic Peptide (BNP) levels. This suggests that serum albumin may be valuable for identifying high-risk patients. Hypoalbuminemia is linked to both the occurrence and severity of viral, bacterial, and fungal infections and serves as a predictor of infectious complications in non-infectious diseases.

keywords: albumin level, mortality rate, hypoalbuminemia

PBi-52

Evaluation of the progesterone effects on the proliferation and apoptosis in the human keratinocyte cell line (HaCaT)

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Psoriasis is a chronic skin condition caused by an overreaction of the immune system. Keratinocytes, as important epidermis cells, are crucial in initiating skin inflammatory responses. In psoriasis, keratinocytes proliferate excessively and differentiate abnormally. Some patients may experience reduced psoriasis symptoms during pregnancy, potentially due to hormonal shifts that affect inflammatory responses and keratinocyte activity. The role of progesterone in improving psoriasis remains unclear, with conflicting results regarding its effects on skin cells. This study aims to explore the expression of membrane progesterone receptors in keratinocyte cell lines and determine whether specific progesterone concentrations promote or inhibit cell proliferation

Methods: The study utilized the HaCaT cells, suspended in RPMI 1640 medium and incubated until reaching 70-80% confluency. Cells were treated with varying concentrations of progesterone in 96-well plates. Cell viability and proliferation were assessed via the MTT assay, which determined absorbance after incubating with MTT and DMSO. Apoptosis was analyzed 72 hours post-treatment using an Annexin/PI kit and flow cytometry for cell staining.

Results: Progesterone significantly reduced viability and induced apoptosis in HaCaT cells ($P \leq 0.05$).

Conclusion: Regarding progesterone's role in reducing keratinocyte proliferation and induced apoptosis, it can be introduced as a promising therapeutic candidate for skin conditions characterized by inflammation and excessive keratinocyte proliferation

keywords: Keratinocytes, HaCaT, Psoriasis, Membrane Progesterone Receptor, Apoptosis

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PBi-54

Biochemical Comparison Of Mouse Models Of Polycystic Ovary Syndrome

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The most commonly administered agents in animal models to reproduce PCOS-like conditions are estradiol valerate, letrozole, high-fat diet (HFD) and testosterone. However, the biochemical findings from different studies have varied. The objective of our study was to investigate biochemical changes in the mouse models of polycystic ovary syndrome.

Methods: 60 NMRI mice (12 per group) were split into control and PCOS models. testosterone enanthate (1 mg per 100 g, s.c for 35 days), testosterone enanthate+ HFD (31 % cow butter, 4 % soybean protein as rat chow and fructose (20 % in drinking water (w.%/v)), estradiol valerate (EV) (IP, 2 mg/kg EV for 28 days), Letrozole (oral administered 0.5 mg/kg for 21 days) and normal control. After drug administration, Vaginal cytology, blood glucose and lipid profile were measured.

Results: Our data showed that higher FBG levels in HFD and TE compared to Letrozole and EV groups when compared to control (p 0.001). Furthermore, the levels of triglycerides and total cholesterol were notably elevated in the HFD and TE groups compared to the Letrozole and EV groups (p 0.01, p 0.05).

Conclusion: These findings suggest that the HFD model exhibits similar biochemical characteristics to PCOS compared to other groups.

keywords: PCOS, letrozole, testosterone enanthate, high-fat diet

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PBi-55

Melatonin reduces Methamphetamine toxicity through inhibition of NLRP3

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Methamphetamine (Meth) is a highly addictive psychostimulant and induces neuroinflammatory responses. Melatonin is a neurohormone that has protective effects and reduces the inflammation in the central nervous system. Our study focused the melatonin effect on memory impairment, NLRP3/IL-1β axis and Gasdermin D and caspase-1 expression in the hippocampus of rat model of Meth use.

Methods: Meth and melatonin were administered to the rats for 21 consecutive days. The memory was evaluated using alternation behavior in Y-maze. NLRP3 and IL-1β were assessed by western blotting and ELISA respectively. Gasdermin D and caspase-1 expression levels were evaluated using qRT-PCR.

Results: The NLRP3 and IL-1β were elevated in the hippocampus following Meth injection. Moreover, Meth increased gasdermine D and caspase-1 expression levels. After 21 days of Meth use, memory impairment was seen in the Y-maze test. Melatonin significantly improved memory and decreased the expression of NLRP3, IL-1β, gasdermin D and caspase-1 in the hippocampus.

Conclusion: Our study revealed that inflammasome formation and pyroptosis pathway are involved in Meth-induced neurotoxicity. Melatonin may be a potential treatment against neurotoxicity and cognitive disorders caused by Meth.

keywords: Methamphetamine, Melatonin, NLRP3, Interlukine-1β, Pyroptosis

PBi-56

Therapeutic potential of Mesenchymal Stem Cells in diabetic wounds

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetic wounds are a type of chronic wound characterized by their persistence and incurability. Recently, the self- regenerative potential of mesenchymal stem cells (MSCs) has led to their use in wound healing through differentiation and immunomodulation. This review summarizes recent advances in stem cell-based treatments of diabetic wounds.

Methods: A majority of finding were collected from PubMed, Google Scholar, and ScienceDirect databases. The therapeutic mechanisms, including direct cell differentiation, paracrine signaling, and use of extracellular vesicles (EVs) derived from MSCs were analyzed. Additionally, we assess the efficacy of various delivery methods, such as injection, bio-carriers, and engineered skin grafts containing MSCs.

Results: The results suggest that MSCs contribute significantly to wound healing through their ability to differentiate into different cell types and promote tissue repair by secreting growth factors and modulating inflammation. The use of exosomes and extracellular vesicles derived from MSCs shows promising results in transporting molecules to the wound site, improving healing outcomes. The studies also highlight the challenges of MSC-based therapies, such as long-term efficacy and cost-effectiveness, which need to be further investigated.

Conclusion: MSCs and their derivatives therapies can be an innovative approach in regenerative medicine. This potential could remarkably enhance patients quality of life and reduce the healthcare costs of chronic wounds. However, further studies and clinical trials are necessary to confirm the long-term efficacy and safety of these therapies.

keywords: DiabeticWounds;StemCells; Mesenchymal StemCells; Regenerative Medicine; Chronic

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PBi-57

The Protective Effect of Berberine Against Glucose-Induced ER stress and Cell Death

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetes mellitus (DM) is one of the most frequent chronic diseases worldwide. In DM, Endoplasmic Reticulum (ER) stress as a compensatory pathway is activated by hyperglycemia. Splicing of XBP1 mRNA known as an important regulator of ER stress. Overactivation of ER stress-depended pathways cause cell death. Caspase-9 activation is critical for intrinsic apoptosis. Berberine (BBR), an isoquinoline alkaloid of the protoberberine type found in an array of plants, is widely recognized for its protective properties against ER stress. This study investigated the effect of BBR in the management of high glucose-induced ER stress and cell death in HepG2 cells

Methods: Toxicity of high glucose and cell viability of HepG2 was detected. In order to investigate the effect of BBR on the viability of cells, HepG2 cells were incubated with different doses of BBR for 24 h in presence of the high glucose in IC50 doses in preventive and therapeutic modalities. Expression levels of XBP1u and XBP1s mRNA were evaluated by polymerase chain reaction (PCR) that was carried out. Furthermore, activation of procaspase-9 was detected by western blot.

Results: The MTT assay indicated the high glucose-induced apoptosis in HepG2 cells. Then, the protective effects of BBR on HepG2 cells against high glucose concentration were investigated in preventive and therapeutic modalities. Untreated group was used as a negative control. RT-PCR and Western blot results revealed the increased XBP1s and activated caspase-9, which indicates the high glucose-induced ER stress and apoptosis. BBR reduces the XBP1s and caspase-9 activation leading cells to survival. Additionally, caspase-9 activation significantly decreased in the berberine-treated groups compared to the positive control group, clearly demonstrating berberine's role in reducing cell death.

Conclusion: This study indicates that BBR, can protect cells from glucose-induced ER stress and cell death. These findings underscore berberine’s potential role in mitigating diabetes-related cellular damage

keywords: Berberine, High Glucose Concentration, ER Stress, Apoptosis, Caspase-9, XBP-1

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PBi-58

New insights in Quality Control in Coagulation Testing

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Coagulation laboratory tests play an important role in patient safety. Quality control refers to statistical methods for monitoring and improving quality, including internal and external processes.

Methods: Articles were reviewed in databases such as PubMed, Google Scholar, and Scopus within the years 1998-2023 using the keywords quality control, coagulation testing, INR, anti-thrombin, proteins C-S, and D-dimer.

Results: Quality control for coagulation tests includes median values for PT, INR, TT, and APTT in normal and therapeutic ranges, while D-dimer and coagulation factors use normal and abnormal ranges. Factor XIII testing utilizes normal and FXIII-deficient plasma controls. Protein S-C, ATIII, and APCR tests use lower normal limits and heterozygous patterns for control. The lupus anticoagulant (LA) test incorporates both positive and negative controls. Performance conditions for antithrombin (AT) are suboptimal at 10%, contrasting with 80% for protein C and 70% for protein S. Significant variability exists in D-dimer concentrations across diagnostic systems, and differences in INR usage have decreased. For PT, recombinant thromboplastin with an ISI below 1.2 is recommended. aPTT should use reagents sensitive to factor deficiencies, and fibrinogen activity is reported in g/L. D-dimer is expressed in mg/L or as DDU and FEU.

Conclusion: This article emphasizes the critical role of quality control in medical laboratories, especially in coagulation tests, for improving patient safety and care. It stresses the need for improved performance goals, standardized methods, and comprehensive quality control programs.

keywords: Quality control, Coagulation testing, Coagulation factors.

PBi-59

Blood tests as game changers: Identifying benign vs. malignant breast masses with circulating biomarkers

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Breast soft tissue masses frequently pose a diagnostic challenge in clinical settings. These masses encompass a diverse range of histological types, which can be broadly categorized into malignant and benign tumors. Conversely, many breast masses are ultimately determined to be benign after histological assessment, leading to reports of unnecessary biopsies. Therefore, the implementation of non-invasive experiments with high diagnostic accuracy is crucial to minimize unnecessary procedures, addressing the dilemma of distinguishing between malignant and benign masses. Our study aimed to assess the effectiveness of circulating biomarker in distinguishing between benign and malignant breast masses in patients with confirmed histopathological diagnoses.

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including breast cancer, benign masses, malignant masses and biomarkers were investigated and combined using Boolean operators (e.g., AND, OR).

Results: The differentiation between malignant and benign breast masses presents significant challenges due to the overlapping imaging characteristics and the subtlety of malignant signs in some cases. Based on evidence, the serum concentrations of glutamic acid and human epidermal growth receptor 2 (HER2) were significantly higher in patients with malignant masses compared to people with benign masses. It has been suggested that each of these biomarkers contributes to the enhancement of tumor growth and the advancement of breast cancer. In addition, it has been reported that the profiles of transcription factor activities based on cell-free DNA (cfDNA) sequencing on plasma samples, along with the accessibility of transcription factor-binding sites specific to breast cancer, can effectively differentiate between benign and malignant breast lesions.

Conclusion: This scooping review indicate that blood can be used as a crucial medium for identifying potential diagnostic biomarkers for breast cancer, including, cfDNA, glutamic acid and HER2. Assessing the levels of these circulating biomarkers can significantly aid in the early detection of breast cancer and help distinguish between patients with malignancies and healthy individuals and overcome the use constraints (low sensitivity and specificity, repeated risky exposure, and high cost) associated with other detection methods, including magnetic resonance imaging, mammography,and ultrasound.

keywords: Human papillomavirus, psychological stress, inflammation, immunity, cervical carcinoma

PBi-60

Evaluation of the antioxidant effect of berberine in organo-metallic beta-cyclodextrin nanostructure

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The development of metal-organic frameworks (MOFs) based on beta-cyclodextrins and metal ions as drug delivery systems for effective treatment has attracted the attention of many researchers. CD-MOFs are promising nanostructures that offer unique properties and can effectively encapsulate drug and improve their pharmacological activity.

Methods: Cyclodextrin-based metal-organic frameworks (CD-MOFs) were synthesized by dissolving cyclodextrin in dimethylformamide (DMF) and adding ZnCl2. To encapsulate berberine, dried CD-MOF was dissolved in ethanol and berberine was added. The physicochemical properties of Ber-CD-MOF and the amount of berberine loading and release in CD-MOF were evaluated. The antioxidant activity of Ber-CD-MOF were measured.

Results: The synthesis of Ber-CD-MOFs was confirmed by scanning electron microscopy (SEM) technique and Fourier Transform Infrared Spectroscopy (FTIR). Encapsulation and release of berberine in CD-MOF was evaluated and significant loading capacity and controlled release of berberine in these structures were demonstrated. Results showed that the antioxidant effect of Ber-CD-MOF are higher than other groups.

Conclusion: These findings indicate that Ber-CD-MOFs can be a promising tool for antioxidant effect and potentially leading to protective effect against various cancers.

keywords: berberine; antioxidant effect; organo-metallic beta-cyclodextrin nanostructure.

PBi-61

Investigating the effects of combination therapy with metformin in the treatment of Acute myeloid leukemia

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Acute myeloid leukemia (AML) represents the most prevalent form of acute leukemia. Despite considerable efforts, the overall prognosis for patients with AML remains poor, and the mortality rate due to relapse is also considerable. Consequently, the disease presents significant treatment challenges. A number of studies have indicated that metformin may serve as a beneficial adjunct to traditional anti-leukemia medications, particularly in enhancing their effectiveness against drug resistance. However, it has been demonstrated to be ineffective when used as a standalone treatment. In this context, combination therapies are currently being investigated as a promising treatment option

Methods: A comprehensive literature search across multiple databases, including PubMed, Google Scholar, Scopus, Embase, and Cochrane, yielded 32 relevant articles up to July 2024. In the course of the database search, search terms such as AML, combination, and metformin were employed in order to identify relevant articles.

Results: The results of the studies indicate that the combination of metformin with gilteritinib, sorafenib, 6-benzylthionosine, venetoclax, diclofenac, diflunisal, and cytarabine reduces intracellular ATP levels, inhibits glycolysis, decreases cytotoxicity, diminishes oxidative phosphorylation, increases the expression of anti-apoptotic proteins, and halts the cell cycle. Furthermore, this combination induces apoptosis, reduces cell growth, and ultimately results in a significant decrease in the burden of AML and an increase in overall survival for patients with AML.

Conclusion: the combination of metformin with other drugs has been shown to have a beneficial effect on patients with AML. It can thus be concluded that the combination of these drugs with metformin may enhance the synergistic effect and improve the treatment of AML patients.

keywords: AML; Combination; Metformin

PBi-62

Understanding Infertility in Iran: Prevalence, Causes, and Societal Implications

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Infertility is a global problem that affects a significant portion of the population and its prevalence varies across cultures and regions. In Iran, infertility brings significant social and psychological challenges and affects family structure and individual well-being. This article examines the prevalence of infertility among Iranian couples by analyzing the data of 3500 patients treated in different fertility clinics.

Methods: Data were collected from multiple studies conducted between 2010 and 2023, focusing on patients seeking infertility treatment in urban and rural centers across Iran. These studies used standard diagnostic criteria for infertility, which mostly followed WHO guidelines. In each study, demographic characteristics, medical history, and reproductive health status of the patients were recorded.

Results: The meta-analysis showed that the prevalence of infertility in Iran was approximately 15.5%. Of the examined patients, 55% experienced primary infertility, and 45% experienced secondary infertility. Notably, patients aged 30–35 years had the highest rate of primary infertility. Delays in marriage, stressful lifestyles, and increased social pressure have been identified as factors affecting the rate of infertility in this population. Common causes of infertility include polycystic ovary syndrome (PCOS), male factor infertility (e.g., low sperm count and motility problems), and hormonal imbalance. Environmental factors, such as exposure to toxins and improper nutrition, are also involved in infertility

Conclusion: The consequences of infertility go beyond medical concerns and affect the social dynamics in Iran. Infertility can lead to stigma, social isolation, and emotional distress. Couples often experience financial burden due to the costs associated with treatment, which can further strain marital relationships. Support systems and counseling frameworks are essential for couples experiencing infertility. Public health initiatives aimed at increasing awareness and educating couples about reproductive health can potentially reduce some of the associated social stigma. Conclusion: This analysis of the prevalence of infertility in Iran provides valuable insights into

keywords: Infertility Prevalence Iran, Reproductive Health, Social Stigma

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PBi-63

The Protective Role of Berberine in Oxidative Stress Caused by High-glucose Condition

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetes mellitus (DM), a chronic and metabolic disorder diagnosed with excessive plasma glucose, is a major worldwide health problem. High glucose condition can cause protein misfolding and mitochondrial dysfunction. It also induces oxidative stress in diabetes mellitus. Oxidative stress, the imbalance between the production and removal of reactive oxygen species (ROS), plays an important role in the pathophysiology of diabetes. Berberine (BBR), an alkaloid, has multiple biological and pharmacological activities. BBR has shown a wide range of pharmacological actions, including hypoglycemic and antioxidant activities. This study assessed the effect of BBR in the management of oxidative stress following high-glucose condition

Methods: To investigate the role of HG and/or BBR on cell death and cell oxidative stress status, we used the MTT assay and qPCR (quantitative polymerase chain reaction), respectively. Toxicity of high glucose and protective dose of BBR was investigated by MTT assay. Then high glucose incubated HepG2 cells were treated with different doses of BBR for 24 h in preventive and therapeutic modalities. Expression levels of antioxidant enzymes genes (SOD, superoxide dismutase; GPx1, Glutathione peroxidase1; CAT, catalase; Nrf2, nuclear factor erythroid2–related factor2; and NQO1, NAD(P)H quinone oxidoreductase 1), anti- apoptotic genes (B- cell lymphoma 2; Bcl2) and the DNA repair gene (Oxo-guanine glycosylase- 1, OGG1) was evaluated by qPCR.

Results: In HepG2 cells cultured with high glucose, all antioxidant enzymes (SOD, GPx1, CAT, Nrf2, and NQO1,) anti-apoptotic gene (Bcl2) and the DNA repair gene (OGG1) were significantly reduced; however, when HepG2 cells were treated with BBR under high glucose condition, the expression levels of all antioxidant enzymes, Bcl2 and OGG1 mRNA were increased in compared with untreated group

Conclusion: Our results showed that BBR has protective effect against glucotoxicity, oxidative stress and apoptosis induced by high glucose in HepG2 cells. Hence, BBR alleviates apoptosis and shows effective potential to address the impaired antioxidant response following elevated glucose levels which observed in diabetes.

keywords: Berberine; High Glucose Concentration; oxidative stress; Apoptosis.

PBi-64

Melatonin and Myocardial Ischemia-Reperfusion Injury

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Medical Biochemistry, Quality control, Trace elements

Background and aim: One of the major causes of morbidity and mortality in the world is attributed to acute myocardial infarction (AMI) which the reperfusion strategy is considered its standard therapy. Melatonin prevents the production of harmful metabolites by free radical scavenging and also induces antioxidant enzyme activities that enable melatonin to attenuate the tissue damages inflicted by reactive oxygen species. This review concentrate on the mechanism of IRI as well as the effects of melatonin administration on IRI in clinical trials.

Methods: We used PubMed for searching related articles.

Results: Melatonin can improve ischemic reperfusion injury (IRI), ameliorate cardiac action, reduce infarcted areas, decrease myocardial perfusion damages, and repair blood flow. Pretreatment with melatonin as a pharmacological agent is associated with reducing myocardial IRI. However, the timing of melatonin administration and the prescription dose need to be further investigated. The impacts of melatonin physiological doses appear to be more effective than pharmacological doses. In addition to melatonin protecting roles against oxidative stress and reducing inflammation in patients with myocardial ischemia, it may have a significant role to improve public health. Indeed, well-designed RCTs and long-term pharmacological melatonin treatment are necessary to prove the pharmacotherapeutic effects of melatonin.

Conclusion: In conclusion, significantly decreased infarct size has been shown as the main effect of melatonin administration on IRI in most of the studies. Melatonin administration generally increases LV function, antioxidant capacity, and decreases apoptosis index and oxidative stress markers. The effects of physiological doses appear to be more effective than pharmacological doses. Since elderly people possess lower levels of melatonin, melatonin replacement therapy may contribute to a decline in myocyte damage followed by ischemic-reperfusion. Due to the controversy between the studies,

further RCTs and long-term pharmacological melatonin treatments are required. keywords: Myocardial infarction; Melatonin; Pharmacotherapeutic

PBi-65

Assuring accuracy and reliability: a comprehensive approach to quality control in clinical laboratories

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Accurate and reliable test results are essential for effective patient care in the clinical laboratories. Errors can lead to misdiagnoses, inappropriate treatment, and adverse outcomes. To reduce these risks, a comprehensive quality control (QC) approach is critical. This article examines the methods that clinical laboratories use for quality assurance, and the importance of implementing these measures for reliable healthcare services.

Methods: A strong quality-control strategy consists of several interconnected components. First, standard operating procedures (SOPs) were developed to guide sample collection, processing, testing, and reporting, ensuring consistency and minimizing variation. Second, internal quality control measures include the analysis of control samples along with patient samples to confirm accuracy and precision, allowing for immediate corrective action if discrepancies occur. Periodic internal audits assess compliance with SOPs and identify areas of improvement. Third, it is important to participate in external quality assessment (EQA) programs to benchmark performance through interlaboratory comparisons. Proficiency testing, a key component of EQA, involves analyzing the same blind sample in multiple laboratories to identify systematic errors and promote continuous improvement. In addition, the integration of automated systems and advanced technologies streamlines laboratory processes, reduces human error, and enhances data analysis through laboratory information systems (LIS) that monitor results in real time.

Results: The implementation of this comprehensive QC approach has resulted in a significant reduction of test errors in clinical laboratories. Advanced training and adherence to SOPs reinforce established practices, whereas internal and external quality control measures provide a solid framework for identifying and addressing issues. In addition, automation has improved time and efficiency, ensuring the timely delivery of results to healthcare providers.

Conclusion: Ensuring accuracy and reliability in clinical laboratories requires a multifaceted quality control approach, which includes SOPs, internal and external assessments, automation, and ongoing staff training. By establishing this comprehensive framework, laboratories can increase test quality and

improve patient safety and clinical outcomes. Finally, investing in quality control measures strengthens laboratory performance and trust in the healthcare system.

keywords: Quality Control ,Accuracy, Reliability , Standard Operating Procedures, Continuous Improvement

PBi-66

Iron Homeostasis in Cancer: Recent Insights into Ferroptosis, Ferritinophagy, and Novel Iron Acquisition Mechanisms

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Iron, essential for various cellular functions, plays a crucial role in cancer development and progression. This review aims to synthesize recent findings on the intricate relationship between iron metabolism and cancer, highlighting potential therapeutic targets.

Methods: A comprehensive literature search was conducted across PubMed, Web of Science, and Scopus databases, spanning the years 2014 to 2024. Search terms included "iron homeostasis," "cancer," "ferroptosis," "ferritinophagy," and "iron acquisition." Original research articles and reviews investigating the multifaceted role of iron metabolism in cancer were included.

Results: The literature review revealed several key findings. Ferroptosis, an iron-dependent form of cell death characterized by lipid peroxidation, emerged as a promising therapeutic target. Studies suggest that modulating ferroptosis could overcome resistance to conventional cancer therapies. Ferritinophagy, the degradation of ferritin for iron release, plays a significant role in cancer cell survival. Disrupting this pathway could sensitize resistant cancer cells to treatment. The NRF2 pathway, a regulator of iron metabolism, emerged as crucial for cancer cell survival. Its ability to protect against ferroptosis makes it a potential target for therapeutic intervention. Furthermore, cancer cells employ sophisticated mechanisms for iron acquisition, including the LCN2-SLC22A17 system and CD44 antigen-mediated uptake. Targeting these pathways could limit iron availability and hinder cancer cell growth. Additionally, studies highlight the role of prominin 2 (PROM2) in packaging ferritin into exosomes, suggesting a mechanism by which iron contributes to cancer metastasis.

Conclusion: The interplay between iron homeostasis and cancer biology is complex, offering numerous opportunities for innovative therapeutic strategies. Targeting iron-related pathways, particularly those involving ferroptosis and ferritinophagy, holds significant promise for cancer treatment. However, further research is crucial to fully understand and exploit these mechanisms for developing effective and targeted therapies against cancer.

keywords: Iron homeostasis, Ferroptosis, Ferritinophagy, Cancer metabolism

PBi-67

Effect of a herbal supplement containing extracts of Silybum marianum, Cynara scolymus, Curcuma longa and Taraxacum officinale on liver function tests and oxidative stress biomarker in patients with Non-alcoholic fatty liver disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Non-alcoholic fatty liver disease (NAFLD) is the most common form of liver diseases in all over the world. Given the high incidence of the disease, further research is an undeniable necessity for its better management. In this research, the efficacy of the supplement on liver function tests and oxidative stress biomarkers were evaluated for the first time in literature, up to our knowledge.

Methods: Participants were 60 patients with NAFLD allocated to two equal groups (Intervention=30 and Comparison=30). Block balanced Randomization method was performed using a computer by a trained nurse. Intervention and comparison groups received 275 mg the extract and placebo as capsule for 12 weeks, respectively. Data were collected by completing a standard questionnaire and performing relevant tests based on common laboratory methods.

Results: The supplement had intermediate effect on malondialdehyde (MDA) level as an oxidative biomarker that was statistically significant too. The magnitude of effects of the supplement on other parameters were overally negligible compared to the comparison and not significant. No side effects were seen in these patients following capsule usage.

Conclusion: In generally, this trial study indicated 12 weeks intake of the supplement had considerable effects on MDA as oxidative stress biomarker.

keywords: NAFLD, Oxidative stress, Liver function test, Herbal supplement

PBi-68

The effect of vitamin D levels on chronic periodontitis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Periodontitis is a persistent inflammatory disease that impacts the gums and the bone structure around the teeth, representing a major public health concern. One factor that has gained growing interest is vitamin D, a fat-soluble nutrient essential for regulating calcium and phosphate levels, supporting bone mineralization, and enhancing immune function. Research has shown that vitamin D is crucial in the onset and progression of periodontitis, highlighting its vital role in supporting periodontal health. This study aims to explore the relationship between vitamin D levels and the occurrence of gingivitis.

Methods: I searched related keywords in the international sites "Google Scholar", "PubMed", "science direct" for original articles and reviews. The searched keywords were vitamin D, periodontal disease and periodontitis . Based on the search result, In this review article, I am examining the different factors influencing the impact of vitamin D on the development of periodontitis.

Results: Numerous studies have examined the relationship between vitamin D levels and periodontitis, consistently showing that vitamin D deficiency increases the risk of developing periodontal disease, while supplementation can improve periodontal health. Benefits of vitamin D include reduced inflammation, improved bone density, and enhanced immune response. Studies indicate that vitamin D has anti-inflammatory properties, as it reduces the levels of pro-inflammatory cytokines while promoting the production of anti-inflammatory cytokines. Furthermore, vitamin D has been found to inhibit the growth of harmful periodontal bacteria, such as *Porphyromonas gingivalis*, helping to mitigate the progression of the disease.

Conclusion: Current research highlights the important role of vitamin D in maintaining periodontal health and preventing periodontitis. A deficiency in vitamin D can increase the risk of developing periodontitis, while the condition itself may exacerbate vitamin D deficiency due to the chronic inflammation and metabolic disturbances it causes. Therefore, assessing vitamin D levels in individuals at risk for periodontitis is essential.

keywords: vitamin D; periodontitis; periodontal disease

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PBi-69

Distinct expression of the CSF2RB gene in PSC cirrhosis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The CSF2RB gene, which encodes the common beta chain of high-affinity receptors for interleukin-3 (IL-3), interleukin-5 (IL-5), and granulocyte-macrophage colony-stimulating factor (GM-CSF), plays a significant role in the immune response. The gene's involvement in immune regulation and cell differentiation could imply a potential link to liver diseases, including cirrhosis. Cirrhosis is often associated with chronic inflammation and immune dysregulation, conditions where cytokines like IL-3, IL-5, and GM-CSF may play a role. The present study aimed to investigate CSF2RB gene expression in cirrhotic tissues.

Methods: In this case-control study, 27 liver tissues with cirrhosis, including 6 tissues with hepatitis B and C viruse infections (HBV/HCV), 6 tissues with autoimmune hepatitis (AIH), 5 tissues with primary sclerosing cholangitis (PSC), 7 tissues with nonalcoholic steatohepatitis (NASH), and 3 tissues with alcoholic and 9 controls were collected. Gene expression of CSF2RB was quantified using qRT-PCR.

Results: The results of the present study indicated that the expression of the CSF2RB gene in cirrhotic tissues was lower than that in the control group, with the exception of PSC cirrhosis. Interestingly, the CSF2RB gene expression in PSC cirrhosis was higher than in the control group; however, this difference was not significant. Additionally, the CSF2RB gene expression in all cirrhotic tissues was significantly lower than that in PSC cirrhosis.

Conclusion: Despite the immune system's involvement in the pathogenesis of most chronic liver diseases, the role of the CSF2RB gene in PSC cirrhosis significantly differs from its role in other types of cirrhosis.

keywords: CSF2RB; cirrhosis; primary sclerosing cholangitis

PBi-70

Evaluating the Efficacy of Sacubitril/Valsartan in Heart Failure Management: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Heart failure involves multiple neurohormonal pathways, with the renin-angiotensin-aldosterone system (RAAS) playing a key role, especially in heart failure with reduced ejection fraction (HFrEF). Biomarkers like natriuretic peptides and neprilysin indicate the activation of these pathways. Inhibiting these pathways, including RAAS, is crucial for treatment. Neprilysin, which breaks down vasoactive peptides, has led to new treatments. Angiotensin receptor-neprilysin inhibitors (ARNi), combining sacubitril and valsartan, counteract angiotensin II effects and enhance natriuretic peptides' activity.

Methods: A systematic literature search was conducted to identify all studies that investigated the ARNi therapy on heart failure in the PubMed (pubmed.ncbi.nlm.nih.gov) database.

Results: In total, 8 studies with 9000 participants have reported on the efficacy of sacubitril–valsartan on the rate of hospitalization amongst heart failure patients. The pooled RR was 0.76 (93% CI: 0.70 to 0.87; I2 = 23%), Patients treated with sacubitril–valsartan showed a notably reduced rate of hospital admissions compared to those on alternative treatments. (p 0.001). In total, 10 studies with 1400 participants have reported on the efficacy of sacubitril–valsartan on the LVEF amongst heart failure patients. The pooled MD was 3.74 (96% CI: 1.93 to 5.55; I2 = 88.4%), indicating that the patients receiving sacubitril–valsartan had significantly higher LVEF when compared to patients receiving any routine medications (p 0.001).

Conclusion: Sacubitril/Valsartan has been effective as a potent therapy in managing heart failure with reduced ejection fraction. This combinational drug significantly reduces mortality and morbidity among patients with heart failure.

keywords: Heart failure, Neurohormone, Neprilysin inhibitor, sacubitril/valsartan, ARNi

PBi-71

How have metallic nanostructures changed the diagnostic methods?

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Nanotechnology has become the field of medical laboratory sciences. The laboratory on the chip, microchips and, microarrays technology, nanoparticles, nanotubes, and other types of nanometer tools and systems have increased the sensitivity and accuracy, increased the speed, increased the efficiency, and of course reduced the costs of various medical diagnostic tests and even provided us with new diagnostic methods. Metal nanostructures and metal oxide are the most important nanostructures in different diagnostic techniques. These materials are essential in the development of biosensors based on colorimetry, separation of biomolecules and cells, improvement of traditional sandwich-based methods, etc.

Methods: From the databases of Google, Scopus, and PubMed, the desired articles in which metal nanoparticles, metal oxides, and pseudo-metals were used in the production of sensors and diagnostic methods were extracted and categorized into different methods.

Results: Gold nanoparticles and iron oxide nanoparticles are the most used among different nanoparticles in the design and construction of diagnostic tools. The development of lab-on-a-chip techniques, Förster resonance energy transfer, and plasmonic biosensors are among the most important techniques in which metal nanoparticles are used.

Conclusion: Direct analysis of DNA, protein, or any biomolecule with high speed, accuracy, and sensitivity can be easily achieved with methods based on nanotechnology, the potential of single molecule detection in biological solutions using nanotechnology is certainly very beneficial for medical diagnosis techniques. In addition to improving and strengthening the traditional laboratory methods of medical diagnosis, nanotechnology provides new methods, tools, and materials that laboratory science specialists can use in the diagnosis of diseases.

keywords: Nanotechnology, metal nanoparticles, medical diagnosis

PBi-72

The Role of Gingival Crevicular Fluid-Derived Mucin and Amylase in Oral Squamous Cell Carcinoma: Insights into Downstream Gene Regulation

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Oral squamous cell carcinoma (OSCC) is a highly aggressive malignancy characterized by poor prognosis and limited treatment options. Gingival crevicular fluid (GCF), an exudate from periodontal tissues, contains various proteins that may reflect local pathophysiological changes. Recent research suggests that mucin and amylase, key components of GCF, are involved in the regulation of downstream signaling pathways implicated in OSCC progression. This review aims to consolidate current knowledge on the roles of GCF-derived mucin and amylase in OSCC and their impact on gene expression, focusing on their potential as diagnostic biomarkers and therapeutic targets.

Methods: A comprehensive literature review was conducted using databases such as PubMed, Scopus, and Web of Science. Relevant studies investigating the molecular and functional roles of mucin and amylase in OSCC were selected. Special emphasis was placed on research exploring their effects on downstream signaling pathways, including PI3K/Akt, NF-κB, and MMP-9.

Results: Evidence indicates that mucin and amylase levels are elevated in GCF from OSCC patients compared to healthy controls. These proteins modulate key downstream pathways that promote tumor cell proliferation, migration, and resistance to apoptosis. Mucin has been shown to enhance cellular adhesion and immune evasion, while amylase contributes to altered metabolic and inflammatory responses. Their combined effects upregulate the expression of genes such as MMP-2, MMP-9, and anti-apoptotic factors, driving OSCC progression. Preclinical studies suggest that targeting these proteins could improve therapeutic outcomes by reducing tumor invasiveness and enhancing chemosensitivity.

Conclusion: GCF-derived mucin and amylase play significant roles in the pathogenesis of OSCC by regulating critical downstream genes and pathways. Their unique presence in GCF makes them promising biomarkers for early detection and monitoring of OSCC. Additionally, therapeutic strategies targeting these proteins offer a novel approach to managing OSCC. Further clinical validation is necessary to translate these findings into routine clinical practice.

keywords: Oral squamous cell carcinoma, Gingival crevicular fluid, Mucin, Amylase

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PBi-73

The Effect Of Red Meat On Human Liver Factors

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The relationship between red meat consumption and liver function has been extensively studied due to its potential health impacts. Liver enzymes such as ALT, AST, and ALP serve as key markers of liver health. However, the evidence linking red meat intake to liver enzyme levels remains inconsistent. This review aims to evaluate the effects of red meat consumption, particularly processed vs. unprocessed varieties, on liver function markers in humans.

Methods: : A systematic search was conducted using Google Scholar for studies published between 2000 and 2023 with proper keywords. Studies that examined the relationship between red meat consumption and liver enzyme levels (ALT, AST, ALP) were included. A total of 18 studies with 200-300 participants were selected for analysis. Data were pooled using fixed- and random-effects models, and heterogeneity was assessed using the I^2 statistic. The quality of the studies was evaluated using the GRADE approach.

Results: The results showed that higher red meat intake was significantly associated with increased ALT and AST levels. Individuals with the highest red meat consumption had a 18% higher ALT and a 15% higher AST compared to those with lower intake. Processed red meat had a stronger effect, with a 22% higher ALT and 20% higher AST. No significant effect was observed on ALP levels.

Conclusion: This analysis indicates that high consumption of red meat, especially processed varieties, may elevate liver enzymes, suggesting possible liver dysfunction. Further research is needed to clarify the underlying mechanisms and assess the impact of different types of red meat on liver health.

keywords: Red meat; liver function; liver enzymes; liver biomarkers.

PBi-74

High prevalence of hypovitaminosis D3 among pregnant women in central Iran: correlation with newborn vitamin D3 levels and negative association with gestational age

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Hypovitaminosis D3 is a significant concern among pregnant women and their newborns because vitamin D3 (Vit-D3) plays a crucial role in embryonic growth, development, and health. This study aimed to evaluate the Vit-D3 status of a group of pregnant Iranian women and its association with newborn Vit-D3 levels, medical and clinical indices after delivery.

Methods: A total of 206 pregnant women and their newborns were assessed for Vit-D3 levels and their correlation with gestational age. Mean±standard deviation (SD) or the orders (non-parametric tests) of variables were compared, and correlation estimations were performed to elucidate any differences or associations between groups, with a confidence interval of at least 0.95.

Results: The mean±SD of mothers' age and gestational age were 29.65±6.18 years and 35.59±1.6 weeks, respectively. Neonatal Vit-D3 levels were associated with maternal age. Using a 30 ng/mL cutoff point for serum Vit-D3 levels, 83.5% of pregnant women and 84.7% of newborns had hypovitaminosis D3. The average Vit-D3 levels of mothers and newborns at delivery time were 23.5±8.07 ng/mL and 20.76±9.14 ng/mL, respectively. Newborn Vit-D3 levels were positively correlated with maternal Vit-D3 serum levels (R=0.744; P0.001) and gestational age (R=0.161; P=0.022). In newborns, head circumference was inversely correlated with bilirubin level (R=−0.302; P0.001) but directly associated with weight (R=0.640; P0.001).

Conclusion: Hypovitaminosis D3 remains a significant challenge for pregnant Iranian women. Maternal Vit-D3 levels provide for the newborn's needs, particularly in the late stages of pregnancy. Therefore, Vit-D3 supplementation and regular monitoring are essential for pregnant women and their newborns.

keywords: Vitamin D, Pregnancy, Newborn, Umbilical cord, Apgar score

PBi-75

The effect of spirulina supplementation on blood pressure in adults: a GRADE-assessed systematic review and meta-analysis of randomized clinical trials

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Medical Biochemistry, Quality control, Trace elements

Background and aim: -Previous studies have yielded controversial results regarding the effect of spirulina on blood pressure (BP), which need updating. So, this updated systematic review and meta-analysis of randomized controlled trials (RCTs) carry out a more accurate estimation of the effect of spirulina on BP in adults.

Methods: We conducted systematic searches (in PubMed/Medline, Scopus, and ISI Web of Science) until April 1, 2024, to identify related RCTs based on PICOS guidelines (population (individuals 18 years old), the intervention (spirulina), the comparison (control or placebo group), the outcomes (systolic BP (SBP) and diastolic BP (DBP), and the study design (RCTs). We evaluated the impact of spirulina on DBP and SBP. Conventional procedures were employed for analysing publication bias, heterogeneity, and sensitivity. The GRADE criteria and the Cochrane assessment method were employed to evaluate the risk of bias (ROB) and certainty of evidence across the studies, respectively.

Results: The result shows spirulina consumption decreases SBP (WMD: -4.41 mmHg, 95% CI: -6.74 to -2.07, I2 = 66.1%) and DBP (WMD: -2.84 mmHg, 95% CI: -4.65 to -1.03 (I2 = 62.3%). Subgroup analysis demonstrated SBP and DBP were still lower in individuals with ≥120 mmHg and ≥80 mmHg, Hypertension (HTN) individuals, overweight individuals, age 50 years, and 8 weeks of intervention. Indeed, we do not observe publication bias, ROB, or interference studies in the overall results of BPs, and based on GRADE, our outcomes have moderate quality. Because of the low number of studies and participants, the dose-response and meta-regression are not significant.

Conclusion: Results of this study demonstrated spirulina intervention decreased SBP and DBP in HTN and overweight individuals, age 50 years, and 8 weeks of intervention. So, spirulina intake decreases BP and could be used in clinical practice. Furthermore, more and high-quality RCTs are needed to establish the clinical efficacy of the spirulina and determine cut-off spirulina interventions based on dose and duration.

keywords: Meta-analysis, Spirulina, Hypertension, Blood pressure

PBi-76

Saffron improves diabetic nephropathy in diabetic rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetic nephropathy (DN) is one of the most important complications of diabetes. Nowadays, more people are using herbal remedies to treat inflammatory disorders because they are readily available, have fewer side effects, and are less expensive. This study investigated the potential antidiabetic benefits of saffron ethanolic extract and on the TLR-4 and S100A8 genes expression in the kidneys of rats with type 1 diabetes.

Methods: 24 male rats were selected by simple random sampling. Animals with a fasting blood sugar level greater than 200 mg/dl were considered diabetic. Rats were randomly assigned to 5 groups: Control group, diabetic group, diabetic + saffron (dose=100) group, diabetic + saffron (dose=200) group, and diabetic + saffron (dose=300) group. Fasting blood glucose (FBG) and the gene expression of TLR-4 and S100A8 were analyzed. ANOVA and Bonferroni post-hoc tests were used for data evaluation.

Results: Diabetes significantly impaired the serum FBG levels and the expression of TLR-4 and S100A8 genes in kidney tissues (P0.001). After treatment with the ethanolic extract of saffron, the FBG was close to the normal range (P0.001). The saffron extract significantly decreased the expression levels of TLR-4 and S100A8 genes in kidney tissues when compared to the diabetic control group (P0.001). In addition, the beneficial effects of saffron were dose-dependent.

Conclusion: The ethanolic extract of saffron has beneficial antidiabetic effects. Saffron reduced the expression of TLR-4 and S100A8 genes. Thus, it may be used as an adjuvant treatment for diabetic complications.

keywords: Saffron, Alcoholic Extract, Gene Expression, Diabetes, rat

PBi-78

Investigating the correlation between serum bilirubin and prediction of coronary heart disease in patients with ischemic heart disease (IHD) referred to Amir al-momenin (AS) hospital in Zabol city.

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Ischemic heart disease (IHD) refers to the lack of oxygen caused by insufficient blood supply, which itself is caused by the imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is coronary epicardial disease. The general aim of the study is to investigate the relationship between serum bilirubin and the prediction of coronary heart disease in ischemic heart patients referred to Amir al Mominin Hospital Zabol city.

Methods: This is a Cross-sectional study in which 200 patients, including 100 patients and 100 controls, were selected. The case group consists of patients referred to the heart clinic of Amir Al-Momenin Hospital in Zabol City whose CAD has been confirmed by a specialist doctor by angiography

Results: Based on the results obtained from this study, the difference between the mean cholesterol, triglyceride, and LDL levels in the case and control groups was not significant. However, HDL and CRP levels are significantly different between the case and control groups.

Conclusion: In general, the results of the research showed that the measurement of bilirubin is proposed as an indicator for predicting the occurrence of coronary artery disease

keywords: Coronary Artery Disease, Serum Bilirubin, Ischemic Heart Disease, HDL, LDL

PBi-79

Evaluation of the Relationship Between Different Variants of Alpha-1 Antitrypsin and the Severity of COVID-19 Disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The outbreak of coronavirus disease in late 2019 led to a significant increase in respiratory illnesses worldwide. Alpha-1 antitrypsin (A1AT), a serine protease inhibitor, is critical for maintaining pulmonary health, and its deficiency is associated with lung diseases. This study hypothesized that specific variants of the SERPINA1 gene, encoding A1AT, influence the severity of COVID-19.

Methods: Forty-two patients aged 25–60 years diagnosed with COVID-19 were hospitalized at Tohid Hospital, Sanandaj, Iran, and categorized into three groups: outpatients, inpatients, and intensive care unit (ICU) patients (14 per group). DNA extracted from nasopharyngeal swabs, along with viral RNA, was used for the amplification of the SERPINA1 gene via polymerase chain reaction (PCR). Electrophoresis was used to evaluate the band quality of PCR products. The amplified products were sequenced using Sanger sequencing, and the quality of the sequences was assessed using Chromas software. CLC and Clustal Omega web-based software were employed to align the sequencing samples and their corresponding amino acid sequences with the SERPINA1 reference gene. The Fisher-Freeman-Halton test was used for the statistical analysis of the data. All statistical analyses were performed using SPSS software version 21 at a significance level of 0.001.

Results: Six variants were identified in the SERPINA1 gene, including three non-synonymous variants causing amino acid changes and three synonymous variants that did not alter the amino acid sequence. Analysis revealed distinct frequencies and impacts of non-synonymous variants across patient groups. In exon 2, the location of 5646 CG variant (A G) was found in 35.71% of hospitalized patients, while

the location of 5892 AG variant (E G) was most frequent in outpatients (50%). Notably, the location of 5895 CG variant (A G) was exclusive to ICU patients, with a 100% frequency, suggesting its potential link to severe COVID-19. Variants were classified using ACMG guidelines into three categories: Variant of Unknown Significance (VUS), Likely Benign, and Benign. Non-synonymous variants were categorized as VUS, while synonymous 3' UTR variants were classified as Likely Benign or Benign.

Conclusion: Structural and functional changes in A1AT, mediated by synonymous and non-synonymous variants, may influence the severity of COVID-19. The identified variants, particularly 5895 CG, may potentially increase susceptibility in COVID-19 patients.

keywords: Alpha1-antitrypsin, COVID-19, SERPIN 1, Single nucleotide polymorphisms, SARS-CoV-2

PBi-80

Induction of apoptosis using siRNA IGF-IR in MCF-7 cell line resistant to 5-fluorouracil

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Medical Biochemistry, Quality control, Trace elements

Background and aim: 5-FU is used to treat a variety of cancers, including breast cancer. Chemotherapy resistance in cancer cells is started by up regulation and down regulation of several factors which would be resulted in cancerphenotype change. Increasing the expression of IGF-1F is one of the key element in this transition that causes the cells do not respond properly to the drug. In the present study, the effect of siRNA targetingIGF-1R onthe apoptosis induction in MCF-7 cancer cell line resistant to 5-FU drug was investigated.

Methods: MCF-7 breast cancer cell line was treated by 5FU to generate resistant cancer cells, then IC50 and cell viability in non-resistant and resistant cells were measured by MTT method. Lipofectamineused for delivery of siRNA targeting IGF-1R into cancer cells.After evaluation the level ofIGF-IR mRNA expression by RT_PCR method, apoptosis was measured using flow cytometry.

Results: The results of IC50 and MTT showed that MCF-7 cancer cells were induced for resistance during 60 days of long-term exposure to certain doses of FU-5 drug. Gene expression of IGF-1R has already been decreased in cancer cells was diminished after resistance process. Flow cytometry analysis indicated that significant elevation of apoptosis were present in resistant cancer cells treated by siRNA targeting IGF-1R.

Conclusion: Resistance has greatly affected the anti-cancer activity of 5FU. Down regulation of IGF-1R as one of genes involved in resistance using siRNAcould decrease the process resulting in better effect of 5FU on cancer cells.

keywords: breast cancer ،siRNA ،MCF-7،IGF٥ ،-FU

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PBi-81

Investigating the Effect of Vitamin E on the Occurrence of Alzheimer's Disease: A Systematic Review Article

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Alzheimer's disease (AD) is a neurodegenerative disorder causing cognitive decline, particularly memory loss, and is the leading cause of dementia in older adults. AD is characterized by amyloid plaque accumulation and neuronal damage, with oxidative stress playing a key role in its progression. Vitamin E, a powerful antioxidant, has gained interest for its potential to reduce oxidative stress and inflammation in AD. This article explores the impact of Vitamin E in preventing AD, focusing on its effects on β-amyloid plaque accumulation and cellular signaling pathways involved in the disease.

Methods: This systematic review was written in 2024 by searching PubMed and Google Scholar databases using the keywords "Vitamin E," "Alzheimer's Disease," "β-amyloid," and "Diet." An initial search identified 1090 articles, of which 70 were found to be relevant. From these, 17 articles were duplicates, 39 were published prior to 2020, and 2 were excluded due to lack of specificity. Finally, 12 articles were selected for the final analysis.

Results: A study conducted in 2004 demonstrated a significant reduction in the accumulation of β-amyloid plaques in the cortex and hippocampus of rats administered Vitamin E compared to the control group(p0.01). This finding suggests a protective role for Vitamin E in mitigating amyloid-induced neurodegeneration. Additionally, a 2014 clinical trial involving 613 patients with AD found that daily administration of 2000 IU of Vitamin E led to a significant slowing of functional decline, as compared to the placebo group. These results highlight the potential benefits of Vitamin E in delaying the progression of cognitive impairments in AD patients. Moreover, a 2019 study investigating the genes involved in Alzheimer's disease found that Vitamin E treatment reduced the expression of key genes and related signaling pathways associated with AD. These findings suggest that Vitamin E may help downregulate inflammatory and amyloidogenic pathways, contributing to the overall neuroprotective effect.

Conclusion: The evidence presented in this review indicates that Vitamin E, as a powerful antioxidant, may play a significant role in reducing oxidative stress and inflammation in the brain. By decreasing oxidative biomarkers, preventing ROS production, and inhibiting the accumulation of β-amyloid plaques and hyperphosphorylated tau(p-tau), Vitamin E appears to offer neuroprotective effects. These effects may potentially complement existing treatments, such as cholinergic inhibitors, in managing Alzheimer's disease. However, further large-scale, long-term clinical studies are necessary to validate these findings and to assess the therapeutic efficacy of Vitamin E in AD.

keywords: Vitamin E, Alzheimer’s Disease, β-amyloid, Diet, Oxidative Stress, Antioxidants.

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PBi-82

Investigation of the Relationship between Constipation and Colorectal Cancer: Systematic Review Article

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Colon cancer is a common and dangerous cancer with increasing prevalence, posing a global health concern. It begins in the epithelial cells of the colon and rectum, progressing to gastrointestinal dysfunction and potential metastasis. Chronic constipation, prevalent in industrialized societies, may increase the risk of colorectal cancer(CRC) by prolonging the contact between carcinogens in feces and the colon mucosa. However, the exact relationship between constipation and CRC remains unclear, requiring further research. This study aims to explore the potential link between chronic constipation and CRC risk and its impact on disease progression.

Methods: This article is a systematic review written in 2024, utilizing data from the Google Scholar and PubMed databases with keywords such as "colon cancer," "colorectal cancer," and "constipation." A total of 310 articles published between 2010 and 2024 were initially identified, and after screening for relevance, language(English), and clinical trial studies, 13 articles were selected for final analysis. These studies include data on the effects of chronic constipation on the onset of colorectal cancer and its correlation with genetic factors and the use of laxatives.

Results: The data analysis revealed conflicting information regarding the relationship between constipation and colorectal cancer. Some studies have shown a potential link between chronic constipation and an increased risk of colorectal cancer, while others have not found a direct association. For instance, a study conducted in 2021 on 3,943 colorectal cancer patients with chronic constipation found a higher percentage of these patients compared to the control group, indicating a possible connection. However, data from 126,650 patients diagnosed with colorectal cancer between 1989 and 2016, as well as genetic data from independent CRC groups (P=0.198), showed no significant relationship between constipation and the rate of colorectal cancer. Moreover, a 2014 study found that although constipation did not correlate with an increased rate of CRC, the use of laxatives was associated with a higher risk of colorectal cancer compared to individuals who did not use laxatives.

Conclusion: This study finds no direct, significant link between constipation and colorectal cancer(CRC). However, laxative use may increase colon cancer risk due to long-term changes in gut microbiota and immune system activation. Constipation could also prolong the contact time between carcinogens in stool and the colon mucosa, potentially raising CRC risk. Although constipation is not an independent risk factor for CRC,it may indirectly contribute to colon cancer by fostering conditions that promote cancer-causing bacteria in the stool. Further large-scale studies are needed to better understand the relationship between constipation and CRC.

keywords: Colorectal Cancer, Constipation, Laxatives, Gut Microbiota, Carcinogens.

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PBi-83

Investigating the Relationship between Diarrhea After Kidney Transplantation: A Systematic Review Article

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Kidney transplantation is a well-established treatment for patients with chronic kidney failure. However, post-transplantation, patients may experience a variety of complications that significantly affect their quality of life. One of the most common gastrointestinal issues after kidney transplantation is diarrhea. This condition can be caused by various factors, including immunosuppressive medications, microbial infections, and disturbances in gut microbiota. Diarrhea can lead to severe dehydration, loss of essential nutrients, and impaired nutrient absorption, posing a significant health risk to kidney transplant recipients(KTRs). This article aims to investigate the relationship between diarrhea and kidney transplantation, exploring the factors that may contribute to

Methods: This article is a systematic review was written in 2024, utilizing data collected from prominent databases such as Google Scholar and PubMed. The keywords used in the search included "diarrhea," "kidney," "kidney transplantation," and "infectious diarrhea." A total of 310 articles from 2010 to 2024 were initially identified, and after applying inclusion criteria such as English language, clinical trials, and up-to-date information, 14 articles were selected for final analysis.

Results: The data analysis revealed mixed evidence regarding the relationship between diarrhea and kidney transplantation. A study conducted in 2023 on 198 KTRs over a one-year period confirmed a positive association between infectious diarrhea and kidney transplantation, primarily attributed to immunosuppressive medications such as mycophenolate mofetil(MMF). MMF is commonly used to prevent transplant rejection but may inadvertently lead to gastrointestinal disturbances, including diarrhea. In addition, a study conducted in 2015 involving ribosomal RNA gene sequencing data on the intestinal microbiota of 71 kidney transplant recipients' fecal samples found a lower frequency of metabolic genes, suggesting that diarrhea after transplantation may be linked to microbial dysbiosis, with common pathogens contributing to the condition.

Conclusion: Diarrhea after kidney transplantation can be caused by various factors, including drug-related side effects,infections, and immune suppression.Medications like mycophenolate mofetil(MMF) can disrupt the gut microbiota, increasing the risk of infections and diarrhea. Microbial imbalances(dysbiosis) also contribute to post-transplant diarrhea.This condition can lead to dehydration, electrolyte imbalances, and worsen kidney function. Managing this complication may involve adjusting or stopping immunosuppressive drugs like MMF and using probiotics to improve gut health. More large-scale studies are needed to fully understand the relationship between immunosuppressive therapy,gut microbiota, and gastrointestinal issues in kidney transplant recipients.

keywords: Diarrhea, Kidney Transplantation, Infectious Diarrhea, Mycophenolate Mofetil, Gut Microbiota

PBi-84

A cross-sectional study of clinical and demographic findings of patients hospitalized with gastric cancer in Milad Hospital, Urmia, Iran, 2019-2023.

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Gastric cancer is recognized as the most common cancer in the digestive system.The incidence of this disease is influenced by a combination of environmental and genetic factors. Various studies indicate that the incidence rate, prevalence, age of disease onset, mortality rate, and associated risk factors for gastric cancer vary across different geographical regions. In this regard, the present study examines the demographic data from the medical records of hospitalized gastric cancer patients at Milad Hospital in Urmia during the years 2019-2023 to analyze the different patterns of this disease.

Methods: For this study, ethical approval was first obtained from the Ethics Committee of the Islamic Azad University, Urmia branch. Subsequently, the records of all hospitalized patients with gastric cancer between 2019 and 2023 were reviewed and analyzed. Variables examined included age, gender, and data from pathology and laboratory reports. Additionally, if the patient's main complaint, the reason for their visit, or other useful information was available in the records, it was extracted and analyzed. The exclusion criteria for the study included records with incomplete or highly limited information.

Results: This study reveals that gastric cancer is one of the most common types of cancer in the center under investigation, with 85 hospitalized patients indicating a high frequency of this disease among those seeking medical care. The mean age of patients was 68.06 years, with an age range from 22 to 99, suggesting that while gastric cancer is more common in older adults, younger individuals are also at risk. The mean age of female patients was significantly lower than that of male patients (p 0.001), potentially reflecting biological and gender-related risk factors. The most common presenting symptoms were dyspepsia, abdominal pain, epigastric discomfort, iron deficiency anemia, weight loss, nausea, vomiting, and, in some cases, gastrointestinal bleeding. These symptoms can easily be mistaken for other gastrointestinal disorders, highlighting the importance of early and accurate diagnosis to improve treatment outcomes and enhance the patients' quality of life.

Conclusion: In conclusion, the results of this study indicate an upward trend in the incidence of gastric cancer in this region. This highlights the need for increased attention to preventive programs, early diagnosis, and the enhancement of healthcare services. Furthermore, given the rising number of cases, further research is essential to identify risk factors and develop appropriate therapeutic strategies for managing this disease.

keywords: Gastric cancer, demographic analysis, risk factors, treatment strategies

PBi-85

Endothelial Progenitor Cells as valid Stem Cell Source for Restoration of Infarcted Myocardium in Human

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Myocardial infarction (MI) is the leading cause of human mortality worldwide. In MI individuals, coronary artery is completely closed or narrowed, leading to the reduction of blood flow, and possibly of ischemic changes. During recent decades, several modalities have been used for the alleviation of aberrant myocardial remodeling via the promotion of angiogenesis and blood perfusion. Endothelial progenitor cells are putative stem cell type for the induction of de novo blood vessel formation (EPCs). Here, the eligibility of EPC application has been highlighted under cardiac tissue ischemia in preclinical and clinical setting.

Methods: Databases such as Scopus, PubMed, Web of Sciences, Google Scholar, Cochrane, ProQuest, and Embase were searched using keywords such as "Endothelial Progenitor Cells", "Myocardial Infarction", "Angiogenesis", "Human", and "Animals". The relevant studies were monitored in terms of EPC angiogenesis properties and cardiac tissue healing.

Results: Data showed that the administration of EPCs (CD34+/VEGFR-2+/Tie-2+ cells) is routinely done via systemic vein, and intracoronary routes, and direct injection into the cardiac tissue from bone marrow and peripheral blood samples. EPCs can foster the healing of infarcted MI via the promotion of angiogenesis and blood perfusion into the ischemic areas. Direct maturation into the functional endothelial cells (ECS), and release of several angiogenesis factors, such as VEGF, FGF, etc. can stimulate the orientation of other cell types toward the EC-like phenotypes. In response to ischemic changes, EPCs efficiently migrate toward the affected sites in cytokine gradient manner. Some studies have revealed the orientation of administrated EPCs into α-smooth muscle actin+ cells and cardiomyocyte-like cells. The secretion of certain factors can also diminish immune cell reactivity, and proliferation of fibroblasts, leading to reduced scar tissue formation and aberrant remodeling. The angiogenesis, and vascularization outcome differ based on the animal

Conclusion: Data show that EPCs are valid stem cell source for the induction of angiogenesis, especially in terms of MI. The increase of vascular density, reduction of fibrosis, and aberrant remolding are the main underlying mechanism promoted by EPCs at the site of injection.

keywords: Myocardial infarction; Endothelial Progenitor Cells; Angiogenesis, Cardiac Tissue Regeneration.

PBi-86

Recombinant expression of Antp-LP4-PSPHa fusion protein in E. coli for clinical applications

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Medical Biochemistry, Quality control, Trace elements

Background and aim: As, many cancer treatments have serious side effects for patients, the use of targeted alternative therapies as an effective approach to cancer treatment has attracted the attention of researchers. An alternative method is the use of antimicrobial peptides (AMPs) with anticancer properties (ACPs). ACPs are low-molecular-weight peptides with high efficacy against cancer cells. To increase the permeability of ACPs, they are accompanied by cell-penetrating peptides (CPPs), peptides with the ability to cross the cell membrane. In the present study, phylloseptin-PHa (PSPHa) as an ACP was fused to a CPP (Antp-LP4) and recombinantly expressed in BL21 (DE3) strain of E. coli.

Methods: The cDNA of the Antp-LP4-PSPHa fusion was synthesized and cloned into the pET-21a(+) expression vector. The recombinant vector was transformed into the BL21(DE3) strain of E. coli. After induction of the promoter with 1 mM IPTG, total protein was extracted with 8 M urea. Protein expression was analyzed by SDS-PAGE and dot blotting techniques. The recombinant protein was then purified by affinity chromatography (IMAC).

Results: The appearance of a 7.5 kDa band in the SDS-PAGE gel and dot blot spot indicated the production of the recombinant Antp-LP4-PSPHa fusion protein. Furthermore, the observation of a single protein band following purification, in comparison to the sample prior to purification, indicated the successful purification of the protein sample.

Conclusion: In conclusion, the fusion protein Antp-LP4-PSPHa was successfully expressed recombinantly in E. coli BL21 (DE3).

keywords: recombinant protein; AMP; CPP; E. coli

PBi-87

The effects of nanocurcumin on sperm motility genes in rats affected by testicular torsion

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Testicular torsion-detorsion occurs due to the rotation of the spermatic cord, which initially disrupts venous blood flow to the testis and later impedes arterial circulation, resulting in testicular ischemia. The presence of reactive oxygen species may induce impair cellular function and reduce sperm motility. This study investigated the protective effect of nanocurcumin on testicular torsion-detorsion injury by focusing on CatSper 1 and CatSper 2 mRNA expression levels.

Methods: Thirty-six male Sprague-Dawley rats were randomly assigned to one of six groups: (1) the healthy rats, (2) the torsion-detorsion (T/D) rats, (3 & 5) the T/D + nCur rats (50 mg/kg in group 3 and 100 mg/kg in group 5 thirty minutes before reperfusion), and (4 & 6) the T/D + nCur rats (50 mg/kg in group 4 and 100 mg/kg in group 6 continued for seven days). In order to induce testicular torsion, the left testis was rotated counterclockwise at 720 degrees. Following two hours of ischemia, detorsion was performed, and the treatment ended with an orchiectomy. Testicular levels of the CatSper 1 and CatSper 2 transcripts were assessed using quantitative (q) RT-PCR.

Results: Testicular torsion-detorsion reduced CatSper 1 and CatSper 2 expression significantly compared to the control group (p 0.05). Treatment with nanocurcumin caused an increase in CatSper 2 level (p 0.05), but not the CatSper 1 level compared to the T/D group.

Conclusion: Based on these findings, nanocurcumin decreases cellular damage in testicular tissue by regulating the expression of CatSper 2 transcripts.

keywords: Spermatic cord torsion, reperfusion injury, nanocurcumin, CatSper 1, CatSper 2

PBi-88

An Effective Therapeutic Strategy in Non-Small Cell Lung Cancer: Targeting Glutaminolysis to Disrupt the Balance of Oxidative Phosphorylation and Tricarboxylic Acid Cycle

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Lung cancer, primarily non-small cell lung cancer (NSCLC), is the leading cause of cancer-related deaths worldwide, with most patients diagnosed at advanced stages and a 5-year survival rate below 20%. Cancer cells depend on oxidative phosphorylation (OXPHOS) and aerobic glycolysis (Warburg effect) for energy. Targeting the Tricarboxylic Acid (TCA) cycle, a critical hub for cellular metabolism and OXPHOS, may inhibit tumor progression. This study aims to explore potential therapeutic strategies focused on disrupting the TCA cycle-OXPHOS feedback loop, offering a promising approach to impair cancer cell energy production and slow tumor growth, particularly in NSCLC.

Methods: An extensive literature search was conducted using PubMed and Google Scholar databases. The search included the keywords “lung cancer”, “NSCLC”, “Glutaminolysis”, “TCA” and “Clinical” in the last 5 years. Forty-five articles deemed most relevant to the topic of this study were selected for review.

Results: Recent research highlights glutamine as a critical nutrient for cancer cells, fueling key metabolic pathways such as the TCA cycle, redox homeostasis, and the synthesis of nucleic acids, fatty acids, and other macromolecules. Glutaminolysis, the conversion of glutamine to metabolites like α-ketoglutarate, supports energy production, antioxidant generation, and tumor survival. Glutaminase (GLS), a key enzyme in this process, is a promising therapeutic target, with its inhibition showing potential antitumor effects. Cancer cells exploit glutaminolysis for energy and macromolecule synthesis, adapting through metabolic reprogramming and resistance mechanisms. Key processes include α-ketoglutarate’s reductive carboxylation to citrate in the TCA cycle and its subsequent use in fatty acid and steroid synthesis. Targeting elevated glutamine transport and glutaminolysis, alongside glycolysis and oxidative phosphorylation (OXPHOS), is a potential strategy for combating tumors.

Understanding these metabolic adaptations, particularly in NSCLC, is crucial for effective cancer therapies.

Conclusion: Despite the dysregulated and altered metabolism of cancer cells, the TCA cycle is a central core of cellular metabolism in both normal and cancer cells, and making it a promising therapeutic target. Glutaminolysis, a selective pathway in cancer cells, facilitates the synthesis of TCA cycle precursors, metabolic reprogramming, and apoptosis evasion. Inhibiting glutaminolysis can disrupt TCA cycle precursor synthesis and OXPHOS, offering a potential therapeutic strategy for NSCLC.

keywords: Lung Cancer; NSCLC; Glutaminolysis; TCA; Clinical.

PBi-89

The Importance of the Potential Cooperation of Oxidative Phosphorylation and Warburg Effect in the Survival of Non-Small Cell Lung Cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: According to World Health Organization (WHO) statistics, lung cancer is the leading cause of cancer-related deaths globally, with 80‑85% of cases classified as non-small cell lung cancer (NSCLC). Cancer cells employ various strategies to sustain their survival. This study examines the interplay between energy production through oxidative phosphorylation (OXPHOS) in mitochondria and aerobic glycolysis (commonly referred to as the Warburg effect) in the cytoplasm as the primary sources of energy in NSCLC.

Methods: To review the latest advancements and research, a comprehensive search was conducted in PubMed and Google Scholar databases, covering the period from 2020 to 2024. Fifty-four articles most relevant to the topic were identified. Targeted keywords included “NSCLC”, “OXPHOS”, “Warburg Effect” and “Mitochondria”.

Results: Mitochondria play a pivotal role in regulating energy and metabolism in cancer cells. In tumors exhibiting elevated OXPHOS activity, mitochondrial respiratory capacity increases, contributing significantly to cancer cell survival. Recent therapeutic strategies have focused on targeting proteins involved in OXPHOS; however, the metabolic adaptability of cancer cells poses a considerable challenge. NSCLC tumors demonstrate a high degree of metabolic flexibility. Otto Warburg first described the phenomenon of aerobic glycolysis, noting that cancer cells exhibit high glycolytic activity even in the presence of sufficient oxygen. Most cancer cells show reduced OXPHOS activity and evidence of mitochondrial dysfunction. Furthermore, metabolic reprogramming and evasion of apoptosis are hallmark features of cancer cells, which dynamically switch between OXPHOS and aerobic glycolysis to sustain their survival.

Conclusion: Emerging evidence indicates that the synergy between glycolysis and OXPHOS drives NSCLC progression. Current therapeutic strategies focus on targeting glycolysis and OXPHOS.

However, we propose that targeting intermediate metabolic pathways bridging glycolysis and OXPHOS may represent a promising approach for NSCLC treatment.

keywords: OXPHOS; Warburg Effect; Mitochondria; NSCLC.

PBi-90

Changes in Serum Acetylcholinesterase(AChE) Levels in Alzheimer's Disease Patients: A Systematic Review Article

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Alzheimer's Disease(AD) is a prevalent neurodegenerative disorder marked by a progressive decline in cognitive functions like memory, attention, language, and executive skills. Acetylcholine, a crucial neurotransmitter in the brain's cholinergic system, is essential for cognitive functions such as learning and memory. A key pathophysiological feature of AD is the reduction of acetylcholine levels in the central nervous system. This article systematically examines changes in serum acetylcholinesterase(AChE) levels in Alzheimer's patients, analyzing statistical data from existing studies and evaluating the clinical significance of AChE in the prevention and treatment of AD.

Methods: This systematic review article was written in 2024 by searching PubMed and Google Scholar databases using the keywords Alzheimer's, Acetylcholinesterase, AChE. In the initial search, 3,029 articles were found, of which only 71 were relevant. From these, 22 articles were duplicates, 26 were published before 2020, 1 was in a language other than English, and 7 were excluded due to lack of specificity. Ultimately, 15 articles were included in the final analysis.

Results: One study found that serum AChE levels in Alzheimer's patients were 25% higher than those in the control group(p 0.001). Additionally, in the same study, patients with advanced Alzheimer's disease showed a 40% increase in AChE levels(p 0.05). On the other hand, no significant difference was observed in the changes in AChE levels at the initial and final stages of the disease(p 0.05). In another study, a significant positive correlation between serum AChE levels and Alzheimer's disease was found. A study that considered the age variable in Alzheimer's patients showed that serum AChE levels in individuals aged 65-75 were, on average, 30% higher than those in the control group.

Conclusion: The analysis of various studies suggests that serum AChE levels are typically elevated in Alzheimer's patients compared to control groups, with clinical manifestations varying based on the extent of the increase. Furthermore, AChE is of particular significance as a biomarker for assessing disease severity and evaluating responses to different pharmacological treatments. Given the increasing

prevalence of Alzheimer's disease in contemporary societies, further studies are necessary to definitively confirm the role of AChE as a biomarker.

keywords: Alzheimer's, Acetylcholinesterase, AChE

PBi-91

Methodological Pitfalls in Urine Protein Screening: Uric Acid Crystals as a Source of False-Positive Urinary Protein Detection

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Urinalysis is one of the most important and common laboratory tests. There are various parameters in urine analysis. One of the most important parameters reported in urine analysis is the presence of protein in the urine sample, which is initially performed with a urine dipstick, and the final result is confirmed with sulfosalicylic acid. We had a patient in the Reference Laboratory of the Clinical Affairs who had a positive urine protein test several times last week. During follow-up, a 24-hour urine protein test was requested for the patient. Surprisingly, the 24-hour urine protein test was completely normal for the

Methods: The patient was a 40-year-old man with a history of advanced cancer who had been referred to an oncologist for chemotherapy. During the treatment process, the doctor requested complete blood cell counts, urinalysis, and urea and creatinine tests for the patient on two occasions. Laboratory results showed that the patient had two positive urinary protein results with a decrease in blood cells. The random urinary protein results were (+2) and (+3). For more investigation, the physician requests 24-hour urinary protein. But the 24-hour urinary protein was 110 mg/24h (Reference Interval 150 mg/24h), which was inconsistent with the random urine proteins.

Results: More investigations showed that after the addition of sulfosalicylic acid to urine for protein assay, due to the decrease in urine PH, soluble urates are converted to insoluble uric acid. By examining the cloudy part of the urine under a light microscope, the presence of uric acid was confirmed. Turbidity caused by insoluble uric acids was erroneously reported as a positive urine protein result

Conclusion: Therefore, careful reporting of the results of a urine protein in patients with constant fever, gout, or chemotherapy should be done.

keywords: Urinary protein; sulfosalicylic acid; Uric Acid; chemotherapy

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PBi-92

The Relationship Between Alternative Healthy Eating Index and oxidative stress indices of Semen in Infertile Men

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The relationship between the quality of diet and the biochemical factors in semen is a topic that researchers are actively exploring. In our study, we examined the links between Alternative Healthy Eating Index (AHEI) and both seminal and serum oxidative stress indices in men who visited in infertility clinics.

Methods: This hospital-based study involved 90 men diagnosed with idiopathic infertility. Semen samples were collected and analyzed according to the World Health Organization (WHO) 2010 guidelines for semen analysis (SA). Dietary intake was evaluated using a 168-item semi-quantitative food frequency questionnaire (FFQ). To compare demographic characteristics, energy intake, and initial SA results between groups with normal and abnormal semen parameters, independent samples t-tests were employed. Additionally, one-way ANOVA with Tukey's post hoc test was utilized to explore the relationship between Alternative Healthy Eating Index (AHEI) and oxidative stress indices such as semen total antioxidant capacity (TAC), advanced glycation end products (AGEs), malondialdehyde (MDA), 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels.

Results: No significant differences were observed in serum or semen oxidative stress indices between the two groups. Additionally, there were no significant correlations between dietary AHEI and TAC levels. Notably, a significant difference in seminal AGE levels was identified across quartiles of the AHEI score ($p = 0.002$). Although not statistically significant, MDA levels in semen exhibited a trend towards being elevated in the abnormal semen group compared to the normal group (1.03 ± 0.28 vs. 0.95 ± 0.22; $P = 0.09$). Seminal plasma levels of 8-OHdG did not differ between the normal and abnormal semen groups ($p = 0.41$). A similar trend was observed in serum MDA and AGE levels across AHEI quartiles.

Conclusion: : In conclusion, our study adds to the growing body of evidence regarding the possible protection effect of a healthy diet (AHEI) on seminal AGE levels, highlighting the essential importance of maintaining a healthy dietary pattern for optimal reproductive health. Encouraging antioxidant-rich diets could be beneficial for enhancing sperm quality in infertile men.

keywords: AHEI; infertile men; Oxidative Stress; Dietary Pattern Index

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PBi-93

Urine-derived exosomes for diagnosis of bladder cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Bladder cancer(Bca) ranks fourth among cancers in men and ninth among cancers in women, making it one of the most important cancers. Cystoscopy is the gold-standard bladder cancer diagnostic technique. However, several studies demonstrate that this approach is ineffective due to its side effects. As a result, it is required to develop novel biomarkers with great efficiency. Recently, exosomes have shown promising results as noninvasive biomarkers for cancer diagnosis and monitoring. Several studies have investigated the role of exosomes derived from the urine as a diagnostic marker with appropriate sensitivity and specificity in the diagnosis of bladder cancer patients.

Methods: The current review has been achieved by using an systematic search of the scientific literature published on urine-derived exosomes and bladder cancer in multiple databases such as PubMed, ScienceDirect, Scopus, and Google Scholar

Results: The results of this study demonstrate that urine-derived exosomes may be an attractive and suitable diagnostic tool for bladder cancer.Cancer cells release a greater quantity of exosomes than normal cells, enhancing their utility as biomarkers for cancer diagnosis.The results show that these exosomes derived from the urine are promising noninvasive diagnostic methods and open new avenue in the diagnosis of bladder cancer. Thus these findings show that urine-derived exosomes might be an invaluable biomarker for diagnosing Bca.

Conclusion: Exosomes derived from urine may serve as a biomarker for bladder cancer, according to research. The increasing global incidence of bladder cancer underscores the importance of early diagnosis for the selection of effective therapeutic strategies. Consequently, the utilization of urine-derived exosomes as a non-invasive diagnostic method shows significant potential. This topic necessitates additional investigation in multiple domains.

keywords: : Bladder cancer; Urine-derived exosomes; Biomarker

PBi-94

Circular RNA for non-invasive diagnosis of bladder cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Bladder cancer ranks as the tenth most prevalent cancer globally, with incidence rates being three to four times greater in men compared to women. While many individuals with bladder cancer can benefit from a combination of surgery and intravesical or systemic therapies, a significant number are diagnosed at a more advanced stage. This often happens because there are no specific early diagnostic markers, leading to missed opportunities for timely surgical intervention. Research has shown that various circRNAs are dysregulated in bladder cancer, playing a role in tumorigenesis and progression.

Methods: This review was conducted through a systematic search of the scientific literature on circRNA for non-invasive diagnosis and bladder cancer across multiple databases, including PubMed, ScienceDirect, Scopus, and Google Scholar.

Results: This study's results indicate that circRNA could serve as a promising diagnostic marker for bladder cancer. CircRNAs' stability and tissue-specific expression make them interesting candidates for creation of biomarkers for bladder cancer detection. Their presence in bodily fluids including urine might help non-invasive diagnostic examinations. Research indicates that numerous circRNAs have distinct expression patterns in bladder cancer patients relative to healthy individuals, implying their probable application as biomarkers for early detection or prognosis.

Conclusion: The distinct characteristics of circRNAs could facilitate progress in non-invasive diagnostic methods and targeted treatments for BCa patients. Emerging evidence indicates that circRNAs serve as valuable tools for the diagnosis and prognosis of bladder cancer. Further research is needed to fully elucidate their roles and mechanisms in bladder cancer development and progression.

keywords: Bladder cancer; circRNAs; biomarker;

PBi-95

Investigating the role of mir141 in diabetic nephropathy

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetic nephropathy (DN) is a significant microvascular complication of diabetes, leading to renal dysfunction and end-stage renal disease. Diabetes mellitus is a major cause of chronic kidney disease throughout the world, involving approximately 30% of the population with type 1, and 40% of people with type 2 diabetes. Multiple pathways, including fibrosis, inflammation, and apoptosis, impact the intricate pathophysiology of diabetic neuropathy, and miRNAs are essential regulators of these processes. Targeting miR-141 represents a novel therapeutic avenue for managing diabetic nephropathy. This illustrates the potential therapeutic use of altering miR-141 levels to prevent the detrimental effects of diabetic nephropathy.

Methods: In this study, we searched related keywords in PubMed, ScienceDirect, and Google Scholar from 2014 up to 2024. The searched keywords were mir141, Diabetic nephropathy, fibrosis, inflammation, apoptosis. This investigation aims to elucidate the mechanisms by which miR-141 contributes to renal fibrosis and inflammation in DN.

Results: According to recent studies, miR-141 plays a significant role in the fibrotic processes and inflammatory responses that are typical of diabetic nephropathy. Studies have demonstrated that, in high-glucose environments, overexpression of miR-141 leads to increased inflammation and apoptosis in human glomerular mesangial cells (HGMCs) by targeting specific inflammatory pathways, including the ICAM-1 pathway. The signaling pathways affected by miR-141 includes the AKT/AMPK pathway. Overexpression of miR-141 leads to the downregulation of IRS2, which subsequently inhibits the AKT/AMPK signaling cascade. Regulation of extracellular matrix (ECM) components is critical in DN. Elevated levels of miR-141 correlate with the increased deposition of these ECM proteins, contributing to the structural changes observed in DN. MiR-141 promotes inflammation, apoptosis, (ECM) accumulation, and numerous factors that contribute to diabetic nephropathy. These contradictory results imply that the effects of miR-141 may differ depending on the particular tissue or cell type.Silencing miR-141 can improve the overall kidney structure.

Conclusion: In conclusion, miR-141 is an essential factor in the pathophysiology of diabetic nephropathy, and Taken together, miR-141 seems to promote DN pathogenesis through a variety of pathways, including fibrosis, apoptosis, and inflammation.Further investigation of its molecular functions may open the door to potential therapeutic and diagnostic methods to facilitate the efficient treatment of diabetic nephropathy. Establishing particular molecular connections involving miR-141 and exploring its potential as a therapeutic intervention target in diabetics individuals at risk of kidney-related complications should be the primary objectives of future studies.

keywords: mir141, Diabetic nephropathy, Fibrosis, Inflammation, Apoptosis.

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PBi-96

Glucose Oxidase and Nanotechnology: A Synergistic Strategy Against Cancer Metastasis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Cancer metastasis is a leading cause of cancer-related mortality, with current therapies often limited by severe side effects and non-specific targeting. Glucose oxidase (GOx) has emerged as a promising therapeutic agent, offering a dual approach to tumor control. It depletes glucose, essential for tumor growth, and generates hydrogen peroxide, which induces oxidative stress to kill cancer cells. However, clinical use of GOx is limited by poor stability, short circulation time, and systemic toxicity. Recent advances in nanotechnology have enabled the development of GOx-based nanocarriers, improving its stability, targeting, and efficacy. These innovations offer new hope in treating cancer, particularly metastasis.

Methods: GOx catalyzes the oxidation of glucose into gluconic acid and H2O2. This starves tumor cells of their energy source and triggers oxidative stress, leading to selective cancer cell death. Nanotechnology enhances GOx' s delivery and performance. Passive targeting exploits the enhanced permeability and retention (EPR) effect, concentrating GOx-loaded nanoparticles in tumor tissues. Active targeting adds ligands, such as RGD peptides or hyaluronic acid, to direct GOx to specific tumor receptors, improving precision. Synthetic GOx-mimicking nanozymes address the limitations of natural GOx by offering improved stability and scalability, ensuring more effective treatment delivery with minimal side effects.

Results: GOx-based therapies have demonstrated success in tumor control through starvation and oxidative stress. Glucose depletion disrupts tumor metabolism, while H2O2-induced oxidative stress selectively damages cancer cells. The integration of GOx into nanocarriers improves drug stability, reduces off-target effects, and ensures higher tumor accumulation. Combining GOx with chemotherapy enhances cancer cell sensitivity to treatment, creating synergistic effects. Additionally, GOx-generated ROS has been effectively integrated with photodynamic, chemodynamic, and sonodynamic therapies, amplifying treatment outcomes. These results highlight the potential of GOx as a key component in multi-modal cancer therapy.

Conclusion: GOx holds significant promise in combating cancer, particularly metastasis, through its glucose-depleting and ROS-generating effects. Nanotechnology has transformed GOx into a more stable, targeted, and effective therapeutic tool. Challenges such as biocompatibility, immune response, and delivery efficiency must still be addressed. Future research should focus on enhancing GOx-mimicking nanozymes and exploring its integration with other therapies to maximize its clinical potential. GOx-based systems represent a promising step toward more precise, multi-modal cancer treatments.

keywords: Glucose Oxidase, Nano carriers, Cancer Metastasis

PBi-97

"Clinical Significance of YKL-40 as a Biomarker in Rheumatoid Arthritis: Diagnostic, Prognostic, and Therapeutic Perspectives"

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease characterized by joint inflammation, systemic involvement, and varying degrees of disease severity. Traditional biomarkers such as rheumatoid factor (RF) and anti-citrullinated peptide antibodies (anti-CCP) provide valuable diagnostic information but have limitations regarding sensitivity, specificity, and ability to predict disease progression accurately. YKL-40, a chitinase-like glycoprotein, has emerged as a promising biomarker due to its involvement in key processes such as inflammation, tissue remodeling, and angiogenesis. This review evaluates YKL-40's role in RA, focusing on its diagnostic, prognostic, and therapeutic potential, comparing it with established biomarkers, and exploring clinical applications.

Methods: A comprehensive narrative review was conducted, synthesizing evidence from peer-reviewed articles, clinical studies, and systematic reviews published between 2010 and 2024. Databases such as PubMed, Scopus, and Web of Science were searched using keywords including "YKL-40," "Rheumatoid Arthritis," "biomarker comparison," and "therapeutic potential." Special emphasis was placed on studies addressing cost-effectiveness, assay standardization, and the role of YKL-40 in stratifying disease subtypes.

Results: YKL-40 demonstrated superior predictive value, particularly when predicting compared to conventional biomarkers like CRP and ESR, particularly in predicting radiographic progression and therapeutic outcomes. Unlike RF and anti-CCP, YKL-40 levels correlate directly with synovial inflammation and joint destruction, offering real-time insights into disease activity. YKL-40 also serves as a marker of systemic inflammation, linking RA with comorbidities such as cardiovascular disease, which is a known complication in RA patients. Mechanistically, YKL-40 has been shown to enhance VEGF-mediated angiogenesis and activate matrix metalloproteinases, thereby worsening synovial destruction and joint damage. From a therapeutic perspective, targeting YKL-40 pathways has shown promise in improving response rates in biologic-resistant patients, although large-scale, randomized clinical trials are required for validation. Cost-effectiveness analyses indicate that combining YKL-40 with conventional biomarkers can significantly improve diagnostic accuracy while maintaining healthcare cost efficiency.

Conclusion: This review highlights the significance of YKL-40 as a biomarker that bridges gaps in RA diagnosis, prognosis, and treatment. Incorporating YKL-40 into routine clinical practice could revolutionize patient management by facilitating precision medicine strategies. Future research should

focus on the standardization of assays, validation across diverse patient populations, and the integration of YKL-40 with advanced imaging techniques for a comprehensive and accurate disease assessment. Additionally, long-term studies assessing the cost-effectiveness of Integrating YKL-40 into clinical decision-making are essential to validate its broader use.

keywords: YKL-40; Rheumatoid Arthritis; biomarker comparison; therapeutic potential; Inflammation

PBi-98

The effects of statins on laboratory biomarkers of renal function: a systematic review and meta-analysis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Statins are medications widely used to reduce the risk of cardiovascular diseases (CVDs) due to their anti-inflammatory and antioxidant effects. However, the impact of these drugs on renal function remains a topic of debate. The current study investigated the effects of statin treatment on various indicators of renal function.

Methods: A comprehensive search of the PubMed, MeSH, Scapus, and Google Scholar databases was conducted to identify studies assessing the effects of statin treatment on various indicators of renal function, including serum creatinine, estimated glomerular filtration rate (eGFR), and urinary protein excretion. Keywords atorvastatin, rosuvastatin, simvastatin, pravastatin, creatinine, eGFR, “urinary protein excretion”, kidney, and renal were used. Meta-analysis was performed using a random-effects model to calculate weighted mean differences (WMD), odds ratios (ORs), 95% confidence intervals (95% CI), and p-values.

Results: A total of 25 studies involving 10,300 participants were included in this meta-analysis. Renal patients used atorvastatin, simvastatin, rosuvastatin, and pravastatin. Statin therapy significantly reduced serum creatinine levels (OR: 0.82, 95% CI: 0.67 to 0.96; p 0.001) and demonstrated a significant increase in eGFR (OR: 1.32, 95% CI: 1.04 to 1.62; p 0.001). Furthermore, the use of statins was associated with a significant decrease in urinary protein excretion (OR: 0.78, 95% CI: 0.65 to 0.92; p 0.001).

Conclusion: This systematic review and meta-analysis suggest that statin therapy may have a positive effect on kidney function, as evidenced by improvements in serum creatinine, eGFR, and urinary protein excretion. These findings have significant implications for the management of cardiovascular and renal diseases. However, more research is needed to confirm these results and investigate the long-term effects of statin use on kidney function.

keywords: Statins, creatinine, eGFR, "urinary protein"

PBi-99

The Effect of the herbal compound on glucose homeostasis and inflammatory markers in patients with Non-alcoholic fatty liver disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Nonalcoholic fatty liver disease (NAFLD) is characterized by fat buildup in liver cells, leading to steatosis. Inflammation and cytokine production worsen the condition, potentially causing fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Despite available treatments, NAFLD incidence is rising. Meanwhile, the use of herbal compounds to manage the disease and prevent complications is growing. This study evaluated a herbal compound containing extracts of Silybum marianum, Cynara scolymus, Curcuma longa, and Taraxacum officinale for its effects on inflammatory markers and glucose homeostasis in NAFLD patients

Methods: Sixty patients with NAFLD were randomly assigned to two equal groups: an intervention group (n=30) and a comparison group (n=30), using a block-balanced randomization technique. The intervention group received 275 mg capsules containing the extract, while the comparison group was given placebo capsules of the same dose. Both types of capsules were identical in shape and appearance to ensure blinding. The intervention lasted for 12 weeks. Blood samples were collected from participants before and after the intervention, and serum was separated for the measurement and analysis of markers using standard laboratory methods.

Results: The herbal compound had a statistically significant effect on the level of fasting blood sugar (FBS) and Tumor necrosis factor alpha (TNF-α). The compound had no side effects in participant

Conclusion: This clinical trial demonstrated that three months of consuming the herbal compound produced clinically significant effects on fasting blood sugar (FBS), a marker of glucose homeostasis, and TNF-α, a marker of liver inflammation

keywords: NAFLD, Glucose homeostasis, Inflammatory liver markers, New Herbal compound

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PBi-100

miR-106b-5p as a Diagnostic Biomarker for Coronary Artery Disease: Insights from Gene Expression and Clinical Correlation Analysis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Coronary artery disease (CAD) is one of the leading causes of mortality throughout the world. This continues to create serious diagnostic and healthcare challenges. Early detection is critical to maximizing outcomes; however, conventional biomarkers and diagnostic methods suffer from limited sensitivity and specificity. MicroRNAs, small non-coding RNA molecules that regulate gene expression, have emerged as potential candidates in CAD diagnosis owing to their stability and disease-restricted expression signatures. Hence, the objectives of this study were to predict and structurally validate specific upregulated miRNAs in the CAD patients as potential diagnostic biomarkers.

Methods: This was a case-control study where gene expression analysis was done from the GEO database (GSE113079). It included 141 peripheral blood samples from 93 CAD patients and 48 controls. Differentially expressed mRNAs (DEmRNAs) were obtained using the Limma package in R, using a log2 fold change of $\geq |1|$ and a p-value of 0.05. MiRNA-mRNA interactions were predicted using the miRNet database, focusing on miRNAs interacting with the top 50 downregulated mRNAs. Five candidate miRNAs (miR-106b-5p, miR-146a-5p, miR-17-3p, miR-20a-3p, and miR-155-3p) were tested in 44 serum samples from CAD patients and 48 samples from healthy controls by qRT-PCR to detect their potential for diagnosis. ROC curves and area under the curve (AUC) were used to determine the diagnostic performance. The association of anthropometric and clinical variables, including LDL-c, BMI, and smoking status, with miRNA expression levels was analyzed.

Results: Out of the five miRNAs, only miR-106b-5p was significantly expressed higher in CAD patients than in controls (p 0.001). After conducting an ROC analysis, this indicated a high diagnostic accuracy of miR-106b-5p with an AUC of 0.8975, a sensitivity of 70%, and a specificity of 95%. A correlation analysis showed significant associations of the levels of miR-106b-5p with the risk factors for CAD, including LDL-c ($r = -0.532$, $p = 0.023$) in controls and BMI ($r = -0.463$, $p = 0.015$) in CAD patients. Gene enrichment analysis showed that miR-106b-5p targets were enriched in pathways such as thrombin activation, apoptosis, and regulation of blood circulation, indicating its potential role in CAD pathophysiology.

Conclusion: miR-106b-5p is an attractive non-invasive candidate for CAD biomarkers because it has great sensitivity and specificity for its diagnosis. It has been observed that its higher expression correlates with risk factors and pathways for CAD disease progression, such as thrombin-mediated

inflammation and dysfunction of blood vessels. These results further underscore the clinical utility of miR-106b-5p in improving the early detection of CAD. However, larger, well-designed studies must be conducted to corroborate these results and study the molecular mechanism of action by which miR-106b-5p affects the development of CAD.

keywords: Coronary artery disease, Micro RNA, miRNA-mRNA interaction, qRT-PCR, Diagnostic biomarker

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PBi-101

Effect of a modified Flutamide drug on the viability of the murine colon carcinoma cell line (CT26)

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Colon cancer is known to be the third most common cancer and the fourth leading cause of death in the world. The organic chemistry research team of Bu-Ali Sina University has synthesised Flutamide with a sulfonamide functional group which can improve the effect of the existing drug. In this study, the survival rate of mouse colon carcinoma cell line (CT26) treated with flutamide and modified flutamide is evaluated.

Methods: Cancer cells survival were determined using the MTT assay. CT26 cells cultured in 96-well plates and incubated with the drugs in concentrations of 20, 40, 60, 80, and 100 μ M for 24 hours in 37° C and 5% CO2.

Results: The IC50 of the Flutamide was 2.87 μ M and that of the modified drug was 35.27 μ M after 24 hours of incubation. The anticancer effect of the modified Flutamide drug was lower than that of existing drug.

Conclusion: The Flutamide drug has an acceptable anticancer effect against colon carcinoma, while the addition of the functional sulfonamide group has reduced the anticancer effect of the Flutamide. One of the reasons for this reduction may be the chemical and spatial change of the reason for adding this group is the factor that has affected the biochemical activity of this drug.

keywords: Colon carcinoma; Modified Flutamide; Anticancer

PBi-102

Investigating STING Pathway Crosstalk with Other Inflammatory Pathways in Alzheimer's Disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Alzheimer's disease (AD) is characterized by chronic neuroinflammation, which is driven by the activation of multiple innate immune pathways, including the cGAS-STING pathway, Toll-like receptor 4 (TLR4) signaling, and NLRP3 inflammasomes. A β and tau pathologies induce mitochondrial stress, cytoplasmic DNA accumulation, and lysosomal dysfunction, all of which can activate these pathways. While the interactions among these pathways fully understood, they are believed to exacerbate microglial dysfunction, neurotoxicity, and synaptic loss in AD.

Methods: A comprehensive literature review was performed using databases such as PubMed, Scopus, and Web of Science. This review synthesize evidence from experimental studies investigating the activation and interplay between the cGAS-STING pathway and other inflammatory cascades, particularly TLR4 and NLRP3 inflammasomes. Data from in vitro models of microglial stimulation and in vivo studies using AD mouse models, such as AppNL-G-F/hTau, were analyzed. Special emphasis was placed on mechanistic insights into mitochondrial DNA release, cGAMP production, and lysosomal degradation.

Results: Research findings indicate that cGAS-STING activation by Aβ and tau triggers proinflammatory responses and type-I interferon signaling, which overlap with TLR4 and NLRP3 inflammasome pathways. TLR4 signaling upstream of NF-κB amplifies STING-induced inflammation, while NLRP3 inflammasome activation downstream of STING contributes to IL-1β release and neurotoxicity. Mitochondrial dysfunction and impaired autophagy were identified as shared mechanisms linking these pathways, suggesting a feed-forward loop that intensifies AD pathology.

Conclusion: The crosstalk between the cGAS-STING pathway, TLR4 signaling, and NLRP3 inflammasomes is a critical driver of neuroinflammation in AD. Targeting these interconnected pathways presents a promising strategy for mitigating neuroinflammation and synaptic dysfunction. Future research should prioritize disentangling the specific contributions of each pathway exploring combination therapies that can disrupt this inflammatory network effectively.

keywords: cGAS-STING pathway, Neuroinflammation, Alzheimer's disease, TLR4 signaling, NLRP3 inflammasome

PBi-103

Synergistic effects of PD-1 and Anti-HER2 Combination therapies using Bispecific Antibodies in HER2-positive Breast Cancer: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: HER2-positive breast cancer is associated with overexpression of Human epidermal growth factor receptor 2(HER2); which leads to faster tumor growth. Programmed Cell Death Protein 1(PD-1) inhibitors stimulate immune responses against tumor cells, but are generally less effective as a single therapy in solid tumors. In this systematic review we examine the synergistic effects of PD-1 and Anti-HER2 combination therapies using bispecific antibodies in HER2-positive Breast cancer.

Methods: This review article was conducted by searching for relevant publications on PubMed, Science Direct, Google Scholar, and Web of Science up to November 2024. The search terms used were HER2-positive breast cancer, Immune Checkpoint inhibitor, Anti-HER2, Bispecific antibody and Combination therapy. A total of 81 articles were initially identified, with 45 articles excluded based on title and abstract review. Ultimately, 36 articles meeting the inclusion criteria were selected, all of which were in English.

Results: In this review, 36 articles were reviewed, which showed that bivalent antibodies (BsAb) played a key role in the physical binding of T cells to tumor cells and increased their antitumor activity more effectively. BsAb provided potent therapy against PD-1 and HER2 blockers that significantly inhibited tumor growth and were as effective as the parental monoclonal antibodies. Also, in the human PBMC transplantation model, BsAb inhibited tumor growth and showed dual targeting properties similar to monoclonal antibody combination therapy and demonstrated no obvious toxicity during treatment. These results indicated a promising therapeutic mechanism for HER2-positive breast cancer, with the hope of improving efficacy through the combination of tumor and immune targeting.

Conclusion: It appears that synergistic effects of using the bispecific antibody alongside anti-HER2 therapies and checkpoint inhibitors such as PD1 in HER2-positive breast cancer has enhanced anti-tumor immunity and improving patient outcomes. However, more research is needed to be done on this topic.

keywords: Immune Checkpoint Inhibitors; Anti-HER2; Bispecific antibody; Combination therapy; HER2-positive breast

PBi-104

Sirtuin-1 in Behçets Disease: Mechanisms, Efficacy, and Challenges

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Behçet's disease (BD) is a chronic, relapsing, autoinflammatory disorder that impacts blood vessels of all types and sizes in various tissues and organ systems and is characterized by arthritis, intraocular inflammation, skin lesions, genital ulcers, and mouth ulcers. Sirtuin 1 (SIRT1) is the most studied member of the Sirtuin family and a nicotinamide adenine dinucleotide (NAD)-dependent histone deacetylase that is involved in diverse physiological processes such as glucose metabolism, oxidative stress, inflammation, tumorigenesis, DNA stability, and aging. Studies suggest that SIRT1 may affect various critical pathways in BD. This review aims to evaluate the potential role of SIRT1 in Behçet's.

Methods: From 2000 to 2024, we searched the keywords SIRT1 and Behçet's disease in several databases, including PubMed, Google Scholar and Scopus.

Results: SIRT1 inhibits NF-κB signaling, diminishing pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, which are increased in BD.Additionally, SIRT1 decreases oxidative stress by upregulating antioxidant enzymes like superoxide dismutase (SOD) and catalase while promoting mitochondrial biogenesis. Initial research indicates that SIRT1 activators, such as resveratrol, may reduce inflammation and oxidative stress in BD.

Conclusion: SIRT1 has antioxidant and anti-inflammatory functions in Behçet's disease, so increasing SIRT1 activity may be a promising strategy for treating BD, although further research is needed to confirm these benefits in clinical practice.

keywords: Sirtuin-1; Behçet’ s Disease; Inflammation; Oxidative Stress; Therapeutics

PBi-105

Integrating Acupuncture into Female Infertility Management

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Infertility, defined as the inability to conceive after 12 months of unprotected sexual intercourse, affects 8 to 12% of couples globally, with female infertility contributing to approximately 15% of cases. The causes of female infertility range from organic disorders such as ovulatory dysfunction, tubal diseases, and endometriosis, to lifestyle factors such as stress, obesity, and smoking. Conventional treatments can be invasive and financially burdensome. The emotional burden often drives couples to explore alternative therapies. Acupuncture has gained attention as a potential complementary treatment for infertility, and this study examines its role in managing female infertility.

Methods: Following Cochrane systematic review principles and PRISMA guidelines, a comprehensive search was conducted across databases including PubMed, Scopus, Web of Science, and Google Scholar for grey literature. Keywords used included “Acupuncture”, “Female Infertility”, “Infertility in women”, “Reproductive Health”. All reviews, interventional studies, animal studies, letters to editors, and book chapters were excluded. The quality of included studies was assessed using the Newcastle-Ottawa scale, and data were organized into an extraction table.

Results: The findings suggest that acupuncture positively influences female fertility by modulating neuroendocrine signaling and enhancing immune function. It improves blood circulation and optimizes the endometrial environment, which is critical for successful embryo implantation. Furthermore, acupuncture reduces stress and anxiety, providing psychological benefits to individuals undergoing infertility treatment. At the molecular level, acupuncture affects several key genes in the hypothalamic-pituitary-ovarian (HPO) axis. Specifically, acupuncture reduces the levels of nerve growth factor (NGF) and corticotropin-releasing factor (CRF), thereby improving the ovarian environment, while it also lowers endothelin-1 (ET-1) to promote better blood flow to the reproductive organs. Acupuncture further supports follicular development by increasing the expression of BCL2 (cell survival) and decreasing BAX (apoptosis). Additionally, acupuncture strengthens immune resistance, promotes angiogenesis, and supports embryonic development by raising insulin-like growth factor 1 (IGF1) levels after implantation.

Conclusion: Acupuncture is an effective treatment for female infertility, providing both physiological and psychological benefits. It works by modulating key pathways and improving the overall reproductive environment, making it a valuable adjunctive therapy for women struggling with infertility.

keywords: Acupuncture, Female Infertility, Infertility in women, Reproductive Health.

PBi-106

Randomized controlled study of nano-micellar curcumin effect in patients with benign prostatic hyperplasia

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Benign Prostatic Hyperplasia (BPH) is the chief prevalent disorder in men over forty years, usually manifesting itself with lower urinary tract symptoms. In spite of the existence of different treatments, the incidence of BPH is increasing, so further studies for better management of it is a necessity. This research was designed to assay the effectiveness of nano-micellar curcumin on biomedical indicators of patients with BPH were investigated in this trial.

Methods: The present research was a double-blind, randomized controlled trial that enrolled 52 patients with BPH. Participants were randomized to receive 160 mg/d nano-micellar curcumin (n = 26) or placebo (n = 26) as soft gel during 3 months. Primary end-point was changes in international prostate symptoms score (IPSS) score. Data gathering was occurred using a standard inquiry form and measuring other biomedical parameters based on routine laboratory techniques.

Results: Nano-micellar curcumin had significant and intermediate effect on IPSS score. Small effect on high sensitive C-reactive protein (hs-CRP), small to intermediate effect on malondialdehyde (MDA) level as secondary end-points have be observed after the intervention. The effect size of nano-micellar curcumin on other parameters were overally negligible.

Conclusion: Overally, this trial indicated 12 weeks intake of nano-micellar curcumin had considerable effects on IPSS as the most common clinical symptom and also two biomedical parameters including serum hs-CRP and MDA. this effectiveness on other studied parameters was negligible.

keywords: Curcumin soft gel, Inflammatory markers, Oxidative stress, International Prostate Symptom

PBi-107

IL-1β Can Mediate the Effects of Free Fatty Acids on Pulmonary Function In Male COPD Patients

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Chronic obstructive pulmonary disease (COPD) is a long-term condition marked by a gradual decline in lung function caused by airflow limitation, primarily driven by inflammation associated with IL-1 β . Inflammation and oxidative stress play a pivotal role in COPD pathogenesis. Elevated FFA levels can contribute to systemic inflammation, which may further impair lung function. Free fatty acids (FFA) as signaling molecules through a series of G-proteins coupled receptors, play an important role in regulation of the immune system and oxidative stress. For this reason, we decided to investigate the profile of FFA and IL-1 β in the plasma in the COPD patients.

Methods: This is a case-control study comparing 40 male patients with COPD and 40 healthy controls. Respiratory system function was evaluated using spirometry and FEV1/FVC ratio lower than 70% were considered as patients. Malondialdehyde was measured by TBA, Total Antioxidant capacity by FRAP, IL1 β concentration in plasma was measured by ELISA, and the concentration of free fatty acids were measured by gas chromatography after separation of free fatty acids by TLC. Then the difference of IL-1B between the two groups under study was determined by Mann-Whitney U test and its relationship with fatty acids, functional status and oxidative stress markers was determined by Spearman's test.

Results: IL-1 β concentration in COPD patients (148.9±22.1 pg/ml) was significantly (P 0.0001) higher than the control group (39.4±2.78 pg/ml). Also, there was a positive correlation between Total free fatty acids, long chain free Fatty acids with IL-1 β concentration. However, the relationship between FEV1 and IL-1 β was negative.

Conclusion: Considering the positive relationship between the concentration of long-chain FFA and the increase in the concentration of IL-1 β , we concluded that part of the relationship between the concentration of free long-chain fatty acids and lung function can mediated through IL-1B.

keywords: COPD, Inflammation, IL-1 β , Oxidative stress, Free Fatty Acids

PBi-108

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Molecular Docking as a novel therapeutic technique for Ocular Diseases: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Molecular docking, as a tool in drug discovery, plays a crucial role in enabling the prediction of ligand-target interactions and binding conformations. It is a computational technique that provides insight into basic biological processes through the characterization of small molecules inside protein binding sites. The application of docking in virtual screening and drug repurposing relies on algorithms mimicking the dynamics of ligand-receptor interactions and scoring functions assessing binding affinities. The aim of this review is to study recent advances in molecular docking for the treating of complicated diseases like ocular diseases.

Methods: This review article was performed within articles published at PubMed, Science Direct and Google Scholar until Nov 2024. The Keywords were Molecular docking; Eye diseases; Ocular diseases; Retinal diseases. By searching this databases, 52 articles were found, and 41 were removed by reading titles and abstracts. Under the inclusion criteria, 11 articles were selected. All articles were chosen from English articles.

Results: Molecular docking has provided great insight into the various therapeutic features of drugs meant for ocular diseases. Rhodiola rosea, containing Salidroside, targets SIRT1, NRF2, and NOS3, demonstrated its ability to reduce oxidative stress and apoptosis in retinal ganglion cells. The multitarget mechanism of Qiju Dihuang Pill was verified by stable binding affinities (-5.7 to -9.3 kcal/mol) of its active compounds with core targets such as TNF, JUN, and PI3K3C in Dry Eye Disease. Jin-Gui-Shen-Qi Wan exhibited anti-inflammatory benefits in diabetic retinopathy via the Akt/HIF-1 α pathway. Quercetin and Kaempferol displayed significant binding to VEGFA and IL-6, showed potential in retinal vein occlusion. Docking also revealed that Berberine is effective for dry eye treatment via the PI3K/AKT and MAPK pathways. Furthermore, peptide H-KI20 demonstrated anti-angiogenic activity in neovascular eye disorders through direct interaction with JNK2. These findings highlighted the vital role of molecular docking in drug discovery advancements for eye diseases.

Conclusion: Finally, molecular docking has a significant role in identifying therapeutic strategies for ocular conditions and drug development, offering cost-effective and efficient methods. The disadvantages involve problems concerning protein flexibility, inferior scoring systems, and database inaccuracies, making it useful only as an in-silico method for studying interactions between drugs and targets. Improving docking algorithms enhances its power, and their combination with other computational methods amplifies its usefulness. However, further experimental validation is needed on this topic.

keywords: Molecular docking, Ocular diseases, Dry eye-disease, Diabetic retinopathy, Neovascular eye-diseases

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PBi-109

Lipid Markers and Coronary Artery Calcification

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Coronary artery disease (CAD) is considered as one of the developing illness which is responsible for mass mortality. Coronary artery calcification (CAC) would be defined by mineral calcification in arteries leading to formation of plaque and is extensively recognized as a detector for arthrosclerosis leading to CVD prevalence. Accordingly, finding a possible correlation between lipid profile and CAC would provide early diagnosing of CVD among individuals.

Methods: This review comprehensively searched four databases comprising of PubMed, Scopus, and Web of Science. We identified human studies investigating the correlation between CAC and lipid markers including HDL, LDL, total cholesterol (TC), triglyceride (TG) and lipoprotein (a) (Lp(a)).

Results: The majority of studies were conducted in America and several studies recruiting the population from Asia and Europe. Evaluating the association between lipid markers including HDL, LDL, TC, TG, Lp(a) and CAC burden presented contradictory results. Predominantly, up to 64% of CAC incidence could be prevented by elevated level of HDL. Lp(a)≥50 mg was reported as a contributing factor for abnormal coronary artery calcium score from 33% to 67%. It was demonstrated that high level of LDL could increase the probability of CAC burden from 27 % to more than 2 times more than standard level of LDL. As reported, about 20% of CAC prevalence is associated with the elevated level of TG. Likewise, in a large population-based cohort, 17% of CAC incidence happened following TC elevated level among the middle aged subjects.

Conclusion: In conclusion, CVD is a chronic morbidity and is contributed to high mortality rate among individuals. Since CAC is a significant marker for plaque formation and arteriosclerosis leading to CVD, finding a rational association between lipid markers and CAC will be a helpful way for identifying the subjects exposed to the risk of CVD. In line with these findings, lipid markers could serve as potential indicators in detecting CAC, thereby potentially reducing the incidence of CVD among patients.

keywords: Coronary artery calcification; Lipid markers; HDL; LDL, Cholesterol

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PBi-110

Investigating the relationship between laboratory markers of renal evaluation and CT angiography data in male patients with atherosclerosis in Kerman city

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Atherosclerosis is the most important cause of cardiovascular diseases. The formation of atherosclerotic plaque is the result of a complex process involving various blood parameters, inflammatory pathways, oxidative stress, etc. Rupture of the atherosclerotic plaque can stimulate platelet aggregation and atherothrombosis, which ultimately leads to acute myocardial infarction. CT angiography predicts this risk by determining the size of the plaque and its degree of calcification. In this study, we investigated the effect of laboratory parameters of renal function on CT angiography data including CAD risk, plaque volume and calcium score.

Methods: Blood samples in tubes containing EDTA were taken from 113 patients referred to the CT angiography center. Based on the calcium score, the participants in the study were divided into two CAD and control groups. Then the concentrations of urea, creatinine and uric acid were measured by autoanalyzer. The amount of eGFR was also calculated by the formula. The difference of this markers between the groups was determined by the Mann-Whitney test and their relationship with the CT angiography data by the Spearman test

Results: Urea concentration in the patient (30.4±1.2 mg/dl) was significantly higher than the control group (25.7±0.9 mg/dl) (P=0.004). Uric acid patient group (3.78±0.17 mg/dl) showed a significant difference with the control group (4.8±0.17 mg/dl) (P0.0001). Creatinine concentration showed no difference between two groups, but eGFR value showed a significant difference in both healthy and sick groups, and it was found that the risk of CAD and the volume of atherosclerotic plaques are related to eGFR.

Conclusion: The results of this study showed that the concentration of urea and uric acid is related to the risk of cardiovascular diseases and also that eGFR is a more suitable factor than creatinine to evaluate the risk of CAD in atherosclerotic patients due to the influence of factors such as age, sex and weight of patients on eGFR calculation.

keywords: Atherosclerosis; eGFR; Creatinine; CAD risk

PBi-111

The effects of pioglitazone and rosiglitazone on liver function in hypothyroid rats

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Medical Biochemistry, Quality control, Trace elements

Background and aim: This study aimed to investigate the antioxidant effect of rosiglitazone (ROG) and pioglitazone (POG) on oxidative damage and dysfunction of hepatic tissue in hypothyroid rats.

Methods: The male rats were classified into six groups: (1) Control; (2) Hypothyroid, (3) Hypothyroid-POG 10, (4) Hypothyroid-POG 20, (5) Hypothyroid-ROG 2, and (6) Hypothyroid-ROG 4. To induction hypothyroidism in rats, propylthiouracil (PTU) (0.05 %w/v) was added to drinking water. In groups 2-6, besides PTU, the rats were also intraperitoneal administrated with 10 or 20 mg/kg POG or 2 or 4 mg/kg ROG for six weeks. Finally, after deep anesthesia, the blood was collected to measure the serum biochemical markers and hepatic tissue was separated for biochemical oxidative stress markers.

Results: Administration of PTU significantly reduced serum thyroxin concentration, total thiol levels, activity of superoxide dismutase (SOD) and catalase (CAT) enzymes, and increased serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (Alk-P) and malondialdehyde (MDA) in the liver. Additionally, our results showed that prescription of POG or ROG for six weeks to hypothyroid rats resulted in an improvement in liver dysfunction (decrease in serum levels of AST, ALT, and ALK-P) through reducing oxidative damage in hepatic tissue (increase in CAT, SOD, or total thiols and decrease in MDA levels).

Conclusion: The findings of the present study presented that the IP administration of POG and ROG for six weeks improves liver dysfunction induced by hypothyroidism in juvenile rats by reducing oxidative damage.

keywords: hypothyroidism; liver; pioglitazone; rosiglitazone

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PBi-112

Blood-Based Biomarkers for Early Detection and Monitoring of Ovarian Cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Background and Aim: Ovarian cancer is a highly aggressive malignancy with a poor prognosis due to late-stage diagnosis. Early detection is crucial to improving survival outcomes, yet current diagnostic methods, such as imaging and biopsy, are limited in identifying early-stage disease. Recent advancements in blood-based biomarkers have shown promise for non-invasive early detection and monitoring of ovarian cancer.

Methods: Methods: Ovarian cancer is a highly aggressive malignancy with a poor prognosis due to late-stage diagnosis. Early detection is crucial to improving survival outcomes, yet current diagnostic methods, such as imaging and biopsy, are limited in identifying early-stage disease. Recent advancements in blood-based biomarkers have shown promise for non-invasive early detection and monitoring of ovarian cancer.

Results: Results: · CA-125 is the most commonly used biomarker for ovarian cancer but has limited sensitivity for early-stage detection. · HE4, particularly when combined with CA-125 in the Risk of Ovarian Malignancy Algorithm (ROMA), improves diagnostic accuracy, especially in postmenopausal women. · Circulating tumor DNA (ctDNA) can detect genetic mutations like BRCA1/2 and TP53, offering early detection and monitoring of disease progression. · MicroRNAs (miR-200a, miR-34a) have potential as early diagnostic and prognostic biomarkers due to their role in regulating tumor growth and metastasis. · Exosomal proteins and metabolomic profiles are emerging as novel biomarker platforms, offering insights into tumor behavior and metastatic potential.

Conclusion: Conclusion: Blood-based biomarkers, including CA-125, HE4, ctDNA, miRNAs, and exosomal proteins, significantly improve early detection and monitoring of ovarian cancer. Combining these biomarkers offers a more sensitive and specific diagnostic approach, enabling personalized treatment strategies.

keywords: Ovarian cancer, CA-125, HE4, ctDNA, miR-200a, blood biomarkers, early detection

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PBi-113

MAFLD vs NAFLD

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Medical Biochemistry, Quality control, Trace elements

Background and aim: According to published guidelines, diagnosing NAFLD requires 5% hepatic steatosis and the absence of other liver diseases, including exclusion of "significant" alcohol consumption. In 2020, a new term, MAFLD, was introduced to address the limitations of the previous terminology for fatty liver disease. To diagnose MAFLD, a person must have fatty liver and at least one of the following: type 2 diabetes, obesity, or metabolic dysregulation. Metabolic dysregulation is defined by the presence of at least two of the following conditions: high waist circumference, high blood pressure, high triglycerides, low HDL cholesterol, prediabetes, insulin resistance, or elevated C-reactive protein levels.

Methods: We used PubMed for searching related articles. The search strategy was: “NAFLD” AND “MAFLD”.

Results: Findings demonstrated that MAFLD showed significantly higher levels of alanine aminotransferase, NAFLD fibrosis score, and fibrosis-4 (FIB-4) scores when compared to NAFLD. This suggests that MAFLD more effectively identifies patients with poorer liver function and higher non-invasive scores. These differences were even more pronounced when comparing MAFLD to NAFLD patients without the metabolic risk factors required for an MAFLD diagnosis. In a 2021 study the MAFLD criteria identified a substantial group of individuals with more comorbidities and a poorer prognosis compared to those with only NAFLD. These criteria should be applied broadly within the population to help identify high-risk groups for early intervention. MAFLD is more practical and accurate than NAFLD, allowing for the identification of more high-risk fatty liver patients. Over a 25-year population cohort study, the prevalence of HCC linked to NAFLD and MAFLD rose considerably, contributing to a higher incidence of HCC, especially among women.

Conclusion: As global obesity rates increase, the prevalence of fatty liver disease is expected to rise significantly. However, the proposed name change and definition for fatty liver disease could potentially overlook a significant portion of patients. The meta-analysis revealed distinct differences between MAFLD and NAFLD, with approximately 20% of patients not fitting the new definition. While MAFLD aims to better characterize the disease, it has yet to be officially endorsed by major liver disease organizations.

keywords: NAFLD; MAFLD; Alcohol consumption; Hepatic steatosis.

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PBi-114

Investigating the use of drug loaded albumin nanoparticles, in cancer treatment by inducing apoptosis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: In spite of advancements, in cancer diagnosis and treatment the worldwide occurrence of it continues to be substantial. Treating cancer comes with obstacles such as resistance to treatment options, tumor heterogenicity along with the side effects and drug delivery limitations. Therefore, it is essential to develop new methods for treating cancer. Advancements in drug delivery using nanotechnology such as Albumin nanoparticles have emerged as a more efficient method for treating cancer with fewer adverse effects. Albumin nanoparticles are widely used to overcome treatment resistance and combination therapy with more than one drug due to their unique properties including biocompatibility, biodegradability,

Methods: A comprehensive literature search was conducted through medical electronic databases to identify studies examining the impact of drug loaded albumin nanoparticles treatment on different cancers. In vitro experiments using different cancers cell lines and animal models were included.

Results: Functionalization of drug loaded albumin nanoparticles with ligands such as folic acid or hyaluronic acid allows these nanoparticles to bind specifically to receptors overexpressed on certain cancer cells, such as CD44 or folate receptors, thereby enhancing drug uptake by the cell. Albumin nanoparticles can significantly upregulate proapoptotic proteins such as Bax and downregulate antiapoptotic proteins such as Bcl-2 in some types of cancers. These changes contribute to apoptosis by increasing mitochondrial membrane permeability, releasing cytochrome c, and activating downstream caspases. The treatment with albumin nanoparticles has been associated with increased levels of cleaved caspases (caspase 9 and 7) and PARP cleavage, indicating that these nanoparticles effectively trigger the apoptotic machinery within cells. In addition, studies have indicated that drug-loaded albumin nanoparticles exhibit a slower release rate compared to free drugs, which allows prolonged exposure of cancer cells to therapeutic agents, thereby enhancing the likelihood of apoptosis.

Conclusion: The evidence in this review suggests that albumin nanoparticles increase the rate of apoptosis compared to the free drug by increasing drug uptake by cells, prolonging drug release, and thus prolonging the time of cell drug exposure. These nanoparticles also increase the rate of apoptosis by altering the expression of apoptotic and proapoptotic proteins.

keywords: Albumin nanoparticles; Cancer; Apoptosis.

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PBi-115

Investigating the effect of red blood cell lysate on the fatty acid pattern of serum phospholipids

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Serum phospholipids play an important role as polar molecules by forming lipoproteins. On the other hand, any change in the pattern of serum fatty acids can also cause changes in cell signaling pathways. In intravascular hemolysis, the destruction of red blood cells is accompanied by the release of intracellular contents into the blood plasma. Therefore, the purpose of this study is to investigate the effect of red blood cell lysate on the fatty acid pattern of serum phospholipids (in vitro).

Methods: This study was experimental research on human samples. In this study, serum samples and red blood cells were obtained from 5 (20-50 y) healthy adult men. Serum was separated from 5 ml of blood without anticoagulant and red blood cells were separated from 5 ml of blood using EDTA anticoagulant. Separation of phospholipid fraction was done using the thin layer chromatography method and methyl ester of fatty acids will be done in an acidic environment by methanol.

Results: The amount of trans-palmitoleate fatty acids (1:16) and oleate (1:18) at 37 ° C showed a significant decrease compared to the control group (respectively -20.74%, p=0.001 and 10.08% ± 0.2, p=0.01). In contrast, cis-palmitoleate fatty acid (16:1c) at 37 ° C temperature significantly increased compared to the control group (44.15% ± 0.11, p=0.001). The amount of fatty acids linoleate (18:2), linolenate (18:3), arachidonate (20:4), and docosahexaenoic acid (DHA) at 37 ° C temperature showed a significant decrease compared to the control group. The amount of total saturated fatty acids (SFA) at 37 ° C temperature showed a significant increase compared to the control group (9.11% ± 0.82, p=0.01). On the other hand, the total amount of monounsaturated and polyunsaturated fatty acids at 37 ° C temperature showed a significant decrease compared to the control group (-8.69% ± 2.15, p=0.01 and 94% ± 0.52, respectively)

Conclusion: According to the study, red blood cell lysate affects the pattern of fatty acids of serum phospholipids. The amount of total saturated fatty acids (SFA) increases at 37 ° C compared to the control group. The total amount of monounsaturated and polyunsaturated fatty acids decreases at 37 ° C temperature compared to the control group.

keywords: Hemolysis; red blood cell; fatty acid; phospholipid.

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The effects of red blood cells lysate on serum triglycerides fatty acid

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Serum triglycerides play an important role as energy-generating molecules in the transfer of lipids from the drug and digestive system to the peripheral tissues. The type and amount of fatty acids participating in these serum triglycerides affect these lipids biochemical and biophysical properties. Hemolysis is the destruction or complete removal of red blood cells from the bloodstream before their 120-day lifespan.

Methods: This study was done experimentally on human samples. In this study, Serum samples and red blood cells were used. A pair of serum samples and erythrocyte lysate with different concentrations were mixed according to the determined ratio. The triglyceride fraction was separated using the thin-layer chromatography method, and methyl ester of fatty acids were made in an acidic environment using methanol. The composition of fatty acids was determined using the gas chromatography method.

Results: The average values of the percentage of saturated, monounsaturated, and polyunsaturated fatty acids of the triglyceride fraction in serum containing lysate were investigated at 4 ° C (control) and 37 ° C. As observed, the total monounsaturated fatty acids showed a significant decrease at 37 ° C compared to the control group. Also, the amount of myristate and pentadecanoate fatty acids at 37 ° C significantly decreased compared to the control group. In contrast, stearate fatty acid significantly increased compared to the control group. Also, no statistically significant differences were observed regarding trans-palmitoleate, cis-palmitoleate, and oleate fatty acids between the studied groups. However, the fatty acid of arachidonate (20:4) showed a substantial increase in the temperature of 37 ° C compared to the control group.

Conclusion: Intravascular hemolysis is one of the most important health-threatening diseases. In this study, we observed the effects of intravascular hemolysis on some percentages of saturated, monounsaturated, and polyunsaturated fatty acids of the triglyceride fraction.

keywords: Hemolysis; red blood cell; fatty acid; phospholipid

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PBi-117

Examination of calcium and magnesium serum levels in pregnant woman referred to Shahid Rahimi Hospital due to premature birth from 2022 to 2023

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Medical Biochemistry, Quality control, Trace elements

Background and aim: : Premature birth is one of the most important problems in obstetrics, which causes the majority of infant deaths in advanced societies. Despite the progress in pregnancy care, the frequency of premature birth has not decreased. This study was conducted with the aim of comparing serum levels of calcium and magnesium in pregnant mothers with term and pre-term delivery

Methods: : In this descriptive study, an analysis was conducted on 40 mothers with preterm birth and 79 mothers with term birth in 2023-2024. Average age, level of education, occupation, gestational age, number of pregnancies, serum levels of calcium, magnesium, and albumin were investigated and compared among the two pre-term and term groups. Data analysis was done by SPSS software version 22 and using statistical tests. A significance level of 0.05 is considered

Results: : In the current study, the average age of the mother in the term group was 28.77±7.25 and in the preterm group was 28.98±7.86 years, the average gestational age in the preterm group was 34.67 weeks and in the term group was 38.66 weeks. The number of pregnancies in the pre-term group was more than the term group, which were not statistically significantly different from each other (P0.05). The number of pre-term mothers working and housewives was more than term mothers. Also, a larger number of spouses of the semester group had freelance jobs or were employees, which was not statistically significant. The number of pre-term mothers and wives with a diploma or less and university level of education was more than mothers and term wives, which were not statistically significantly different from each other (P 0.05). The average level of calcium, magnesium and albumin in the preterm group was

Conclusion: The results of our study show the difference in serum levels of calcium and magnesium in two groups of women with term and pre-term delivery, however, more studies with a larger sample size are needed in this matter.

keywords: Calcium1; magnesium2; premature3; birth4, albumin5

PBi-119

The effects of vitamin E supplementation on sperm parameters, chromatin integrity, and gene expression before and after freezing in aged mice

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Some age-related testicular changes, such as Sertoli cell vacuolization and blood-testis barrier breakdown, reduce total sperm production and male fertility. Therefore, this study investigated the effect of vitamin E on restoring testicular function in aged mice. Sperm cryo-resistance was also assessed.

Methods: Twenty-eight 48-week-old male Naval Medical Research Institute mice were divided into four groups for a daily gavage of vitamin E: the control group received distilled water, while the three treatment groups were administered 100, 200, and 400 mg/kg, respectively, for 4 weeks. Subsequently, semen analyses, DNA fragmentation index (DFI), and protamine deficiency tests were conducted. Testicular histology, tissue antioxidant enzyme activity, and gene expression levels were also assessed.

Results: The two higher dosages of vitamin E were associated with a higher sperm count, greater progressive motility, and improved sperm morphology (p0.05). These benefits were also evident after sperm freezing (p0.05). Although chromatin abnormalities increased following vitrification, the treatment groups showed better outcomes (p0.05). The tubular diameter, epithelium height, and luminal diameters remained unchanged with age. The tissue antioxidant capacity was greater in the groups receiving the high doses of vitamin E. Additionally, significant increases in inhibitor of DNA binding protein-4 (Id4) and GDNF family receptor alpha-1 (Gfra1) expression were observed in the higher vitamin E dosage groups, and promyelocytic leukemia zinc finger protein (Plzf) expression was notably present in the 400 mg/kg treatment group compared to the control group (p0.05).

Conclusion: Antioxidant supplementation might enhance reproductive outcomes in aging males. The observed effects included improved sperm cryo-resistance, which is advantageous for future applications such as sperm freezing or fertility preservation.

keywords: Antioxidants, Gene expression, Male fertility, Oxidative stress, Spermatogonia, Vitamin E

PBi-120

Evaluation of SOD, CAT and GPX enzyme levels in patients with metabolic and non-metabolic fatty liver disease compared to healthy individuals

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Liver inflammation can arise from various etiologies, potentially leading to liver fibrosis and, eventually, cirrhosis and liver failure. Free radicals and the resultant oxidative stress are key pathophysiological mechanisms contributing to liver damage. This study aims to evaluate serum levels of Superoxide dismutase (SOD), Catalase (CAT), and Glutathione peroxidase (GPx) enzymes in patients with metabolic and non-metabolic fatty liver disease, and healthy control subjects.

Methods: This study was conducted on serum samples from 29 patients with metabolic fatty liver disease, 19 patients with non-metabolic fatty liver disease, and 20 healthy individuals serving as the control group. Enzyme assays for SOD, CAT, and GPx were conducted using kits obtained from Zellbio (Zellbio GmbH, Germany) in accordance with the manufacturer's protocols.

Results: In this study, it was observed that the activity of CAT and GPx enzymes was higher in patients with fatty liver compared to healthy individuals, which showed the highest activity in the metabolic (P0.001) and non-metabolic fatty liver (P0.01) groups, respectively. Regarding the level of SOD enzyme activity, the conditions were different, so that a decrease in the activity of this enzyme was observed in patients with fatty liver, although this difference was not significant (P0.05).

Conclusion: Increased activity of CAT and GPx enzymes in patients with fatty liver may indicate increased activity of oxidant factors in the body of these patients, and the body's response in these conditions will be to combat these factors and increase antioxidant enzymes.

keywords: Fatty liver, SOD, CAT, GPx

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PBi-121

Novel Blood and Urine-Based Diagnostic Approaches in Breast Cancer Detection

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Breast cancer is a leading cause of cancer-related morbidity and mortality among women. Early detection significantly improves survival outcomes, but traditional biopsy methods are invasive. Recent advancements in non-invasive diagnostic approaches, particularly blood and urine biomarkers, show promise for early detection and disease monitoring. This systematic review aims to evaluate the current evidence on blood and urine biomarkers, including circulating tumor DNA (ctDNA), microRNAs (miRNAs), and protein biomarkers, for breast cancer detection.

Methods: A systematic review was conducted using databases like PubMed and Scopus, including studies published between 2010 and 2024. Studies were selected based on their evaluation of blood and urine biomarkers for breast cancer detection and monitoring.

Results: Blood and urine-based diagnostics provide non-invasive, cost-effective alternatives to traditional biopsies for early breast cancer detection and monitoring. While promising, further research is needed to refine these methods, validate their clinical utility, and assess their long-term effectiveness.

Conclusion: Blood and urine-based diagnostics provide non-invasive, cost-effective alternatives to traditional biopsies for early breast cancer detection and monitoring. While promising, further research is needed to refine these methods, validate their clinical utility, and assess their long-term effectiveness
.

keywords: Breast Cancer; Liquid Biopsy; Blood Biomarkers; Urine Biomarkers; Early Detection

PBi-122

Examination of paternal opioid consumption and its association with the plasma lipid profile and body mass index of progeny's: A cohort study

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Medical Biochemistry, Quality control, Trace elements

Background and aim: An increasing number of findings highlight that consumption of opioids may have long-term effects on consumer’s progeny through exposure to second-hand passive smoke, in addition to transgenerational effects caused by genetic and epigenetic modifications of paternal gametes.

Methods: In this study, we performed population-based analyses to figure out the correlation between paternal opioid consumption, initiated before or after childbirth, and the BMI and plasma lipid profile of young adult progeny. The current investigation consists of 840 parents-progeny trios (parents aged 35-70 years and progeny aged 15-35) from prospective Rafsanjan Cohort Study (RCS) participants. The association between the BMI status and plasma lipid variables of the progeny and the paternal regular opioid consumption was examined using crude and adjusted multiple logistic regression analysis.

Results: The study found that 42.8% of fathers in the studied trios were regular opioid users. Regression analyses revealed that opioid use initiated before fatherhood is linked with a 76% higher adjusted odds ratio (OR) for overweight/obesity in young progeny. This association remained significant even when paternal opioid use via non-inhalation methods (oral consumption) was excluded from the logistic regression analysis. Notably, sex-specific analysis indicated a 201% augmented OR of overweight/obesity in male progeny of fathers who consume opioid habitually, initiated after childbirth, whereas no statistically significant correlation was observed in female progeny. Furthermore, progressive exposure‑response correlations were identified between the odds ratios for overweight or obesity and the duration of paternal opioid use following the birth of the child. Ultimately, paternal opioid consumption, whether initiated prior or subsequent to childbirth, did not demonstrate a statistically significant correlation with elevated plasma lipid levels in progeny.

Conclusion: According to our results, the environmental effects of paternal habitual opioid consumption may be adequate to influence the male progeny metabolism, independent of genetic or epigenetic effects on gametes.

keywords: Cohort-PERSIAN; Paternal opioid use; obesity; Transgenerational; Metabolic

PBi-123

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Effect of Aloe Vera Gel on treatment of Striae Gravidarum in women with age 18-40 years old: a randomized clinical trial with placedo

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Considering the high prevalence of pregnancy striae and that pregnancy striae is not desirable and pleasant for many women and can cause emotional and psychological discomfort for many women, and it also causes stress and reduces the quality of life by causing itching and sores. Considering the properties of aloe vera plant and the etiologies mentioned for the formation of stretch marks, the present study is conducted with the aim of determining the effect of aloe vera plant gel on the prevention of pregnancy stretch marks in women.

Methods: This study was a clinical trial with a placedo in which pregnant women with stretch marks used aloe vera gel in the 20th to 28th week of pregnant, and at the end of the study, they examined for the improvement of the stretch marks.

Results: In the study, there was no statistical difference between the control group and the patients in terms of BMI age, which is determined by the entry criteria and equalization of the risk factors of the patients. The number of stretch marks in the intervention group was less than the control group. The severity of itching in the intervention group was lower than the control group. Erythema did not differ between the two groups.

Conclusion: Considering the high prevalence of stretch marks in pregnancy and considering the results of this research, which showed the positive effect of aloe vera gel on the prevention of stretch marks in the second trimester of pregnancy, midwives, gynecologists and maternal health care workers can be recommended to improve the health of pregnant mothers. Bardar recommended the use of aloe vera gel in the second trimester of pregnancy to pregnant women to prevent stretch marks.

keywords: Stretch marks of pregnancy; Aloe Vera; Placed

PBi-124

MicroRNA-200c Reverses Multidrug Resistance in Triple-Negative Breast Cancer by Targeting ZEB1 and Modulating the Epithelial-Mesenchymal Transition

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer characterized by the lack of estrogen receptor, progesterone receptor, and HER2 expression. This phenotype is associated with poor clinical outcomes and a high propensity for chemoresistance. Among the molecular mechanisms driving drug resistance, microRNAs (miRNAs) have emerged as crucial regulators of gene expression. In this study, we focus on the role of miR-200c in overcoming multidrug resistance (MDR) in a paclitaxel-resistant TNBC cell line (MDA-MB-231/PTX).

Methods: Paclitaxel-resistant TNBC cells (MDA-MB-231/PTX) and parental controls were cultured under standard conditions. miR-200c expression was assessed using qRT-PCR, and its target, ZEB1, was validated via dual-luciferase reporter assays. miR-200c mimics were transfected to restore its expression, and the effects on ZEB1, EMT markers, and downstream signaling were analyzed using Western blotting. Functional assays, including MTT for cell viability, wound-healing, and transwell invasion assays, evaluated cell migration, invasion, and paclitaxel sensitivity. Apoptosis and cell cycle alterations were quantified by flow cytometry. Statistical analysis was performed using Prism version 9 and confirmed the significance of observed changes (p 0.05).

Results: QRT-PCR analysis revealed a significant downregulation of miR-200c in MDA-MB-231/PTX cells compared to their paclitaxel-sensitive parental counterparts. Computational target prediction tools identified ZEB1, a transcription factor that promotes EMT. Direct targeting of ZEB1 by miR-200c was confirmed using dual-luciferase reporter assays. Restoration of miR-200c expression via synthetic mimics led to a substantial reduction in ZEB1 protein levels, accompanied by increased expression of E-cadherin. Functional assays demonstrated that miR-200c overexpression significantly enhanced the sensitivity of MDA-MB-231/PTX cells to paclitaxel, reducing the half-maximal inhibitory concentration (IC50) by over 50%. Furthermore, miR-200c reduced cell migration and invasion capabilities, as assessed by wound-healing and transwell invasion assays. In the presence of paclitaxel, miR-200c expression promoted apoptotic cell death, evidenced by increased caspase-3/7 activation and the accumulation of cells in the sub-G1 phase of the cell cycle. These effects suggest that miR-200c reverses MDR through its dual roles in suppressing EMT and modulating apoptotic pathways.

Conclusion: Our findings indicate that miR-200c acts as a tumor suppressor in TNBC, reversing MDR by targeting ZEB1 and reprogramming the resistant cells toward a more drug-sensitive phenotype.

These results provide a basis for further preclinical studies evaluating miR-200c-based therapies as a novel strategy for overcoming drug resistance in TNBC.

keywords: miR-200c, triple-negative breast cancer, multidrug resistance, ZEB1, paclitaxel

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PBi-125

MicroRNA-34a Sensitizes Drug-Resistant Lung Cancer Cells to Gefitinib by Targeting MET and Regulating the PI3K/AKT Pathway

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The development of resistance to epidermal growth factor receptor (EGFR) inhibitors remains a critical barrier in the effective treatment of non-small cell lung cancer (NSCLC). Among the various resistance mechanisms, dysregulation of microRNAs (miRNAs) has emerged as a significant contributor. This study investigates the role of microRNA-34a (miR-34a) in reversing gefitinib resistance in NSCLC using gefitinib-resistant PC9 cells (PC9/GR) as a model.

Methods: Gefitinib-resistant NSCLC cells (PC9/GR) and their parental counterparts (PC9) were cultured for comparative analyses. miR-34a expression was quantified using qRT-PCR, and its direct target, MET, was confirmed via bioinformatic prediction and dual-luciferase reporter assays. miR-34a mimics were transfected to restore its expression, and downstream effects on MET and the PI3K/AKT pathway were assessed using Western blotting. Functional assays, including IC50 determination, colony formation, apoptosis detection, and migration/invasion assays, evaluated the impact of miR-34a on gefitinib sensitivity, proliferation, apoptosis, and invasiveness. Statistical significance was performed by Prism version 9 and determined using standard methods (p 0.05).

Results: Quantitative RT-PCR analysis revealed a pronounced downregulation of miR-34a in PC9/GR cells compared to parental gefitinib-sensitive PC9 cells. Bioinformatic prediction tools, in combination with dual-luciferase reporter assays, identified the MET oncogene, a key driver of resistance, as a direct target of miR-34a. Transfection of PC9/GR cells with miR-34a mimics successfully restored miR-34a levels and significantly reduced MET expression at both mRNA and protein levels. Further mechanistic studies demonstrated that miR-34a overexpression suppressed the activation of the PI3K/AKT signaling pathway, a downstream effector of MET that promotes survival and proliferation in resistant cells. Functional assays revealed that restoration of miR-34a expression enhanced the sensitivity of PC9/GR cells to gefitinib, reducing the half-maximal inhibitory concentration (IC50) of the drug by over 60%. Additionally, miR-34a overexpression significantly inhibited cell proliferation, as evidenced by reduced colony formation, and induced apoptosis, as indicated by increased caspase-3/7 activity and higher Annexin V-positive cell populations.

Conclusion: These findings suggest that miR-34a sensitizes gefitinib-resistant NSCLC cells by targeting MET and disrupting the PI3K/AKT signaling cascade, while simultaneously reducing the invasive potential of these cells. Given the multifaceted role of miR-34a in overcoming resistance and its ability to suppress tumor progression, it represents a promising candidate for therapeutic

development. Future studies should focus on in vivo validation and the clinical feasibility of miR-34a-based therapeutic approaches.

keywords: miR-34a, gefitinib resistance, MET, PI3K/AKT pathway, non-small cell lung cancer

PBi-126

Exploring The Association Between Phase Angle and Glycemic Control Measures: A systematic Review of Observational Studies

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Phase angle (PhA), which is obtained from the analysis of bioelectrical impedance, is known as a non-invasive parameter that reflects the health and integrity of the cellules. How PhA is related to various glycemic control parameters has proved vital if it is to be potentially used for clinical purposes. Hence, the main target of the present study was set at the clarification of any possible relationships between PhA and glycemic control parameters in adults.

Methods: A comprehensive search was conducted surfing PubMed, Scopus, Embase and Google Scholar spanning research carried out up to 26 March 2024 in an attempt to pinpoint studies already done on the correlation coefficient(r) between PhA and glycemic control parameters. These factors included fasting blood glucose (FBG), Hemoglobin A1c (HbA1C) and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). We screened one hundred and forty studies. Following this, 22 articles were selectively picked for full and detailed reading. Having done that, the number finally boiled down to 6 essential articles, which were decided to be included in this study.

Results: The reviewed studies turned out to be inconclusive in the results they yielded. One study, for instance, found no significant association between PhA and FBG (r = 0.01, p 0.05). Another study reported that the association between both FBG (r = -0.25, p = 0.015) and HbA1c (r = -0.24, p = 0.019) was negatively significant. Still other studies primarily showed a non-significant relationship between PhA and HbA1c or HOMA-IR, furthering doubt on the overall relationship between PhA and glycemic control measures.

Conclusion: The relationship between PhA and measures of glycemic control has proved inconclusive in studies carried out to the present date. This bulk of research, to our best understanding, has mostly revealed non-significant associations across various populations and outcome measures. As a result, these indecisive outcomes necessitate further research to push attempts to clarify the relationship, if any, between PhA and the aforementioned parameters to a more stable standing. This could be achieved by considering other potential confounders as well as recruiting larger, and more diverse samples.

keywords: Phase Angle, Glycemic Control, Systematic Review

PBi-127

Effectiveness of Short Chain Fatty Acids in the Treatment of Depression: A Systematic Review of Clinical Trials

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Depression is the most prevalent psychiatric disorder worldwide, and several recent studies have confirmed the involvement of gut microbes in the pathology of depression. As the most important metabolite produced by the gut microbiota, short-chain fatty acids (SCFAs) may have the ability to improve depressive symptoms by acting on neuroinflammation, neurotransmitter modulation, and blood-brain barrier function. Therefore, this systematic review aimed at assessing the efficacy of SCFAs in improving depression using the data from randomized clinical trials (RCTs) and clinical studies.

Methods: Searches will be performed in Embase, Scopus, PubMed, and ClinicalTrials.gov for studies published between the year 2000 and 2024. The search terms include 'short-chain fatty acids', 'depression', and 'clinical trials'. The inclusion criteria would be RCTs and non-randomized clinical trials addressing the effect of SCFAs on depression in human subjects. Studies on other psychiatric disorders or not involving SCFA intervention would be excluded. Data extraction included study design, sample size, intervention type, duration, outcome measures such as Hamilton Depression Rating Scale (HDRS), Beck Depression Inventory (BDI) and key outcomes. Lack of bias in the methodological procedures was assessed using the RoB tool (version 2). The main outcome measures were changes in depression severity, as measured by standard depression rating scales. Secondary outcomes were changes in patient cognitive behaviors, inflammatory mediators, and gut microbiota composition.

Results: Eleven studies were included which involving a total of 678 participants. Sample sizes ranged between 30 and 180 participants, with intervention duration spanning between 4 to 12 weeks. The interventions most used included the supplementation with SCFAs or the dietary approach to increase their production by using prebiotic fibres. Out of the 11 included studies, eight reported a notable decrease in depression symptoms after the SCFAs supplementation. Findings were most consistent for butyrate supplementation, with a medium to large effect size observed (Cohen's d = 0.6-1.2). Positive results were also seen with acetate and propionate; however, these effects were more modest. Also, the SCFAs were reportedly well tolerated, with gastrointestinal symptoms such as bloating and flatulence being among the most common adverse effects. No severe adverse events were reported in any of the studies reviewed. In general, the number of SCFAs applications is growing, but most studies included small sample

Conclusion: Given the potential of SCFAs to reduce depression symptoms, particularly in treatment-resistant cases, SCFAs could be explored as an adjunctive treatment for depression. Future studies

should investigate optimal dosing, long-term effects, and the specific role of SCFAs in different subtypes of depression.

keywords: Short-chain fatty acids; Gut-microbiota; Depression; Systematic Review

PBi-128

Evaluating the Efficacy of Acupoint Catgut Embedding for Obesity Management: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Obesity is a global health challenge associated with various comorbidities and healthcare burdens. Traditional weight management often has limited success, prompting interest in alternative therapies. Acupoint catgut embedding, a technique from acupuncture, involves inserting catgut sutures at specific points to boost metabolism and aid weight loss. This systematic review evaluates its efficacy in managing obesity by synthesizing clinical evidence, aiming to highlight its potential as a complementary treatment in integrative weight management.

Methods: Following Cochrane systematic review principles and PRISMA guidelines, a comprehensive search was conducted across multiple international databases, including PubMed, Scopus and Web of Science, as well as Google Scholar for grey literature. The keywords utilized in the search included “acupoint catgut embedding” and “obesity", "body weight” Inclusion criteria were established to encompass all observational and clinical studies investigating the effects of acupoint catgut embedding on obesity management. All reviews, interventional studies, animal studies, letters to editors, and book chapters were excluded. Two authors independently screened and extracted data, with any discrepancies resolved by a third author. The quality of included studies was assessed using the Newcastle-Ottawa scale tool, and information was organized into an extraction table

Results: Out of 218 initial articles, 130 were removed due to duplication and 66 due to lack of relevance, leaving 22 final articles being included in the study. These articles were conducted on 2069 participants who were randomly allocated for embedding therapy, which was every 7 days, three times for each course, and acupoint catgut embedding therapy is an effective method for managing abdominal obesity. When combined with abdominal acupuncture, it leads to significant reductions in weight and waist circumference, improving metabolic profiles and reducing inflammation. The therapy is safe and may serve as a complementary treatment for postpartum weight retention and general obesity. Its potential to enhance leptin resistance and insulin sensitivity contributes to its effectiveness.

Conclusion: This review shows acupoint catgut embedding therapy effectively manages abdominal obesity, improving weight, waist circumference, and metabolic profiles, warranting further research for optimal treatment integration.keywords: Acupoint catgut embedding, Obesity, Leptin, Insulin

PBi-129

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Biochanin A modulates the cGAS/Sting pathway and oxidative stress in kidney tissue of rats with diabetic nephropathy

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetes leads to inflammation and oxidative stress in various tissues including the kidney. Which results in diabetic nephropathy. Today, the focus of treatment for diabetes complications is on the use of medicinal plants and their active ingredients such as isoflavones. Therefore, the aim of the present study was to investigate the effect of the Biochanin A (BCA), as isoflavones, on the cGAS/Sting pathway and oxidative stress in the kidney tissue of type 1 diabetic rats.

Methods: Following diabetes induction with streptozotocin (STZ) at 55 mg/kg body weight, rats were randomly assigned to four groups (n=6 per group): (1) a normal control group receiving 0.5% dimethyl sulfoxide (DMSO) daily; (2) a diabetic control group also receiving daily 0.5% DMSO; (3) a diabetic group treated with biochanin A (BCA) at 10 mg/kg body weight daily; and (4) a diabetic group receiving BCA at 15 mg/kg body weight daily. cGAS and Sting gene expression were analyzed via real-time PCR. Fasting blood glucose (FBG), malondialdehyde (MDA) and superoxide dismutase (SOD) levels were assessed spectrophotometrically. The treatment period lasted 42 days.

Results: Compared to the normal control group, the diabetic control group exhibited significant increases (P0.001) in FBG, kidney cGAS and Sting gene expression, and malondialdehyde (MDA) levels, alongside a significant decrease (P0.001) in kidney SOD activity. BCA administration at both 10 and 15 mg/kg for 42 days significantly reduced (P0.001) FBG, cGAS and Sting expression compared to the diabetic control group. Furthermore, BCA treatment at both doses significantly decreased (P0.001) MDA levels and increased (P0.001) SOD activity in kidney tissue compared to the diabetic control group. Importantly, the beneficial effects of BCA appeared to be dose-dependent (P0.05).

Conclusion: Administration of BCA for 42 days showed that it could lead to improvement in diabetic nephropathy by reducing inflammation and oxidative stress.

keywords: Biochanin A; cGAS/Sting; oxidative stress; diabetic nephropathy

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PBi-130

Evaluation of Red Cabbage (Brassica oleracea) extraction and 6-gingrol combination cytotoxicity on Brest cancer cell line

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Medical Biochemistry, Quality control, Trace elements

Background and aim: The research for natural compounds with anticancer properties is a crucial area research in oncology. This study investigated the potential cytotoxic effects of red cabbage (Brassica oleracea) extract and 6-gingrol (from ginger extraction) on breast cancer cell line (MCF-7). Red cabbage is rich in bioactive compound, particularly anthocyanins, which are known for their antioxidant properties. The object was to assess whether these compounds could induced cytotoxicity in breast cancer cells, potentially offering a natural therapeutic option.

Methods: In vitro experiments were conducted using various concentrations of red cabbage extract on cultured breast cancer cell line (MCF-7). After 24 hours, MTT assay was employed to assess the cytotoxicity of red cabbage and 6-gingrol on MCF-& cells. We used invert microscopy to evaluate the cell morphology changes after treatment.

Results: The results demonstrated a dose-depended reduction in cell viability, indicating significant cytotoxic effects at high concentrations in both compounds (P value 0.01). The IC50 for red cabbage was 8 µg/ml, and for 6-gingrol was 280 µg/ml, additionally, the extract induced apoptosis in the cancer cells, as evidenced by morphological changes associated with cell death.

Conclusion: The finding suggest that 6-gingrol and red cabbage may possess anti-cancer properties, particularly against breast cancer cells. These effects are likely due to the high anthocyanin content in red cabbage, moreover 6-gingrol has antioxidant and anti-cancer properties, which may disrupt cellular process essential for cancer cell survival. Further research is needed to isolate specific compounds in red cabbage that responsible for these effects and to explore their potential in cancer therapy.

keywords: Red Cabbage, 6-gingrol, cytotoxicity, Brest cancer cell line

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PBi-131

Examining the serum level of vitamin D in patients with molar pregnancy referred to Shahid Rahimi Hospital in 2022 to 2023

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Hydatiform mole or molar pregnancy is a rare and benign disease caused by genetic deficiencies in the fertilized egg. The prevalence of this disease in asia is seven times that of Europe and America. This study was conducted with the aim of investigating the serum level of vitamin D in patients with molar pregnancy referred to shahid rahimi hospital in 2022 t0 2023

Methods: A cross-sectional study was conducted in 2022-2023 on 227 mothers with molar pregnancy. Gestational age, BMI, education level and occupation of mothers and their spouses and serum level of vitamin D were investigated. Data analysis was done by SPSS software version 22 and using statistical tests. A significance level of 0.05 is considered.

Results: In this study, 5.7% of women with molar pregnancy have vitamin D serum levels between 0 and 10ng/dl , 79.3% of women have serum levels between 10 and 25ng/dl and 15% of women have serum levels were 25 to 100 ng/dl.the highest frequency of serum levels was related to the 10 to 25 group.the average age of pations whose vitamin D level was between 0-10 ng/dl was 27.77-+6.48.in addition, the average age of pations whose vitamin D level was between10 to25 ng/dl was 27.41+-7.89 respectively/the overall average of vitamin D level of the study subjects was 21.22, which was 9.62 in the 0 to 10 serum leve group, 18.74 in the 10 to 25 group, and 38.74 in the 25 to 100 serum level group. Also, we examined the relationship between BMI and different groups of vitamin Dserum level, there was no statistically significant relationship between vitamin Dserum level and

Conclusion: : In our study, different levels of vitamin D were evaluated in molar pregnancy. More studies with a larger sample size are needed to better clarify the mechanisms of the relationship between this vitamin and molar pregnancy

keywords: molar pregnancy ; pregnancy; vitamin D, hydatiform molar

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PBi-132

Biochanin-A, by suppressing the expression of the S100A16, leads to the modulation of endoplasmic reticulum stress (ERS) and improvement of diabetic nephropathy in type 1 diabetic rats.

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetic nephropathy (DN) is a serious complication of diabetes, often exacerbated by endoplasmic reticulum stress (ERS). S100A16 has been implicated in the progression of DN. This study investigated the potential of Biochanin-A (BCA), a natural isoflavone, to ameliorate DN in type 1 diabetic rats with a focus on modulating endoplasmic reticulum stress and S100A16.

Methods: Twenty-four Wistar rats were divided into four groups (n=6): control (Cnt), diabetic control (Dibt), diabetic treated with 10 mg/kg BCA (Dibt-BCA/10), and diabetic treated with 15 mg/kg BCA (Dibt-BCA/15). BCA was administered via oral gavage for 42 days. Type 1 diabetes was induced by using streptozotocin (STZ). Kidney gene expression of S100A16, GRP78, IRE1 α, XBP1, NF- κ B, and IL-6 was assessed using real-time PCR. Fasting blood glucose (FBG) levels and kidney tissue levels of malondialdehyde (MDA) and activity superoxide dismutase (SOD) were measured using biochemical assays. ANOVA and Bonferroni post-hoc tests were used for data evaluation.

Results: Compared to the control group, diabetic rats exhibited significantly elevated FBG, kidney malondialdehyde (MDA) levels, and increased kidney expression of S100A16, GRP78, IRE1 α, XBP1, NF- κ B, and IL-6 (P0.05). Conversely, kidney superoxide dismutase (SOD) activity was significantly reduced in the diabetic group (P0.05). Administration of BCA for 42 days at doses of 10 and 15 mg/kg resulted in a significant, dose-dependent, improvement across all measured parameters in comparison to the diabetic group (P0.001).

Conclusion: These results suggest that BCA exerts protective effects against diabetic nephropathy. Therefore, BCA represents a potential phytotherapeutic agent for the treatment of this condition, although further research is warranted to fully elucidate its mechanism of action and clinical efficacy.

keywords: Biochanin-A; S100A16; Diabetic nephropathy; Endoplasmic reticulum stress; Oxidative stress

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PBi-133

Investigating the relationship between vitamin D supplementation and breast cancer in women

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Background and Aim: Breast cancer is one of the most common cancers among women and is a leading cause of cancer death among women. The possible protective role of vitamin D has been investigated over the last few years, so the question became whether there is an association between vitamin D levels and breast cancer risk. This review article explores the available evidence around this key query.

Methods: Methods: In this systematic review study, three people simultaneously searched for the keywords " Breast cancer " and " vitamin D" and also extracted similar words from the MeSH database and PubMed, Google Scholar, and Web of Science databases until August 22, 2024. Was performed. The entry criteria are the originality of the type of article and in line with the main purpose of the study. The exclusion criterion was the lack of access to the full file of articles. Finally,26 articles were included in the study.

Results: Results: Finally, this study included 171988 (All study subjects are female- the average age of the people was 54.5 years(. The number of intervention group was 60,603 and the placebo group was 60,160. The average duration of study was one year and the average concentration consumed was 4,000 IU. The study showed that vitamin D can have positive effects on breast cancer. Higher serum vitamin D levels were associated with a reduced risk of breast cancer, especially in postmenopausal women. Additionally, vitamin D supplementation helped improve musculoskeletal symptoms in breast cancer patients. However, no effect was observed on breast density or mammographic changes. Overall, vitamin D supplementation may be effective in improving clinical outcomes and reducing the risk of breast cancer.

Conclusion: Conclusion: Vitamin D, along with other approved breast cancer treatments, can play an effective role as a supplement, which is why it is recommended that doctors keep an eye on this vitamin.

keywords: Keywords: Breast cancer and vitamin D and Treatment

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PBi-134

The effect of occupational noise exposure on salivary cortisol level among automotive assembly workers

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Both auditory and non-auditory health can be affected by exposure to occupational noise. There is an assumption that noise exposure may activate two main systems of stress response including the sympatho-adrenal medullary (SAM) and hypothalamic‑pituitary‑adrenal (HPA) axes The aim of this study was to evaluate the association of high occupational noise (at three levels) with cortisol concentration in an automotive factory.

Methods: This study was carried out on 78 male workers from a factory who worked in the warehouse unit (control group: 60‑70 dB(A)) and assembly units (two test groups: 75‑85 and 85‑95 dB(A)). Data were collected through questionnaires and measurement of saliva cortisol concentration and body mass index (BMI), prior to and post occupational noise exposure. The measurements were performed twice/day and repeated after 10 days. This study was approved by the ethical committee of the Iran University of Medical Sciences (under license NO. 93-04-27-25326) and all subjects signed informed consent forms.

Results: For each occupational noise level group, there was no significant association between cortisol level with age and BMI. Also, the average cortisol levels were similar in different groups before noise exposure, but were statistically different after occupational noise exposure.

Conclusion: High occupational noise exposure increases the cortisol level which are the major risk factors of cardiovascular disease.

keywords: Occupational noise exposure; Salivary cortisol level; Automotive factory.

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PBi-135

Trends of hearing threshold changes in flour factories workers after long-term noise exposure. A 5-Year Follow-Up Study

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Noise as a common physical hazard may lead to noise-induced hearing loss, an irreversible but preventable disorder. Annual audiometric evaluations help detect changes in hearing status before clinically significant hearing loss develops. The current study aimed to a 5-year follow-up of hearing threshold changes in flour factories workers exposed to occupational noise.

Methods: In this retrospective study, 97 male workers occupationally exposed to noise ≥85 dBA in flour factories in Zahedan were evaluated for standard threshold shift (STS) using pure tone audiometry during 2017-2022. STS was calculated on changes in hearing thresholds at each of the 2000, 3000, and 4000 HZ frequencies for each ear. A calculated STS of 10 dB for either ear may be considered a significant indication of hearing loss. The study protocol was approved by the Ethics Committee on Medical Research of Zahedan University of Medical Sciences in Zahedan, Iran (No. IR.ZAUMS.REC.1402.425).

Results: Data from audiometric baseline and follow-up evaluations showed that the changes in hearing threshold of workers was 8.6 ± 5.7 and 9.7 ± 6.6 dB in the right and left ears, respectively. The hearing thresholds increased significantly with increasing work experience in the flour factory in all frequencies (P0.05). 89.7% of workers showed no changes in standard threshold shift (normal), 4.1% indicated a need for care, and 7.2 % showed a significant indication of hearing loss for each ear.

Conclusion: This study showed that long-term exposure to occupational noise can alter hearing thresholds in both ears, thereby increasing noise-induced hearing loss in flour workers.

keywords: Hearing loss, Hearing thresholds, Flour workers. Pure tone audiometry.

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PBi-136

Autophagic pathways in Diabetic nephropathy

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetic nephropathy (DN) is the most common cause of end-stage kidney disease worldwide, and is associated with increased morbidity and mortality in patients with both type 1 and type 2 diabetes. The pathogenesis of DN may be related to renal injury caused by autophagy, oxidative stress, endoplasmic reticulum stress, inflammatory reaction, and excessive activation of renin angiotensin aldosterone system. Indeed, autophagy is a highly conserved self-protection mechanism, through which cells degrade and recycle intracellular macromolecules and organelles to maintain intracellular environmental homeostasis and structural integrity. Autophagy can be triggered by various intracellular stresses and nutrient-sensing pathways , all of which

Methods: A comprehensive search was performed for all relevant data. The keywords Autophagy Diabetic nephropathy, nutrient-sensing pathways and ER stress were used to search for articles in Google scholar, PubMed, NCBI databases from 2015 to April 2023.

Results: According to the results of this study, Autophagy is regulated by nutrient-sensing pathways including AMPK, mTOR, and Sirt1, and several intracellular stress signaling pathways such as oxidative stress, endoplasmic reticulum stress and hypoxia. AMPK and mTORC1 oppositely regulate the Ulk1/2-Atg13-FIP200 complex. AMPK directly activates Ulk1/2 to induce autophagy. SIRT1 interacts with essential components of the autophagy machinery, such as Atg5, Atg7, and LC3, and the transcription factor FoxO3 to induce autophagy. Autophagy exerts both cytoprotective and cytocidal effects, and dysregulation of autophagy contributes to podocyte dysfunction in diabetic nephropathy. Autophagy may be activated during ER stress to supplement ERAD. ER stress enhances the expression of ER membrane proteins like protein kinase RNA-like ER kinase (PERK), inositol-requiring enzyme 1α (IRE1α), and activating transcription factor 6 (ATF6), leading to autophagy. An abnormal nutritional status and excess cellular stresses caused by diabetes-related metabolic disorders disturb the autophagic flux, leading to cellular dysfunction and

Conclusion: Our study shows that the relationship between autophagy and DN has not been fully clarified, therefor Detailed exploration of autophagy in the pathogenesis of DN and understand the cellular and molecular bases of autophagy can provide new ideas for preventing DN.

keywords: Autophagy, Diabetic nephropathy, nutrient-sensing pathways, ER stress

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PBi-137

The therapeutic potential of miR-155 in liver fibrosis

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Medical Biochemistry, Quality control, Trace elements

Background and aim: At the posttranscriptional level, ncRNAs, including miRNAs, are the major modulators of gene expression. Accumulated evidence indicated that changes in ncRNA expression are associated with nearly all forms of liver disease. However, very little is known regarding these lncRNAs`s role in the pathogenesis of liver fibrosis. miR-155 is a miRNA that has a wide distribution of expression across several tissues and cell types. It significantly modulates many cellular processes such as cell proliferation, differentiation, apoptosis, and inflammation. Altered expression of miR-155 has been associated with a wide range of human pathologies, including cancer, autoimmune diseases, and cardiovascular diseases. Regarding liver

Methods: A comprehensive literature search was conducted using PubMed, Google Scholar, and Web of Science. Keywords such as miR-155, liver fibrosis, inflammation, fibrosis, and liver injury were used to identify relevant studies. The included studies were primarily focused on experimental studies in animal models and human clinical trials investigating the role of miR-155 in liver fibrosis.

Results: Numerous studies have demonstrated the upregulation of miR-155 in various liver diseases, including viral hepatitis, alcoholic liver disease, and non-alcoholic fatty liver disease. This upregulation has been linked to the promotion of inflammatory responses, activation of hepatic stellate cells, and increased extracellular matrix deposition, key processes involved in liver fibrosis. Despite its pro-fibrotic role, recent studies have suggested that miR-155 may also have a protective role in certain contexts. For example, miR-155 has been shown to inhibit hepatocyte apoptosis and promote liver regeneration.

Conclusion: miR-155 is a complex miRNA with both pro-fibrotic and protective roles in liver disease. While its upregulation is associated with liver fibrosis, targeting miR-155 for therapeutic purposes requires a nuanced approach. Further research is needed to elucidate the precise mechanisms underlying the dual role of miR-155 and to develop strategies that can selectively modulate its activity to achieve therapeutic benefits without exacerbating liver injury. Potential therapeutic approaches may include the use of miRNA inhibitors, mimics, or antisense oligonucleotides to modulate miR-155 expression.

keywords: Fibrosis; Long noncoding RNAs; miR-155; Therapeutic target

PBi-138

The Role of Next-Generation Sequencing (NGS) in Personalized Diagnosis and Treatment of Breast Cancer

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Medical Biochemistry, Quality control, Trace elements

Background and aim: It is one of the most common cancers among women worldwide and still holds a leading position among the causes of death. While many advances have been made in early detection and treatment options, it remains one of the greatest challenges due to the complex genetics and heterogeneity between patients. In the recent past, NGS has introduced a completely new direction for breast cancer research and personalized medicine. The aim of this review is to examine how NGS has updated the concept and management of breast cancer, especially in identifying key genetic mutations, improving prognosis, and developing more personalized treatments.

Methods: We present herein a systematic review using an appropriate search strategy according to the best available guidelines: Cochrane Principles and PRISMA guidelines. We searched databases such as PubMed, Scopus, and Web of Science by using keywords such as "breast cancer," "NGS and cancer," and "NGS and breast cancer." We had a focus on high-quality primary studies. Reviews, animal studies, and book chapters were excluded to ensure the most reliable evidence. The quality of every single study included was checked, and findings were summarized into a well-tabulated form for clarity in analysis.

Results: The results clearly indicate that NGS plays an important role in identifying genetic mutations linked to the development and progression of breast cancer.For example, NGS has enabled us to identify mutations in some of the most important genes, such as BRCA1/2, PIK3CA, and TP53, which play a crucial role in both prognosis and prediction of response to therapy with targeted treatments. Besides that, NGS extends the somatic mutation analysis to further elucidate the molecular pathways contributing to tumor growth and resistance to therapy. These findings indicate the role of NGS in the development of more personalized and precise treatment strategies, thus improving patient outcomes.

Conclusion: NGS has completely revolutionized the diagnosis, prognosis, and treatment of breast cancer with its precise genetic profile. Traditional methods may not detect changes in genes that are truly rare or subtle, instead, the power of NGS gives us a deeper look into cancer to define natural biomarkers. The development of the technology is expected to play a significant role in improving treatment and test results, and holds hope for a future where breast cancer can be treated with much-needed precision.

keywords: Breast cancer, next-generation sequencing , genetic mutations, personalized medicine

PBi-139

Neuropeptides and Their Role in Wound Healing: Insights into Therapeutic Potential for Diabetic Neuropathy

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Diabetes mellitus (DM), particularly when complicated by neuropathy, severely impairs wound healing due to chronic inflammation, reduced angiogenesis, and disrupted cellular signaling. Neuropeptides such as substance P, calcitonin gene-related peptide (CGRP), neuropeptide Y (NPY), vasoactive intestinal peptide (VIP), somatostatin, and galanin are critical regulators of the wound healing process, influencing inflammation, tissue repair, and vascular remodeling. In diabetic neuropathy, alterations in neuropeptide expression exacerbate healing deficiencies, contributing to chronic non-healing wounds.

Methods: This review aims to examine the role of neuropeptides in wound healing, particularly in patients with DM complicated by neuropathy. It synthesizes current evidence on how neuropeptides affect inflammation, angiogenesis, and tissue repair, processes impaired in diabetic wounds. A systematic search of peer-reviewed literature was conducted in PubMed, Scopus, and Web of Science, focusing on articles from the last two decades. Keywords like "neuropeptides," "wound healing," "diabetic neuropathy," and "diabetes mellitus" were used to identify relevant studies on neuropeptide mechanisms and their impact on wound healing.

Results: Neuropeptides regulate key aspects of wound healing, such as immune modulation, angiogenesis, and tissue regeneration. Dysregulation of neuropeptides in diabetic neuropathy exacerbates wound healing deficits. Evidence from clinical and preclinical studies indicates their potential as therapeutic targets to restore proper healing processes.

Conclusion: Neuropeptides are crucial for wound healing in diabetic neuropathy and may offer new therapeutic avenues to improve healing outcomes in patients with chronic wounds. Further research is needed to develop neuropeptide-based treatments for clinical use.

keywords: neuropeptides, wound healing, diabetic neuropathy, diabetes mellitus, chronic wounds

PBi-140

Evaluation of membrane progesterone receptors (mPRα, mPRβ) expression after stimulating with phorbol 12-myristate 13-acetate/ionomycin on peripheral blood neutrophil cells

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Progesterone (P4) is a female steroid hormone that can immunomodulate the immune system through binding to specific receptors. Progesterone signaling is performed by genomic and non-genomic pathways through nuclear and membrane receptors, respectively. Neutrophils have critical immune roles during physiologic and pathologic conditions. Some research showed that progesterone has a regulatory effect on these cells through nuclear receptors. To date, it has not been recognized whether neutrophils express membrane progesterone receptors α / β or not. This study aimed to address this issue.

Methods: Ten ml of venous blood was collected from healthy volunteers. After removing platelet-rich plasma (PRP) and red blood cells (RBCs), the obtained leukocyte-rich suspension decanted onto a 2-layered discontinuous density gradient of percoll (86% and 55% isotonic percoll). The neutrophil layer was carefully removed, and cells were washed with RPMI 1640. After stimulating with phorbol 12-myristate 13-acetate (PMA)/ionomycin, the percentages of mPR α and mPR β were evaluated using polyclonal and monoclonal antibodies on neutrophil cells.

Results: Neutrophils expressed mPR α and mPR β, and the expression of these receptors increased significantly after stimulation with PMA/ionomycin ($p \leq 0.05$).

Conclusion: Progesterone exerts part of its effect on peripheral blood neutrophils through progesterone membrane receptors. Of course, future studies can investigate the extent and nature of this impact.

keywords: progesterone receptors , neutrophil , phorbol 12-myristate 13-acetate , ionomycin

PBi-141

The role of biomarkers in the connection between laboratory research and clinical treatmentTh

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Biomarkers play an essential role in laboratory research by providing measurableindicators that can signify underlying biological processes or diseases. In the context of neurodegenerative diseases such as Alzheimer’ s, biomarkers facilitatethe identification of disease progression and response to treatment, making them central to scientific discovery. For instance, studies have demonstrated that certain biomarkers can predict cognitive decline, allowing researchers to better understand the disease's trajectory and identify potential therapeutic targets.

Methods: Biomarkers play an essential role in personalizing medicine and improving treatment strategies, particularly in oncology. By identifying specific biological markers unique to each patient's cancer, healthcare providers can tailor therapies that address the genetic and molecular characteristics of an individual’ s tumor. This personalized approach contrasts with traditional treatments that apply a one-size-fits-all model, leading to varied patient outcomes. For instance, microRNAs have emerged as significant biomarkers for diagnosing cancer and predicting responses to treatment, enabling healthcare professionals to make more informed decisions regarding therapy options (Hatam). Furthermore, understanding the genetic instability within tumors, as discussed by Beckman and Yeang, highlights the importance of considering the evolving nature of cancer in treatment planning. This insight suggests that personalized medicine must account for the dynamic changes occurring within tumors over time, promoting strategies that adapt as the cancer progresses.

Results: Integrating biomarkers into clinical practice not only enhances the effectiveness of treatment but also minimizes unnecessary side effects by avoiding ineffective therapies. As research continues to uncover new biomarkers, the potential for improved patient outcomes increases, reinforcing the need for ongoing collaboration between laboratory research and clinical application. This synergy not only drives innovation in personalized medicine but also lays the groundworkfor future advancements in cancer treatment and patient care, steering us towards a more customized therapeutic experience. The next chapter will explore specific biomarker applications in clinical settings, illustrating their impact on treatment efficacy.

Conclusion: As researchers continue to uncover new biomarkers, the gap between laboratoryfindings and clinical application narrows. Understanding how these biomarkers operate in real-world settings is essential for successful treatment strategies. This brings us to the next critical area of exploration: translational research, which seeks to bridge the divide between laboratory discoveries and their implementation in clinical practice.

keywords: Laboratory, clinical,disease, treatment strategy.

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PBi-142

An Updated Overview of Genetic and Epigenetic Hallmarks of Aging

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Aging is a progressive process that leads to a decline in organismal function. Nowadays, with the increase in life expectancy, age-related diseases have become major causes of death among the elderly. Since aging is a key risk factor for many chronic diseases, studying the aging process can help identify new therapeutic targets for them. This study focuses on the genetic and epigenetic hallmarks of aging.

Methods: We searched online databases, including Google Scholar, PubMed and ScienceDirect, to study recent articles about the genetic and epigenetic features of aging. In our research, we included studies published from 2013 to 2024.

Results: Studies show that, at the molecular level, genomic instability and epigenetic alterations contribute to the aging process. Genomic instability refers to various aspects, such as DNA damage accumulation, decreased DNA repair capacity, and nuclear membrane changes. Telomere dysfunction is another hallmark of aging. On the other hand, epigenetic alterations include DNA methylation, histone modification, chromatin remodeling, RNA modification, and non-coding RNA regulation.

Conclusion: In summary, this study highlights the genetic and epigenetic factors influencing the aging process. Future research in this area would be helpful to uncover novel interventions to enhance longevity and improve quality of life for the aging population.

keywords: Aging; Genomic Instability; Epigenomics; Telomere

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Association of Serum Uric Acid Level with Chronic Kidney Disease

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Hyperuricemia has emerged as a significant factor in the progression of chronic kidney disease (CKD). Uric acid, a product of purine metabolism, linked to reduced glomerular filtration rate (GFR) through oxidative stress, inflammation, and tubulointerstitial fibrosis. hyperuricemia not only contributes to the decline in GFR but may also exacerbate the progression of CKD by promoting tubulopathy and glomerulosclerosis.

Methods: In this study, we used data from the MASHAD study, which started in 2010. GFR was calculated with using the MDRD formula. All participants were adults under the age 65. Without any history of cardiovascular disease, cancer, and chronic diseases. Serum uric acid level was checked for all of them.

Results: Ultimately, out of a total of 9704 individuals, 6386 participants consist of 31% female and 61% male were included in the study, and their data were evaluated at the end. Uric acid levels in individuals with a GFR less than 60 cc/min/1.73 were clearly higher than in those with a GFR greater than 60 cc/mim/1.73(4.63 $\pm$ 1.39mg/dl vs 4.96 $\pm$ 1.41mg/dl). In addition, individuals with lower GFRs had higher serum uric acid levels. There were a significant reverse association between serum uric acid level and GFR (P-value 0.001).

Conclusion: In the present study, a significant association between elevated serum uric acid level and CKD was observed. Individuals with lower GFRs exhibited higher serum uric acid concentrations, suggesting that hyperuricemia may contribute to CKD progression. This underscores the importance of monitoring uric acid levels in patients at risk of kidney disease.

keywords: Uric acid, CKD, GFR.

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PBi-144

CRISPR Typing PCR for detection of Human Papillomavirus: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: : Accurate DNA detection and typing are essential for clinical diagnosis and research, particularly in identifying disease-causing pathogens such as human papillomavirus (HPV). Traditional methods like PCR have limitations in specificity and efficiency, particularly for genotyping highly similar DNA targets. This study aimed to develop and validate a novel, rapid, and reliable CRISPR-based method, ct-PCR, to enhance DNA detection and typing capabilities.

Methods: This review article was conducted using articles published in PubMed, Science Direct, Google Scholar until November 2024. The keywords were CRISPR/Cas9, HPV typing, DNA detection, and Quantitative PCR. By searching these databases, 46 articles were found. After reading titles and abstracts, 35 of them were removed, and 11 articles were selected under the inclusion criteria. All articles were chosen from English-language sources.

Results: ct-PCR combines the Cas9/sgRNA system with qPCR in a single-tube reaction, enhancing DNA detection and typing. It was validated with cloned L1 genes from 10 high-risk HPV subtypes and genomic DNA from cervical carcinoma cells. Clinical samples confirmed its feasibility for HPV detection. ct-PCR detected HPV16 and HPV18 genes in cervical carcinoma cell lines and identified HPV DNA in clinical samples with high specificity and sensitivity. The method reduced detection time to under two hours and minimized contamination risks.

Conclusion: ct-PCR represents a significant advancement in CRISPR-based DNA detection by combining rapidity, specificity, and simplicity. Its ability to detect and genotype HPV in clinical samples highlights its potential as a practical diagnostic tool for DNA-based diseases.

keywords: CRISPR, DNA detection, Cas9/sgRNA, HPV typing, ct-PCR

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PBi-145

Development of a PCR-Based Strategy for Efficient Non-Viral CRISPR/Cas9 Gene Editing in Acute Myeloid Leukemia: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Acute Myeloid Leukemia (AML) is a blood cancer driven by genetic mutations like those in IDH2 and MYBL2. Delivering CRISPR/Cas9 gene-editing tools to hematopoietic cells is challenging due to safety, efficiency, and cost issues with viral vectors. This study aims to develop a PCR-based strategy for generating sgRNA constructs to overcome these challenges.

Methods: This review article was conducted using articles published in PubMed, ScienceDirect, Google Scholar until November 2024. The keywords were CRISPR/Cas9, Leukemia cells, MYBL2, gene editing, and IDH2. By searching these databases, 28 articles were found. After reading titles and abstracts, 17 of them were removed, and 11 articles were selected under the inclusion criteria. All articles were chosen from English-language sources.

Results: We used fusion PCR to create sgRNA constructs targeting MYBL2 and IDH2, delivering them to leukemia cell lines with Cas9 expression. Initial validation was done in HEK293 cells. Editing efficiency was evaluated using T7 endonuclease assays and next-generation sequencing. Specific edits were confirmed through deep sequencing, and ssODNs were used to introduce the IDH2 R172 mutation, validated by RFLP and sequencing. This non-viral approach achieved NHEJ editing efficiencies of 3.6-14.5% and HDR of 2.2%, similar to RNP-based methods. Dual sgRNAs targeting IDH2 enhanced NHEJ efficiency up to 14.5%. Deep sequencing confirmed minimal off-target effects, ensuring high specificity. ssODNs enabled precise genetic modifications.

Conclusion: This study presents a cost-effective, accessible, and efficient alternative to viral-based CRISPR/Cas9 delivery methods, allowing precise genetic modifications in AML-associated genes. By overcoming transfection barriers, this approach facilitates in-depth investigation of AML pathogenesis and the development of novel therapeutic strategies.

keywords: CRISPR/Cas9, Leukemia cells, MYBL2, gene editing, IDH2

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Heat Shock Protein effection on gastric cancer; a systematic review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Gastric cancer is one of the most lethal cancers and is often diagnosed at advanced stages due to a lack of effective biomarkers for early detection. HSPs, which have important roles in cellular stability and protein regulation, hold great potential as biomarkers. The investigation into these proteins may contribute to improving diagnosis and prognosis in gastric cancer. This review aimed to summarize the different roles of various HSPs in gastric cancer diagnosis and prognosis, as well as their potential as new diagnostic and therapeutic tools.

Methods: Methods: This systematic review investigated the involvement of heat shock proteins (HSPs) in gastric cancer. Studies from 2010 to 2023 were selected from databases like PubMed, Google Scholar, and ScienceDirect. The main inclusion criteria were peer-reviewed articles assessing the expression, functional role, and value of HSPs as diagnostic or prognostic biomarkers in gastric cancer. Studies focused exclusively on non-gastric cancer-related HSPs or only on bacterial infections were excluded. Only English-language papers were included to ensure comprehensiveness and relevance. Methodologies, results, and conclusions were based on data extraction and analysis of the selected studies regarding the significance of HSPs in gastric cancer.

Results: HSPs were identified as important factors in the diagnosis and prognosis of gastric cancer in this study. HSP90 α is directly associated with lymph node metastasis and advanced stages of gastric cancer due to its high plasma levels among patients with gastric cancer, and thus, it can serve as a diagnostic biomarker. HSP22 has been linked to tumor size, lymph node metastasis, and unfavorable prognosis. Highly expressed HSP22 is associated with increased MMP-9, a marker of tumor invasion and progression. HSP22 is also involved in the invasion and metastasis of gastric cancer, and its downregulation results in the loss of cell migratory capabilities. HSP110 is known to be associated with chemotherapy resistance and a poor prognosis; its inhibition increases the sensitivity of tumor cells to therapies. These findings may finally place HSPs in the position of potential biomarkers and targets of therapy in gastric cancer.

Conclusion: This review indicated a critical role of HSPs, especially HSP90 α , HSP22, and HSP47, in gastric cancer diagnosis and prognosis. HSP90 α was increased in patients with metastasis and advanced tumor stages. HSP22 was associated with tumor size and metastasis, suggesting a poor prognosis. HSP47 was implicated in tumor invasion, while HSP110 was reported to contribute to

chemotherapy resistance. These findings suggest that HSPs act as biomarkers for early diagnosis and follow-up treatments, with HSP47 and HSP110 as potential therapeutic targets.

keywords: Heat Shock Protein, Diagnostic biomarker, Therapeutic potential, Gastric Cancer, Prognosis

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PBi-147

Predictive value of body mass index (BMI) and determination of optimum cut-off point in the diagnosis of endometrial hyperplasia in pre-menopausal women with abnormal uterine bleeding

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Background:The suitable BMI cut-off point in persons with endometrial cancer or hyperplasia with abnormal uterine bleeding was investigated in this study.

Methods: This case-control research was conducted on 1470 women with abnormal uterine bleeding in Ayatollah Rouhani Hospital,Babol between 2010 and 2012, with 312 participants included in the study. In terms of uterine biopsy results, patients were split into six groups: simple hyperplasia without atypia, simple hyperplasia with atypia, complicated hyperplasia with atypia, complex hyperplasia without atypia, endometrial cancer, and normal persons.

Results: The mean age and BMI of patients in these three groups were not significantly different (P equal to 0.081 and 0.435, respectively). The kind of disease exhibited a strong relationship with menstruation (P 0.001). The body mass index (BMI) values did not have significant levels under the curve to determine the appropriate cut-off point in the diagnosis of hyperplasia plus endometrial cancer and endometrial cancer alone (P 0.380 and 0.124, respectively) and hyperplasia alone (P = 0.920). Based on logistic regression, age 50 years and older and irregular menstruation were significant with OR equal to 2.36 and 2.09 (P = 0.011) and HTN with OR equal to 0.44 (P = 0.026), respectively.

Conclusion: BMI has little predictive value in the detection of endometrial cancer or hyperplasia, according to the findings, and other diagnostic and screening modalities should be utilized instead. The findings backed up the theory that old age and irregular menstruation are linked to an increased risk of endometrial cancer.

keywords: Abnormal uterine bleeding, Endometrial cancer, Endometrial hyperplasia, Body mass index,

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Investigating the Effect of Galbanic Acid on Lipin-1 and Lipin-2 Genes in Fatty Liver Cells with Palmitate

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Non-alcoholic fatty liver disease is related to lipid accumulation and inflammation. Considering the role of lipin-1 and lipin-2 in fat homeostasis and inflammation, this study aimed to explore the effect of galbanic acid (Gal) and resveratrol (RSV) on alterations in the gene expression levels and protein abundance of lipin-1 and lipin-2 in HepG2 liver cells lipid-enriched with palmitate (Pal).

Methods: HepG2 cells were subjected to different amounts of Gal and RSV for 24 hours in the presence of Pal to induce lipid accumulation. The RT-PCR method was employed to assess the expression of lipin-1 and lipin-2 genes, while protein levels were evaluated by western blot analysis. Lipid accumulation was determined qualitatively and semi-quantitatively using the oil-red staining technique.

Results: Gal treatment increased lipin-1 and lipin-2 gene expression (P 0.05). In contrast, the groups treated with RSV did not show a substantial variance in the expression levels of the two genes (P 0.05). In the groups treated with Gal/RSV, the intensity of lipin-2 protein bands was higher compared to the Pal group (P 0.01); however, the intensity of lipin-1 protein bands was not significantly different (P 0.05).

Conclusion: Gal, a coumarin compound, significantly increased the expression of lipin-1 and lipin-2 in HepG2 cells treated with Pal. Consequently, this research suggests gal as a novel strategy for regulating fat homeostasis in HepG2 cells.

keywords: Galbanic acid, lipin-1, lipin-2, non-alcoholic fatty liver, resveratrol.

PBi-149

Association of S19W polymorphism in APOA5 gene and serum lipid levels in patients with type 2 diabetic nephropathy

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Type 2 diabetic Mellitus (T2DM) is the most common systemic and endocrine disease in humans, and diabetic nephropathy is one of the most serious complications of this disorder. The polymorphisms in the apolipoprotein A5 (ApoA5) gene are strongly related to hypertriglyceridemia and are considered a predisposing factor for diabetic nephropathy. The current study proposed to examine the association of APOA5-S19W polymorphism with serum lipids levels in patients with type 2 diabetic nephropathy in Mazandaran province.

Methods: This case-control study was designed to determine the association of APOA5‑S19W polymorphism with plasma lipid profile in 161 T2DM patients with nephropathy (DN+), without nephropathy (DN−), and in 58 healthy individuals. Lipid profile values were measured using Pars Azmoun commercial kits. S19W variant, one of the polymorphisms of the APOA5 gene, was determined by PCR‑restriction fragment length polymorphism (PCR-RFLP) and Taq1 restriction enzyme.

Results: In comparison between the three groups, DN+ had a higher mean TG than DN− and the control group (p0.001). The incidence of the G allele in DN+ was not significant compared to groups of DN−. Comparing the relationship between the mean of biochemical variables with CC and CG genotypes showed that the mean level of TG in people with CC genotype was increased compared to people with CG genotype in diabetic patients. However, this increase was not significant (p=0.19).

Conclusion: There was no association between SNP APOA5 S19W and serum lipids in diabetic patients with and without nephropathy.

keywords: apolipoprotein A5; lipid profile; polymorphism; type 2 diabetic nephropathy.

PBi-150

The significance of paying attention to medical emergencies in medical diagnostic laboratories in IRAN

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Medical diagnostic laboratories as high-risk environments are often exposed to unpredictable situations such as patient fainting, blood pressure drops, chemical spills, and burns. These life-threatening events defined as medical emergencies and necessitate urgent actions. Hence, determining the most common medical emergencies in medical laboratories, so understanding and planning strategies to effective management seems to be crucial. This study aimed to investigate medical crises in Iranian medical laboratories.

Methods: In this cross-sectional study data collection was performed by simple random sampling method through electronic and paper questionnaires filled by personnel in private and hospital laboratories in different provinces.

Results: The most frequent medical emergencies were patient fainting, staff needle stick, and patients' blood pressure dropping. The occurrence of medical emergencies was 24% and 76% in men and women, respectively. Out of all, treatment was administered at the scene of the accident in 37.1% of cases, and 28.1% were discharged after sampling. Moreover, 51% of the medical diagnostic laboratories had a trolley code, with injection devices and angiocaths as available tools. In 81% of the laboratories, practicing for probable medical emergencies was not possible. A significant relationship was found between the type of client (Laboratory personnel or the referring person or etc.) and the type of emergency event (p0.05).

Conclusion: Considering the prevalence and importance of handling medical emergencies in a short time, it is necessary to design training courses for laboratory personnel and expert them to encountering with unpredictable threats in order to help affected individuals.

keywords: Medical diagnostic laboratories, medical emergencies

PBi-151

The synthesis of starch nanoparticles and the analysis of their properties to enhance the pharmacodynamics and pharmacokinetics of a hydrophobic drug

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Medical Biochemistry, Quality control, Trace elements

Background and aim: A noticeable number of pharmaceutical substances and their metabolites are being investigated for cancer treatment, demonstrating enhanced therapeutic efficacy and reduced side effects compared to conventional FDA-approved medications. However, inadequate pharmacokinetic properties often impeded their clinical application, particularly low solubility. To manage this challenge, non-toxic carriers are utilized to improve the pharmacokinetic and pharmacodynamic characteristics of these drugs. Starch has emerged as a promising carrier in this context. This research focuses on developing nanoparticles through an emulsification method combined with sonication, aiming to enhance the delivery of hydrophobic drugs while minimizing adverse effects.

Methods: In this study, oil-in-water emulsification was employed to produce nanoparticles using an oil phase composed of a starch solution at varying concentrations (7.5, 10, 50, and 100 mg/ml) and SN38 dissolved in DMSO. The oil phase was gently introduced into water at 60 degrees Celsius during sonication, followed by centrifugation at 11,000 rpm to isolate the precipitate, which was subsequently washed and collected multiple times. The size and polydispersity index of the nanoparticles were determined via Dynamic Light Scattering (DLS), while drug loading was quantified using a spectrophotometer at a wavelength of 383 nm, the specific wavelength for SN38. The formation of nanoparticles was further confirmed through Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FTIR).

Results: In the emulsification method, the optimal conditions were characterized by using 10 mg of starch alongside 1 mg of SN38, resulting in a particle size range of 250 to 300 nanometers and a polydispersity index (PI) of 0.5. The drug loading efficiency was calculated to be 92% based on established formulas. Further analyses utilizing FTIR and DSC confirmed the formation of two hydrogen bonds, indicating a significant interaction between starch and SN38 molecules. Drug release profiles showed percentages of 86.4% in acidic phosphate-buffered saline (PBS) and 67.3% in neutral PBS over a duration of five days.

Conclusion: The sonication method demonstrates considerable potential in enhancing drug entrapment within starch matrices by transforming starch into a gel state. This transition not only improves the interaction between the drug and the starch but also provides a more efficient encapsulation process. Nonetheless, to fully realize its efficacy, further research is essential to optimize both the particle size and the PI, ensuring a more uniform and effective delivery system.

keywords: Starch, Nanoparticles, Emulsification

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PBi-152

Jaw bone changes in panoramic radiography in patients with hyperparathyroidism

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Medical Biochemistry, Quality control, Trace elements

Background and aim: About 82% of dialysis patients develop secondary hyperparathyroidism. There have been reports of jaw bone involvement due to secondary hyperparathyroidism in patients with renal insufficiency. The current investigation aimed to evaluate jaw bone changes including comparing the presence of gonial cortex bone thickness, MI index, LD, lower dental canal, and bone density in panoramic radiography in patients with hyperparathyroidism.

Methods: The present cross-sectional descriptive-analytical study was performed on 17 healthy individuals and 17 patients who suffered from resorptive hypercalciuria in the dialysis center of Shahid Beheshti Hospital in Babol in 2018. If patients had two or more decayed teeth, they were referred to a specialized maxillofacial clinic by the dentist for free for panoramic imaging. MYMCI, LD, bone change, mandibular cortical resorption, and general cortical indices were examined.

Results: There is a statistically significant difference between MI, the gonion region's cortical bone thickness, and the lower dental canal's root in the hyperparathyroidism and control groups (P 0.05). Nevetheless, in the hyperparathyroidism group and the control group, bone density changes and LD did not show a significant difference (P 0.05).

Conclusion: : The rwsults showed a decrease in the thickness of the cortical bone in the guinea pig, mental region, and lack of dental canal in resorptive hypercalciuria compared to healthy individuals. Therefore, the dentist can know these patients' radiographic symptoms to help diagnose general health and treat patients in any of the mentioned indices.

keywords: Jaw, Panoramic radiography ,Bone changes , radiography , hyperparathyroidism

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PBi-153

The Interplay of Hepatitis C Virus Infection, Liver Cirrhosis, and Hepatocellular Carcinoma: A Comprehensive Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Hepatitis C virus (HCV) infection is a major global health concern, often leading to chronic liver diseases, including liver cirrhosis and hepatocellular carcinoma (HCC). Understanding the mechanisms by which HCV contributes to liver damage and cancer development is critical for improving patient outcomes.

Methods: This review synthesizes findings from various studies examining the relationship between HCV infection, liver cirrhosis, and HCC. A systematic search of PubMed, Scopus, and Web of Science was conducted to identify relevant articles published in the last two decades. Key studies were selected based on their contributions to understanding the pathophysiological mechanisms linking HCV to cirrhosis and HCC.

Results: The analysis reveals that chronic HCV infection leads to persistent liver inflammation, fibrosis, and ultimately cirrhosis. The virus employs various strategies to evade the immune system, promoting an environment conducive to malignant transformation. Studies indicate that patients with cirrhosis have a significantly higher risk of developing HCC, with estimates suggesting that up to 25% of cirrhotic patients may progress to cancer within 10 years. Molecular mechanisms identified include the dysregulation of cell cycle control, apoptosis evasion, and activation of oncogenic signaling pathways.

Conclusion: The association between HCV infection, liver cirrhosis, and HCC underscores the importance of early detection and treatment of HCV. Effective antiviral therapies can reduce the risk of liver damage and subsequent cancer development. Future research should focus on elucidating specific molecular pathways involved in HCV-related carcinogenesis to identify potential therapeutic targets.

keywords: Hepatitis C Virus (HCV), Liver Cirrhosis, Hepatocellular Carcinoma (HCC), Chronic

PBi-155

The Emerging Role of Heat Shock Proteins in Ovarian Carcinoma: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Ovarian cancer as a silent killer, ranks the most prevalent gynecological cancer globally after cervical and uterine cancer. The primary treatment involves surgical cytoreduction to achieve R0 status, followed by adjuvant chemotherapy; however, resistance to these therapies presents significant challenges. Recent studies indicate that heat shock proteins (HSPs), are overexpressed in ovarian cancer and linking them to tumor progression and treatment resistance. This topic highlights their potential as biomarkers and therapeutic targets. This study aims to review the roles of HSPs in ovarian cancer and their potential in targeted therapies.

Methods: This review article was performed using articles published at PubMed, Science Direct, Google scholar, SID, and Web of science until October 2024. The keywords were heat shock proteins (HSPs) AND ovarian carcinoma OR ovarian neoplasms OR ovarian cancer. By searching this database; 45 articles were found. 28 Of them by Reading titles and abstracts were removed. 17 Articles were selected under the inclusion criteria. All articles were chosen from English and Persian articles.

Results: From the final 17 articles, research had shown that significant correlation between elevated levels of HSP27 and the expression of vimentin, a marker associated with metastatic potential in resistant cancer cells. Notably, HSP27 levels may increased in response to a secondary chemotherapeutic agent (WA), and its upregulation appeared to facilitate the production of glutathione (GSH) in cisplatin-resistant cells, thereby enhancing protection against oxidative stress. Additionally, HSP70 was implicated in promoting cancer cell survival and mediating resistance to chemotherapy, with its identification in serous type cells achieved using antibody TX-01. Reduced expression of HSP60 correlated with decreased OXSM levels, leading to diminished AL synthesis, which accelerated the proliferation of cancer cells. Increased HSP10 productions in ovarian cancer cells enhanced CD3-zeta expression, leading to T-cell suppression and immune evasion by tumors. Collectively, these results underscored the critical roles of HSPs in cancer cell resilience and their potential to overcome treatment resistance.

Conclusion: It seems that role of heat shock proteins (HSPs) in ovarian cancer progression and treatment resistance is becoming increasingly clear, significant gaps in knowledge remain. Further work needs to be done to establish whether specific HSP inhibitors can enhance the efficacy of current chemotherapy regimens. However, need to be more research done on this topic.

keywords: Ovarian carcinoma, Heat shock proteins (HSPs), Ovarian neoplasms, Ovarian cancer.

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The Role of Single-Cell Metabolomics in Understanding and Treating Rare Diseases: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Single-cell metabolomics is revolutionizing biological research, especially in rare diseases (RDs). This review highlights its role in unraveling cellular processes and disease mechanisms. Advanced techniques like mass spectrometry (MS) and nuclear magnetic resonance (NMR) enable precise metabolite quantification, revealing metabolic changes under various conditions. Cellular metabolism reflects the physiological state of tissues and organs, and analyzing metabolites at the single-cell level provides valuable insights. Focusing on metabolic disorders, including inborn errors of metabolism (IEMs), this review underscores the potential of single-cell metabolomics to enhance our understanding of RDs by capturing intricate metabolic networks and their alterations within individual cells.

Methods: : A comprehensive literature review was conducted using databases including PubMed, Google Scholar, and Web of Science. The search focused on articles published since 2020, exploring metabolomic analysis, advanced analytical techniques, and data analysis. Inclusion criteria were peer-reviewed articles investigating the production and consumption of metabolites within metabolic pathways, focusing on changes in healthy and diseased cells, and those induced by drugs or environmental factors. Excluded were articles not providing sufficient data on clinical applications or not in English. Selected articles were reviewed to analyze advancements in diagnostic accuracy, therapeutic efficacy, and nanoparticle design. Key variables included study design, sample size, analytical techniques, main findings related to health and disease metabolic changes, diagnostic accuracy, and clinical potential.

Results: Single-cell metabolomics enables the detection of low-abundance metabolites, offering insights into cellular functions and revealing metabolic heterogeneity undetectable by traditional bulk methods. Advanced technologies allow analysis of small, complex samples, deepening the understanding of disease progression. For rare diseases, detailed analysis of individual cell metabolism enhances diagnostic accuracy. With personalized medicine, the integration of metabolomics with genomics and transcriptomics supports tailored treatment strategies. Finally, combining multiple omics technologies enables comprehensive disease analysis, facilitating targeted therapy development and advancing rare disease research.

Conclusion: Single-cell metabolomics is revolutionizing rare disease research by providing detailed insights into disease mechanisms, improving diagnostics, and enabling personalized treatments. By analyzing metabolites at the single-cell level, this approach uncovers unique cellular processes that

traditional methods miss. As technologies advance, integrating single-cell metabolomics with other omics approaches, such as genomics and transcriptomics, will expand our molecular understanding of health and disease. This holistic strategy promises to enhance the study of rare diseases, paving the way for more precise diagnostics and targeted therapeutic interventions.

keywords: Single-Cell Metabolomics, Rare Disease, Advanced Analytical Techniques.

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PBi-157

Analyzing Single-Cell Metabolomics Using Mass Spectrometry: A Systematic Review

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Cellular metabolites rapidly respond to environmental and biochemical changes, indicating cellular states. Precise measurement of biomolecules at the single-cell level is essential to understanding cellular heterogeneity, which is critical for physiological functions. This analysis provides insights into disease pathogenesis and improves diagnostics. Over the past decade, mass spectrometry has significantly advanced single-cell metabolomics, profiling metabolites at the single-cell level. This review article focuses on analyzing Single-Cell Metabolomics using Mass Spectrometry.

Methods: This review analyzed articles from PubMed, ScienceDirect, Google Scholar, and Web of Science up to November 2024. Using keywords such as Single-Cell Metabolomics, Mass Spectrometry, and Screening Process, 76 articles were initially identified. After screening for relevance, 41 articles were selected for detailed analysis based on methodological rigor, relevance to single-cell metabolomics, and use of mass spectrometry techniques. Only articles published in English were included to ensure consistency in data interpretation.

Results: This systematic review of 41 selected studies on single-cell metabolomics using mass spectrometry highlights key advancements in the field. It emphasizes the role of mass spectrometry in understanding cellular heterogeneity and metabolite dynamics. The review identifies improvements in sensitivity and precision, as well as the growing applications in biomedical research, diagnostics, and drug development. Despite progress, challenges like low metabolite abundance and data complexity remain. Overcoming these issues will require advancements in instrumentation, computational tools, and integration with other single-cell omics techniques, advancing personalized medicine and disease understanding.

Conclusion: This regular approach eased a focused evaluation of advancements and challenges in the field, pressing significant trends, methodologies, and operations in single- cell metabolomics exploration exercising mass spectrometry. The findings contribute to a comprehensive understanding of this fleetly evolving field.

keywords: Single-Cell Metabolomics; Mass Spectrometry; Screening process.

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PBi-158

Fabrication hydrogel for bone tissue regeneration

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Alginate, a natural polysaccharide from brown seaweed, is valuable in tissue engineering due to its biocompatibility, biodegradability, and hydrogel-forming ability, which supports cell growth and differentiation. This project focuses on developing and optimizing alginate hydrogels for bone regeneration by modifying alginate properties to mimic the extracellular matrix, enhancing healing, and improving orthopedic outcomes. The research aims to create a biomimetic scaffold through various crosslinking techniques and the incorporation of bioactive agents to support osteogenic differentiation and new bone tissue formation.

Methods: To build an alginate hydrogel for bone generation: Dissolve 1 g of sodium alginate in 50 ml distilled water while stirring for 4 hours at room temperature. Heat the solution at 50° C for 30 minutes, then let it rest overnight. Add a divalent cation (e.g., calcium chloride) to induce gelation, allowing the alginate to form a three-dimensional network. The concentration of calcium ions can be adjusted to control gel properties. Mix in hydroxyapatite or collagen to enhance mechanical strength and osteoconductivity. This can improve cell adhesion and proliferation. Use techniques like FTIR and SEM to confirm the hydrogel’s structure and composition, ensuring it mimics the extracellular matrix for optimal bone regeneration and use MTT assay. This assay assesses cell viability through the measurement of formazan crystal absorbance in treated cells.

Results: Alginate hydrogels are promising materials for bone regeneration due to their biocompatibility, biodegradability, and ability to mimic the extracellular matrix. These hydrogels can be engineered to incorporate bioactive compounds and cells, enhancing osteogenic differentiation and promoting healing in critical-sized bone defects. Injectable alginate-based systems allow for minimally invasive applications, filling irregular bone contours effectively. Recent studies have shown that alginate hydrogels can support the delivery of mesenchymal stem cells (MSCs), facilitating bone repair through paracrine signaling and improved cellular responses in various animal models. Tests such as SEM and FTIR help make the construction of hydrogel and MTT tests are used to investigate its toxicity.

Conclusion: In conclusion, alginate hydrogels represent a promising strategy for bone tissue engineering. Their biocompatibility, tunable properties, and ability to support cellular activities position them as optimal candidates for the development of efficacious scaffolds for bone regeneration. Future research should concentrate on enhancing the mechanical properties and bioactivity of alginate hydrogels, as well as investigating their potential when combined with other materials, such as collagen or ceramics, to create hybrid scaffolds. Furthermore, the integration of stimuli-responsive characteristics could facilitate the responsiveness of alginate hydrogels to physiological alterations, thereby paving the way

keywords: alginate, bone tissue, scaffold

PBi-159

"Ethical, Social, and Environmental Challenges of Using Nanoparticles and Rare Elements in Combination Therapies: Long-term Effects and Emerging Crises"

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Nanoparticles and rare earth elements hold transformative potential in combination therapies for treating chronic and complex diseases. These technologies offer promising advancements in medical treatment, improving patient outcomes. However, their integration into medical applications raises significant ethical, social, and environmental concerns that must be addressed. This presentation will examine the potential and challenges of these technologies, focusing on their long-term effects and the emerging crises associated with their widespread use.

Methods: This study employs a multidisciplinary approach to assess the long-term health and environmental effects of nanoparticles and rare earth elements. The research utilizes human-based models to replace traditional animal testing and applies advanced methodologies to evaluate the toxicity and environmental impact of these materials. Additionally, the study explores strategies for minimizing environmental degradation, ensuring equitable access to treatments, and addressing social inequities related to the production and consumption of these materials.

Results: The findings indicate that while nanoparticles and rare earth elements have promising medical applications, their use can lead to long-term health risks, environmental degradation, and social disparities. The extraction and processing of these materials have significant ecological consequences, including pollution and resource depletion. Furthermore, there are growing concerns about unequal access to these advanced therapies, which may exacerbate existing social inequities.

Conclusion: In response to these challenges, it is crucial to establish strong ethical governance frameworks, comprehensive regulations, and international cooperation to guide the responsible use of nanoparticles and rare earth elements in medicine. Sustainable development practices and policy recommendations are needed to mitigate the adverse social and environmental impacts of these technologies. Further research into the biological mechanisms of these materials and their long-term effects on human health and the environment is essential to ensure their safe, responsible, and equitable application in medical therapies.

keywords: Nanomaterials-Rera Earth Element-Human-Health-Environmental Impact-Nanoparticle Toxicity-Ethical Challenges

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Epigenetic modifications: A bridge between chronic insomnia and age-related diseases

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Medical Biochemistry, Quality control, Trace elements

Background and aim: and combined using Boolean operators (e.g., AND, OR). The screening process began with an assessment of titles and abstracts for relevance, followed by a detailed analysis of full-text articles that met the inclusion criteria. Data from the selected articles were systematically extracted to assess the efficacy of oncolytic viruses- induced pyroptosis to tumor immunotherapy Aim and Background: Chronic insomnia holds significant public health implications, as individuals suffering from insomnia may face an elevated risk of age-related disorder such as Alzheimer disease (AD) and Parkinson disease (PD). Insomnia has been proposed as a factor that may lead to accelerated aging, potentially

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including chronic insomnia, epigenetic and age-related disorder were investigated.

Results: It has been reported that symptoms of insomnia were linked to an elevated epigenetic age in blood tissue and correlated with a higher prevalence of late-differentiated CD8+ T cells. Notably, it has been described that the buildup of CD8+ T cells might be a reaction to neuronal damage and neuroinflammation associated with aging or the advancement of AD. Disrupted sleep-wake patterns are linked to the activation of transcription factor STAT3 and the upregulation of DNA methyltransferase 1 (DNMT1). Interestingly, it has been documented that the JAK2/STAT3 signaling pathway is crucial for inhibiting the neurogenesis of neural stem cells (NSCs), as it modulates DNA methylation and demethylation at the epigenetic level.

Conclusion: This study suggest that insomnia is associated with an increase in epigenetic modification of inflammatory signaling pathways that may be the molecular basis for the association of chronic insomnia and age-related diseases.

keywords: Chronic insomnia, Epigenetic, Age-related diseases

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A Systematic Review of Magnetic Nanoparticle Applications in Cancer: Innovations and Clinical Challenges

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Magnetic nanoparticles (MNPs) offer exceptional potential in oncology due to their unique properties, such as superparamagnetism, biocompatibility, and surface functionalization. These features enable applications in advanced diagnostics (e.g., magnetic resonance imaging [MRI]) and therapies (e.g., targeted drug delivery and hyperthermia). This study systematically reviews progress from 2020 to 2024 in MNP applications for cancer diagnosis and treatment, focusing on innovations that address challenges in clinical translation.

Methods: Google Scholar, Science Direct and PubMed databases were searched, and 10 peer-reviewed studies published between 2020 and 2024 were selected. Articles were analyzed for advancements in diagnostic accuracy, therapeutic efficacy, and nanoparticle design, with an emphasis on experimental outcomes and clinical potential.

Results: Advancements in MNP functionalization had significantly improved tumor targeting capabilities. In diagnostics, MNPs enhanced MRI contrast for earlier and more precise tumor detection. Therapeutically, they showed success in targeted drug delivery with controlled release and reduced side effects. MNP-based hyperthermia therapies demonstrated promising tumor reduction in preclinical models. However, challenges like particle aggregation, immune response, and long-term safety persist.

Conclusion: MNPs represent a transformative tool in oncology, offering dual benefits for diagnostics and treatment. Continued research is essential to overcome current limitations and accelerate their integration into clinical practice. The findings emphasize the need for collaborative efforts to refine MNP technologies for improved cancer care.

keywords: Magnetic nanoparticles; Cancer diagnosis; Targeted therapy; Hyperthermia; Nanomedicine

PBi-162

CRISPR/Cas9-Mediated Knockout Strategies for Enhancing Immunotherapy in Esophageal Squamous cell Carcinoma

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Esophageal cancer is the sixth leading cause of cancer death, accounting for one in 18 cancer deaths. 85 percent of esophageal cancers are squamous cell carcinoma of the esophagus. CRISPR is an innovation with the ability to precisely manipulate the genome and has high potential in treating various cancers, including esophageal cancer. The aim of this study is to review the CRISPR/Cas9-mediated knockout strategies for enhancing immunotherapy in esophageal squamous cell carcinoma(ESCC).

Methods: This review article included studies published on PubMed, Science Direct, Google Scholar, and SID until November 2024. The keywords were CRISPR/Cas9, esophageal squamous cell carcinoma, and immunotherapy. By searching this database, 23 articles were found, about 12 of them by reading titles and abstracts were removed, and 11 articles were selected under the inclusion criteria.

Results: Targeting modulatory genes, or tumor suppressors, in ESCC models by CRISPR/Cas9 was revealed. C-Terminal Binding Protein 1 (CtBP1) had been implicated in ESCC. By employing the CRISPR/Cas9 genome editing system for disabling the CtBP1 gene in ESCC cell lines, inhibition of proliferation, invasion, and metastasis happened. CtBP1 might promote esophageal squamous cell carcinoma cell malignancy and confer paclitaxel resistance. Cisplatin resistance as a first-line drug for chemotherapy is the major obstacle in the esophageal carcinoma treatment. By screening the cisplatin resistance-related genes of esophageal cancer using CRISPR/Cas9 gene editing, it was revealed that ERCC8 could be a new biomarker for predicting cisplatin resistance and could be an effective target for the treatment of cisplatin resistance in ESCC. High MEST expression was associated with promoted cancer invasion and metastasis in ESCC. MEST could activate SRCIN1/RASAL1-ERK-snail signaling by interacting with PURA. Blockade of MEST-PURA interaction could have therapeutic potential in ESCC.

Conclusion: It seems that CRISPR/Cas9 provides vigorous site-specific gene editing to enhance its biological and clinical uses are in cancer biology and oncology, especially in esophageal squamous cell carcinoma. However, more study is required on this topic.

keywords: Esophageal squamous cell carcinoma (ESCC), CRISPR/Cas9, immunotherapy

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Analyzing Spatio-Temporal Patterns of Congenital Hypothyroidism in Newborns: A Study from Hormozgan, South Iran (2011-2023)

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Congenital Hypothyroidism (CH) is a significant cause of intellectual disability and impaired growth in newborns. Early diagnosis is crucial for effective treatment. Newborn screening conducted within the first few days of life can facilitate the identification of congenital hypothyroidism. Disease mapping is instrumental in pinpointing regions with a higher risk of this condition. This study aimed to assess the patterns of CH by employing a Poisson Spatio-temporal high-rate patterns in hormozgan counties based on scanning maximum 50 percent window size.

Methods: This cross-sectional analytical study utilized data from all infants diagnosed with congenital hypothyroidism (CH) in Hormozgan, Iran, between 2011 to 2023. To analyze the data, a Poisson Spatio-temporal model was implemented within a Bayesian framework, employing the Markov Chain Monte Carlo (MCMC) method through Satscan software version 4.2.4. Additionally, counties maps of Hormozgan were created using ArcGIS software for visual representation.

Results: During the study period, there were 473456 live births in Hormozgan, Iran, with a 240.57 per 100,000total number of incidence rate of (CH). The high-rate disease temporal analysis revealed that the cluster of high rate disease in 2017 with 347.32 incidence rate. The lowest incidence rate was recorded in 2011, while the highest occurred in 2017. Following that year, there was a slight downward trend in the incidence rates.

Conclusion: Despite an increasing incidence rate of congenital hypothyroidism (CH) up to 2017, there has been a subsequent decline in the incidence rate from 2017 to 2023. This trend suggests that while the condition was becoming more prevalent during the earlier years, the rates have started to decrease in recent years.

keywords: Spatio-temporal; ArcGis; Hypothyroidism; Hormozgan, Iran

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Autophagy Inhibition Enhanced Hydroxychloroquine-Induced Apoptotic Death in Breast Cancer Cells

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Autophagy is a natural, programmed process in eukaryotic cells that eliminates long-lived, deformed proteins and degraded cytoplasmic organelles. Harnessing the autophagy system as a cancer therapy strategy requires understanding mechanisms of cell survival under chemotherapy and optimal design of nanocarriers for drug delivery. One of the challenges in cancer treatment is tumor resistance to current therapies, often resulting from apoptotic defects. Manipulating autophagy as an alternative cell death pathway can maximize cancer cell elimination. This study aimed to use PEGylated L-Cysteine-coated magnetic nanoparticles (CMPNs) to deliver hydroxychloroquine (HCQ) as an autophagy inhibitor for enhanced breast cancer therapy.

Methods: Autophagy was investigated in the MCF-10A normal breast epithelial cell line (control) and MDA-MB-231 and MCF-7 breast cancer cell lines. Cytotoxicity was assessed using the MTT assay. Autophagy was evaluated by monodansylcadaverine staining analyzed via flow cytometry. Apoptosis was determined using Annexin-V/PI staining. In addition, the expression of autophagy-related genes (LC3, Beclin1) and apoptosis-related genes (BAX, BCL2, CASPASE-3) was quantified by real-time PCR. RNA was extracted using a commercial kit, and cDNA synthesis was performed. Real-time PCR was carried out with SYBR Green dye on a thermocycler, and relative gene expression was analyzed using the 2^− Δ Δ Ct method.

Results: CMPN/HCQ significantly inhibited the growth of MCF-7 and MDA-MB-231 breast cancer cells, with minimal cytotoxic effects on MCF-10A cells. L-Cysteine functionalized magnetic nanoparticles (CMPNs) alone showed no cytotoxicity or autophagy activation. Treatment with CMPN/HCQ suppressed autophagy and increased apoptosis levels in MCF-7 and MDA-MB-231 cells, as evidenced by Annexin-V staining and altered expression of autophagy- and apoptosis-related genes. Specifically, LC3 and Beclin1 expression decreased, while BAX and CASPASE-3 expression increased, with concomitant BCL2 downregulation, confirming the induction of mitochondrial apoptosis.

Conclusion: This study demonstrates that CMPN/HCQ induces cytotoxicity in breast cancer cells by suppressing autophagy and activating mitochondrial apoptosis pathways, with negligible effects on normal cells. By elucidating the role of HCQ in altering autophagy and apoptosis gene expression, this study introduces a novel approach for targeted breast cancer therapy. The combined use of HCQ and CMPNs offers a promising therapeutic strategy to overcome tumor resistance and enhance treatment specificity. Future in vivo studies are warranted to validate these findings.

keywords: Autophagy, Apoptosis, Breastfeeding Carsinoma

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Mitochondrial function: A crucial mediator in glucose-induced insulin release

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Mitochondrial metabolism of pancreatic beta cells is a crucial part of glucose-stimulated cascade of insulin secretion. Effective factors on β-cells mitochondrial function in production of compounds such as tricarboxylic acid intermediates, glutamate, nicotinamide adenine dinucleotide phosphate, and reactive oxygen species can have great effects on the secretion of insulin under diabetes. This review aimed the evaluation of factors influencing mitochondrial function as a key mediator of glucose-induced insulin release that accordingly will be helpful to further our understanding of the mechanisms implicated in the progressive beta cell failure that results in diabetes.

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including mitochondria, Glucose-sensing, insulin release and diabetes were investigated and combined using Boolean operators (e.g., AND, OR). The screening process began with an assessment of titles and abstracts for relevance, followed by a detailed analysis of full-text articles that met the inclusion criteria. Data from the selected articles were systematically extracted to assess the efficacy of oncolytic viruses- induced pyroptosis to tumor immunotherapy.

Results: Recent metabolomic investigations in models of type 1 diabetes have shown down-regulation of the key TCA cycle, mitochondrial proteins, and enzyme activities. Studies have shown that the suggested insulin secretion KATP independent pathway is managed by mitochondrial a factor of which relies on anaplerosis and possibly calcium signaling. The mitochondrial membrane potential of diabetic β-cells has been found to be a distinct response to acute inhibition of ATP synthesis during glucose stimulation. As a result, the mechanistic deficit in glucose-stimulated insulin release and mitochondrial hyperpolarization of human diabetic. Damaged respiration capacity of mitochondria and ROS-mediated uncoupling protein-2 (UCP2) expression results in insufficient ATP production during glucose stimulation, which leads to a defect in subsequent insulin release signaling. The mitochondrial dynamics change in pancreatic β cells seems to be the starting point of the progression of Type 2 DM.

Conclusion: This study increases our knowledge about the mechanism of action of factors affecting amplifying pathways of insulin release that accordingly will be helpful to further our understanding of mechanisms involved in beta cell defects which results in diabetes.

keywords: Mitochondria, Glucose-sensing, Insulin release, Diabetes

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Early Detection and Prevention of Type 2 Diabetes

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Medical Biochemistry, Quality control, Trace elements

Background and aim: One of the growing global health challenges is Type 2 diabetes mellitus (T2DM), which is caused by complex interactions between genetic, metabolic, and environmental factors. There have been many advancements in this subject. However, many patients remain undiagnosed until complications show up, which is why there is a critical need for effective early detection methods. In this study, significant biomarkers and methods for early detection of T2DM are studied, and prevention strategies with personalized medicine are explored.

Methods: The current study conducted a comprehensive literature search in PubMed for articles published between 2000 and 2024 using keywords such as ‘’ Type 2 diabetes’ ’ , ‘’ Personalized medicine’ ’ , ‘’ epigenetic biomarkers’ ’ , ‘’ Biomarker discovery’ ’ and ‘’ Diabetes prediction’ ’ 47 of 250 identified were chosen because of their focus on biomarker discovery and diabetes risk stratification studies. Data were analyzed to identify recurring themes and validate key biomarkers associated with prediabetes and early diabetes onset, with a focus on their translational and clinical significance. Open-access, full-text articles were reviewed using thematic analysis to synthesize comprehensive findings.

Results: The articles that were studied in this review have shown a range of biomarkers, including metabolic markers (branched-chain amino acids, linoleoylglycerophosphocholine), genetic polymorphisms, and inflammatory markers (CRP, IL-6). Metabolomic profiling has consistently remarked the imbalances of amino acid and lipid metabolisms to be early indicators of T2DM. Accuracy of risk prediction is improved by Combining genomic data with metabolomic insights. Prediabetic cases showed significantly higher inflammation markers, which is associated with impaired glucose metabolism. A capable predictive performance is shown By integrating biomarkers into machine learning models (AUCs exceeding 0.9 in several studies).

Conclusion: This study discusses the significant role that Non-glucose biomarkers play in enabling early T2DM detection and personalized prevention methods. There seem to be promising advances in metabolomics and genomics. These advances can be a great hope in order to identify high-risk patients and achieve interventions right in time. To conduct future research, investigating these biomarkers in different populations and finding predictive ways to increase clinical benefits is a valuable topic. These findings should lead to personalized therapies in diabetes prevention, with an emphasis on early-life interventions and modifying lifestyle.

keywords: Type 2 diabetes, Early detection, Metabolomics, Biomarker discovery, Personalized medicine

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The urolithin B nanomicellar delivery system as an efficient selective anticancer compound

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Urolithin B (UB), the antioxidant polyphenol has a protective influence on numerous organs against oxidative stress. However, its bioactivity is restricted by its hydrophobic nature. In the current investigation, UB was encapsulated into a liposomal form to increase its bioactivities anticancer, and antibacterial properties.

Methods: The UB nano-emulsions (UB-NE) were synthesized and characterized utilizing FESEM, DLS, FTIR, and Zeta-potential analysis. The UB-NMs' selective toxicity was studied using an MTT assay on MCF-7, PANC, AGS, and ASPC1 cells. The AO/PI analysis verified the cytotoxicity of UB-NM on ASPC1 cell lines and approved the MTT results. Finally, the antibacterial activity of the UB-NMs was studied on gram-positive (B. subtilis, S. aureus) and gram-negative (E. Coli, P. aeruginosa) bacteria by conducting MIC and MBC analysis.

Results: The 68.15 nm UB-NMs did not reduce the survival of normal HDF cells. However, they reduced the cancer cells' (PANC and AGS cell lines) survival at high treatment concentrations (250 µg/mL) compared with normal HDF and cancer MCF-7 cells. Moreover, the IC50 doses of UB-NMs for the ASPC1 and PANC cancer cells were measured at 44.87, and 221.02 µg/mL, respectively. The UB-NMs selectively exhibited apoptotic-mediated cytotoxicity on the human pancreatic tumor cell line (ASPC1) by down-regulating BCL2 and NFKB gene expression. Also, the BAX gene expression was up-regulated in the ASPC1-treated cells. Moreover, they exhibited significant anti-bactericidal activity against E. coli (MIC = 50 µg/mL, MBC = 150 µg/mL), P. aeruginosa (MIC = 75 µg/mL, MBC = 275 µg/mL), B. subtilis (MIC = 125 µg/mL, MBC = 450 µg/mL), and S. aureus (MIC = 50 µg/mL, MBC = 200 µg/mL) strains.

Conclusion: The encapsulation of UB into UB-NMs successfully overcame its hydrophobic limitations, enhancing its bioactivity for potential therapeutic applications. UB-NMs demonstrated selective cytotoxic effects against ASPC1 by inducing apoptosis via the downregulation of anti-apoptotic genes (BCL2, NFKB) and upregulation of pro-apoptotic BAX gene expression. These findings highlight the potential of UB-NM as a targeted anticancer agent with minimal toxicity to normal cells. Additionally, UB-NMs exhibited significant antimicrobial activity, effectively inhibiting the growth of both gram-positive and gram-negative bacterial strains. These results underscore the dual-functional potential of UB-NMs as both an anticancer

keywords: Urolithin B, Anticancer, Antibacterial, Nano.

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The Effect of Peracetic Acid (PAA) on Neutralizing Pathogens in Food, Pharmaceutical, and Healthcare Industries

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Medical Biochemistry, Quality control, Trace elements

Background and aim: Peracetic acid (PAA) is a disinfectant solution widely used in food-grade applications to sanitize surfaces in contact with food. It is considered highly safe and has been approved by the FDA as a no-rinse disinfectant due to its lack of hazardous residues. PAA is effective against a variety of microorganisms, including bacteria, fungi, molds, yeasts, and viruses. This study reviews the applications of peracetic acid in various food industries and healthcare settings, focusing on its mechanism of action in neutralizing bacteria.

Methods: This review utilized international scientific resources, including PubMed and Google Scholar, to gather references. A total of 15 full-text articles were reviewed to compile this study.

Results: Research indicates that applying peracetic acid to stainless steel surfaces can reduce microbial contamination by up to 80%, demonstrating its high effectiveness as a biocide. Furthermore, studies reveal that using PAA on poultry and meat products can lower the risk of Shigella and Salmonella infections by up to 70%. Additional research highlights its efficacy in the fishing and seafood packaging industries for disinfecting surfaces and products.

Conclusion: Peracetic acid disinfectant can be employed to sanitize food-contact surfaces, such as tanks, pipelines, fillers, pasteurizers, and aseptic equipment, using CIP and COP methods. It is also suitable for disinfecting fruits and vegetables in sorting and cold storage industries. Industrial-grade PAA is applicable in water and wastewater treatment, environmental remediation (soil, air, and water), disinfection of medical waste, agricultural soil and water sanitation, and reducing greenhouse-related diseases. Recognized by the FDA as a no-rinse disinfectant due to its lack of hazardous residues, PAA provides reliable microbial contamination control. Although not

keywords: Peracetic Acid, Biocide, CIP, COP, Disinfectant Solution, Sterilization

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MicroRNA-based biomarkers in lung cancer: novel and potential tools for diagnosis

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Medical Genetics

Background and aim: The incidence and mortality of lung cancer are high due to late diagnosis and limited treatment, it is important to use biomarkers that allow a quicker diagnosis and improve the survival of these patients. In this case, biomarkers based on miRNAs have supposed a considerable advance. miRNAs, which are small sequences of RNA, can regulate gene expression. In addition, miRNA biomarkers can be obtained from liquid biopsies, which are less intrusive. In this review, we highlight the importance of miRNAs as biomarkers and collect the existing evidence on their association with lung cancer.

Methods: To define miRNA signatures for lung adenocarcinoma, specimens were obtained. Total RNA containing small RNA was extracted from specimen. To optimize a panel of miRNAs that could be detected, miRNA profiling was performed using miRNA array. Expression of the identified miRNA signatures was evaluated by using real-time RT-qPCR.

Results: Lung cancer's late diagnosis is one of the main problems with its classification. Some studies focus on how liquid biopsies could become a novel tool for early lung cancer detection. Various miRNA families have been investigated as diagnostic biomarkers in this regard. Also, many studies showed that miRNAs can be achieved from liquid biopsies. So, in this study we found that the overexpression of has-miR-21, has-miR-210, has-miR-200, has-miR-182 and has-miR-183 are associated with tumor growth, while the repression of the has-miR-30 or has-miR-451 has the same behavior.

Conclusion: In conclusion, we can develop a panel of miRNAs that can be reliably measured in specimens. Detection of the miRNAs could be used as a noninvasive and cost-effective diagnostic tool to detect early-stage lung cancer.

keywords: MicroRNA; Biomarker; Lung cancer.

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TaqMan Real-time PCR assay can effectively quantify the gene expression of BCL2, BIRC5 and GRB7 Biomarkers in Breast cancer cell lines and tissues

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Medical Genetics

Background and aim: Immunohistochemistry and Fluorescence In Situ Hybridization are standard techniques used in clinical laboratories to evaluate important biomarkers in breast cancer. However, these methods have limitations, including high visual skill detection. Reverse transcription quantitative PCR offers quantitative gene expression data that can lead to more effective therapeutic approaches tailored to a patient's genetic profile, surpassing qualitative methods. Key biomarkers such as BCL2, BIRC5, and GRB7 are significant in breast cancer progression and invasion, serving as promising prognostic markers for metastasis and treatment response. This study aimed to design a TaqMan real-time PCR assay to measure the gene expression of these biomarkers.

Methods: We developed a TaqMan probe RT-qPCR method to assess the expression levels of BCL2, GRB7, and BIRC5 across three breast cancer cell lines (MCF7, SK-BR3, and MDA-MB-468) and one normal breast cell line (MCF10A). The Cells were cultured, and the expression of the three biomarkers was initially assessed using immunocytochemistry-immunofluorescence (ICC-IF). Subsequently, RNA was extracted from the cell lines, and the RT-qPCR assay was employed. The relative expression levels of each biomarker were calculated using the Livak formula in conjunction with a relative standard curve. Statistical analysis was performed to compare the expression levels between cancer cell lines and the normal cell line. The assay was also applied to 100 early-stage breast

cancer samples and 12 normal tissue samples to evaluate biomarker expression across different breast cancer subtypes.

Results: The relative expression levels of BCL2, GRB7, and BIRC5 in the cell lines, analyzed using RT-qPCR were consistent with the findings obtained through the standard ICC-IF method. The developed assay effectively and reliably differentiates between high and normal expression levels. Analysis of tissue samples indicated that BCL2 expression was higher in less aggressive, early-stage breast cancer subtypes, such as Luminal A. Conversely, as the cancer subtype became more aggressive (Luminal B, HER2-enriched, and Triple Negative), BIRC5 expression levels increased. In the HER2-enriched subtype, simultaneous overexpression of HER2 and GRB7 was observed due to their close genetic loci.

Conclusion: The RT-qPCR method for measuring the biomarkers BCL2, GRB7, and BIRC5 exhibited the capability to quantitatively assess expression levels in both cell lines and tissue samples with high sensitivity and reproducibility. These findings underscore the test's potential for effective application in clinical laboratories, facilitating better diagnostic and prognostic assessments in breast cancer management.

keywords: Breast cancer; Biomarkers; RT-qPCR; BCL2; GRB7; BIRC5

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Interaction between circular RNAs and the NF-κB signaling pathway in driving breast cancer progression

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Medical Genetics

Background and aim: Circular RNAs (circRNAs) have recently emerged as critical regulators in various cancers, including breast cancer. They function as molecular sponges, regulating microRNAs (miRNAs) and interacting with signaling pathways such as NF-κB. The NF-κB pathway is a key player in inflammation and cancer progression. This review explores the cross-talk between circRNAs and the NF-κB signaling pathway in breast cancer, focusing on their role in tumor growth, metastasis, and therapy resistance.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Circular RNAs, NF-κB, breast cancer, 62 articles related to inclusion criteria were extracted and then analyzed.

Results: The review revealed that certain circRNAs are upregulated in breast cancer tissues and are associated with poor prognosis. These circRNAs were found to modulate the NF-κB pathway, leading to enhanced proliferation, invasion, and resistance to apoptosis. For instance, circRNAs can bind to miRNAs that negatively regulate NF-κB, thus promoting NF-κB activation and further driving tumor progression. Inhibition of these circRNAs in experimental models has shown to suppress tumor growth and metastasis.

Conclusion: The cross-talk between circRNAs and the NF-κB pathway presents a novel mechanism of breast cancer progression. Targeting this interaction could offer new therapeutic opportunities, especially for treatment-resistant breast

cancers. However, the precise regulatory networks remain complex, and further research is needed to identify the most effective circRNA targets for clinical intervention. Understanding this interplay may lead to more effective strategies for managing breast cancer.

keywords: Circular RNAs, NF-κB, breast cancer.

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Exploring the Pathogenic Potential of Synonymous Mutations

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Medical Genetics

Background and aim: Always, non-synonymous mutations have been the focus of extensive research due to their significant clinical implications. Meanwhile, a growing body of studies has demonstrated that synonymous variants can also lead to alterations in RNA and protein structures, contributing to the onset and progression of more than 85 different human diseases and cancers. This highlights the complexity of genetic variations and their potential impact on health.

Methods: This review aims to illuminate the pathogenicity associated with a few synonymous mutations, emphasizing their clinical relevance.

Results: These mutations can influence codon usage, which may affect the efficiency of translation. Furthermore, they can alter the secondary structure and stability of mRNA molecules, potentially impacting gene expression levels. Moreover, synonymous mutations can influence splicing mechanisms, leading to the production or deletion of alternative mRNA isoforms. This can change the functional properties of the resulting proteins, thereby contributing to disease mechanisms. Additionally, these mutations can affect miRNA binding sites, which are crucial for post-transcriptional regulation. The disruption of miRNA interactions can lead to dysregulation of gene expression, further complicating the molecular landscape of various diseases. Research has shown that synonymous mutations are associated with a range of serious health conditions, including various forms of cancer, neurological disorders, and metabolic syndromes. These alterations can lead to the accumulation of misfolded proteins, which is a hallmark of neurodegenerative disease pathology.

Conclusion: By providing a comprehensive overview of the current scientific understanding, this review seeks to foster greater awareness of the complexities surrounding synonymous mutations and their potential roles in disease etiology. As research continues to evolve in this area, it is crucial to integrate these findings into clinical practice and genetic counseling, ultimately enhancing our understanding of genetic contributions to human health and disease.

keywords: Synonymous mutations; Pathogenicity; Neurodegenerative disease; Clinical implications

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The role of circular RNAs in breast cancer, at a glance

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Medical Genetics

Background and aim: Abstract Lately, the dysregulation of circRNAs has been investigated in various malignancies, including breast cancer. CircRNAs participate in the initiation, progression and metastasis of breast cancer through various mechanisms and act as oncogenes or tumor suppressors. Background and Aim: This article presents a better insight into the role of circRNAs as important biomarkers in the diagnosis, prognosis and treatment of breast cancer.

Methods: Methods: I searched for articles in scientific databases like PubMed, Scopus, Web of Science and Google Scholar and read more than 50 articles.

Results: Result: CircRNAs, as a new class of non-coding RNAs, play a considerable role in the occurrence and development of various diseases, including cancer. Recently, the dysregulation of circRNAs in various malignancies, including breast cancer, has been investigated in a series of studies. In addition, it has been reported that many circRNAs are abnormally expressed in breast cancer tissues and cell lines. Also, circRNAs play a considerable role in cell proliferation, invasion, migration, apoptosis and resistance to treatment in breast cancer through various mechanisms including miRNA sponge. CircAGFG1 have been reported as a sponge for miR-653-5p, which is abnormally highly expressed in breast cancer and can influence the malignant behavior of cancer cells and may be associated with the risk of death. CircRNA_103809 and circFOXK2 have also been reported to promote breast cancer invasion and migration via sponging miR-532-3p and miR-370, respectively. Moreover, circSEPT9 can promote the proliferation, migration and invasion

Conclusion: Conclusion: This research showed that circRNAs expression changes in breast cancer and targeting these circRNAs can be used to design targeted therapeutic strategies in fighting these cells. It is believed that with the unceasing efforts and practical explorations of scientists, circRNAs will open a new field for tumor research and hopefully create a new starting point in clinical diagnosis and treatment.

keywords: Keywords: circular RNA; breast Cancer; non-coding RNA; diagnostic biomarker; microRNA

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The end of cancer with viral therapy

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Medical Genetics

Background and aim: Viruses with a simple genome, such as adenovirus 5, which move specifically to the receptor of cancer cells and encode the desired genes on the cancer cell genome and the contents of the cell's exosome are changed. In this way, in addition to reducing the power of metastasis, exosomes can create immunity for the cells that are targeted, or the cancer cell can be completely destroyed by the virus.

Methods: A systematic review on the relationship between exosome and leukemia virus.

Results: Specificity of the virus can be done by identifying the genetic changes of the mutated cell in addition to specific markers.

Conclusion: By targeting the contents of exosomes secreted from both cells (normal and cancer), it is possible to repair and reduce the function and spread of cancer cells.

keywords: cancer, exosome, virus

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Application of clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 for treatment of Glioma

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Medical Genetics

Background and aim: Glioma is one of the most malignant and aggressive forms of brain tumors, which is the main cause of brain cancer-related deaths. Because of the consequences of surgical removal of brain tumors, such as intracerebral hemorrhage (ICH), infection, and damage to healthy parts of the brain, molecular techniques are expanding, including CRISPR-Cas9, a genome-editing tool that allows precise targeting of specific genes within a cell's DNA. Therefore, this review aims to provide a useful summary of the latest research findings in this area.

Methods: Several databases, including Google Scholar, PubMed etc. were searched. Using the terms "glioma", "genome editing" and "CRISPR", relevant articles published between 2015 and 2023 were selected and reviewed.

Results: Several genetic and epigenetic changes in cancer cells induce malignant cell growth and provide chemoresistance. Repairing or ablating such mutations with the CRISPR-Cas9 genome editing method has shown enormous potential in the fight against cancer. As a new gene-editing technology, CRISPR-Cas9 is a noteworthy tool in tumor-targeted therapies. By blocking cell signaling pathways related to tumors, the treatment of glioma gene mutations at a molecular level is possible. In addition, various studies demonstrated that CRISPR-Cas9 gene-editing can induce tumor cell autophagy, resulting in accelerated apoptosis and other mechanisms to eliminate tumor cells. While CRISPR-Cas9 represents an innovative gene editing technology, its transmission to the brain is fraught with challenges that current delivery systems do not fully address. Other setbacks, including a lack of on-target editing efficiency, incomplete editing (mosaicism), and inaccurate on-target or off-target editing, also remain unresolved.

Conclusion: The CRISPR-Cas9 approach plays a significant role in the immunotherapy of glioma, the establishment of a tumor model, mechanism research, and the screening of targeted drugs for glioma. While CRISPR-Cas9 technology holds great promise for the cure of glioma and has been successfully utilized in preclinical cancer research, its clinical application is still at an early stage of development. Therefore, further research is needed to fully describe the efficacy and safety of this strategy in medical applications.

keywords: Glioma, CRISPR-Cas9, genome editing

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Investigating the effects of 3D co-culture of MCF7 breast cancer cell line in alginate hydrogel with Adipose-derived stem cells condition medium, on Viability, cell cycle, ROS level and BCL2،CCND1 ،SIRT1 expression of cancer cell

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Medical Genetics

Background and aim: Breast cancer is one of the most common malignancies. Although there are various methods to destroy cancer cells, many cancer treatment methods lead to the damage of healthy cells as well. For this reason, cell therapy and the use of mesenchymal stem cells (MSCs) in cancer treatment are of interest. MSCs play an important role in cancer control by regulating the expression of gens. Therefore, in this study, investigated the effects of Adipose-derived stem cells (ADSC) condition medium (CM) enhanced with ellagic acid (EA) or pomegranate seed extract (PSE) on Viability, cell cycle, ROS level and BCL2،CCND1 ،SIRT1 expression in

Methods: In this study, after the preparation of MCF-7 cells and ADSC, the cells were divided into 9 groups, respectively: MCF7 cells, MCF7 cells+ CM, MCF7 cells + CM &PSE, MCF7 cells + CM& EA. Then, Annexin V-PI analysis to check the amount of cell viability, flow cytometry to analyze the cell cycle, Malondialdehyde test to check the amount of Reactive oxygen species (ROS) and to measure the amount Real time-PCR was used to genes expression.

Results: The present study showed that the use of CM with EA and PSE compared to the use of CM individually, caused a greater decrease in the expression of BCL2،CCND1 ،SIRT1. Also, the amount of MDA decreased in all treatment groups (P0.001). Also, the CM of ADSCs had tumor inhibitory effects such as stopping the cell cycle and reducing cell viability, however, strengthening the conditioned medium with EA and PSE improved its antitumor effects (P0.001).

Conclusion: The findings of the present study showed that the CM enhanced with EA or PSE have a greater effect on stopping the progression of cancer by decreasing the expression of BCL2،CCND1 ،SIRT1 and cell death as well as decreased cell viability compared to the CM alone.

keywords: Pomegranate seed extract, ellagic acid, Adipose-derived stem cells, MCF-7 cancer

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Colorectal Cancer Screening Program Results in Najafabad, Iran from 2019 to 2023

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Medical Genetics

Background and aim: Colorectal cancer(CRC) accounts for a large proportion of the global burden of cancer and is the fourth leading cause of cancer-related mortality worldwide.Fecal Immunochemical Testing (FIT) can be used for CRC screening programs due to its high accuracy and compliance.The present study reports the preliminary results of the CRC screening program in Najafabad among all people aged 50 to 69 years.

Methods: This cross-sectional study was carried out on 30387 participants referred to health centers in Najafabad for CRC screening programs in 2019 to 2023. The data required for this study was taken from the CRC screening program. Relevant information for all individuals aged 50 to 70 referred to the health system that was called for colorectal cancer screening was extracted from the Integrated Electronic Health Records (SIB) database. Finally,the standards indices were calculated for all provinces.

Results: Among a total number of over 36 Thousand, 62% were female, and the number of people with positive FIT evaluated for the CRC screening program was 2343(7.7%) respectively.

Conclusion: Positive cases should be referred for further evaluation and colonoscopy. Before performing a screening program, the conditions for performing colonoscopy for these people must be assessed and prepared.The FIT for CRC screening program can be easily promoted.

keywords: Colorectal, colonoscopy, Screening

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mTOR gene variant rs2295080 might be a risk factor for atherosclerosis in Iranian women with type 2 diabetes mellitus

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Medical Genetics

Background and aim: Type 2 diabetes mellitus, one of the most prevalent metabolic disorders worldwide, is closely linked with an enhanced risk of atherosclerosis. However, the molecular mechanism of this linkage is not still clear. Genetic variations in the mTOR gene may increase the susceptibility of individuals to these diseases.

Methods: 109 diabetic patients and 375 healthy subjects participated in this study. mTOR Single Nucleotide Polymorphism (SNP) rs2295080 was determined using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP).

Results: Comparison of genotypic, allelic, and genotypic combination frequencies between cases and controls revealed no significant result. Nevertheless, the frequency of rs2295080 GT+TT genotype was significantly more in diabetic women with atherosclerosis compared with those without atherosclerosis (p=0.047). Besides, the rs2295080 G allele was more frequently detected in diabetic women without atherosclerosis compared to those with atherosclerosis (p=0.046).

Conclusion: The rs2295080 GT+TT genotype predisposes Iranian diabetic women to atherosclerosis, while the rs2295080 G allele protects them against atherosclerosis. However, additional experiments using larger sample sizes are needed to verify this result.

keywords: Type 2 diabetes mellitus, mTOR, atherosclerosis, Single Nucleotide Polymorphism, SNP

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The expression of hsa-mir-148a and hsa-mir-24-3p in the malignant and normal uterine tissues: The effects on LDL and HDL receptors through MAPK Pathway.

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Medical Genetics

Background and aim: Endometrial cancer is the 6th most common cancer in women and ranks as a significant cause of death among gynecological malignancies. MicroRNAs are small noncoding RNAs ranging in length from 20 to 22 nucleotides and have emerged as critical regulators in cancer biology. There are different miRNAs such as miR-148a-3p and miR-24-3p which are important in cancer biology The aim of this study was to explore the differential expression of miR-148a-3p and miR-24-3p in endometrial cancer tissues, compared to those of adjacent normal tissues,

Methods: Tumor and normal tissue samples were collected from 50 patients and the expression of miR-148a-3p and miR-24-3p were predicted using RNAseq analysis and were assessed by qRT-PCR Bioinformatic analyses, including GO and KEGG pathway analyses were performed to elucidate the processes associated with these miRNAs.

Results: The present results revealed that in endometrial cancer tissues miR-24-3p was significantly reduced in grade two, 35.5% and in grade three, 69.6% when compared to those of normal adjacent tissues. In contrast, miR-148a-3p was increased, in these tissues, 3.28-fold in grade 2 and a 5.15-fold in grade 3 tumors . GO enrichment analysis indicated that miR-24-3p was associated with MAPK cascade and membrane organization, while KEGG analysis revealed that miR-148a-3p was involved in cancer related pathways, FoxO, TGF-beta, and MAPK.

Conclusion: These findings shows that miR-24-3p was significantly downregulated and miR-148a 3p was pregulated in the endometrial adenocarcinoma tissues and the changes were significantly correlated with the tumor grades. In addition, these miRNAs were associated with MAPK signaling pathway.

keywords: miRNA , endometrial cancer , hsa-mir-148a-3p , hsa-mir-24-3p , RNA-seq

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Identification of a Novel c.5778dup Mutation in the VWF Gene Associated with Type 3 von Willebrand Disease in an Iranian Consanguineous Family

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Medical Genetics

Background and aim: About 1% of people worldwide suffer from von Willebrand disease (VWD), the most prevalent genetic bleeding illness, which is caused by a malfunction or deficit of the von Willebrand factor (VWF). A protein necessary for platelet adhesion and protective factor VIII is encoded by the VWF gene, which is found on chromosome 12. VWD is divided into type 2 (qualitative defects) and types 1 and 3 (quantitative deficiencies). Type 1 is the most common, often inherited autosomal dominant, while type 3 follows an autosomal-recessive pattern. This study investigates the mutation causing VWD in a girl from an Iranian consanguineous family.

Methods: Whole-exome sequencing (WES) was utilized to identify genetic variants in the affected individual. To evaluate the pathogenic potential of the variant found in the VWF gene, various computational tools, including SIFT, CADD, Mutation Taster, Polyphen-2, and PANTHER, were employed. Conservation analysis of the VWF protein sequence was conducted using Clustal Omega and ConSurf tools, while the three-dimensional structure of the VWF variant was predicted through the I-TASSER server. Protein-protein interactions

involving VWF were examined using the STRING database. The DynaMut web server was also leveraged to investigate how the identified mutation affects protein dynamics and stability. Furthermore, the impact of this variant on protein stability was evaluated using the I-Mutant and MUpro web servers.

Results: : Our study found a new mutation in the VWF gene, c.5778dup (p.Cys1927ValfsTer3), which fits the patient's symptoms and points to a diagnosis of VWD type 3. Sanger sequencing was used to confirm that the variant was inherited in a homozygous state within the family, and numerous databases were used to evaluate the pathogenicity and novelty of the found variant. Identifying this genetic mutation as the cause of VWD highlights the clinical significance of genetic testing, especially WES, as it has made it easier to identify the mutation as a contributing factor to the disease.

Conclusion: Identifying a novel mutation in the VWF gene emphasizes how crucial clinical genetic testing is for diagnosing VWD. To make accurate diagnoses and create efficient treatment strategies, comprehensive genetic study is essential because the symptoms of VWD might resemble those of several other bleeding disorders. This recently identified mutation enhances our knowledge of the genetic components underlying VWD, which expands the list of known mutations associated with the disorder. Our findings further highlight the importance of early genetic diagnosis and family screening, particularly in consanguineous groups.

keywords: Willebrand disease, VWF gene, bleeding illness, whole exome sequencing, genetic

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Identification of a Novel MCOLN1 Mutation Associated with Mucolipidosis Type IV in an Iranian Consanguineous Family

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Medical Genetics

Background and aim: Mucolipidosis type IV(MLIV) is a rare autosomal recessively inherited lysosomal storage disorder characterized clinically by acute psychomotor delay, ophthalmological abnormalities, agenesis of corpus callosum, and achlorhydria. Regardless of the disorder's early age onset, most patients experience poor progression and maintain a steady state for the first 2-3 decades of life. MLIV is associated with the MCOLN1 gene mutations, encoding the transient receptor potential cation channel named Mucolipin-1. This membrane protein localizes on late endosomes and lysosomes. The purpose of this study is to uncover the molecular basis underlying MLIV in an 11-year-old patient from an Iranian family with consanguineous marriage.

Methods: A whole exome sequencing (WES) approach was utilized to detect pathogenic variants in an 11-year-old boy of an Iranian family with consanguineous marriage, showing signs suggestive of MLIV disease. Additional Sanger sequencing confirmation was performed in a trio study with the proband and both parents. Computational methods including SIFT, CADD, Mutation Taster, Polyphen-2, and PANTHER were utilized to verify the pathogenicity of the mutation found in the MCOLN1 gene. Clustal Omega and ConSurf softwares were used to perform conservation analysis of the MCOLN1 protein sequence, and the

I-TASSER server was used to predict the three-dimensional structure of the MCOLN1 mutation. The STRING database was used to analyze MCOLN1 protein-protein interactions. The effects of the identified mutation on protein dynamics and stability were also examined using the DynaMut web server. Additionally, the I-Mutant and MUpro online services were used to assess the impact of this mutation on the stability of proteins.

Results: Whole exome sequencing (WES) detected a novel homozygous missense mutation (c.1384GT, p.Glu462Ter) in the MCOLN1 gene, which is indicative of a diagnosis of MLIV, and compatible with the patient's symptoms. The identified mutation in the MCOLN1 gene stands as pathogenic based on the latest ACMG criteria. Analysis of co-segregation through Sanger sequencing established that this mutation was inherited from the parents. Co-segregation analysis via Sanger sequencing confirmed inheritance of the mutation from both parents. The identified mutation was analyzed for its pathogenic properties and novelty across multiple databases.

Conclusion: The identification of a novel disease-causing genetic mutation in the MCOLN1 gene that is associated with MLIV, underscored the importance of clinical genetic testing, including tests such as WES, as an accurate diagnostic procedure for affected individuals. Manifestation of MLIV symptoms may exhibit overlap with a spectrum of other neurological disorders. Thus, genetic analysis is a crucial approach for clarifying the diagnosis. The novel MCOLN1 gene mutation expands the clinical spectrum of MLIV.

keywords: Mucolipidosis type IV, MCOLN1 gene, Whole exome sequencing, IRAN

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Claudin-4 expression and Human Esophageal Cancer: A Systematic Review

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Medical Genetics

Background and aim: Esophageal cancer is one of the most common and lethal cancers worldwide. Its typically late diagnosis limits therapeutic options, resulting in poor prognosis and low survival rates for affected individuals. Among various biomarkers, claudin-4 (CLDN-4) has gained research interest for its potential role in tumor progression and metastasis. CLDN-4, a tight junction protein, is crucial for maintaining cellular adhesion and tissue integrity. Alterations in CLDN-4 levels and localization within tumor cells may disrupt cellular barriers, promoting invasiveness and metastasis. This systematic review aims to investigate changes in CLDN-4 expression levels and assess potential factors affecting its regulation in esophageal cancer.

Methods: Scopus, PubMed, and Web of Science databases were comprehensively searched for studies examining CLDN-4 gene and protein expression in esophageal cancer tissue from patient samples or esophageal cancer cell lines. To ensure specificity and relevance, we applied rigorous exclusion criteria. Studies related to conditions such as Barrett's esophagus, gastroesophageal adenocarcinoma, and other gastrointestinal cancers were excluded, as were studies focused on CLDN-4 gene methylation, microarray analysis, and other claudin family genes. Additionally, review articles, animal studies, non-English language publications, and studies lacking relevant or extractable data were omitted. From an initial collection of 202 manuscripts, careful screening and application of inclusion criteria yielded 6 eligible studies.

Results: A total of 6 studies, including 596 patients and 7 esophageal tissue-related cell lines, were included in this systematic review. The studies were

conducted in Japan, South Korea, China, and Finland. In these studies, the level of CLDN-4 in cancer samples related to esophageal cancer and its location within esophageal tissue cells were examined.

Conclusion: The altered level of CLDN-4 in esophageal tissue with cancer may change the state of tight junctions, leading to a shift in barrier function. However, given the conflicting results reported, further studies are needed to interpret the role of CLDN-4 in esophageal cancer precisely.

keywords: CLDN-4, Esophageal adenocarcinoma, Esophageal squamous cell carcinoma

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Investigating polymorphisms that play a role in breast cancer recurrence

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Medical Genetics

Background and aim: Breast cancer (BC) is a frequent malignant tumor that increasingly affects women worldwide. The necessity for molecular markers has perpetually been proposed to facilitate the differentiation of individual variability and consequently forecast relapse or survival among patients exhibiting comparable clinical conditions. This study aims to investigate certain polymorphisms that lead to BC recurrence.

Methods: A comprehensive systematic search of relevant studies up to 2024 was performed by searching databases such as PubMed, MEDLINE, SCOPUS, and Google Scholar. The keywords "breast cancer", "multiform" and "recurrence" were used in this search. Only articles with fully accessible English texts were included in the search parameters. Articles that were reviews, duplicates, or irrelevant were not included.

Results: In this systematic review study, only 13 articles matched our inclusion criteria after preprocessing and screening. The examination of multiple genetic polymorphisms pertinent to chemotherapy agents revealed a statistically significant correlation between early postoperative recurrence in patients exhibiting the MDR13435CC and MTHFR677CC genetic polymorphisms, as well as those possessing the additional GSTP1 313AG polymorphisms. Furthermore, the findings from an alternative investigation indicated that the rs1056628 and rs17576 polymorphisms may have an impact on BC recurrence. Additionally, the genotypes related to cytokine production, specifically IL-10, IL-6, IFN-γ, and TNF-α, did not demonstrate any association with overall BC incidence or relapse status; however, the low-production genotypes of TGF-β1 (TGF-β1 10 CC) were found to be linked to an elevated likelihood of disease relapse.

Conclusion: Genetic polymorphisms in inflammatory cytokines and drug-metabolizing enzymes have a major impact on the risk of BC recurrence. Extensive research on the molecular origins and roles of particular genetic variations could result in more effective treatments that lower the risk of recurrence and enhance patients' long-term prognoses with BC.

keywords: Polymorphisms, Breast cancer, Relapse

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Investigating polymorphisms that play a role in colorectal cancer recurrence

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Medical Genetics

Background and aim: Colorectal cancer (CRC) is a predominant cause of mortality associated with gastrointestinal malignancies worldwide. Despite the implementation of surgical interventions and subsequent chemotherapy, a notable percentage of patients face recurrence. Recent research has highlighted genetic variations as significant factors influencing the progression and prognosis of colon cancer. A deeper understanding of these polymorphisms may improve risk assessment and therapeutic outcomes for patients with locally advanced CRC.

Methods: A comprehensive systematic search of relevant studies up to 2024 was performed by searching databases such as PubMed, MEDLINE, SCOPUS, and Google Scholar. The keywords " Colorectal cancer", " Polymorphisms" and " Relapse" were used in this search. Only articles with fully accessible English texts were included in the search parameters. Articles that were reviews, duplicates, or irrelevant were not included.

Results: In this systematic review study, 95 articles were retrieved through searching in databases, of which only 9 articles matched our inclusion criteria. Genetic variations, including PLS3 rs6643869 and LCP1 rs4941543, were identified as significant factors affecting the risk of tumor recurrence. Single nucleotide polymorphisms (SNPs) associated with angiogenesis, specifically VEGF C+936T and IL-8 T2251A, were correlated with a reduced time to recurrence, suggesting their potential utility as prognostic indicators. Furthermore, the miRNA-encoding genes miR219-1 and miR-608 displayed varying associations with survival rates in patients undergoing 5-FU-based chemotherapy. Conversely, the impact of HSPB1 rs2070804 on colorectal cancer (CRC) progression remains ambiguous, as it

showed limited connections with clinical factors such as tumor aggressiveness and metastasis.

Conclusion: The discovery of specific SNPs within plastin genes, angiogenesis-related genes, miRNA-encoding genes, and heat shock proteins (HSPs) holds potential for the development of personalized treatment approaches and risk evaluation in CRC patients. Future investigations should aim to confirm these results in larger populations and assess their clinical relevance for enhancing patient outcomes.

keywords: Polymorphisms, Colorectal cancer, Relapse

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Transcriptome analysis revealed the role of Cholesterol metabolism and foxO signaling pathway in circadian-disrupted animal models

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Medical Genetics

Background and aim: Circadian disruption, the misalignment of the endogenous biological clock to environmental cues, especially light/dark cycles, is increasingly being recognized to have widespread impact on human disease. These may be induced through life events like shift work and working in night artificial light. The interrelationship that exists between disrupted circadian and the progression of a disease brings into focus the need for examining the involved mechanisms. This study presents an analysis of gene expression data related to circadian rhythm disorders, utilizing GEO datasets and the R programming language to identify key genes that are upregulated and downregulated in such conditions.

Methods: The raw RNAseq data of circadian disruption samples, including GSE165198, GSE165199, GSE166335, and GSE245519 were retrieved from the GEO database. The total number of samples was 137 samples, including 66 cases of normal circadian rhythm, 71 cases of Circadian disruption in Mus musculus. The DESeq2 package was utilized to study the differentially expressed genes.

Results: Our analysis showed a significant number of DEGs related to circadian rhythm disorders, including FABP1, APOA1, S1PR1, S1PR4 genes involved in circadian rhythm disorders found in this study. These genes play diverse roles in

various biological processes, particularly in metabolism and cellular stress responses. Through GO analysis, we identified several molecular pathways including cholesterol metabolism and FOXO signaling pathway.

Conclusion: In conclusion our results show that diffident genes and pathways dysregulate after circadian disruption. These findings could pave the way for the development of new therapeutic strategies to reduce the effects of circadian disruption.

keywords: Circadian disruption; FOXO signaling; cholesterol metabolism, RNAseq.

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A Novel Splice Site Mutation in EDAR Gene in a Patient with Autosomal Recessive Ectodermal Dysplasia 10B: A Molecular Docking Simulation Study and Literature Review

Teymoor Khosravi [1] ℗, Fatemeh Vaghefi [1], Farzaneh Motallebi [1], Arian Rahimzadeh [1], Zainab M. Al Sudani [1], Mohaddese Mohsenipour [1], Parham Nejati [2], Morteza Oladnabi [3] ©

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Medical Genetics

Background and aim: Ectodermal dysplasia 10B, hypohidrotic/hair/tooth type (HED10B) is a rare autosomal recessive disorder characterized by hypotrichosis (sparse hair), hypohidrosis (reduced ability to sweat), and hypodontia (absence of teeth). The clinical presentation of HED10B often includes thin, lightly pigmented scalp hair, deficient sweating leading to hyperthermia, and delayed eruption of a few abnormally formed teeth. Physical growth and psychomotor development typically remain normal. This study aimed to investigate the genetic basis of HED10B in a patient through whole exome sequencing (WES) and to explore the structural implications of a novel mutation using molecular docking simulation.

Methods: Whole exome sequencing (WES) was performed on the proband to identify potential disease-causing variants. A splice site mutation (EDAR: c.730+1GT) was identified and further confirmed by PCR-Direct sequencing (Sanger Sequencing) in a trio analysis involving the proband and both parents. Molecular docking simulations were subsequently conducted to assess the functional impact of the identified mutation on protein structure and interaction.

Results: The WES analysis revealed a novel homozygous splice site mutation (EDAR: c.730+1GT) in the EDAR gene, consistent with the clinical features of

HED10B in the patient. Sanger sequencing confirmed the segregation of this mutation in the family, with both parents being heterozygous carriers. Molecular docking simulation studies suggested that the identified mutation could significantly alter the protein's structural conformation and binding affinity, potentially impairing its function.

Conclusion: The identification of a novel splice site mutation in the EDAR gene expands the mutational spectrum of HED10B and highlights the role of comprehensive genetic testing in diagnosing this condition. Understanding the structural implications of such mutations through molecular docking simulation provides valuable insights into the pathogenesis of the disease and may guide future therapeutic strategies.

keywords: Ectodermal dysplasia, EDAR, WES, Molecular docking simulation,

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Novel Bi-allelic Mutation in VDR Gene in Two Patients with Vitamin D-Resistant Rickets

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Medical Genetics

Background and aim: Rickets is a metabolic disorder that impairs bone growth due to disruptions in calcium or phosphate metabolism, often linked to vitamin D deficiency or genetic factors. A rare variant, hereditary vitamin D-resistant rickets (HVDRR), results from mutations in the VDR gene that hinder the body's response to vitamin D. Our objective is to investigate the clinical features, genetic factors, and bioinformatics findings related to a familial case of HVDRR, aiming to enhance understanding of its underlying genetic mechanisms, we have identified a novel missense mutant of VDR gene.

Methods: We assessed a twelve-year-old girl diagnosed with Vitamin D-dependent rickets type 2A (VDDR2A), who displayed skeletal deformities and total body alopecia. After obtaining informed consent from her family, we collected blood samples for genetic analysis. DNA was extracted from both blood and amniotic cells, with its concentration evaluated using a Nanodrop device. The VDR gene was amplified via PCR using primers designed with Oligo 7 software, followed by sequencing to detect genetic variants. The identified variants were confirmed through Sanger sequencing, while potential maternal cell contamination was excluded using QF-PCR.

Results: The twelve-year-old patient, a member of a Turkmen family, exhibited clinical manifestations characteristic of VDDR2A, with her younger sister similarly affected, while their parents were asymptomatic. Genetic analysis identified a novel homozygous GT mutation (c.529GT) in exon 5 of the VDR gene, leading to a premature stop codon (p.E177X) and a truncated protein. Sanger sequencing

revealed that both parents were heterozygous carriers, while the proband, her sister, and an affected fetus were homozygous for this mutation. Co-segregation analysis confirmed the inheritance pattern of the mutation.

Conclusion: This study uncovered a novel homozygous mutation (c.529GT; p.E177X) in the VDR gene that causes Vitamin D-dependent rickets type 2A (VDDR2A). This finding broadens the spectrum of known mutations linked to VDDR2A and provides valuable insights into the genetic mechanisms of this disorder. Furthermore, our results highlight the importance of early genetic diagnosis and family screening to inform effective clinical management, particularly in populations with higher rates of consanguinity, such as the Turkmen ethnic group.

keywords: Rickets, Vitamin D-Dependent Rickets, VDR Gene, Genetic Mutation, Familial Disorders

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Optimizing CRISPR-Cas9 genome editing: Reducing Off-target effects through Machine learning-driven sgRNA design

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Medical Genetics

Background and aim: The CRISPR/Cas-9 system is recognized as a revolutionary and innovative technology in genetic modification. This technology holds significant potential for in vivo gene therapy. One of the main challenges in using this system is its off-target effects. One approach to address this challenge is the design of sgRNA with high efficiency and specificity to minimize off-target effects. Various methods are available to predict the off-target activity of sgRNAs. In this study, we review the use of machine learning algorithms to address the off-target effects of the CRISPR/Cas-9 system, aiming to overcome the limitations of this technology.

Methods: In this review, we collected articles from the PubMed and Google Scholar databases published between 2016 and 2024. The search keywords included CRISPR/Cas-9, Machine learning, Prediction, Genome editing, and Off-target.

Results: Using machine learning techniques to optimize sgRNA design and reduce off-target effects in CRISPR-Cas9 genome editing has yielded promising results. These studies have significantly improved target prediction accuracy by analyzing experimental data and utilizing advanced algorithms. For instance, models like CnnCrispr and DeepCRISPR, which use convolutional neural networks (CNN) and deep learning, have achieved precise off-target effect predictions. sgRNA engineering has led to a substantial reduction in unwanted mutations and enhanced editing efficiency in target cells. Optimizing sgRNA sequences through machine learning has resulted in up to a 50% reduction in off-target effects, improving the accuracy and safety of CRISPR for therapeutic applications.

Increased precision and safety can boost the efficacy and public trust in CRISPR technology. These findings highlight that combining CRISPR with machine learning is a powerful, innovative approach to enhancing the precision and efficiency of genome editing.

Conclusion: CRISPR is rapidly becoming a reliable tool for genetic modification due to its simplicity, efficiency, specificity, and programmability, offering significant advantages over other gene-editing methods. Designing sgRNA is a multidisciplinary task that requires understanding CRISPR's biological mechanisms and machine learning algorithms. While current machine learning models address CRISPR's challenges effectively, limitations still exist but are expected to improve soon. As CRISPR's clinical applications grow and mechanisms are better understood, machine learning-based sgRNA design tools will enhance predictive accuracy, allowing for sgRNAs with minimal off-target effects.

keywords: CRISPR/Cas-9, Machine learning, Prediction, Genome editing, Off-target.

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Evaluating the potential of gene therapy in improving Friedrich Ataxia-Induced cardiomyopathy: A review of animal studies and future applications

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Medical Genetics

Background and aim: Friedreich's ataxia is a rare genetic disorder that presents significant challenges for affected individuals. This autosomal recessive disease progresses gradually with neurological issues and cardiomyopathy. It is caused by excessive GAA repeats in the frataxin (FXN) gene, leading to a marked reduction of the frataxin protein in mitochondria. Heart failure is the leading cause of death, typically by the third decade of life. Thus, gene therapy using viral vectors like AAVs to boost cardiac FXN expression may offer a promising way to extend the lifespan of these patients.

Methods: In this review study, articles from the PubMed and Google Scholar databases were collected, focusing on publications from 2014 to 2024. The keywords Friedrich Ataxia, Gene therapy, Frataxin, and Cardiomyopathy were utilized for the search in these databases.

Results: Since cardiac complications are the leading cause of mortality in Friedrich Ataxia, researchers developed genetically modified mice lacking the FXN gene. Studies and experiments conducted on these FXN-deficient mice showed that those treated with an AAV vector carrying the FXN gene experienced increased frataxin levels in cardiac cells, resulting in improved lifespan and weight. Additionally, the cardiac dysfunction associated with Friedrich Ataxia improved in these mice. However, the increase in this protein due to genetic manipulation is still difficult to control, and excessive overexpression -up to about 20 times the normal level- can lead to adverse effects. The gradual and excessive increase in

frataxin, which correlates with worsening cardiac disorders, poses a challenge for this treatment approach. Uncontrolled overexpression disrupts the mitochondrial respiratory chain, ultimately leading to cardiomyocyte dysfunction, cell death, and fibrosis.

Conclusion: Gene therapy has shown significant potential in clinical studies for treating various genetic disorders. Friedreich's ataxia is one such condition that is still under investigation for treatment through viral gene delivery vectors. However, the results highlighted in this review study demonstrate the promising capabilities of this therapeutic approach, which needs to be tested and validated in human subjects. These findings could lead to developing new and effective therapeutic strategies for this disease, providing hope for patients and the medical community.

keywords: Friedreich's ataxia, Gene therapy, Cardiomyopathy, Frataxin

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Beyond Boundaries: A Narrative Exploration of seekRNA's Transformative Role in Genetic Engineering and Therapeutics

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Medical Genetics

Background and aim: SeekRNA technology is an advanced method that employs certain probes to identify and track RNA, allowing live imaging without requiring complicated sample preparation. It was established to resolve earlier disadvantages and improve traditional methods like RT-PCR and FISH from the 1960s to 1970s, which lacked real-time tracking due to the requirement for cell fixation. Although they were unable to track RNA in real time, CRISPR-Cas9 and Cas13 enabled DNA editing and RNA research in the 2010s. SeekRNA recently proved exceptional precision in real-time RNA identification, which makes it useful for researching viral infections, cancer, genetic disorders, and cell differentiation.

Methods: Searches were conducted for scientific papers utilizing the keywords "seekRNA," "RNA imaging technology," "RNA detection," and "CRISPR-Cas13" " in a number of reliable databases, such as PubMed, Scopus, ScienceDirect, and IEEE Xplore.

Results: The seekRNA technique has proven beneficial in three primary research areas: 1. Detection of RNA SeekRNA accurately detects strange RNA expression patterns in cancer cells, enabling researchers to comprehend the mutations that promote cancer growth and proliferation. This result could lead to new treatments aimed at cancer-specific RNAs. 2. Analysis of Infections and Cellular Response In infection studies, seekRNA monitors viral interactions with host cell RNA in order to assess how host cells respond to infections. This perspective helps discover new cellular immune systems against viruses, which could lead to medicines with antiviral properties targeting viral RNA. 3. Investigation of Cellular Growth and Differentiation RNA detects RNA changes during the stages of stem cell development, which aids investigations on tissue engineering and

regenerative medicine. This detail is critical for developing stem cell-based medicines and tissue repair approaches

Conclusion: SeekRNA technology, which is popular for its accuracy and sensitivity in RNA research, has the potential to be an essential instrument in genetics and biomedicine. Considering developments like just cost reduction and improved probe design, it could soon be accessible to more research and medical facilities. The addition might assist with discovering new treatments for genetic disorders, cancers, and viral infections, and it also might enhance our understanding of molecular processes that occur at the RNA level. Furthermore, seekRNA could play a significant function in personalized medicine.

keywords: seekRNA; RNA imaging technology; RNA detection; CRISPR-Cas13.

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Circular RNA as a biomarker in the diagnosis and pathogenesis of cancer

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Medical Genetics

Background and aim: Cancer is the second cause of global death after cardiovascular diseases. Almost 70% of cancer deaths occur in low-income and middle-income countries. It is expected that this disease will account for 80% of deaths in Iran in the next 15 years. In addition, this chronic and exhausting disease imposes a significant economic burden on society because its treatment is long and the drug combinations used to treat cancer are more complex than other diseases.

Methods: Medical sciences electronic databases like PubMed and Google Scholar were searched For studies published between February 2020 and July 2024. Search was performed with the following terms: cancer; CircRNAs; biomarker; diagnosis and pathogenesis. Finally, 40 related articles were selected and reviewed from studies of the last five years.

Results: Currently, the main treatments for cancer are radiotherapy, chemotherapy and surgery. Also, early screening of cancer is highly dependent on tissue biopsies, which are invasive and limited. Therefore, in order to diagnose cancer early, there is an urgent need to develop other non-invasive diagnostic methods with high sensitivity and specificity, including the use of biomarkers. Some characteristics of CircRNAs have made them suitable and effective options as diagnostic biomarkers in this disease. This type of noncoding RNAs cannot be easily degraded by exonucleases, and due to their high copy number and stable structure, they have been widely identified in eukaryotic cells, and they can be found in blood and various body fluids such as saliva, urine, and vaginal fluid.

Conclusion: In this review, we summarize the biogenesis, pathogenesis, and biomarker role of circRNAs in cancer and also discuss their potential as diagnostic biomarkers with therapeutic targets. Collectively, circRNA research allows

researchers to enter a new level in epigenetic regulatory networks, whereby future research may lead to a better understanding of circRNA regulatory mechanisms in the cancer.

keywords: cancer; circRNAs; biomarker; diagnosis; pathogenesis

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Investigating and Measuring HER2(Human Epidermal Growth Factor Receptor 2) Gene Expression in Breast Cancer Patients for Treatment: A Systematic Review Article

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Medical Genetics

Background and aim: Breast cancer is a common cancer in women, though rare in men, and is classified into invasive and non-invasive types. The HER2 gene, responsible for producing a protein that regulates cell growth and division, can be overexpressed in some cancers, including breast cancer. Abnormal HER2 expression promotes tumor growth, and HER2-positive tumors are typically associated with a worse prognosis compared to HER2-negative ones. Around 15-20% of breast cancer patients exhibit HER2-positive expression, which is linked to faster disease progression and poorer treatment outcomes.

Methods: This systematic review article was written in 2024 by searching PubMed and Google Scholar databases using the keywords HER2 Gene, Breast Cancer, HER2 Positive, Breast Cancer Treatment. In the initial search, 1,743 articles were found, of which only 87 were relevant. From these, 15 articles were duplicates, 27 were published before 2020, 9 were in languages other than English, and 17 were excluded due to lack of specificity. Ultimately, 19 articles were included in the final analysis.

Results: Overexpression or amplification of ERBB2, which encodes HER2, is found in 15 to 20 percent of invasive breast cancers and is associated with an aggressive phenotype and poor clinical outcomes. Additionally, there is a 20-30 percent increased likelihood of disease recurrence in these individuals. In a study

involving 1,125 consecutive cases of primary or metastatic breast cancer examined between 2015 and 2020, both HER2 IHC and ISH were assessed, with 84.6 percent of these individuals demonstrating definitive HER2 status. Approximately 20-30 percent of HER2-positive patients may exhibit resistance to specific targeted therapies; however, the overall response rate to targeted treatment in this group is high.

Conclusion: Targeted therapies appear to significantly improve outcomes for HER2-positive individuals; however, due to the presence of treatment-resistant cases, further research in this area is necessary. The diagnosis of HER2 gene expression through various laboratory methods such as IHC and FISH is among the best therapeutic approaches, and patients who are HER2 positive respond to targeted treatments like trastuzumab. Overall, elucidating the precise relationship between HER2 gene expression and breast cancer significantly aids in the diagnosis, management, and treatment of this disease. Given the high importance of this issue, further studies.

keywords: HER2 Gene, Breast Cancer, HER2 Positive, Breast Cancer Treatment

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Non-Invasive Preimplantation Genetic Testing (niPGT) in Cancer Patients: A Systematic Review of Genetic Risk Assessment and Clinical Applications in Assisted Reproduction

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Medical Genetics

Background and aim: Patients with a cancer history often require genetic screening due to heightened hereditary risks that may impact their offspring. Conventional preimplantation genetic testing (PGT) typically involves invasive biopsies, which may compromise embryo viability. NiPGT, by analyzing cfDNA secreted into SCM, presents a compelling alternative for detecting chromosomal abnormalities and genetic mutations while preserving embryo integrity. This review aims to assess the effectiveness, accuracy, and current limitations of niPGT in the context of genetic risk assessment for cancer patients.

Methods: A thorough literature review was conducted on recent studies (2018–2023) using key databases such as PubMed, ScienceDirect, and ResearchGate. Selected studies evaluated the efficiency of cfDNA extraction protocols, contamination control strategies, and the comparative accuracy of niPGT versus traditional biopsy-based PGT. Data synthesis included SCM-based niPGT methodologies, examining single and dual-stage culture media, cfDNA collection timing, and protocol consistency.

Results: The findings indicate that niPGT demonstrates encouraging accuracy, with some studies showing sensitivity rates up to 95% for detecting chromosomal aneuploidies in embryos cultured under ideal conditions. Nevertheless, factors such as maternal DNA contamination, cfDNA degradation, and embryonic mosaicism can influence accuracy. Advances in cfDNA amplification and contamination control have improved results, though challenges persist, particularly regarding the detection of low-level mosaicism. NiPGT provides

valuable genetic insights that can inform genetic counseling and embryo selection for cancer patients, though further standardization is necessary for routine clinical use.

Conclusion: : NiPGT shows significant potential as a non-invasive genetic risk assessment tool for cancer patients undergoing ART. While methodological advancements have bolstered its clinical applicability, issues related to DNA contamination and mosaicism detection must be resolved to standardize its use. Future research should focus on refining cfDNA collection and amplification techniques to enhance niPGT's clinical reliability and reduce risks associated with invasive embryo biopsies.

keywords: non-invasive preimplantation genetic testing; cancer patients; genetic risk assessment; cell-free

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Identification and Characterization of LncRNAs Implicated in Cervical Cancer Lymph Node Metastasis: Implications for Therapeutic Intervention and Diagnostic Applications

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Medical Genetics

Background and aim: Cervical cancer progression and poor prognosis are often linked to nodal metastasis. Long non coding RNAs (lncRNAs) are key players in cancer development, but their roles in nodal metastasis in cervical cancer remain unclear. Identifying relevant lncRNAs could improve diagnostics and treatment options. This study aims to identify lncRNAs associated with nodal metastasis in cervical cancer using data from The Cancer Genome Atlas (TCGA-CESC). By pinpointing dysregulated lncRNAs, the study seeks to discover potential biomarkers for diagnosis and prognosis, ultimately aiding in the management of cervical cancer.

Methods: The cancer genome atlas's TCGA-CESC dataset contains cervical cancer samples that were evaluated using a bioinformatics technique. Next, we assess the expression value of significantly dysregulated lncRNAs across different cervical cancer stages using the cancer genome atlas's pathological features on nodal metastasis as a guide. To better diagnose and treat cervical cancer, it is important to identify the genes that cause nodal metastasis.

Results: Bioinformatics analyses have revealed that SPINT1-AS1, LINC00958, and PLBD1-AS1 lncRNAs hold significance in the context of cervical cancer. Notably, these lncRNAs have been implicated in cervical cancer nodal metastasis, thereby emphasizing their role in disease progression. Furthermore, it has been observed that these genes exhibit expression across all stages of cervical cancer, underscoring their potential as diagnostic and therapeutic targets.

Conclusion: Our study suggests that bioinformatic approaches can identify highly expressed lncRNAs in lung cancer nodal metastasis, offering potential diagnostic and prognostic biomarkers for affected patients.

keywords: Cervical cancer, Nodal metastasis, Biomarker, LncRNAs, Bioinformatics.

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A Novel Analytical Approach to Unveil Key Biomarkers in COPD: Highlighting DCN's Role in Disease Pathogenesis

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Medical Genetics

Background and aim: Chronic Obstructive Pulmonary Disease (COPD) is a common respiratory condition marked by persistent airflow limitation, often due to prolonged exposure to harmful gases. It includes emphysema, which damages alveoli, and chronic bronchitis, marked by a prolonged cough. Typical symptoms are shortness of breath, coughing, and mucus production. While traditional diagnostics like spirometry and imaging are widely used, they have limitations in detecting early-stage disease. Recent advances, such as biomarker and exhaled breath analyses, offer improved sensitivity and specificity. This study aims to uncover molecular insights into COPD using microarray data analysis to identify differentially expressed genes (DEGs) and potential Biomarkers.

Methods: Microarray data analysis was conducted using two datasets, GSE64614 and GSE37768, from the GEO database, encompassing a total of 259 samples across three groups: COPD patients, healthy smokers, and healthy non-smokers. To enhance analytical robustness, we performed two distinct comparisons: COPD patients vs. healthy smokers and COPD patients vs. healthy non-smokers. Data processing was conducted in R (version 4.2.2), including background correction, log2 transformation, and quantile normalization. Differential expression analysis applied a false discovery rate (FDR) threshold with p-value 0.05 and log fold change (LogFC) ±1.34. Hub genes were identified using the STRING database and visualized in Cytoscape V3.10.2. Top hub genes were selected based on degree, closeness, and betweenness scores using the Cytohubba plugin. Additionally, miRNA-target interactions were explored using TargetScan to assess regulatory relationships potentially relevant to COPD.

Results: Differential expression analysis revealed 846 genes in the COPD vs. healthy smoker comparison and 741 genes in the COPD vs. healthy non-smoker comparison. In the first analysis, eight key hub genes were identified through Protein-Protein Interaction (PPI) network analysis using STRING and Cytoscape: LUM, TFRC, SIRPA, PDGFRA, DCN, HAVCR2, IL1R1, and KITLG. The second comparison identified five hub genes: MMP2, COL1A1, EGFR, DCN, and TIMP3, with DCN appearing in both analyses, suggesting its potential role in COPD pathology. Further analysis confirmed DCN's extracellular localization and secretory nature. miRNA-target interaction analysis highlighted several microRNAs, including hsa-mir-122-5p, hsa-mir-129-5p, hsa-mir-140-3p, and hsa-mir-222-3p, as regulators of DCN.

Conclusion: This study identified key hub genes, particularly DCN, associated with COPD through differential expression analysis and PPI network construction. The presence of DCN across both comparisons and its regulation by specific miRNAs suggests its potential role in COPD pathogenesis, particularly in extracellular matrix remodeling. These findings highlight DCN as a potential biomarker and therapeutic target, providing a molecular basis for future diagnostic and treatment strategies that could improve COPD patient outcomes.

keywords: COPD, Differential Expression Analysis, DCN, miRNA-Target Interaction, Biomarker

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A Review of COVID-19 Effective Pharmaceutics Based on Molecular Targets and Single Nucleotide Polymorphisms

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Medical Genetics

Background and aim: COVID-19 is a highly contagious viral disorder which declared a global pandemic and results in more than 6 million mortalities worldwide since the late December 2019. Given that it remains a major health issue, finding the best treatments to counteract the effects of COVID-19 is critical, and numerous drugs are suggested and employed in clinical trials against COVID-19. Based on currently disseminated scientific documents, this review article gave a summary of prospective therapies in the management of COVID-19. We presented a comprehensive description of their molecular mechanisms and demonstrated the function of the target cells in COVID-19 virus infection after

Methods: We wrote this review article by studying various databases and examining different sources

Results: As previously noted, inflammatory factors such as IL-1R, IL-6R, IL17A, IL17RA, JAK1, and JAK2 may be potential targets for anti-COVID-19 drugs. However, all of these genes have SNPs that can affect gene expression, are linked to other inflammatory illnesses, and interfere with therapeutic function. Table 1 in the appendix contains detailed information on SNPs in these genes based on SNPEDIA and DBSNP. Although there has been few research on the interactions between their SNPs and medications, multiple studies have shown a link between interleukin 6 and two SNPS, rs12083537 and rs2228145, and tocilizumab function. The rs2228145 SNP (single nucleotide polymorphism) results in a shift from guanine (G) to adenine (A) at position -174 in the IL-6R promoter region, which has been linked to variance in response to tocilizumab treatment in patients with

rheumatoid arthritis (RA). The A allele has been linked to increased IL-6R production and activity, while the G

Conclusion: COVID-19 is classified as an inflammatory disease. Given its high mortality rate, determining the optimum treatment plan and appropriate medications is critical. In this Review, we discussed many effective medications used in COVID-19 individuals with mild to severe symptoms. We attempted to collect and identify medications as well as briefly discuss their molecular target. However, this review didn't include all medicine used for COVID-19 treatment and we only mentioned those with clear evidence of high efficiency and performance. Furthermore, we provided SNPs associated with medicines administered against COVID-19. Finally, this

keywords: COVID-19, treatment, anti-interleukin, Antiviral, drugs, SNP

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miR-21 as Potential Plasma Biomarkers in the Acute Phase of Ischemic Stroke

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Medical Genetics

Background and aim: Stroke is the major cause of disability in the world. Identification of molecular biomarkers in the acute phase of stroke is important in diagnostic and therapeutic applications. miR-21 is a highly expressed microRNA in the central nervous system. Here, the efficacy of miR-21 as a potential biomarker in the acute phase of ischemic stroke has been evaluated

Methods: 200 patients (in the first 12 hours after ischemic stroke) and 200 healthy subjects were examined. miR-21 was assessed using qRT-PCR. Stroke etiology and infarct size were investigated. The National Institutes of Health Stroke Scale (NIHSS) was also evaluated.

Results: Compared to the healthy controls, ischemic stroke patients showed increased miR-21 expression (P 0.0001). The area under the ROC curve for miR-21 was 0.90. The level of miR-21 showed significant differences among various subtypes of stroke etiology and infarct size. The baseline NIHSS values were correlated positively with miR-21 (r=0.78).

Conclusion: Our result suggested that dysregulation in miR-21 may be a potential biomarker in occurrence and severity of ischemic stroke.

keywords: Ischemic Stroke, miR-21, Stroke etiology, Infarct size

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The Role of HSP70 in Colorectal Cancer: From prognosis to the Potential as a diagnostic marker and a Therapeutic Target: A Systematic Review

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Medical Genetics

Background and aim: A leading cause of cancer that results in death is colorectal cancer (CRC) but by early diagnosis, we can improve survival rates. Heat shock protein 70 (HSP70) levels in CRC tissues correlate with aggressive tumor traits and could increase metastasis. For early detection, this protein may work as a biomarker for advanced disease stages. The aim of this study is to review the role of HSP70 in the development and progression of colorectal cancer as well as its potential as a diagnostic marker and therapeutic target.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Web of Science until November 2024. The keywords were HSP70, Heat shock protein 70, Colorectal Cancer, Colorectal Neoplasm, Prognosis, Diagnostic biomarker and Therapeutic potential. By searching this database,83 articles were found,45 of them by Reading titles and abstracts were removed.38 articles were chosen under the inclusion criteria. All articles were selected from English articles.

Results: In this review, ultimately, 38 articles were concluded. Heterogenous expression of the HSP70 in CRC cells seemed to promote survival proliferation and resistance against apoptosis, at the same time enhancing immunogenicity and immune evasion. Immunohistochemistry and Western blotting as major experiments confirmed its high levels in CRC tissues and participation in apoptosis, autophagy, and inflammation. CRC patients had high serum levels of HSP70, which displayed some promise as a diagnosis of biodegradable per se with respect to early detection and its relevance in monitoring. Inducing knockdown of HSP70 showed good results in diminishing the survival of CRC cells and also

improved chemotherapy with respect to apoptosis. Perhaps most preliminary exploration on immunotherapy has examined the role of HSP70 as a potential means to enhance the anti-tumor immune response against CRC. Overall, rising interactions of HSP70 with an extremely large number of pathways endorsed the hypothesis of its involvement in cancer

Conclusion: It appears that HSP70 largely participates in colorectal cancer processes by the promotion of tumor survival, proliferation, and immune evasion. High serum levels of HSP70 are present in CRC patients and may suggest a prospective selection as a clinical diagnostic marker. Inhibition of the HSP70 showed great improvement in factor therapy but requires more issues to be resolved before entering clinical application.

keywords: HSP70; Colorectal Cancer; Prognosis; Diagnostic biomarker; Therapeutic potential

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A Novel Analytical Approach and Clinicopathological Insights in Lung Adenocarcinoma Biomarker Discovery

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Medical Genetics

Background and aim: Lung adenocarcinoma (LUAD) is among the primary causes of cancer-related mortality globally, constituting a significant subset of lung cancer cases. Characterized by an aggressive clinical course and poor prognosis, LUAD presents an urgent need for advanced diagnostic and therapeutic approaches. Conventional diagnostic techniques, including imaging and biopsy, are often invasive, costly, and time-intensive, which restricts their effectiveness and accessibility. Consequently, there is a critical demand for efficient strategies to facilitate early detection and management of LUAD. This study aims to identify key biomarkers and explore the association of gene expression profiles with clinicopathological data.

Methods: RNA-Seq datasets for lung and normal tissue samples were sourced from TCGA and processed using the TCGAbiolinks package in R. Differentially expressed genes (DEGs) were identified based on criteria of p-value 0.05 and a log fold change ≥ 3. Additionally, lung cancer microarray data underwent meta-analysis to assess DEGs in lung cancer versus healthy tissues, utilizing R packages with a p-value 0.05 and a log fold change (LogFC) ≥ 3.12. Subsequently, a Protein-Protein Interaction (PPI) analysis was performed, and hub genes were identified. Further investigation, leveraging clinical data from the UALCAN (https://ualcan.path.uab.edu) database, explored associations between gene expression and clinicopathological features, including cancer stages, smoking status, patient ethnicity, and age. This integrative approach provides insights into potential biomarkers and their association with clinical data.

Results: The RNA-Seq analysis identified 365 DEGs, while the microarray meta-analysis, conducted across six datasets, revealed 411 DEGs. Among these, 54 genes were consistently identified across both analyses. PPI networks were constructed, and hub genes were identified using the STRING database and Cytoscape, highlighting KIF11, MMP3, EGLN3, and MMP12. Expression correlations of these genes with clinicopathological data were examined using clinical records from 515 lung cancer patients and 59 controls. Notably, KIF11 and EGLN3 expression was elevated in stage 4 patients compared to earlier stages and controls and was higher in smokers versus non-smokers, while MMP3 and MMP12 showed greater expression in non-smokers. Additionally, KIF11 and EGLN3 were more highly expressed in individuals of Asian ethnicity, whereas MMP3 and MMP12 expression was higher in Caucasians. All four genes displayed increased expression in the 21-40 age group compared to other age groups.

Conclusion: The study identifies key biomarkers in LUAD, including KIF11, MMP3, EGLN3, and MMP12, which show significant associations with clinicopathological factors. Elevated expression of KIF11 and EGLN3 in advanced-stage patients, particularly among smokers and specific ethnic groups, suggests their potential as prognostic markers. Similarly, distinct expression patterns of MMP3 and MMP12 in non-smokers underscore their potential as diagnostic targets. This integrative analysis, utilizing RNA-Seq, microarray meta-analysis, and clinical correlations, highlights promising biomarker candidates that could enhance early diagnosis and personalized treatment strategies for LUAD.

keywords: Lung Adenocarcinoma, Biomarkers, Clinicopathological Analysis, Gene Expression Profiling

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Circadian clock disruption in pancreatic cancer

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Medical Genetics

Background and aim: One of the risk factors affecting its development and progression is the Circadian clock (CC) disruption. CC is a 24-hour cycle that regulates the rhythm of alertness and sleepiness, metabolism, hormone secretion, and cell cycle. The function of this cycle is regulated by the day and night environmental signals. CC is located in a part of the hypothalamus known as the SupraChiasmaticNucleus (SCN). Any disruption in its function and the genes involved in it (e.g., BMAL1, CLOCK, PER, and CRY) has been proven to cause various cancers, including pancreatic cancer.

Methods: By reviewing the databases of PubMed, Science Direct, Google Scholar, and Scopus on CC dysfunction, we investigated its role in the development and progression of pancreatic cancer.

Results: The invasion and metastasis of pancreatic cancer to other organs and tissues occur due to the decreased expression of genes in the CC process.

Conclusion: According to the function of the CC genes related to tumor suppressor factors, they can be used as therapeutic targets or diagnostic biomarkers.

keywords: Circadian clock; Pancreatic cancer; Genes expression

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Aptamers as novel targeted therapeutics in colorectal cancer: A Systematic Review

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Medical Genetics

Background and aim: Colorectal cancer (CRC), as the second leading cause of global cancer deaths, poses critical challenges in clinical settings. Aptamers have great specificity and affinity with target molecules, making them ideal alternative therapeutics. This study aims to review the effect of Aptamer on colorectal cancer.

Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until November 2024. The keywords were Aptamer, Aptamer conjugated, Colorectal Neoplasms, Colorectal cancer, treatment, therapy, and therapeutics. By searching this database, 38 articles were found, 29 of them were removed by reading the title and abstracts, and 9 articles were selected under the inclusion criteria. All articles were chosen from English and Persian articles.

Results: Finally, 9 articles were included in this study. There were 4 aptamers that have therapeutic effects on CRC. AuNPs coated with Dox-loaded oligonucleotides (Dox-oligomer-AuNP, DOA) An efficient targeted DDS could be developed for CRC treatment by targeting PrPC. EGFR, HER2, folate receptor, transferrin receptor, and DDSs are appropriate cancer targets an oligonucleotide with an aptamer (Apt) sequence to target PrPC, which was then used to fabricate the PrPC-targeted Dox DDS (PrPC-Apt-functionalized doxorubicin-oligomer-AuNPs (PrPCApt DOA)) which could effect on the mitochondrial functions, proliferation, and apoptosis of CRC cells. EpCAM targeting TSIIA-encapsulated poly (amino acid) NPs (EpCAM-TSIIA-NPs) has higher cytotoxicity, better water solubility, and better targeting ability, and can effectively suppress the proliferation and

metastasis of tumors. EpCAM-aptamer-guided survivin RNAi effectively downregulated survivin both in colorectal cancer cells in vitro and in vivo for CRC, which was able to enhance the sensitivity towards 5-FU or oxaliplatin in colorectal cancer stem cells, increase

Conclusion: It seems that aptamers have beneficial effects on mitochondrial functions, proliferation, apoptosis, and metastasis of CRC. Moreover, it can effectively downregulate colorectal cancer cells in vitro and in vivo. However, more studies are needed on this topic.

keywords: Aptamer, Colorectal Neoplasms, Colorectal cancer, therapy, therapeutic

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Crispr-cas 9 as an effective therapeutic factor in hepatitis b: A systematic review

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Medical Genetics

Background and aim: Hepatitis B is a viral infection that can lead to acute and chronic liver diseases. According to WHO, there are 254 million people were living with chronic hepatitis B infection in 2022, with 1.2 million new infections each year. There is no specific treatment. This review aims to explore the potential of CRISPR-Cas9 gene-editing technology as a therapeutic approach for Hepatitis B, with a focus on its impact on HBV replication and viral persistence through modifications of closed circular DNA (cccDNA). By analyzing recent research, the review seeks to assess the effectiveness and limitations of CRISPR-Cas9.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, SID until November 2024. The keywords were CRISPR-Cas9, Hepatitis B, HBV and Therapy. By searching this database; 35 articles were found, 20 of them by Reading titles and abstracts were removed. 15 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: Finally, 15 articles were selected under the inclusion criteria. Current options for treating chronic HBV, like interferons or nucleos(t)ide analogs, could only suppress the virus replication and they did not omit the pathogen. By using HBV-specific guide RNAs (gRNAs) and CRISPR-Cas9 to observe closed circular DNA (cccDNA) changes after gene editing, the levels of HBV cccDNA, total HBV DNA, pre-genomic RNA and HBV antigen (HBsAg, HBeAg) were significantly reduced. Although CRISPR/Cas9 was a genetic tool that could modify HBV DNA and minichromosomal cccDNA, it required a viral vector for expression and delivery, which raised concerns for human therapy.

Conclusion: It seems that the application of HBV-targeting gRNAs to infected cells shows that CRISPR-Cas9 may effectively interfere with HBV replication. However, more research is required for this subject.

keywords: CRISPR-Cas9; Hepatitis B; gRNAs; Treatment; cccDNA

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The frequency of Rs1048943 polymorphism in the CYP1A1 gene among men referring to infertility treatment centers in East Azerbaijan

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Medical Genetics

Background and aim: Infertility is a reproductive disorder defined as the inability to conceive after 12 months of regular, unprotected intercourse. Male infertility accounts for approximately 45% of cases in infertile couples. Various environmental and genetic factors contribute to male infertility, and the CYP1A1 gene is among the genes implicated. Specific polymorphisms within CYP1A1 have been linked to male infertility, with rs1048943 being one of the most significant. This study examines the frequency of this polymorphism in infertile men from northwest Iran.

Methods: Sperm samples were collected from Tabriz Jihad Daneshgahi Center, and DNA extraction was carried out. DNA samples of suitable quality were retained for further analysis. The Tetra ARMS PCR method was employed to study the rs1048943 polymorphism. PCR amplification was performed using gene-specific primers to target the region of interest, and genotypes were determined based on band patterns observed on gel electrophoresis. Statistical analysis was conducted using SPSS, with a p-value threshold of 0.05 for significance

Results: The genotype frequencies in the patient group for TT, AA, and AT were 52%, 4%, and 44%, respectively. In the control group, the frequencies were 32%, 16%, and 52%, respectively

Conclusion: The differences in genotype frequencies and allelic frequencies between the patient and control groups were not statistically significant.

keywords: Male infertility, CYP1A1 gene, rs1048943, polymorphism, genetic factors

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Impact assessment of Sclareol on endoplasmic reticulum stress in KATO III human gastric carcinoma cancer cell lines

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Medical Genetics

Background and aim: The main goals of chemotherapy are to increase apoptosis or cell death and to stop the cell cycle in cancer cells. One of the very important factors inducing apoptosis in cancer cells is to increase the stress of the endoplasmic reticulum system. In this study, the authors intended to investigate the effect of Sclareol on the ATF6 pathway as well as the effect of two other sub-genes, VEGF and E2F1, associated with the UPR pathways.

Methods: The target population in this research was KATO III human gastric carcinoma cancer cells, which were purchased from the Pasteur Institute of Iran, and they were cultured in the cell culture laboratory until their number reached at least 100,000 cells/well. The cells were treated with concentrations of 0, 20, 40, 60, 80 and 100 µM of Sclareol for 5 hours. Analyzing the expression of the genes- expressed in the research objectives- derived from gastric cancer cells before and after treatment with Sclareol was performed using Quantitative Real Time-PCR from the spheres of cell lines cultured in suspension.

Results: ATF-6 gene expression significantly increased in genes with doses of 20, 40 and 60 µM of Sclareol (P0.0001). On the other hand, it was shown that the level of VEGF gene expression was significantly reduced in genes with doses of 20, 40 and 60 µM of Sclareol (P0.001). Also, there was a significant increase in E2F1 gene expression in doses of 20, 40 and 60 µM of Sclareol (P0.003).

Conclusion: From the results obtained from the present study, it can be concluded that the administration of Sclareol may be useful for reducing the expression of VEGF gene and for increasing the expression of ATF-6 and E2F1 genes, which are responsible for increasing the stress of the endoplasmic reticulum system, in KATO III human gastric cancer cells. The doses of 40 and 60 µM of Sclareol were considered to be effective doses.

keywords: Gastric Cancer- The Endoplasmic Reticulum System Stress- Sclareol - KATO

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S100A12 and RAGE Expression in Human Bladder Transitional Cell Carcinoma: a Role for the Ligand/RAGE Axis in Tumor Progression?

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Medical Genetics

Background and aim: Transitional cell carcinoma (TCC) and prostate cancer are the most frequent cancers in the male genitourinary tract. Measurement of biological biomarkers may facilitate clinical monitoring and aid early diagnosis of TCC. The aim of the present investigation was to detect the mRNA levels of S100A12 and RAGE (receptor for advanced glycation end products) in patients suffering from bladder TCC.

Methods: To explore the involvement of S100A12 and RAGE genes, total RNA was harvested from cancer tissues and samples obtained from normal non-tumorized urothelium of the same patients. Quantitative PCR (qPCR) was subsequently employed to determine the mRNA levels of S100A12 and RAGE.

Results: The results showed that mRNA expression of S100A12 and RAGE was significantly up-regulated in the cancer tissue.

Conclusion: According to the results presented in the current study, mRNA expression of S100A12 and RAGE might be as a useful biomarker for TCC. Therefore, this ligand-receptor axis possibly plays important roles in the development of TCC and may serve either as an early diagnostic marker or as a key factor in monitoring of response to treatment. More research is required concerning inhibition of the S100A12-RAGE axis in different cancer models.

keywords: TCC - bladder cancer - S100A12 - RAGE

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ABCB1 Promoter Methylation: A Potential Biomarker and Therapeutic Target in Ulcerative Colitis Pathogenesis

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Medical Genetics

Background and aim: The ATP-binding cassette subfamily B member 1 (ABCB1) gene, also known as MDR1, plays a crucial role in drug transport and cellular detoxification. Dysregulation of ABCB1 expression due to epigenetic modifications, such as promoter methylation, has been implicated in various inflammatory diseases, including ulcerative colitis (UC). Altered ABCB1 gene expression may affect gut barrier integrity and inflammatory response, making ABCB1 promoter methylation a potential biomarker for UC progression and severity.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords ABCB1, Ulcerative Colitis, Biomarker, Therapy., 65 articles related to inclusion criteria were extracted and then analyzed.

Results: Results show that UC patients exhibit significantly higher levels of ABCB1 promoter methylation compared to controls, resulting in reduced ABCB1 expression in colonic epithelial cells. This downregulation is associated with increased intestinal permeability and inflammation, key features of UC pathology. Furthermore, elevated ABCB1 promoter methylation was correlated with disease severity, suggesting its potential as a prognostic marker. Treatment interventions, including certain anti-inflammatory drugs, were found to partially reverse methylation changes, thereby restoring ABCB1 expression.

Conclusion: The findings support ABCB1 promoter methylation as a contributing factor in UC pathogenesis. Hyper-methylation leads to decreased ABCB1 expression, which compromises gut barrier function and exacerbates inflammation. Targeting epigenetic modifications to restore ABCB1 expression

could offer a novel therapeutic approach for UC. Further research is needed to validate these findings in larger cohorts and explore therapeutic agents that can modulate methylation status. ABCB1 promoter methylation represents a promising biomarker and therapeutic target for managing ulcerative colitis.

keywords: ABCB1, Ulcerative Colitis, Biomarker, Therapy.

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Evaluation of MLH1 gene promoter methylation in peripheral blood mononuclear cells as biomarker for colorectal cancer diagnosis and prognosis.

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Medical Genetics

Background and aim: Various pieces of evidence have shown that peripheral blood mononuclear cells (PBMCs) can reflect the epigenetic profile of tissues they interact with, such as malignant cells through tumor-derived exosomes. The hypermethylation of MLH1 promoter is a well-defined epigenetic alteration in the development of colorectal cancer (CRC). In the present study, we aimed for the first time to assess the diagnostic and prognostic value of the methylation level of MLH1 promoter in PBMCs of patients with CRC.

Methods: The methylation level at the promoter region of MLH1 was quantitatively analyzed in 60 CRC patients and 60 non-cancerous subjects via methylation-quantification of endonuclease-resistant DNA (MethyQESD).

Results: Our data showed a significant increase in methylation of MLH1 in CRC patients compared to healthy subjects (P0.001). Moreover, by determining an optimal cutoff value, the specificity of MLH1 hypermethylation for precise diagnosis of healthy subjects was 75% and the its sensitivity for CRC diagnosis was 76.7%. With receiver operating characteristic (ROC) curve analyses, we found that MLH1 promoter methylation holds a likelihood of 76.8% for distinguishing between CRC patients and healthy individuals (P0.001). Besides, our findings represented that MLH1 methylation levels was significantly increased in CRC

patients with higher tumor stages, suggesting a probable correlation between an increased percentage of methylation and tumor progression (P0.001). However, no statistically significant association was found between methylation status of MLH1 and microsatellite instability (MSI), age, and gender stratifications (P0.05).

Conclusion: Our results propose that MLH1 methytlation status in PBMCs can be used as a promising diagnostic and prognostic biomarker and reliable factor for CRC screening.

keywords: MLH1, colorectal cancer, Biomarker, diagnosis.

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Methylation-based testing in PBMCs as a promising biomarker for colorectal cancer diagnosis and prognosis

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Medical Genetics

Background and aim: Colorectal cancer (CRC) remains one of the leading causes of cancer-related mortality worldwide, emphasizing the urgent need for reliable and non-invasive biomarkers for early detection, diagnosis, and prognosis. Recent studies have identified DNA methylation patterns in peripheral blood mononuclear cells (PBMCs) as potential biomarkers for CRC. This systematic review aims to evaluate the diagnostic and prognostic utility of methylation-based testing in PBMCs in CRC.

Methods: We conducted a comprehensive literature search across multiple databases, including PubMed, Scopus, and Web of Science, to identify studies evaluating the methylation status of the gene promoters in PBMCs from CRC patients. Inclusion criteria comprised original research articles assessing methylation levels using validated quantitative methods.

Results: The review consistently demonstrated that promoter sequence of MGMT, MMP9, PLOD1, RUNX3, NDRG4, TFPI2, ITGA4, TUSC3, MLH1 were hypermethylated in CRC patients compared with healthy controls. The pooled sensitivity and specificity for CRC diagnosis based on PBMC methylation markers were 87% and 82%, respectively. Higher methylation levels of these genes were associated with advanced disease stages and poorer prognosis, indicating their potential as diagnostic and prognostic biomarkers. Importantly, these methylation markers also showed potential for early detection of CRC, providing a significant advantage in improving patient outcomes through earlier intervention.

Conclusion: Methylation-based testing in PBMCs represents a promising non-invasive approach for CRC diagnosis, prognosis, and early detection. Further

large-scale studies are warranted to validate these findings and explore their clinical application in routine CRC screening and management.

keywords: colorectal cancer, PBMCs, Methylation, Biomarker.

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Rel-A/PACER/miR7 Axis May Play a Role in Radiotherapy Treatment in Breast Cancer Patients

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Medical Genetics

Background and aim: Radiotherapy has become the standard form of treatment for BC. Radioresistance is an issue that limits the effectiveness of RT. Therefore, predictive biomarkers are needed to choose the appropriate RT for the patient. Activation of the proinflammatory transcription factor, NF-κB, is a frequently noted pathway in BC. Investigating the relationship between RT and alterations in gene expression involved in the immune pathway can help better control the disease. This research investigated the impact of RT on the expression levels of Rel-A, PACER, and miR-7 within the NF-κB signaling pathway.

Methods: Blood samples (n = 15) were obtained from BC patients during four different time intervals: 72 hours prior to initiating RT, as well as one, two, and four weeks following RT completion. Samples were also collected from 20 healthy women who had no immune or cancer-related diseases. Blood RNA was extracted, and cDNA was synthesized. Gene expression level was determined using RT-PCR.

Results: There was a significant difference in the expression level of Rel-A between patients and normal individual blood samples (p 0.05). After four weeks of RT, qRT-PCR revealed a significant downregulation of miR-7 and upregulation of Rel-A and PACER in BC patients. Also, there was a significant association between Rel-A expression and monocyte numbers during RT (p 0.001).

Conclusion: The expression level of PACER, miR-7 and Rel-A, changed after RT; therefore, these genes could be used as diagnostic and therapeutic RT markers in BC.

keywords: Breast cancer, Radiation biomarkers, Radiotherapy

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Evaluation of the Effect of Radiotherapy on CCL5/miR-214 -3p/MALAT1 Genes Expression in Blood Samples of Breast Cancer Patients

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Medical Genetics

Background and aim: Current cancer therapies include chemotherapy, radiation therapy, immunotherapy, and surgery. Despite these treatment methods, a major point in cancer treatment is early detection. RNAs (mRNA, miRNAs, and LncRNA) can be used as markers to improve cancer diagnosis and treatment. This research examined how radiotherapy affected CCL5, miR-214, and MALAT-1 gene expression in the immune pathway in peripheral blood samples from radiation therapy-treated breast cancer patients.

Methods: Before and after radiotherapy, peripheral blood was collected from 15 patients in four steps. Blood samples were collected in an outpatient facility from 20 healthy female volunteers with no history of malignant or inflammatory conditions. RNA was extracted from the blood samples and cDNA was synthesized. CCL5, miR-214, and MALAT-1 gene expression were determined by real-time polymerase chain reaction (RT-PCR). CCL5 protein levels in the serum were determined in 80 samples (60 BC and 20 healthy controls) using Quantikine Enzyme-Linked Immunosorbent Assay (ELISA) kits (R&D Systems). The data were then statistically evaluated.

Results: There was a significant difference between CCL5 levels in tumoral and adjacent normal blood samples (p 0.05). The results also show that the level of gene expression and serum concentration of CCL5 protein in different phases of radiotherapy is significantly different. On the other hand, the expression level of the miR-214 gene was significantly decreased in patients compared to the control

group, but this decrease was not significant for the MALAT-1 gene (p 0.05). Also, after each stage of radiotherapy, the expression level of these two genes showed a decrease, but in the fourth week after radiotherapy, this decrease was significant (p 0.05).

Conclusion: Radiotherapy is associated with a decrease in the expression of miR-214 and MALAT-1, as a result, an increase in the expression of CCL5. An increase in the concentration of CCL5 protein is accompanied by an increase in the level of monocytes, which ultimately causes the infiltration of macrophages and can ultimately cause cancer recurrence. It is suggested that these genes can probably be used as diagnostic and therapeutic radiotherapy markers in breast cancer.

keywords: Breast cancer, radiotherapy, ELISA, miR-214, CCL5, MALAT-1

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Impact of ATM and SLC22A1 Polymorphisms on Therapeutic Response to Metformin in Iranian Diabetic Patients

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Medical Genetics

Background and aim: Metabolic syndrome and its pathological sequel, type 2 diabetes are considered as important global health problems. Metformin is the most common drug prescribed for patients with this disorder. Consequently, understanding the genetic pathways involved in pharmacokinetics and pharmacodynamics of this drug can have a considerable effect on the personalized treatment of type 2 diabetes.

Methods: In this study, we evaluated the association between rs11212617 polymorphism of ATM gene and rs628031 of SLC22A1 gene with response to treatment in newly diagnosed type 2 diabetes patients. We genotyped rs11212617 and rs628031 polymorphism by PCR based restriction fragment length polymorphism (RFLP) and assessed the role of this polymorphisms on response to treatment in 140 patients who have been recently diagnosed with type 2 diabetes and were under monotherapy with metformin for 6 months.

Results: Response to metformin was defined by HbA1c and fasting blood sugar (FBS) values. Based on such evaluations, patients were divided into two groups: responders (n= 63) and non-responders (n= 77). No significant association was found between these polymorphisms and response to treatment (OR= 0.86, [95% CI 0.52–1.41], P= 0.32) for rs11212617 and (OR= 0.45, [95% CI 0.64–1.76], P= 0.45) for rs 628031.

Conclusion: The reported gene variants in ATM and SLC22A1 are not significantly associated with metformin treatment response in type 2 diabetic patients in an Iranian population.

keywords: Metformin, type 2 diabetes, pharmacogenetic

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Role of Non-coding RNAs in the Pathogenesise of Endometriosis (Ems)

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Medical Genetics

Background and aim: Endometriosis (EMs) is a chronic gynecological disorder caused by endometrioid-like tissue growing outside the uterus, significantly impacting women's quality of life and fertility. Its rising incidence, especially in young women, is compounded by delayed diagnosis due to non-specific symptoms and the absence of reliable biomarkers. Current treatments include surgery and hormonal therapy, emphasizing the need for improved diagnostic and therapeutic approaches. Recent research highlights the regulatory roles of long non-coding RNAs (lncRNAs), functional RNA molecules over 200 nucleotides, in EMs pathogenesis. LncRNAs influence gene expression through epigenetic regulation, miRNA sponging, and signal pathways, analyzed using qRT-PCR and siRNA techniques.

Methods: in this review, we searched Google scholar, PubMed from 2015 up to November 2024 with keywords such as Endometriosis (Ems), Long non-coding RNAs and etc.

Results: By searching these databases, 30 research articles were retrieved and among 10 were included in the study. LncRNAs play diverse roles in endometriosis (EMs) through various mechanisms. As competing endogenous RNAs (ceRNAs), lncRNAs like H19 and LINC01018 regulate gene expression and promote inflammation via miRNA sponging. In exosomes, CHL1-AS1 enhances endometrial stromal cell (ESC) proliferation and migration by competing with miR-610. Antisense lncRNAs such as AFAP1-AS1 and CCDC144NL-AS1 influence transcription and epigenetics, facilitating ESC invasion and epithelial-mesenchymal transition (EMT). Hypoxia-related lncRNAs, including MALAT1 and aHIF, drive angiogenesis and EMT under low oxygen levels. Additionally, lncRNAs exhibit abnormal expressions in EMs. For instance, H19 upregulates pathways

linked to recurrence and infertility, while MALAT1 regulates apoptosis and autophagy via NF-kappaB and PI3K/AKT pathways. UCA1 supports ESC proliferation and inhibits apoptosis, with increased expression correlating with infertility. Other lncRNAs, like FTX, MEG3, and HOTAIR, further impact EMT, angiogenesis, and metastasis in EMs progression.

Conclusion: Despite advancements, challenges such as RNA instability, off-target effects, and immune responses limit the clinical application of lncRNAs in EMs. Large-scale cohort studies are necessary to ensure safety and efficacy. LncRNAs regulate angiogenesis, EMT, and oxidative stress, influencing EMs progression. Their potential as biomarkers and therapeutic targets for early diagnosis and treatment remains promising. Future research should prioritize in vivo studies and innovative detection methods to address current limitations and enhance the clinical translation of lncRNA-based strategies in managing endometriosis.

keywords: Endometriosis (Ems), Long Noncoding RNAs (lncRNAs), Epithelial-Mesenchymal Transition (EMT), Biomarkers.

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RUNX3 Methylation in PBMCs as a Biomarker for Rheumatoid Arthritis: An Exploratory Study

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Medical Genetics

Background and aim: Rheumatoid arthritis (RA) is a debilitating autoimmune condition marked by chronic inflammation and joint destruction. The search for reliable molecular biomarkers has become increasingly important for improving diagnosis and disease management. RUNX3, a transcription factor, plays a crucial role in immune regulation and has been implicated in the pathogenesis of various autoimmune diseases, including RA. This study investigates the methylation status of the RUNX3 gene in peripheral blood mononuclear cells (PBMCs) to assess its potential as a biomarker for RA

Methods: The methylation levels of the RUNX3 promoter were analyzed in PBMCs from 72 RA patients and 72 healthy controls using the methylation-quantification of endonuclease-resistant DNA (MethyQESD) method. Data analysis focused on evaluating the diagnostic value and correlation with clinical features such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)

Results: The study revealed that the mean methylation level of RUNX3 in RA patients was 44.08±16.67%, compared to 40.44±24.13% in healthy controls, indicating no significant difference (P: 0.295). Besides, there was not significant difference in methylation level of RUNX3 between RA patients with an age of onset ≤35 and those with an age of onset 35 (P: 0.542). However, a significant positive correlation was found between RUNX3 methylation levels and clinical indicators, namely CRP (P0.001) and ESR (P: 0.014), suggesting a potential link to disease activity

Conclusion: While the methylation levels of RUNX3 did not differ significantly between RA patients and controls, the observed correlation with CRP and ESR levels points to its possible role in monitoring disease activity. Further research is needed to clarify RUNX3 utility in the clinical management of RA and to explore its prognostic capabilities

keywords: Rheumatoid arthritis, RUNX3 gene, Methylation, Biomarker

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MMP9 Promoter Methylation in PBMCs: A Breakthrough in RA Diagnosis and Prognosis

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Medical Genetics

Background and aim: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by systemic inflammation and joint damage. Traditional markers for RA diagnosis, such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), have limitations, including variable sensitivity and specificity. Recent advancements in molecular biomarkers, particularly DNA methylation analysis, offer a promising alternative for improving diagnostic accuracy and prognostic evaluation. This study evaluates the methylation levels of the MMP9 gene in peripheral blood mononuclear cells (PBMCs) as a potential biomarker for RA

Methods: We examined the methylation levels of the MMP9 promoter in PBMCs from 72 RA patients and 72 healthy controls using methylation-quantification of endonuclease-resistant DNA (MethyQESD). The data were analyzed to determine the diagnostic utility and correlation with clinical features, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)

Results: Our results demonstrated a significant difference in MMP9 methylation levels between RA patients and healthy controls. The mean methylation level in RA patients was 38.23±28.62%, compared to 62.27±19.68% in controls (P0.001). Using an optimal cutoff value, the specificity for correctly identifying healthy subjects was 72.22%, and the sensitivity for diagnosing RA was 73.61%. The receiver operating characteristic (ROC) analysis revealed a diagnostic power (AUC) of 0.756 (P0.001) for MMP9 promoter methylation. Moreover, there was a significant negative correlation between MMP9 methylation levels and clinical

features such as CRP and ESR levels (P0.001). However, there was no significant difference in methylation levels between RA patients with an age of onset ≤35 and those with an age of onset 35 (P: 0.515)

Conclusion: Our findings suggest that methylation levels of the MMP9 promoter in PBMCs can serve as a promising non-invasive biomarker for the diagnosis, prognosis, and early detection of RA. The significant difference in methylation levels between RA patients and healthy controls, along with the demonstrated diagnostic power, supports the potential clinical utility of this biomarker in routine screening and management of RA

keywords: Rheumatoid arthritis, MMP9 gene, Methylation, Biomarker

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The role of mir-7-5p in cancer: function, prognosis, diagnosis, and therapeutic implications

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Medical Genetics

Background and aim: One of the important and conserved microRNAs (miRNAs), miR-7-5p, is involved in several pathological mechanisms, including cell proliferation, apoptosis, migration, and metastasis. Dysregulation of this miRNA's expression is correlated with multiple diseases, especially cancer. Its role as a tumor suppressor has been demonstrated in various types of cancer, such as colorectal cancer, lung cancer, bladder cancer, breast cancer, and glioblastoma. Furthermore, several studies have highlighted the prognostic and diagnostic value of this miRNA, which could be valuable for the diagnosis and treatment of certain disorders

Methods: review article.

Results: We present an overview of the latest findings regarding miR-7-5p's role in the development of cancer, its action mechanisms, and expression, based on in vivo, in vitro, and human research. Additionally, we discuss the function of miR-7-5p as a prognostic biomarker in cancer and explore its potential as a therapeutic target

Conclusion: miR-7-5p could be as a prognostic biomarker and potential therapeutic target in cancer.

keywords: microRNA • miR-7-5p • Cancer • Diagnosis • Prognosis •

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Introducing a novel TRAPPC10 gene variant as a potential cause of developmental delay and intellectual disability in an Iranian family

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Medical Genetics

Background and aim: TRAPP complexes are crucial components for intracellular transport and cellular organization. Their role in vesicle trafficking, particularly through their involvement in the secretory pathway, make them more important in neurodevelopmental mechanisms. This study aims to identify novel genetic variants associated with developmental delay and intellectual disability by analyzing a consanguineous Iranian family.

Methods: Here, we performed whole-exome sequencing on an Iranian family, originating from a small population. The patient presented with severe developmental delay, microcephaly, and behavioral abnormalities.

Results: Through our analysis, we discovered a new biallelic TRAPPC10 variant (NM_003274.5): c.3222CA; p.(Cys1074Ter) that is a potential cause for these specific clinical characteristics.Previous functional analysis suggest that the mutation causes premature termination of protein translation, likely leading to nonsense-mediated decay because of biallelic loss of functional TRAPPC10 protein which leads to severe developmental delay, microcephaly, and behavioral abnormalities such as aggression and autistic traits.

Conclusion: The aim of this research is to discover a novel variant in the TRAPPC10 gene that is responsible for a particular neurodevelopmental condition,

dominantly characterized by developmental delay, intellectual disability, and microcephaly. These findings advance the comprehension of TRAPP-related diseases and emphasize the need for further exploration into the impact of TRAPPC10 on the development of the nervous system.

keywords: TRAPPC10, Intellectual Disability, Developmental Delay, Microcephaly, TRAPP II complex.

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Reduced Expression of miR-19b in Seminal Plasma as a Potential Biomarker for Non-Obstructive Azoospermia Diagnosis and Male Fertility Assessment

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Medical Genetics

Background and aim: Non-obstructive azoospermia (NOA) represents the most severe type of male infertility, with few available treatment options. MicroRNAs (miRNAs) are key regulators of spermatogenesis and have gained attention as potential biomarkers for diagnosing NOA and forecasting the outcomes of assisted reproductive technologies. This research focuses on analyzing the expression levels of miR-19b in the seminal plasma of NOA patients, comparing them to those with impaired sperm quality and normozoospermic controls.

Methods: The study involved 35 normozoospermic individuals, 35 individuals with impaired spermatogenesis, and 15 patients diagnosed with NOA. RNA was isolated from seminal plasma, followed by the synthesis of complementary DNA (cDNA). The expression levels of miR-19b were quantified across the groups using quantitative real-time PCR (qRT-PCR).

Results: The analysis of miR-19b expression showed a statistically significant 3.6-fold reduction in the NOA group compared to the control group (p 0.05). Conversely, no significant difference in miR-19b expression was observed between the NOP group and the control group, indicating no substantial upregulation or downregulation. However, a significant difference was found between the NOA and NOP groups, with the NOA group displaying notably lower miR-19b expression than the NOP group (p 0.05).

Conclusion: The expression of miR-19b in seminal plasma could serve as a potential biomarker for diagnosing NOA and assessing male fertility, providing valuable insights for personalized strategies in managing male infertility.

keywords: Infertility, Non-obstructive azoospermia, seminal plasma, miRNA, miR-19b

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Novel Advances in Cell-Free Therapy for Premature Ovarian Failure (POF): A Comprehensive Review

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Medical Genetics

Background and aim: Premature ovarian failure (POF), is a condition characterized by the early decline of ovulation function. POF is a complex disorder that can be caused by various factors, and the idiopathic form represents a significant proportion of POF patients. Hormone replacement therapy (HRT) is currently considered the first-line treatment for POF. This review aims to provide a comprehensive overview of recent advancements in platelet-rich plasma (PRP), in vitro activation (IVA), stem cell therapy, exosome therapy, microRNAs, and mitochondrial targeting therapies as a promising cell-free therapeutic approach in reproductive medicine. PLT-Exos, a new generation of cells, has been used to treat POF

Methods: search in pubmed and google scholar

Results: Eight clinical trials using PRP application, three involving IVA, and five involving stem cell transplantation are now underway, and the results should be known within the next two years, according to ClinicalTrials.gov. Meticulous experimental and clinical designs will shed light on the safety and effectiveness of these novel therapies for infertility in POF.

Conclusion: A condition with a diverse origin, POF affects up to 3.7% of all females worldwide. Although infertility is seen to be the most crippling aspect of the illness, HRT can aid with its symptomatology and long-term health implications. The reinterpretation of ovarian reserve as a dynamic, rather than static, cell population has prompted research into novel biological strategies for ovarian rejuvenation, including PRP, exosome therapy, IVA, stem cell therapy,

microRNAs, therapies. Intraovarian PRP administration is one of these experimental techniques that has been well explored, is less invasive, and has

keywords: PRP, Exosome therapy, In vitro activation, Stem cell therapy,

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Assessment of the prevalence of coronavirus and influenza A virus

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Medical Genetics

Background and aim: Coronavirus (COVID-19) and influenza A virus (IAV) represent a difficult challenge for humanity. The present study investigated the prevalence of COVID-19 and IAV infection at Khatam Al-Anbia Hospital, Zahedan, Iran.

Methods: A total of 110 patients, with laboratory-confirmed COVID-19 and AIV tests by reverse transcription polymerase chain reaction (RT-PCR) at Khatam Al-Anbia Hospital were assessed in Zahedan for 32 weeks. RT-PCR test, which detects genetic material called RNA from the virus, is an accurate and reliable test for diagnosing COVID-19 and IAV. To perform the test, we used a swab (similar to a long Q-Tip) to collect a sample from the throat. We took a sample from the middle part of the throat (pharynx), just beyond the mouth.

Results: Of the 110 participating patients with respiratory symptoms, patients were 4.5% positive for COVID-19, 0.9% positive for AIV, and 94.6% Negative for COVID-19 and AIV tests. Patients had a mean age of 53 years. The participants were 38.1 % male and 61.8 % female. Most patients with respiratory symptoms were hospitalized in the internal medicine department (69.0 %).

Conclusion: Vaccination appears to have been effective in reducing COVID-19 and AIV. Increased awareness of these data may help guide appropriate treatment choices for patients with respiratory symptoms in the future.

keywords: coronavirus; influenza A virus; RT-PCR;

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Identification of a novel mutation of Platelet-Derived Growth Factor-C (PDGFC) gene in a girl with Non-Syndromic cleft lip and palate

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Medical Genetics

Background and aim: Cleft lip with or without cleft palate (CL/CP) is a prevalent congenital malformation. Approximately 16 candidate loci for CL/CP have been identified in both animal models and humans through association or genetic linkage studies.One of these loci is the platelet-derived growth factor-C (PDGFC) gene. In animal models, a mutation in the PDGFC gene has been shown to lead to CL/CP, with PDGF-C protein serving as a growth factor for mesenchymal cells, playing a crucial role in embryogenesis during the induction of neural crest cells.

Methods: In this study, we present the identification of a novel frameshift mutation in the PDGFC gene, which we hypothesize to be associated with CL/CP, within a consanguineous Iranian family.

Results: The proband was a 3-year-old girl with non-syndromic CL/CP. A history of craniofacial clefts was present in her family. Following genetic counseling, karyotype analysis and whole-exome sequencing (WES) were performed. Cytogenetic analysis revealed normal results, while WES analysis showed that the proband carried a homozygous c.546dupA (p.L183fs) mutation in the PDGFC gene. Sanger sequencing confirmed that her parents were carriers of the mutation.

Conclusion: The c.546dupA (p.L183fs) mutation of PDGFC has not been previously reported and was not found in human genome databases. We speculate that the c.546dupA mutation of the PDGFC gene, identified in the Iranian patient, may be responsible for the phenotype of non-syndromic CL/CP (ns-CL/CP). Further

studies are warranted to explore the specific pathogenesis of the PDGFC mutation in ns-CL/CP..

keywords: Cleft lip; Cleft palate; Cleft lip with/without cleft palate; platelet-derived

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The Potential of CRISPR-Cas9 Technology in the Treatment of Sickle Cell Disease: A Systematic Review

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Medical Genetics

Background and aim: Sickle cell disease (SCD), a common inherited blood disorder, is caused by a point mutation in the beta-globin gene. Worldwide, SCD is very fatal and poses a very difficult proposition for patients. CRISPR-Cas9 technology is a powerful and novel vector for genetic engineering. It originates from a genome-editing system that bacteria have in their defense mechanisms. This technology can be used to repair genome mutations and cure genetic disorders. This review will cover the potential of CRISPR-Cas9 in the treatment of sickle cell anemia.

Methods: This review article was conducted using articles published in PubMed, Google Scholar, and ScienceDirect between 2021 and 2024. The keywords were "CRISPR-Cas9 AND sickle cell anemia OR sickle cell disease OR SCD AND treatment." A search of these databases resulted in 90 articles being found, 67 of which were excluded based on titles and abstracts. A total of 23 articles were selected according to the inclusion criteria.

Results: Finally,23 articles were included in the study.The CRISPR-Cas9 technology has become incredibly popular in the treatment of sickle cell anemia.In SCD,a point mutation in the beta-globin gene causes this disorder.The body creates an abnormal hemoglobin called HbS,which makes red blood cells sickle-shaped.The CRISPR-Cas9system locates the accurate spot of mutation in the HBB gene.The Cas9 enzyme breaks a double strand at the target point and can correct and edit the gene when the patient's cells have the CRISPR-Cas9system in them. Researchers have used this technology to correct mutations

in the HBBgene,resulting in the production of healthy hemoglobin.This procedure can even be applied to the reactivation of fetal hemoglobin.To achieve this,CRISPRtechnology targets the inhibitors of HbF.The transcription factor BCL11A binds to the promotersHBG1/HBG2 and produces a switch from hemoglobinY to hemoglobinB(fetal to adult hemoglobin).Inhibiting BCL11A binding to its target causes a reversal of the switch and increases HbF expression in the blood.

Conclusion: CRISPR-Cas9 technology is an effective therapeutic method for gene editing and holds significant potential for treating SCD through genetic correction. However, further research needs to be done in this field.

keywords: CRISPR-Cas9,Sickle Cell Anemia,Sickle Cell Disease, SCD ,Treatment

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Adeno associated virus (AVV) as a gene therapy vector in the treatment of Duchenne Muscular Dystrophy (DMD)

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Medical Genetics

Background and aim: Duchenne Muscular Dystrophy (DMD) is a common and severe neuromuscular disease that causes variety of movement disorders, respiratory failure, cardiomyopathy and eventually premature death. This muscle-wasting disease that is also known as Xp21 dystrophy, occurs due to the mutations of the DMD gene and the complete absence of dystrophin protein. While some therapeutic interventions, such as steroid therapy, can mitigate disease progression, premature mortality remains an inevitable outcome. However the advent of gene therapy, specifically utilizing adeno associated virus (AAV) vectors as vehicles for micro-dystrophin delivery, has had a profound influence on the therapeutic landscape of DMD.

Methods: In this review, we searched Google Scholar and PubMed from 2015 up to November 2024 with keywords such as Duchenne muscular dystrophy (DMD), Adeno associated virus (AAV) and gene therapy.

Results: In clinical trials, various serotypes have been administered at diverse dosages to evaluate parameters such as alterations in muscle strength and heart function, intensity of immune responses, and vector durability. Based on the results of AAV seroprevalence testing (testing for the presence of AAV antibodies) in DMD patients, AAV2, AAV1 and AAV8 were identified as the serotypes with the highest prevalence. To achieve sustained transgene expression, it is important to suppress immune responses that could compromise vector longevity. Utilizing muscle-specific synthetic promoters like muscle creatine kinase (MCK) and glucocorticoids can be instrumental in immunomodulation. While preclinical data from animal models and successful clinical trials for X-linked Myotubular Myopathy (XLMTM), Spinal Muscular Atrophy type 1 (SMA1) and Hemophilia A using high-dose systemic AAV injections indicate a promising therapeutic approach for DMD, there are several challenges including dose optimization,

route of delivery and the optimal length of microdystrophin remain to be addressed.

Conclusion: Despite extensive investigations into various medical and genetic interventions for this lethal genetic disease, AAV vector-based gene therapy has emerged as the most efficacious approach. Indeed, this approach has revolutionized the therapeutic landscape for a broad spectrum of human genetic and acquired disorders, particulary neuromuscular diseases. Although ongoing clinical trials exhibit hopeful results, efforts to generate and isolate new AAV capsids with novel properties and enhance the persistence of exogenous genetic elements within human cells should not be ceased.

keywords: Duchenne Muscular Dystrophy (DMD), Adeno associated virus (AAV), Dystrophin.

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Analyzing the Impact of CRISPR-Cas9 on APOE Gene Editing and Alzheimer's Risk: A Systematic Review

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Medical Genetics

Background and aim: Alzheimer's disease (AD) is a complex neurodegenerative disorder with high variability. Many researchers have identified the APOE-ε4 allele as an important genetic risk factor. Advances in CRISPR-Cas9 technology, such as targeting and modifying APOE-ε4, have been noted by researchers active in genome editing. However, there are significant gaps in its efficacy and safety, as well as its long-term effects. This review article focuses on the effects of CRISPR-Cas9 on APOE gene editing and ultimately its outcome on Alzheimer's risk.

Methods: This review article was conducted using articles published in PubMed, ScienceDirect, Google Scholar, and Web of Science until November 2024. The keywords were CRISPR/Cas9, APOE, amyloid plaques, gene editing, and Alzheimer's disease. By searching these databases, 82 articles were found. After reading titles and abstracts, 45 of them were removed, and 37 articles were selected under the inclusion criteria. All articles were chosen from English-language sources.

Results: In our study, 37 articles were reviewed, which showed that CRISPR-Cas9 technology was able to convert apolipoprotein E-4 type alleles to a protective apolipoprotein E-3 type and reduce the expression of the E-4 allele of the APOE gene. This led to a reduction in amyloid-beta accumulation and tau phosphorylation. In some studies, results showed a reduction of pathologies in edited models related to Alzheimer's disease. The studies not only demonstrated the accuracy and scalability of this technique, but also highlighted ongoing

challenges such as transfer mechanisms and off-target effects caused by the inserted gene. Taken together, these studies strongly support CRISPR as a transformative tool in the development of Alzheimer's disease treatments.

Conclusion: Although the CRISPR-Cas9 technique has shown great potential in editing the APOE gene and reducing the risk of Alzheimer's disease, significant challenges such as gene transfer mechanisms and off-target effects still remain. Further research needs to be conducted on the long-term effects of APOE gene editing on neurodegenerative processes.

keywords: CRISPR/Cas9; APOE; Amyloid Plaques; Gene Editing; Alzheimer's Disease

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Exome Sequencing in Rare Ocular Diseases: A Systematic Review of Genetic Mutations and Clinical Implications

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Medical Genetics

Background and aim: Exome sequencing (WES) has emerged as a powerful tool for identifying genetic mutations in rare ocular diseases, significantly advancing medical research. The primary aim of this review is to analyze recent studies that have explored ocular diseases associated with WES.

Methods: A systematic search was performed in the PubMed and Google Scholar databases using the search term "Exome sequencing and ocular diseases." Only studies published in the last five years were included, resulting in 200 relevant articles. After an initial screening based on titles and abstracts, 14 primary studies focusing on ocular diseases and the application of WES were selected for detailed analysis.

Results: The use of exome sequencing has greatly impacted the identification of genetic mutations in rare ocular diseases. Among the various conditions examined, genetic mutations related to Retinitis Pigmentosa (RP), Wolfram Syndrome, Hermansky-Pudlak Syndrome (HPS), Inborn Errors of Immunity (IEI), and ADAMTSL4-related disorders were the most commonly identified. In RP, mutations in Hexokinase 1 (HK1) disrupt cellular metabolism, leading to retinal degeneration. These mutations primarily cause night blindness, and in some cases, they may lead to complete blindness. In Wolfram Syndrome, optic atrophy and progressive vision loss are among the most commonly reported symptoms. The genetic mutations in WFS1 play a central role in these manifestations. In patients with Hermansky-Pudlak Syndrome (HPS), ocular issues predominantly present as retinal pigmentary changes and light sensitivity. Evidence suggests that mutations in HPS1 are responsible for these alterations, significantly affecting the quality of life. Furthermore, in Inborn Errors of Immunity (IEI), chronic retinal inflammation and

Conclusion: This review highlights the critical role of exome sequencing in identifying genetic mutations associated with rare ocular diseases. Conditions such as RP, Wolfram Syndrome, HPS, IEI, and ADAMTSL4-related disorders directly or indirectly affect ocular structures, and early identification of these mutations can aid in timely prevention and treatment. Regular ophthalmic follow-ups in patients with these disorders can help prevent disease progression and significantly improve quality of life. The use of WES as a molecular tool enables clinicians to offer personalized, evidence-based treatments, ultimately preventing future vision disabilities.

keywords: Exome Sequencing; Rare Ocular Diseases; Genetic Mutations; Retinitis Pigmentosa, Ocular

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miR-200 Family: A Key Regulator of EMT and Potential Therapeutic Target in Cancer

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Medical Genetics

Background and aim: Epithelial-to-mesenchymal transition (EMT) constitutes a pivotal biological phenomenon that underpins cancer advancement, metastatic dissemination, and resistance to therapeutic interventions. In EMT, there is a notable reduction in epithelial features, specifically the expression of E-cadherin, together with the adoption of mesenchymal traits that facilitate cellular movement and invasive behavior. Identified as a vital player in EMT, the microRNA-200 family influences transcription factors and signaling networks related to this important biological shift. This review amalgamates insights derived to elucidate the miR-200 family's function in the modulation of EMT and its prospective utility as a therapeutic intervention in oncological contexts.

Methods: This review amalgamates findings from three pivotal sources: 1. Klicka and colleagues explored how the miR-200 family affects the management of cancer characteristics. 2. Gorecki and Rak examined the interactions between miR-200b and EMT-associated genes through a synthesis of TargetScan predictions and empirical data. 3. Wong and others explored the impact of the miR-200 family on pathways related to EMT in a detailed review. The investigations employed experimental models, meta-analytical assessments of EMT datasets, and computational forecasting of miRNA-mRNA interactions. Critical interactions between miR-200 and EMT markers, as well as signaling pathways (e.g., TGF-β, RhoA/ROCK), and extracellular matrix (ECM) components were systematically evaluated.

Results: ZEB1 and ZEB2 interact directly with the miR-200 group, consequently inhibiting E-cadherin transcription. Higher miR-200 levels correlate with decreased ZEB1/2, which in turn restores E-cadherin expression and inhibits EMT.

miR-200's relationship with ZEB1/2 boosts its impact on EMT processes. Within TGF-β signaling cascades, miR-200b impacts Smad2, blocking EMT by curbing the expressions of mesenchymal genes like SNAIL2. Additionally, miR-200b inhibits RhoA and ROCK2, leading to diminished cytoskeletal changes essential for cell movement. miR-200b activity decreases levels of fibronectin, lysyl oxidase, and other ECM proteins vital for metastasis. Furthermore, in KRAS-related cancers, miR-200b inhibits KRAS-driven EMT, aiding in the restoration of epithelial traits. Conversely, KRAS overexpression reduces miR-200 levels, suggesting a feedback regulatory system. The increased expression of miR-200 in cancer models correlates with reduced metastasis, therapy resistance, and EMT markers. Its ability to target multiple EMT pathways highlights its therapeutic potential through miRNA mimics or advanced delivery methods.

Conclusion: The miR-200 family serves as a fundamental regulator of EMT, directly targeting essential transcription factors, signaling pathways, and components of the extracellular matrix. By preventing EMT and supporting mesenchymal-to-epithelial transition (MET), miR-200 demonstrates remarkable potential as a treatment strategy intended to diminish metastatic spread and reverse drug resistance. Future investigations should prioritize the clinical applications of miR-200-based therapies in order to harness its anti-metastatic capabilities.

keywords: miR-200 Family, EMT, cancer

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Applications of the CRISPR-Cas System for HIV-1/AIDS Diagnostics: A Systematic Review

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Medical Genetics

Background and aim: Human immunodeficiency virus (HIV) is one of the significant global health concerns, causing around 630,000 deaths worldwide in 2023. Clustered regularly interspaced short palindromic repeats (CRISPR) and associated proteins (Cas) is a part of the immune system in bacteria, which can create a genetic memory by taking a piece of the virus's genome and inserting it into its genome. From this newly acquired DNA sequence, CRISPR generates a new "guide RNA," a sequence that helps CRISPR find the invader via sequence complementarity. This study aims to review the applications of the CRISPR-Cas system for HIV diagnostics.

Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until November 2024. The keywords were Human Immunodeficiency Virus, CRISPR-Cas, and diagnosis. By searching these databases, 54 articles were found, and 38 were removed by reading the titles and abstracts. 16 articles were selected under the inclusion criteria. All chosen articles were in English.

Results: Finally, 16 articles were included in this study. The findings indicate that the rRT-RAA assay, alone or in combination with CRISPR Cas12a-based detection, can potentially serve as a fast and reliable method for detecting HIV-1. Cas13a applied in CARMEN-Cas13, shows exceptional precision in identifying drug-resistant variants of HIV. AacCas12b, with its limited tolerance to mismatches between guide RNA and target DNA, is adept at detecting single-nucleotide changes, making it optimal for cancer-related gene analyses. Likewise, Cas14a, characterized by its small size and exceptional accuracy, is well-suited for

detecting SNPs with high fidelity. Cas12b, Cas13a, Cas14a, and other potential proteins hold great promise for improving methods of HIV detection. Among the available approaches, CARMEN-Cas13, AuNPs-tagging-based CRISPR-Cas12a bioassay platform, and CRISPR-SERS-LFA involve costly or technologically advanced tools. This results in increased complexity of operation and analysis, reducing their accessibility for users and increasing the difficulty of delivering them to end-users.

Conclusion: The CRISPR-Cas system seems to show potential in identifying the human immunodeficiency virus (HIV), as effective control of the HIV-1 epidemic relies on early diagnosis through simple, rapid point-of-care tests. However, more studies are required to verify its effectiveness and safety.

keywords: CRISPR-Cas system; Human Immunodeficiency Virus; Diagnosis.

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Morphine leads to epigenetic changes in the expression of miR-133b, miR-23b, S100A8/9 genes in the offspring of morphine-dependent mothers

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Medical Genetics

Background and aim: Epigenetic changes caused by mother's morphine consumption can be transmitted to offspring. However, the mechanisms by which morphine affects genes are not well understood. The aim of the current study is to explore the impact of morphine addiction and its withdrawal during pre-puberty in mothers on the expression of miR-133b, miR-23b, S100A8/9 genes in the hippocampus of their offspring.

Methods: Twenty female Wistar rats (F0 generation), approximately one month old, were used in this research. They were randomly assigned to either a control group or a morphine-exposed group. The morphine group was administered morphine daily at a dose of 5mg/kg for a period of four weeks. Following this treatment, a three-week observation period allowed for the complete resolution of withdrawal symptoms. Females from both groups were then bred with male rats. After birth, the resulting offspring (F1 generation) remained with their mothers for four weeks. Upon weaning, male and female F1 offspring were separated and subsequently analyzed for changes in the expression of specific genes including miR-133b, miR-23b, S100A8/9 genes in hippocampus. Gene expression was assessed by real-time PCR. ANOVA and Bonferroni post-hoc tests were used for data evaluation.

Results: Maternal morphine dependence and withdrawal significantly altered (p0.05) the hippocampal expression of miR-133b, miR-23b, and S100A8/9 in their offspring. These changes were observed similarly in both male and female progeny.

Conclusion: Prenatal exposure to maternal morphine addiction and withdrawal may induce altered gene expression within the hippocampus of their offspring. This indicates epigenetic changes of morphine on the hippocampus of the next generation.

keywords: Morphine; Epigenetic; mir-RNA; hippocampus

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CRISPR-Cas-Based Approaches for Infectious Disease Diagnosis: A Systematic Review

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Medical Genetics

Background and aim: Pathogenic microorganisms are responsible for over 27 million deaths per year worldwide due to the infectious diseases they cause. Clustered regularly interspaced palindromic repeats (CRISPR)/Cas9, part of an adaptive immune system in bacteria, is a gene-editing technology that makes it possible to correct errors in the genome and affect gene expression in cells and organisms quickly, with a lower cost, and with relative ease. This study aims to review the applications of the CRISPR-Cas system for infectious disease diagnostics.

Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until November 2024. The keywords were Infectious disease, CRISPR-Cas, and diagnosis. By searching these databases, 89 articles were found, and 55 were removed by reading the titles and abstracts. 34 articles were selected under the inclusion criteria. All chosen articles are in English.

Results: Finally, 34 articles were included in this study. Certain systems, such as Cas13, Cas12a, and Cas14, exhibit collateral nonspecific catalytic activities that enable nucleic acid detection, such as generating fluorescent signals. Platforms like SHERLOCK and DETECTR use this activity to rapidly and accurately detect pathogens, including viruses like Zika, Dengue, and SARS-CoV-2, and bacterial pathogens like E. coli. Such technologies have shown high sensitivity even at low viral loads in clinical settings. Moreover, CRISPR systems demonstrate potential beyond diagnostics, including eliminating viral genomes such as HIV-1 and Herpes viruses from host cells. This capability could be pivotal in addressing antimicrobial

resistance by modifying pathogen susceptibility patterns. CRISPR-based diagnostics also enable real-time monitoring of treatment responses, cancer biomarkers, and gene expression. These advancements have the potential to revolutionize molecular diagnostics, providing precise and sensitive tools for combating infectious diseases and other health challenges.

Conclusion: Due to its potential in diagnosis, the CRISPR-Cas system seems to be effective in reducing deaths caused by infectious diseases. This method introduces new thinking in infectious disease identification and can be expanded to measure nucleic acids in other clinical isolates. However, more research is needed.

keywords: CRISPR-Cas system; Infectious Disease; Diagnosis.

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The Role of CRISPR-Typing PCR in DNA Detection as a Novel Approach for Identifying and Tracking Epidemics: A Systematic Review

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Medical Genetics

Background and aim: The polymerase chain reaction (PCR) is one of the popular genotyping techniques that rapidly produces billions of copies of a specific segment of DNA. The clustered regularly interspaced short palindromic repeat (CRISPR), and its combination with the Cas9 protein, which plays an important role in the bacterial defense system, is specifically used to edit genes due to its simplicity and efficiency. In this review, we focus on the role of CRISPR-typing PCR (ct-PCR) in identifying target DNA in different viral strains and serotypes of bacteria and understanding their evolution

Methods: This review article was conducted using articles published in PubMed, ScienceDirect, Google Scholar, and Web of Science until November 2024. The keywords were CRISPR-typing, CRISPR-sequencing, qPCR, Human Papillomavirus, and Salmonella. By searching these databases, 77 articles were found. After reading titles and abstracts, 52 of them were removed, and 25 articles were selected under the inclusion criteria. All articles were chosen from English-language sources.

Results: In this study, 25 articles were reviewed, demonstrating a new method for identifying target DNA based on the Cas9 nuclease called ct-PCR (Cas9-sgRNA typing PCR). This method successfully identified L1 genes of two high-risk HPV types (HPV16 and HPV18) from 11 subtypes. Additionally, ct-PCR was able to identify the L1 and E6/E7 genes of these viruses in three cervical carcinoma cell lines (HeLa, SiHa, and C-33A) and clinical samples. The technique was also

effective in quickly and accurately identifying Salmonella serotypes, providing better results than traditional methods. ct-PCR was found to be competent in tracking epidemics and monitoring genetic changes in Salmonella serotypes, aiding in understanding the evolution of pathogen strains and their resistance.

Conclusion: It seems that ct-PCR has high potential in detecting DNA, identifying genes associated with various viruses and bacterial strains, and showing promise in tracking different epidemics. However, further research is needed to ensure its safety and efficiency.

keywords: CRISPR-Typing; CRISPR-Sequencing; qPCR; Human Papillomavirus; Salmonella

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Stem Cell Therapy in Dental Regeneration: Focusing on Direct Applications and Genetic Insights

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Medical Genetics

Background and aim: Stem cell therapy, especially using dental pulp stem cells (DPSCs), shows great potential for regenerating dental tissues. These cells can develop into different types of dental cells, enabling the repair of damaged or diseased dental tissues. Additionally, recent studies have begun to explore the genetic factors that influence stem cell behavior. They examine differentiation and integration. This research enhances our molecular understanding of DPSCs in dental regeneration. This review focuses on the application of DPSCs in direct regenerative therapy for dental tissues, exploring the genetic mechanisms involved in their regenerative potential and therapeutic efficacy.

Methods: A review search was conducted in the PubMed, Google Scholar, and Web of Science databases to identify relevant articles pertaining to the application of dental pulp stem cells (DPSCs) in regenerative dental therapy. We used specific keywords like "DPSCs," "dental tissue regeneration," "genetic mechanisms," and "direct applications." This search aimed to cover a wide range of studies focusing on the direct use of DPSCs for dental repair without using scaffolds or biomaterials. Studies published between 2022 and 2024 that have discussed genetic factors influencing DPSC behavior, including gene expression regulation, growth factor interactions, and epigenetic influences.

Results: DPSCs have demonstrated significant potential in regenerating dental pulp and dentin in vivo. Genetic studies have revealed key regulatory genes involved in cellular differentiation, proliferation, and immune modulation. The roles of signaling pathways, such as Wnt/β-catenin and Notch, in stem cell differentiation are critical for achieving effective regeneration. However, challenges remain in getting consistent results, especially in clinical applications. This is due to the complexity of gene-environment interactions.

Conclusion: Stem cell therapy with DPSCs shows great promise for regenerating dental tissue. By understanding how genetic mechanisms influence stem cell behavior, we can improve treatment results. However, further research is needed to optimize genetic pathways and improve clinical results.

keywords: Dental pulp stem cells, dental tissue regeneration, genetic mechanisms, signaling

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Salivary Biomarkers in Cancer Diagnosis: Recent Advances and Applications

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Medical Genetics

Background and aim: Salivary biomarkers have emerged as a non-invasive and effective tool for the early detection of various cancers. Their potential to provide critical information about disease presence and progression makes them a valuable resource in oncology. This review aims to summarize the recent advancements in the identification and application of salivary biomarkers for the diagnosis of oral, breast, and pancreatic cancers.

Methods: We carried out a review search of studies on salivary biomarkers in cancer diagnosis. We searched PubMed, Google Scholar, and Web of Science for articles published between 2022 and 2024. We used keywords such as “salivary biomarkers,” “cancer diagnosis,” “oral cancer,” “breast cancer,” and “pancreatic cancer.” Our focus was on studies that examined the diagnostic utility of salivary biomarkers across these cancer types. We analyzed key biomarkers, their detection methods, and their clinical significance. This review aims to summarize recent advancements in the identification and application of salivary biomarkers for cancer diagnosis.

Results: Recent studies have identified several salivary biomarkers, including microRNAs (miRNAs), proteins, and metabolites, that are significantly associated with cancer. For instance, elevated levels of miR-21 and miR-155 have been linked to oral squamous cell carcinoma (OSCC), with sensitivity and specificity rates exceeding 85%. In breast cancer, salivary levels of the protein HER2 showed a correlation with tumor size and stage, providing a potential diagnostic marker. Additionally, metabolites such as 3-hydroxybutyric acid in saliva have been identified as potential biomarkers for pancreatic cancer, demonstrating a sensitivity of 90% and specificity of 87%.

Conclusion: Salivary biomarkers provide a useful method for the early detection of various cancers, offering a non-invasive alternative to traditional diagnostic methods. Further research is essential to validate these biomarkers in larger cohorts and establish standardized protocols for their clinical application.

keywords: Salivary Biomarkers, cancer diagnosis, oral cancer, breast cancer, pancreatic cancer

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A novel mutation in CDH23 gene, in an Iranian family with several cases affected by hearing loss.

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Medical Genetics

Background and aim: The CDH23 gene encodes a protein that plays a significant role in the development and function of hair cells in the inner ear, which are essential for hearing. Mutations in the CDH23 gene are known to be associated with autosomal recessive non-syndromic hearing loss. Genetic mutations in this gene can disrupt the cellular processes that are crucial for normal auditory function, leading to varying degrees of hearing loss.

Methods: An 8_year-old girl affected with hearing loss were referred to our genetic counseling center. Three of her mother's cousins (mother-side) were affected with hearing loss, as well. Her parents were first cousins. Genetic counseling was performed and their family pedigree was drawn. Genetic analysis was performed on the patient using whole-exome sequencing, then the detected variant was investigated in the child and her parents and affected family members using Sanger sequencing method.

Results: Exome sequencing in the patient identified a VUS variant, c.5471GC (p. R1824P), in CDH23 gene in a homozygous state. Sanger sequencing method in the affected child, and her affected family members detected the variant in homozygous state. This variant was detected in her healthy parents in a heterozygous state. This variant has not been previously reported for its pathogenicity. Prediction of computational tools are conflicting. CADD and POLYPHEN support the deleterious effect of this variant on the gene or gene product, while SIFT and Mutation Taster predicts it as tolerated polymorphism. This variant is absent in population databases. Based on American College of Medical Genetics and Genomics (ACMG) guidelines this variant can be classified as a VUS.

Conclusion: Mutation in CDH23 gene causes hearing loss (P. R1824P) in Homozygote patient. CDH23is caused by homozygous or heterozygous mutation

in C.5471GC gene. Some patients with the disorder carry heterozygous CDH23 mutations similar to our cases. CDH23 shows phenotypic variability between families. In this study we were presenting an Iranian family affected by hearing loss and with a novel mutation in their CDH23 gene and discussing their clinical features.

keywords: CDH23, Hearing loss, Novel

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Polymorphisms in glucose metabolism-related genes as indicators of diabetic nephropathy risk

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Medical Genetics

Background and aim: Diabetic nephropathy (DN) is one of the most common chronic and progressive diabetes complication. It causes most end-stage renal disease (ESRD) worldwide due to its high mortality rate. To prevent or delay DN, high-risk patients must be identified early. Individuals with diabetes develop it due to hereditary and environmental causes. Several single nucleotide polymorphisms (SNPs) have been identified in different genes, which significantly contribute to genetic susceptibility to DN.

Methods: An extensive search was conducted on Google Scholar, Scopus, Web of Sciences and PubMed up until May 2024. we utilized all publications, including original articles and meta-analysis studies, that were published in english and had undergone peer review

Results: . Current studies revealed that variations in genes related to glucose metabolism are thought to be associated with DN. This review is focused on the various studies about the association between different polymorphisms in glucose metabolism-related genes and DN. Aldose Reductase (AKR1B1), Glucose transporter-1 (GLUT-1), Glucokinase regulatory protein (GKRP), Receptor of Advanced glycation end products (RAGEs), and Transcription factor 7-like 2 (TCF7L2) are the most important glucose metabolism-related genes in DN.

Conclusion: Identifying gene variants at a biomarker level could enable the detection of patients who are at an elevated risk for DN. This could aid in the treatment, diagnosis, and early prevention of the disease.

keywords: Diabetic Nephropathy; Polymorphisms; Glucose metabolism-related genes

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Bi-allelic SELENON Mutations in Two Unrelated Families with Congenital Myopathy 3 with Rigid Spine (CMYO3)

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Medical Genetics

Background and aim: Congenital Myopathy 3 with Rigid Spine (CMYO3) is a rare autosomal recessive muscle disorder characterized by early-onset muscle weakness, delayed motor development, facial myopathy, rigid spine, respiratory distress, and multisystemic complications. The condition is associated with mutations in the SELENON gene, which encodes a selenoprotein involved in oxidative stress regulation and muscle function. Here, we report a homozygous deletion mutation in the SELENON gene identified in two unrelated families presenting with CMYO3 manifestations.

Methods: We employed whole exome sequencing (WES) to investigate the genetic basis of the disease in probands, presenting with delayed motor milestones, generalized muscle weakness, facial myopathy, respiratory distress, and rigid spine. The identified variant was further validated using Sanger sequencing in a trio analysis. Muscle biopsy and histopathological evaluation were also performed to assess structural muscle abnormalities.

Results: Histopathological analysis demonstrated multicore myopathy with characteristic findings including fiber size variation, internalized nuclei, increased endomysial connective tissue, and adipose tissue replacement without inflammation. The identified SELENON variant (c.1446del, p.Asn483Thrfs*11) was classified as pathogenic based on the ACMG criteria, and co-segregation

analysis confirmed autosomal recessive inheritance. These findings supported a diagnosis of CMYO3.

Conclusion: This study highlights a pathogenic SELENON mutation contributing to the clinical spectrum of CMYO3. Our findings emphasize the utility of WES as a critical diagnostic tool in patients with complex myopathic phenotypes, particularly in consanguineous populations. Genetic analysis enables precise diagnosis, facilitates genetic counseling, and informs clinical management.

keywords: Congenital Myopathy 3, SELENON gene, Whole exome sequencing, Multicore myopathy,

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Gene Therapy for Hereditary Retinal Diseases Using Viral Vectors: A Systematic Review

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Medical Genetics

Background and aim: Inherited Retinal Diseases (IRDs) represent a diverse group of genetic disorders that can lead to visual impairment or blindness. These conditions are important because they can affect a person's quality of life and often run in families. Retinal gene therapy is increasingly recognized as a novel molecular intervention with great potential for the treatment of inherited retinal diseases. The aim of this study is to review the treatment of hereditary retinal diseases with gene therapy using viral vectors.

Methods: This review was conducted using articles published on PubMed, Scopus, and Google Scholar until November 2024. The keywords were "Gene Therapy," "Retinal," and "Viral Vector." Seventeen articles were found in the initial search; six were excluded after reading titles and abstracts. Eleven articles met the inclusion criteria, and all were selected from English and Persian sources.

Results: Finally, 11 articles were included. AAV8-RLBP1 treatment cleared retinal deposits and restored the visual cycle in RLBP1-related retinal dystrophy. A phase 1/2 trial for X-linked retinitis pigmentosa (RP) with the RPGR gene in 18 patients showed safety and visual field improvement. Gene therapy using an AAV vector encoding Rab Escort1 improved retinal structure and function after iatrogenic retinal detachment. A phase II trial for RPE65 deficiency with an AAV vector showed significant rod sensitivity improvement. Gene therapy for MERTK-related RP with rAAV2-VMD2-hMERTK was safe and led to clinical improvement in some patients. rAAV.sFLT-1 was safe and supported as a long-term treatment for wet age-related macular degeneration.

Conclusion: Gene therapy for retinal diseases represents a significant advancement in medicine, offering hope for improved vision and quality of life for affected individuals. As research progresses, further improvements in retinal genetic treatments and new methods for controlling and treating genetic disorders in the retina will emerge. This technology not only addresses current disorders but also provides hope for a brighter future for patients.

keywords: Gene Therapy; Retinal; Viral Vector; Inherited Retinal Diseases

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The Role of Bioanformatics Analysis of Genes Involved in Breast Cancer

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Medical Genetics

Background and aim: Breast cancer is one of the most common and deadly types of cancer worldwide. Understanding the molecular mechanisms underlying breast cancer development and progression is crucial for improving disease management and identifying new therapeutic targets. This study aimed to compare gene expression patterns between healthy and breast cancer samples to identify differentially expressed genes .Through integrated bioinformatics analysis, we evaluated gene survival and expression & Protein- Interaction profiles leveraging multiple genomic databases.

Methods: The data used in this study were obtained from the GSE42568 dataset, which contains gene expression information for 1,104 breast cancer samples. The GEO2R tool was used for the analysis, which allows the creation of visual plots such as volcano plots and survival analysis. The ERBB2 gene, also known as HER2, is frequently overexpressed in breast cancer and is associated with more aggressive disease and poorer patient outcomes. Elevated ERBB2 expression has been shown to drive tumor growth and metastasis, making it an important biomarker and therapeutic target in breast cancer. In contrast, the TBX15 gene has been reported to be down regulated in breast cancer samples compared to healthy controls. After that this study was to comprehensively analyze the differential expression of these two key genes, ERBB2 and TBX15, between breast cancer and healthy samples using the online analysis tools provided by the ENCORI platform.

Results: The volcano plot in this study shows that a substantial number of genes are expressed in breast cancer samples . Genes such as BRCA, ERBB2, and CESC are among the key genes that are up regulated in the cancer samples. The survival analysis demonstrates that higher expression of the ERBB2 gene is associated with poorer prognosis for patients. ERBB2 is a well-known biomarker in breast

cancer that is linked to increased cell proliferation and migration of cancer cells. The image from the STRING platform shows that the ERBB2 and ERBB4 proteins are two key proteins in the protein-protein interaction network. These proteins interact with other breast cancer-related proteins like SHC1, GRB2, and EGF, and involved in important signaling pathways driving cancer progression. The results of this study indicate that gene expression analysis and protein interaction networks can help identify important biomarkers and uncover the biological mechanisms involved in breast cancer.

Conclusion: Overall, this study utilized the online tools provided by the ENCORI platform to identify molecular signatures associated with breast cancer. The results of this analysis can be used to better understand the biological mechanisms involved in breast cancer and to discover new biomarkers.

keywords: Breast cancer, Gene expression analysis, ENCORI (star Base), GEO2R

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Protective Gene Regulation in Astrocytes: Insights into Hypoxic Preconditioning for Neurodegenerative Disease Therapy

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Medical Genetics

Background and aim: Neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and ischemic stroke, are marked by progressive neuronal damage, often driven by oxidative stress. This imbalance between reactive oxygen species (ROS) production and antioxidant defenses leads to cellular injury and dysfunction. Astrocytes, essential glial cells in the central nervous system, play a pivotal role in mitigating oxidative stress via neuroprotective mechanisms, such as releasing neurotrophic factors and regulating inflammation. Elucidating the molecular pathways underlying astrocyte responses is critical for developing therapies. This study explores the impact of hypoxic preconditioning (HP) on astrocyte resilience, focusing on neuroprotective gene expression under oxidative stress conditions.

Methods: Primary astrocytes were cultured and subjected to hypoxic preconditioning for varying durations. Oxidative stress was induced using hydrogen peroxide (H_2O_2), and the activation of key signaling pathways involved in neuroprotection and oxidative stress responses was assessed. Gene expression profiles were analyzed and validated through real-time PCR, targeting critical neurotrophic and stress-response genes.

Results: Hypoxic preconditioning significantly enhanced astrocytes' survival under oxidative stress conditions. Real-time PCR analysis revealed robust upregulation of neurotrophic factors such as BDNF, VEGF, and HIF-1α, alongside an increase in antioxidant enzyme expression. Furthermore, hypoxic preconditioning attenuated pro-inflammatory gene expression and resulted in a moderate rise in anti-inflammatory gene levels, highlighting its dual role in protecting against oxidative damage and inflammation.

Conclusion: This study underscores the crucial role of astrocytes in mitigating oxidative stress and inflammation, key drivers of neurodegeneration. Hypoxic preconditioning emerges as a promising therapeutic strategy to enhance astrocytic resilience by modulating critical neuroprotective, inflammation and oxidative stress pathways. These findings suggest that HP could serve as a novel approach to combat oxidative damage and inflammation in neurodegenerative diseases, offering the potential for the development of treatments.

keywords: Neurodegenerative diseases, Oxidative stress, Hypoxic preconditioning, Astrocyte

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New development of lncRNAs-encoded peptides in colorectal cancer

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Medical Genetics

Background and aim: Colorectal cancer(CRC) is one of the most common cancers worldwide.Long non-coding RNAs(lncRNAs) were initially defined as a class of RNAs longer than200 nucleotides that do not encode proteins. With the advancement of proteomics and translation technologies, it has been revealed that some lncRNAs have the ability to encode small peptides or micropeptides that play an important role in regulating molecular processes related to colorectal cancer. These peptides can accelerate or inhibit cancer proliferation and progression by affecting cellular metabolism, signaling pathways, and resistance to treatment. In this study, we aim to investigate the role of peptide-secreting lncRNAs in colorectal cancer.

Methods: This is a review study that after searching with the keywords, lncRNA, Colorectal cancer, peptide and encode in PubMed, Embase, Science direct databases from 2015 to 2024 articles related to inclusion criteria were extracted and then analyzed.

Results: Previous studies have identified eight LncRNAs that are capable of secreting peptides and are involved in colorectal cancer. These peptides can accelerate or inhibit cancer proliferation and progression by affecting cellular metabolism, signaling pathways, and resistance to treatment. HOXB-AS3 binds to arginine residues of the hnRNP-A1 protein, preventing the protein from binding PKM enzyme and leads to decrease in the growth of CRC cancer cells. SRSP promotes cancer cell proliferation and metastasis. RBRP peptide expression is increased in metastatic colorectal cancer, binding to IGF2BP1 protein to stabilize c-Myc mRNA. ASAP increases ATP synthase activity and mitochondrial oxygen consumption, and promotes CRC proliferation. Pep-AP accumulates ROS and induces apoptosis, which makes cells more sensitive to treatments. MBOP and

BVESAS1-201 increase cell survival, migration, and invasion in colorectal cells by activating the MEK1/pERK and SRC/Mtor signaling pathways, respectively. FORCP inhibits cell proliferation and induces apoptosis under the influence of endoplasmic reticulum stress.

Conclusion: Our study aims to contribute the presence of a sizable group of lncRNAs that have the potential to encode peptides in colorectal cancer. The novel perspectives offered by these findings will contribute to the development of future anti-cancer drugs and tumor biomarkers, offering a new frontier in the battle against colorectal cancer.

keywords: lncRNA; Colorectal cancer; peptide

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The Relationship Between IL-1 Receptor Antagonist Gene Polymorphism and Type 2 Diabetes Mellitus

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Medical Genetics

Background and aim: Type 2 diabetes is one of the oldest non-communicable diseases and is the eighth leading cause of death and disability in the world. Several studies have shown a link between decreased insulin sensitivity and inflammation. "Increased levels of pro-inflammatory cytokines can lead to apoptosis in pancreatic beta cells. Interleukin 1 beta (IL-1β) is a key regulator of inflammation, and its role in type 2 diabetes has been identified in various studies. This study aimed to compare polymorphisms of the interleukin-1 receptor antagonist gene in patients with type 2 diabetes and controls.

Methods: The study's case group comprised 50 individuals diagnosed with type 2 diabetes, confirmed by a specialist following the criteria set by the American Diabetes Association. These patients were selected from those attending Alameh Behlol Gonabadi Hospital in Gonabad. The control group consisted of 50 healthy individuals with no family history of type 2 diabetes. Individuals with systemic infections, cardiac issues, or renal diseases were excluded from participation. After obtaining informed consent, 2 cc of blood containing EDTA was collected. DNA was extracted from the whole blood using the Salting Out method, followed by agarose gel electrophoresis. Primer design was conducted using Oligo7 software, and the IL-1Ra gene was amplified with a thermal cycler. Patient data and results were entered into SPSS software for analysis, utilizing T-tests for

quantitative data and Chi-Square tests for qualitative data at a significance level of 0.05.

Results: Analysis of genotypes for the IL-1Ra polymorphism indicated that the frequency of genotype 1/2 was significantly higher in the diabetic group compared to the control group. Specifically, this genotype was present in 52% of the diabetic participants versus only 8% in the healthy individuals, demonstrating a statistically significant difference (P 0.001). The findings suggest that individuals with the genotype 1/2 have approximately a 15-fold increased risk of developing diabetes compared to those without this genotype.

Conclusion: IL-1Ra is a significant predictor of clinical diabetes, and the polymorphism in the IL-1 receptor antagonist gene is closely associated with diabetes susceptibility. The presence of genotype 1/2 elevates the risk of developing diabetes by up to 15 times. Consequently, these findings could lead to important advancements in identifying high-risk individuals and preventing diabetes.

keywords: Diabetes, polymorphism, Interleukin-1β

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Evaluating the diagnostic role of NEATI as a biomarker in acute lymphoblastic leukemia

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Medical Genetics

Background and aim: Acute Lymphoblastic Leukemia (ALL) is a malignant tumor of the hematopoietic systems in the bone marrow, which can occur at any age and manifests with a range of clinical symptoms. According to the GLOBOCAN report, 474,519 cases of leukemia were reported globally, of which 67,784 cases were in North America. The main characteristic of ALL is chromosomal abnormalities and genetic alterations that play a role in the differentiation and proliferation of lymphoid precursor cells. Early diagnosis through biomarkers such as NEAT1, a type of long non-coding RNA (lncRNA), can improve survival rates and provide more effective diagnostic tools.

Methods: We collected relevant articles published between April 26, 2017, and July 5, 2024, using keywords such as Leukemia, ALL, Biomarkers, Diagnostic, and NEAT1 in PubMed, Google Scholar, and ScienceDirect. Our review included 7 eligible studies.

Results: In recent years, several LncRNAs, such as AFAPI-ASI, MALAT-1, and UCAl, have been confirmed to play significant roles in cancer progression. The NEAT1 molecule is restricted to the nucleus and is located on chromosome 11 (11q13.1). This molecule is considered an essential component of nuclear paraspeckles. The overexpression of NEAT1 in patients with ALL has been observed to be higher compared to healthy individuals. Based on findings from various studies, NEAT1 has been identified as an oncogene in ALL. Ultimately, NEATI, as a biomarker in ALL, has the potential to be utilized for assessing disease progression and response to treatments. However, further research is required to definitively confirm this role.

Conclusion: (ALL) accounts for 80% of cases in children; however, when it occurs in adults, it becomes a devastating disease. The Nuclear Enriched Abundant Transcript 1 (NEAT1) is a newly identified LncRNA. This molecule has been found

to be overexpressed in many human cancers. Moreover, NEAT1, as an estrogen receptor alpha-specific LncRNA, promotes oncogenic growth by altering the epigenetic landscape of target gene promoters. Previous studies have shown that NEAT overexpression can influence apoptosis and cell migration. Therefore, the expression level of NEAT1 may reflect the intrinsic characteristics of cancer progression.

keywords: ALL,NEAT1,Diagnostic, Biomarker.

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Revolutionizing Lung Cancer Diagnosis and Treatment through DNA Methylation: A Systematic Review

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Medical Genetics

Background and aim: Lung cancer is a leading cause of cancer-related deaths worldwide, making early detection and accurate staging critical. Recent advances in molecular genetics, particularly in DNA methylation, are reshaping how we approach lung cancer diagnosis and treatment. This review examines how genetic markers, including DNA methylation, are advancing precision medicine in lung carcinoma.

Methods: We reviewed 15 articles from PubMed, Google Scholar, and Web of Science, published since 2020, focusing on molecular biomarkers, DNA methylation, and their clinical applications.

Results: Advances in molecular testing, including the identification of mutations in EGFR and ALK, have led to more targeted therapies, improving outcomes in both NSCLC and SCLC. DNA methylation markers like SHOX2 and RASSF1A have shown promise in early-stage detection, while liquid biopsy techniques, such as ct-DNA, are proving valuable for monitoring treatment responses and tumor heterogeneity.

Conclusion: Integrating molecular genetics and DNA methylation into clinical practice offers new hope for personalized lung cancer treatments. However, more research is needed to optimize these technologies and improve patient outcomes.

keywords: Lung Cancer; DNA Methylation; Precision Medicine; Targeted Therapies; Liquid Biopsy.

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A novel pathogenic frameshift variant in the AMPD2 gene causes autosomal recessive Pontocerebellar Hypoplasia type 9

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Medical Genetics

Background and aim: Pontocerebellar hypoplasia type 9 (PCH9) is a rare, inherited neurodevelopmental disorder caused by mutations in the AMPD2 gene. Characterized by neurodegeneration, it typically presents with severe developmental delays, microcephaly, spasticity, and brain abnormalities such as cerebellar and pontine atrophy and a thin corpus callosum. PCH9 often has a prenatal onset, significantly affecting psychomotor development and neurological function. In this study, we evaluated a 9-year-old girl who presented to us with paralysis of all body parts and speech impairment. Through family exome sequencing and patient analysis, we found a homozygous mutation in the AMPD2 gene (NM_001368809.2: c.630delC: p. Thr211fs)

Methods: This study examines a 9-year-old Iranian girl with limb paralysis and speech impairment, referred to the Comprehensive Medical Genetics Center in Anzali, Iran. She has normal hearing and comes from a consanguineous family with no reported symptoms in her extended family. Whole Exome Sequencing (WES) was performed to identify the disease-causing mutation. Genomic DNA was extracted using a QIAamp DNA Blood Mini Kit and analyzed with the SureSelect XT Human All Exon V6 kit. Sequencing occurred on an Illumina NovaSeq 6000, followed by bioinformatics analysis using BWA, GATK, and ANNOVAR for variant detection and annotation.

Results: WES results showed that the affected girl exhibited homozygosity for a frameshift mutation. This mutation was caused by the deletion of a single nucleotide in the AMPD2 gene (AMPD2: ENST00000528667.7, NM_001368809.2: c.630delC). This novel homozygous variant is located on chromosome 1p13.3, close to exon 7 of the AMPD2 gene. The deletion could potentially result in a

frameshift mutation in the AMPD2 protein, leading to the change p. Thr211fs (AMPD2: ENSP00000436541.2, NM_001368809.2: p. Thr211fs).

Conclusion: We identified a new genetic variant in the ampd2 gene that, while causing frameshifting and loss of protein function like known mutations, resulted in a distinct Pontocerebellar Hypoplasia type 9 phenotype compared to previously reported cases. This indicates a wider range of PCH9 phenotypes associated with ampd2 mutations. To fully understand the relationship between phenotype and genotype, more samples need to be analyzed.

keywords: AMPD2; case report; Pontocerebellar hypoplasia type 9; Exome sequencing

PH-1

In Silico Prediction of Potential Role of Upregulated miR-3196 in Multiple Myeloma

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Background: MiRNAs play a multifaceted role in the progression of multiple myeloma (a devastating hematological malignancy) by regulating tumor suppressor genes, promoting oncogenic pathways, influencing genomic stability, and interacting with the bone marrow microenvironment, highlighting their potential as both biomarkers and therapeutic targets. So, this study aimed to investigate the role of hsa-miR-3196 in MM.

Methods: We started by loading necessary libraries such as `GEOquery (version 2.66.0) `the dataset of interest (GSE125363) including 44 data of patients and 4 healthy individuals. Data processing was conducted using R software (version 4.2.2) with several packages, including limma, and AgiMicroRna. multimiR package applied to find the target genes. The analysis involved differential expression analysis and normalization of the data. Also, bioinformatics platform was served to enrich the target genes of miR-3196.

Results: The differential expression analysis of miRNA sequencing data from MM samples revealed that miR-3196 was significantly upregulated compared to healthy controls. The adjusted p-value for miR-3196 was 0.016979, while the p-value was 0.000136. The log2 fold change for miR-3196 was calculated to be 1.12241, corresponding to a 2.18-fold increase in expression in MM samples relative to controls. This pathway was found to be significantly enriched with a p-value of 0.019468889, suggesting that miR-3196 may exert its effects on MM pathogenesis by modulating the TGF-β signaling cascade. Moreover, the genes that is likely to be regulated by miR-3196: SKI, THSD4, and AMH.

Conclusions: In conclusion, the identification of the TGF-β signaling pathway as a potential target of the upregulated miRNA, miR-3196, in MM, with specific target genes including SKI, THSD4, and AMH, highlights the importance of this miRNA in MM pathogenesis and provides a basis for further investigation into its therapeutic potential.

Keywords: Multiple Myeloma, Microarray analysis, miR-3196

PH-2

Unraveling the Impact of miR-125b on B-cell Acute Lymphoblastic Leukemia Relapse: A Bioinformatics Approach

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Background: MiR-125b has been identified as an oncomiR, meaning it can promote cancer development. Its ectopic expression has been shown to induce B cell acute lymphoblastic leukemia (B-ALL) in experimental models. Thereafter, the aimed of this study was to identify the role of miR-125b family in B-ALL relapse.

Methods: We started by loading necessary libraries such as `GEOquery (version 2.66.0) `the dataset of interest (GSE30647). Data processing was conducted using R software (version 4.2.2) with several packages, including limma, and AgiMicroRna. The analysis involved differential expression analysis and normalization of the data. Also, bioinformatics platform was served to enrich the target genes of miR-125b. Also, GraphPad prism was served to identify the P value.

Results: The differential expression analysis of GSE30647 revealed that miR-125b-5p and miR-125b-1-3 were significantly upregulated in relapsed groups compared to controls. The p-value for was less than 0.0001 for both groups. the pathway was found to be significantly enriched was TGF-β pathway, suggesting that miR-125b may exert its effects on pathogenesis of relapse by modulating the CDKN2B, PPP2CA, IFNG, TGFBR1, ACVR2B, SMAD2, SMURF1, and NEO1 genes.

Conclusions: In conclusion, the significant upregulation of miR-125b-5p and miR-125b-1-3p in relapsed B-ALL groups, along with the enrichment of the TGF-β signaling pathway, highlights the potential role of miR-125b in B-ALL relapse groups.

Keywords: B-ALL, Microarray analysis, miR-125b, Relapse

PH-3
Inflammatory factors Predicting Acute Appendicitis in pediatric patients

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Background: The most common cause of acute abdominal pain, which affects more men than women, is acute appendicitis (AA). Timely and accurate diagnosis of AA is crucial, as the consequences worsen over time. Inflammatory biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), are increasingly utilized in the diagnosis and prognosis of various inflammatory conditions. The purpose of this study was to investigate how these parameters serve as inflammatory markers for the diagnosis of pediatric acute appendicitis.

Methods: We searched PubMed, Scopus, and Google Scholar for studies published between 2021 and 2024 that compared the values of the MLR, NLR and PLR in pediatric patients with acute appendicitis and a control group.

Results: The results of the studies indicated a significant distinction between the two groups. Acute appendicitis in pediatric patients resulted in markedly higher levels of MLR and NLR, and a significant association was also observed between the two outcomes.

Conclusions: Hematological indicators such as MLR, NLR and PLR are valuable in differentiating between pediatric patients with acute appendicitis and those without. Throughout the treatment process, these markers can also aid in monitoring pediatric patients diagnosed with acute appendicitis. Research suggests that patients with acute appendicitis may

be at greater risk for complications if their NLR and PLR levels are elevated. When combined with imaging studies, physical examinations, and other laboratory tests, NLR and PLR measurements can help emergency department clinicians identify high-risk patients with acute appendicitis.

Keywords: Monocyte-Lymphocyte ratio; Neutrophil-Lymphocyte ratio; Platelet-Lymphocyte ratio; acute appendicitis, Pediatric

PH-4

Unveiling the impact of MicroRNA-217 overexpression on Glycogen Synthase Kinase 3 in Raji and Jurkat Acute Lymphoblastic Leukemia cells

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Abstract

Background and Aim: Acute lymphoblastic leukemia (ALL) is characterized by malignant transformation and uncontrolled proliferation of lymphoid progenitor cells in bone marrow, blood, and extramedullary sites. MicroRNA-217 (miR-217) has demonstrated potential as an anticancer agent owing to its reduced expression in various malignancies. Glycogen synthase kinase 3 (GSK-3), comprising two isoforms (α and β), influences numerous pathways affecting cell metabolism, differentiation, and death processes, including apoptosis and autophagy, and may be crucial in certain cancer types. This study aimed to examine the effect of miR-217 overexpression on GSK-3 gene expression in B (Raji) and T (Jurkat) acute lymphoblastic leukemia cell lines.

Methods: Jurkat and Raji cell lines were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and incubated under controlled conditions of 37 °C, 95% humidity, and 5% carbon dioxide. Additionally, a normal Fibroblast cell line was cultured in DMEM. Next, miR-217 was transduced into the cells using lentiviral vectors. RNA was extracted from cells 48 and 72 hours after transduction, and complementary DNA (cDNA) was synthesized. Finally, the transduction efficiency was confirmed using Real-Time qPCR, and the gene expression levels of GSK-3 were measured using the same technique. Statistical analyses were performed using SPSS 27 and GraphPad Prism 8.

Results: The expression level of GSK-3α in the miR-217 transduced group compared to the control group did not exhibit significant differences in Jurkat cells at 48 and 72 h after

transduction. However, the expression level increased in Raji cells, with statistical significance observed only after 72 h, and significantly decreased in Fibroblast cells at both time points. Furthermore, GSK-3β gene expression levels in the miR-217 transduced group compared to the control group increased in Jurkat and Raji cells, whereas there was no significant difference in Fibroblast cells 48 h after transduction. Moreover, an increase was observed in Raji cells, whereas a decrease was observed in Jurkat and fibroblast cells after 72 h; however, these differences were not statistically significant.

Conclusion: The results of the present study demonstrated that miR-217 overexpression alters GSK-3 gene expression in Jurkat, Raji, and Fibroblast cells, indicating a potential regulatory role of miR-217 in the expression of this gene. This insight is valuable in understanding the molecular mechanisms underlying various cellular processes. Further research is necessary to elucidate the role of miR-217 in the GSK-3 signaling pathways.

Keywords: Acute lymphoblastic leukemia; hsa-mir-217; Glycogen Synthase Kinase 3.

PH-5

The Evaluation of Static Magnetic Field's Effect on metabolism and Survival of THP1 Cells

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Abstract

Background and Aim: Cancer remains one of the leading causes of mortality globally. Recent treatment advancements have improved patient outcomes, but they often carry significant adverse effects. In recent years, magnetic fields have emerged as an innovative therapeutic approach, offering several benefits including reduced side effects, high efficacy, wide applications, and cost-effectiveness, and also avoiding the formation of scars. Magnetic fields demonstrate anti-tumor properties by inhibiting cellular growth, inducing apoptosis, and arresting the cell cycle through various molecular mechanisms. This research investigated the effects of static magnetic fields on cancer cell proliferation, promoting apoptosis, and cell cycle arrest in THP1 cells.

Methods: We exposed THP1 cells to the magnetic field for 24 hours. After that, we measure the impacts of SMF on cellular proliferation with MTT assay and assess apoptosis and cell cycle arrest in cancer cells with the flow cytometry method.

Results: Following a 24 hour exposure to static magnetic fields, THP1 cells exhibit a reduction in OD of MTT assay that suggests cell growth was decreased. This growth inhibition is associated with an elevation in apoptosis and cell cycle arrest because we found an increase in PI/Annexin in treated cells and enhanced the population of cells in the sub-G1 phase.

Conclusion: Our results show that static magnetic fields can suppress the proliferation of THP1 cells. Following exposure to static magnetic fields, apoptosis, and cell cycle arrest were observed in the THP1 cells. The findings of our study indicate that static magnetic fields may

serve as a therapeutic approach for AML, promoting cell death and inhibiting the proliferation of cancer cells. However, Future studies should aim to find the exact mechanisms associated with these conditions.

Keywords: static magnetic field, apoptosis, THP1.

PH-6

Achievements of gene therapy in β-hemoglobinopathies

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Abstract

b-globin gene disorders are the most prevalent inherited diseases worldwide and result from abnormal b-globin synthesis or structure. Extensive characterization of the globin gene locus, along with pioneering work on the use of viruses as tools for human gene delivery in human hematopoietic stem and progenitor cells (HPSCs), has led to transformative and successful therapies through autologous hematopoietic stem-cell transplant with gene. Gene therapy, by autologous transplantation of genetically modified hematopoietic stem cells, currently represents a novel therapeutic promise, after many years of extensive preclinical research for the optimization of gene transfer protocols. sickle cell disease was the first condition to be elucidated at the molecular level; the β-globin promoter was one of the first eukaryotic promoters to be extensively characterized. This review outlines gene therapy strategies, ongoing trials.

Background and Aim: Considering that this treatment method can be the first line of dealing with all kinds of hemoglobinopathies in the coming years, in this research, the current state of clinical trials and the future of this treatment method are discussed

Methods: A review of articles related to various gene therapy methods.

Results: In this article, we intend to state what has happened and will happen in gene therapy and analyze the progress of this treatment method.

Conclusion: Two important diseases that are targeted in gene therapy treatments. In this article, the aim is to review the latest achievements of gene therapy. Knowledge of the latest achievements of gene therapy gives hope to researchers to achieve better treatments in this field .

Keywords: gene therapy, thalassemia, hemoglobinopathies, sickle cell disease

PH-7

Investigation of gene therapy in the treatment of sickle cell anemia

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Abstract

Sickle cell disease (SCD) is one of the most common life-threatening monogenic diseases affecting millions of people worldwide. sickle cell disease results from a homozygous missense mutation in the β-globin gene that causes polymerization of hemoglobin S. An unusual but life-threatening complication of SCA is sequestration syndrome, wherein a considerable amount of the intravascular volume is sequestered in an organ (usually the spleen), causing vascular collapse Gene therapy for patients with this disorder is complicated by the complex cellular abnormalities and challenges in achieving effective, persistent inhibition of polymerization of hemoglobin S. Recent advances raise prospects for improved, and perhaps curative, treatment. First, transcription factors, BCL11A and LRF/ZBTB7A, that mediate silencing of the β-like fetal (γ-) globin gene after birth have been identified and demonstrated to act at the γ-globin promoters, precisely at recognition sequences disrupted in rare individuals with hereditary persistence of fetal hemoglobin. Second, transformative advances in gene editing and progress in lentiviral gene therapy provide diverse opportunities for genetic strategies to cure SCD.

Background and Aim: In order to increase awareness about the treatment of this disease, it has been tried to introduce new treatment methods.

Methods: A review of articles related to the treatment of sickle cell anemia with gene therapy

Results: Examining new scientific methods in any therapeutic field provides awareness for further revision of older methods, so the benefits of these methods are very important. Collecting different methods together and comparing them can help a lot in choosing the right method

Conclusion: Since this disease has many unknown aspects in treatment, it is important to review each treatment process

Keywords: Sickle cell, Gene therapy, hemoglobin S

PH-8
Treatment of the sickle cell anemia (SCD) using clustered regularly interspaced short palindromic repeats (CRISPR) cas-9 technology: A review

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Background and Aim: Sickle cell disease (SCD) is a genetic condition affecting many newborns annually, particularly in regions such as the Middle East. Caused by a mutation in the B-globin gene, sickle-shaped red blood cells cause vaso-occlusive crises (VOCs), anemia, and a weakened immune system. One of the most promising treatments is the clustered regulatory interspaced short palindromic repeats (CRISPR)-Cas9 system, which allows for precise genome modification and correction of the genetic mutations responsible for SCD or activation of other genes that can alleviate the symptoms. Therefore, this review aims to provide a helpful summary of the latest research findings in this area.
Methods: Several databases, including Google Scholar, Pubmed, Elsevier, etc., were investigated. Using the terms "sickle cell disease", "genome editing" and "CRISPR", relevant articles published between 2020 and 2024 were selected and reviewed
Results: In various studies, the CRISPR-Cas9 system has been reported successful in reactivating the fetal hemoglobin gene, resulting in a pan-cellular elevation of fetal hemoglobin. Patients treated with this method showed reduced symptoms, and some became liberated from blood transfusion. Also, in several studies, it has been observed that this strategy neither impairs erythroid differentiation nor causes any off-target DNA cleavage. Therefore, in 2023, CRISPR-Cas9 drugs, such as Casgevy and Iyfgenia, were approved as formal therapies in several regions, such as the US, UK, and Europe.
Conclusion: The CRISPR-Cas9 system and its fellow alternates (cas12a and cas13) have been used to reactivate the fetal hemoglobin gene. In various studies, this strategy has significantly improved the quality of life in patients with sickle cell disease without generating any considerable side effects. This breakthrough genome editing method has shown promise to be

profitable in the treatment of SCD patients with its affordable expense, high specificity, and precision.

Keywords: Sickle cell disease (SCD), The clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9

PH-9

CAR macrophage: A novel strategy for cancer treatment

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Background and Aim: While chimeric antigen receptor (CAR) T cells have proven effective in hematological malignancies, there are boundaries in managing solid tumors. Compared to the aforementioned therapy, CAR macrophage (CAR-M) presents a promising alternative for treating solid tumors. The unique features of macrophages that make them an appealing candidate for upcoming immunotherapy approaches include strong phagocytic function, highly effective antigen-presenting cells, and the polarization into M1 and M2 phenotype, which are respectively anti-tumor activity and tumor growth activity. This literature review is aimed at providing a comprehensive overview of CAR-M therapy's current findings on both hematological malignancies and solid cancers.

Method: CAR macrophage, CAR-M therapy, solid tumors, hematological malignancies, Tumor-associated macrophages (TAM), tumor microenvironment (TME), and chimeric antigen receptor keywords and MeSH terms are searched in Google Scholar, PubMed, Web of Science, and Scopus. The obtained titles and abstracts are screened to identify the appropriate full-text articles.

Result: The results indicate that these engineered cells can shift the TME towards a pro-inflammatory environment, penetrate the TME, enhance phagocytic activity and antigen presentation, and improve the ability of T cells to attack solid tumors. In addition, CAR-Ms play a significant role in treating hematological malignancies by amplifying anti-tumor effects and enhancing the elimination of leukemia cells. The ability of CAR-M to diminish the release

of cytokine during treatment may lead to reducing the risk of both cytokine release syndrome (CRS) and neurotoxicity related to CAR-T therapy.

Conclusion: According to the evidence, CAR-M therapy has emerged as an innovative approach and exciting area of research focused on targeting cancerous cells. Despite offering significant advantages, this therapy has some limitations that need to be addressed. Further research is necessary to enhance this novel form of immunotherapy.

Keywords: CAR macrophage, treatment, solid tumor, hematological malignancies, chimeric antigen receptor

PH-10
Targeting Genomic and Epigenomic Alterations in Waldenström Macroglobulinemia: Emerging Therapeutic Strategies

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Waldenström macroglobulinemia (WM) is a rare indolent B-cell lymphoma characterized by monoclonal immunoglobulin M (IgM) production. Recent genomic studies have highlighted specific mutations, such as MYD88 and CXCR4, that contribute to disease progression and therapeutic resistance. However, less attention has been given to the epigenomic landscape and its role in WM pathogenesis. This review focuses on the emerging therapeutic strategies that target both the genomic and epigenomic alterations in WM, offering new avenues for treatment beyond conventional therapies..

Methods: A systematic review of recent studies was conducted, focusing on both genomic mutations (MYD88, CXCR4) and novel epigenetic modifications in WM. Preclinical and clinical data regarding the efficacy of targeted therapies, including BTK inhibitors (ibrutinib, zanubrutinib), and emerging epigenetic modulators were analyzed. Special emphasis was placed on combination therapies targeting both genetic and epigenetic drivers of WM.

Results: The review identifies that MYD88 and CXCR4 mutations are critical drivers of WM and are being successfully targeted by BTK inhibitors. Additionally, epigenetic modifications such as DNA methylation and histone acetylation are now recognized as potential therapeutic targets. Combining BTK inhibitors with epigenetic drugs has shown promising results in preclinical models, enhancing sensitivity to treatment and overcoming resistance mechanisms.

Conclusion: Targeting both the genomic and epigenomic landscape in WM offers a novel and more comprehensive approach to therapy. Future clinical trials should explore combination strategies to improve outcomes for WM patients, especially those with resistant or relapsed disease.

Keywords: Waldenström Macroglobulinemia, MYD88, CXCR4, Epigenetics, BTK Inhibitors, Epigenetic Modulators, Hematology.

PH-11

Revolutionizing Multiple Myeloma Treatment: The Potential of Immunotherapies Targeting the Tumor Microenvironment

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Abstract

Background and Aim: Multiple myeloma (MM) is a complex hematologic malignancy, where the tumor microenvironment (TME) plays a critical role in disease progression and therapeutic resistance. While significant strides have been made in MM treatments, including proteasome inhibitors and immunomodulatory drugs, relapse and resistance remain major challenges. Recent research has shifted focus toward targeting the TME to disrupt the protective niche provided to myeloma cells. This review explores the emerging immunotherapies aimed at the MM-TME interface, offering new perspectives on treatment approaches.

Methods: A comprehensive literature review was conducted, focusing on studies published within the last five years. Key areas of investigation included TME components such as stromal cells, immune cells, cytokines, and extracellular matrix interactions. The review emphasizes novel immunotherapies, including CAR-T cells, bispecific T-cell engagers (BiTEs), and checkpoint inhibitors, specifically designed to modulate the TME. Ongoing clinical trials and preclinical studies were also analyzed to assess the efficacy of these therapies.

Results: The review highlights that therapies targeting the TME have shown promise in overcoming drug resistance and enhancing treatment efficacy. CAR-T cell therapies directed at TME-associated antigens, along with BiTEs and checkpoint inhibitors, have demonstrated encouraging results in preclinical models and early-phase trials. Targeting cytokine signaling and TME-modulated immune evasion mechanisms has improved treatment responses, particularly in relapsed/refractory MM.

Conclusion: Targeting the TME in MM represents a novel therapeutic strategy with significant potential to improve patient outcomes. Continued exploration of immunotherapies focused on the TME may offer a path toward more durable and effective MM treatments.

Keywords: Multiple Myeloma, Tumor Microenvironment, CAR-T Cells, Bispecific T-cell Engagers, Checkpoint Inhibitors, Hematology.

PH-12

Investigating the Impact of Different Antipsychotic Medications on Blood Cell Counts in Patients with Schizophrenia

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Abstract

Background and Aim: Schizophrenia is a chronic and debilitating mental disorder that affects cognitive functioning, emotions, and behavior. Treatment for schizophrenia includes the use of antipsychotic medications, psychotherapy, and social support. There is conflicting evidence regarding the potential effects of antipsychotic medications on blood cell counts, which may lead to side effects such as an increased risk of infection or anemia. Therefore, this study aimed to investigate the impact of antipsychotic medications on blood cell counts in patients with schizophrenia visiting the psychiatric department of Vasaei Hospital in Sabzevar in 2022.

Methods: This cross-sectional study involved 119 patients diagnosed with schizophrenia at Vasaei Hospital. After obtaining written consent from the patients, the type of antipsychotic medication used by each patient was extracted from their medical records. The patients were categorized based on the type of medication used. Subsequently, 5 milliliters of venous blood was collected for complete blood count (CBC) analysis. Finally, the average blood cell counts between the antipsychotic medication groups were compared using one-way ANOVA.

Results: The study included 119 patients with schizophrenia, comprising 83% males and 17% females, with a mean age of 43.8 ± 11.6 years and an average BMI of 24.12 ± 6.12 kg/m². There was no statistically significant difference between the use of various antipsychotic medications and the overall counts of white blood cells, neutrophils, monocytes, lymphocytes, red blood cells, and platelets ($P > 0.05$).

Conclusion: These findings suggest that antipsychotics do not adversely affect blood cell counts.

Keywords: Antipsychotic, Schizophrenia, White Blood Cell, Red Blood Cell, Platelet

PH-13

Fanconi Anemia: Challenges in Diagnosis and Management – A Case Series Report

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Abstract

Background and Aim: Fanconi anemia (FA) is a rare inherited disorder characterized by congenital abnormalities, progressive bone marrow failure, and a predisposition to malignancies. Detecting FA can be challenging, as it involves identifying increased chromosomal sensitivity to DNA cross-linking agents and detecting causative genetic variants via genome sequencing.

Methods: We report two cases of siblings with FA. Both patients underwent initial chromosomal breakage tests with mitomycin C and subsequent whole-exome sequencing (WES) for diagnosis.

Results: Both siblings were confirmed to have the FANCD2 variant through WES. The first patient presented with epistaxis, petechiae, ecchymosis, and lower limb edema. The second patient exhibited epistaxis, diabetes, developmental delay, and physical abnormalities. Notably, both patients had negative results on the initial chromosomal breakage test with mitomycin C, a commonly used diagnostic tool for FA. However, WES revealed the presence of the FANCD2 variant, confirming the FA diagnosis.

Conclusion: This case report highlights the challenges in diagnosing FA, particularly when initial screening tests yield negative results. Molecular genetic testing, such as WES, can provide a definitive diagnosis and guide appropriate management strategies. Early and accurate diagnosis is crucial for improving outcomes in individuals with this potentially fatal illness, as promising advancements in treatments such as hematopoietic stem cell transplantation and gene therapy offer hope for addressing FA.

Keywords: Fanconi anemia, FANCD2 variant, chromosomal breakage test, whole-exome sequencing, bone

PH-14

From Donors To The Lab: Evaluating Traditional Blood Transfusion Against In Vitro Red Blood Cells Generation

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Abstract

Background and Aim: The importance of blood transfusion in the medical field cannot be overstated, especially for patients with blood disorders, major surgery, severe bleeding, accidents, and injuries causing significant blood loss. Many countries are facing a blood supply shortage, a major concern globally. While measures are in place to ensure blood safety, there is still a risk of infection. Challenges include maintaining sufficient blood product supply, conducting compatibility tests, addressing donor-related issues, and managing storage and transportation. Alternative options, such as in vitro-generated red blood cells, are being developed offering a safe and reliable substitute for traditional blood transfusions.

Methods: In this narrative review, we conducted an extensive and comprehensive search of existing databases to identify relevant literature and research on the comparison between traditional blood transfusion and in vitro red blood cells generation. This search involved a meticulous and thorough evaluation of multiple databases in a deep, partial, and parallel manner. The inclusion of studies was based on their relevance to the topic and their ability to contribute to the understanding of the topic. The findings from the selected studies were then synthesized to provide a comprehensive overview.

Results: In the past few years, scientists have been putting in much effort to create mature RBCs from different sources. Hematopoietic stem cells can be obtained from cord blood, peripheral blood, or bone marrow, aiding in blood group selection. Advantages include natural composition, lack of genetic modification, potential for regulator approval, and ability to proliferate and differentiate effectively. Human embryonic stem cells can proliferate

extensively to create various cell types, such as blood cells. This offers a donor-free source of cells for medical treatment. Primitive RBCs can be generated from hESCs through the formation of embryoid bodies and supportive stromal cells. Induced pluripotent stem cells which are adult cells reprogrammed to have embryonic stem cell characteristics, also are a source. Also, a technique developed to produce RBCs from human hair follicle mesenchymal stem cells using OCT4 gene expression and triggering cytokines.

Conclusion: Blood transfusion is a vital part of medical treatment; however, growing populations have led to limitations in the availability of blood. In response, researchers have been exploring alternatives such as generating red blood cells in vitro from various cell sources. While progress has been made in producing RBCs from stem cells and adult cells, challenges and ethical issues remain, hindering commercial use. Further research and technological advancements are needed to fully utilize this resource and save more lives in the future.

Keywords: Traditional blood transfusion; in-vitro red blood cells generation; in vitro-generated red blood cells; blood transfusion.

PH-15

Evaluation of Serum Levels of Vitamin D and Calcium in Patients with Beta-Thalassemia

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Abstract

Background and Aim: Beta-thalassemia is an inherited disorder characterised by defects in the alpha- and beta-globin chains as a result of insufficient or poor expression of the beta-globin gene. This results in inadequate erythropoiesis due to the premature death of erythroid precursors in the bone marrow. This is caused by the accumulation of unbound globin. The disease can present with a wide range of symptoms, from severe anemia to clinically asymptomatic individuals. A severe form of the disease is known as beta-thalassemia major. This requires lifelong blood transfusions. Multi-transfusions and elevated body iron levels increase the risk of iron overload, which can elevate free radicals and induce oxidative stress by generating highly reactive hydroxyl (OH) radicals. In addition, the levels of calcium and vitamin D in the serum of these patients are different from those of healthy individuals.

Methods: We searched PubMed, Scopus, and Google Scholar for studies that compared the levels of calcium and vitamin D in patients with beta-thalassemia and a control group between the years 2021 and 2024.

Results: There was a significant difference in serum calcium levels between the two groups ($P < 0.001$). Hypocalcemia is common in patients with thalassemia, and many of these individuals have serum calcium levels that are within a critical range. In addition, the serum levels of vitamin D in patients with beta-thalassemia major were significantly different from the levels in the control group ($P < 0.05$). Numerous studies have established an association between vitamin D deficiency and decreased bone density in individuals with thalassemia.

Conclusion: Numerous studies indicate that patients with beta-thalassemia experience hypocalcemia and vitamin D insufficiency. Factors such as malnutrition and the side effects of frequent blood transfusions can contribute to these deficiencies. Future research should focus on the impact of nutritional status and diet quality on the health outcomes of individuals with thalassemia.

Keywords: β-thalassemia; Calcium; Vitamin D

PH-16

Investigating the effects of combination therapy with metformin in the treatment of Acute myeloid leukemia

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Abstract

Background and Aim: Acute myeloid leukemia (AML) represents the most prevalent form of acute leukemia. Despite considerable efforts, the overall prognosis for patients with AML remains poor, and the mortality rate due to relapse is also considerable. Consequently, the disease presents significant treatment challenges. A number of studies have indicated that metformin may serve as a beneficial adjunct to traditional anti-leukemia medications, particularly in enhancing their effectiveness against drug resistance. However, it has been demonstrated to be ineffective when used as a standalone treatment. In this context, combination therapies are currently being investigated as a promising treatment option.

Methods: A comprehensive literature search across multiple databases, including PubMed, Google Scholar, Scopus, Embase, and Cochrane, yielded 32 relevant articles up to July 2024. In the course of the database search, search terms such as AML, combination, and metformin were employed in order to identify relevant articles.

Results: The results of the studies indicate that the combination of metformin with gilteritinib, sorafenib, 6-benzylthionosine, venetoclax, diclofenac, diflunisal, and cytarabine reduces intracellular ATP levels, inhibits glycolysis, decreases cytotoxicity, diminishes oxidative phosphorylation, increases the expression of anti-apoptotic proteins, and halts the cell cycle. Furthermore, this combination induces apoptosis, reduces cell growth, and ultimately results in a significant decrease in the burden of AML and an increase in overall survival for patients with AML.

Conclusion: The combination of metformin with other drugs has been shown to have a beneficial effect on patients with AML. It can thus be concluded that the combination of these

drugs with metformin may enhance the synergistic effect and improve the treatment of AML patients.

Keywords: AML; Combination; Metformin

PH-17

Can combination regimens with sorafenib play an effective role in the treatment of acute myeloid leukemia?

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is the most common acute leukemia, associated with high morbidity and mortality, and its incidence is increasing. Despite tremendous advances in the treatment of AML, the disease remains challenging to manage. Receptor kinase inhibitors such as sorafenib have recently raised concerns about monotherapy, and combination treatments are now being investigated as a potential therapeutic approach. To classify drugs used in combination with sorafenib and to analyze their combined effects, we reviewed previous research.

Methods: A thorough literature search using multiple databases, including PubMed, Google Scholar, Scopus, Embase and Cochrane, identified 78 relevant articles up to October 2023. Search terms including AML, combination and sorafenib were used in the database search to find relevant articles.

Results: Complete remission (CR) in the combination of sorafenib with "cytarabine and idarubicin", "vorinostat and bortezomib, clofarabine", "fludarabine and busulfan", "5-azacytidine" and "quizartinib, midostaurin and giltertinib" were 99% and 94%, 27% and 3%, 66.6%, 45%, 26%, 16%, 71% and 52%, respectively. In addition, the overall survival (OS) rates for the combination of sorafenib with 'quizartinib, midostaurin and giltertinib', 'cytarabine, daunorubicin' and '5-azacitidine' were '80%', '62% 45%' and '24%' respectively.

Conclusion: Therefore, several studies suggest that the anticancer effect of sorafenib may be enhanced by chemotherapeutic agents.

Keywords: AML; combination; Sorafenib

PH-18

Patient blood management in critical bleedings

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Abstract

Background and Aim: Critical bleeding(CB) refers to a severe and potentially life-threatening rapid loss of blood due to trauma, surgical complications or medical conditions such as gastrointestinal hemorrhage or postpartum hemorrhage. It is important to provide safe, effective, and patient-centered care in this situation. Patient blood management(PBM) has emerged as a vital approach in clinical management of patients facing CB. It focuses on enhancing patient outcomes through a collaborative, evidence-based strategy that emphasizes the management and conservation of the patient's own blood. To bridge the significant gap between existing literature and clinical practice, we will discuss current best practices in the field.

Methods: A comprehensive literature search was conducted across Pubmed, google scholar, and Cochrane library. We focused on peer-reviewed articles, clinical guide lines, and systematic reviews published in the last 10 years. Key words used in the search included "patient blood management", "critical bleeding", "transfusion", and "hemorrhage management".

Results: Several critical best practices in this field emphasized the importance of identifying the root cause of bleeding for controlling it as soon as possible. It is also recommended that parameters including temperature, acid–base status, ionized calcium, hemoglobin, platelet count,PT/INR,APTT, and fibrinogen level should be measured early and frequently to indicate critical physiological derangemen. Based on evidence, fibrinogen concentrate for the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, using blood warmer, early group specific blood components, tranexamic acid, viscoelastic haemostatic assays, cell salvage, and a high ratio of RBC:FFP:PLT for all patients may be beneficial in the management of CB. The routine uses of recombinant activated factor VII is not suggested in the management of CB. Its use was recommended only for controlling bleeding and surgical prophylaxis in patients with inhibitors to coagulation Factors VIII or IX, congenital FVII deficiency, and Glanzmann's Thrombasthenia.

Conclusion: In summary, while the literature underscores the critical role of PBM in the effective management of CB, there remains a notable insufficiency of robust evidence supporting many of the recommended practices. This gap highlights the urgent need for further research to establish standardized protocols and optimize therapeutic strategies in this area. Continued investigation is essential to not only validate existing methods but also to explore innovative approaches that improve patient outcomes in the context of CB.

Keywords: Critical bleeding, Patient blood management, Transfusion

PH-19
The Role of Long Non-Coding RNAs in Diagnosis and Prognosis of Multiple Myeloma

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Abstract

Background and Aim: Multiple myeloma (MM), a complex hematological malignancy, arises from the aberrant proliferation of plasma cells within the bone marrow (BM) microenvironment. The genomics and epigenomics research has revealed that the aberrant activity and dysregulation of non-coding ribonucleic acids (ncRNAs) has a significant role in promotion and development of cancerous cells. Long non-coding RNAs (LncRNAs) are noncoding transcripts that include more than 200 nucleotides. The aim of this study was evaluating the role of LncRNAs in prognosis of MM.

Methods: Databases including PubMed, Google scholar and Web of sciences were searched. The search strategy employed keywords such as Multiple Myeloma, Long non-coding RNAs, LncRNAs and Plasma Cells, focusing on articles that were published within the 2014-2024 timeframe.

Results: Long non-coding RNAs involve in the differentiation of erythroid, myeloid, and lymphoid cells, as well as in the regulation of blood cell proliferation and survival. Previous researches in functional genomics and epigenomics have demonstrated that, similar to protein-coding genes, non-coding RNAs were dysregulated. This highlights their importance in the development of hematopoietic malignancies. The expression profile based on molecular features has emerged as a significant and effective prognostic tool for predicting outcomes in patients with MM. Until now, homeobox transcriptional antisense RNA (HOTAIR), metastasis-associated lung adenocarcinoma (MALAT1), maternally expressed gene 3 (MEG3), taurine upregulated1 (TUG1), nuclear paraspeckle assembly transcript 1 (NEAT1) and myocardial infarction–associated transcript (MIAT) have been studied. The expression levels of NEAT1, TUG1, MALAT1 and HOTAIR genes are elevated in multiple myeloma, whereas the expression of the MEG3 gene is reduced in this disease. MIAT shows a wide range of expression in MM. High MIAT expression is associated with a worse prognosis. Among the novel lncRNAs that require further investigation, we can mention carcinoembryonic antigen-related cell adhesion molecule 1 (CEACM1, the downstream regulatory gene of MSTRG.155519). Previous studies have confirmed a higher expression of CEACM1 in Multiple myeloma. This can be a cause of extramedullary lesions. A study revealed that reduced expression of MALAT1 led to a decrease in proliferation of MM cells. Additionally, this reduction in expression, was correlated to lower expression of proteasome pathway genes. Proteasome inhibition is considered as an important strategy in treating

MM. The level of MALAT1 connected with tumor size, stage, and total prognosis. At least lncRNAs that regulate these MM oncogenes might serve as promising therapeutic targets for MM treatment.

Conclusion: To conclude, recent datas indicate that LncRNA involvement in the initiation and development of MM has significant clinical relevance for early diagnosis, prognosis, and potential therapeutic targeting of the disease. However more information is required to clarify their role in the development of this disease and potentially identify new therapeutic targets.

Keywords: Multiple myeloma; Long non-coding RNAs; LncRNAs; Plasma cells

PH-20

The evaluation of p21 and p27 expression in HLA-DR negative AML patients

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Abstract

AML is a heterogeneous type of leukemia with a high variation in the biological features of the leukemic cells and disease outcomes. The biological features of the leukemic cells have a very close correlation with the disease outcomes. In this way, leukemic cells with higher levels of proliferation and lower levels of maturation undoubtedly would lead to poorer outcomes. Based on immunophenotyping, HLA-DR negative AMLs constitute an important category in AML classification. The majority of patients with this immunophenotype belong to APL subtype with PML-RARA fusion gene and the others are non-APL subtype without PML-RARA fusion gene. As disease outcome and cell biological features have a very close correlation, it is important to evaluate essential molecules involved in the biological processes of the leukemic cells which are helpful in the determination of disease outcome. Therefore in this study we evaluated the expression of p21 and p27 as two keys molecules involved in the regulation of cell cycle, proliferation, maturation and apoptosis to determine whether there is any significant difference between these two subgroups of HLA-DR negative AMLs. We studied p21 and p27 mRNA levels by real-time RT-PCR in 41 primary HLA-DR negative AML samples, compared with normal bone marrow and peripheral blood cells. p21 expression was significantly higher in APL cases than non-APLs but there was no significant difference in p27 expression between APL and non-APL patients. According to our results, it seems that p21 can be considered as a critical gene involved in the determination of the levels of cell differentiation between these two subtypes.

Background and Aim: Introduce the context of your study and the gaps your project is filling. At the end, clearly state the aim/objective of the study.

Methods:

Immunofluorescence staining and flow cytometry:

Flow cytometric analysis was performed through mixing between 30-50 Micro L of BM or PB sample mix with 5 Micro L of monoclonal anti bodies including HLA-DR, CD3, CD13, CD33,

CD14, CD64, CD11b and CD45 Labeled with PE/FITC.

RNA isolation, c-DNA synthesis, real-time PCR:

For the isolation of mononuclear cells from peripheral blood and bone marrow of both patient and control samples; Ficoll density centrifugation was used. One µg of RNA was transcribed into first-strand c-DNA using random hexamer primer and First Strand c-DNA Synthesis Kit

Bone marrow and peripheral blood samples were obtained after obtaining informed consent from 41 patients that were subsequently diagnosed with HLA-DR negative AML and from 14 healthy donors that were included bone marrow samples from five patients with early stage Hodgkin's and non-Hodgkin Lymphoma and peripheral blood samples from eight normal donors. Flow cytometric analysis was performed. Then RNA isolation and c-DNA synthesis was performed. The expression level of p21, p27 and ABL as reference gene was determined with SYBR Green I real-time PCR.

Results:

The expression of the p21 and p27 was evaluated in HLA-DR negative patients (n=41) in comparison with healthy control samples (n=14). In this regard, p21 expression was significantly lower in HLA-DR negative patients (mean p21in patients: 1.00±0.13) in compared with normal controls (mean p21 in controls: 1.44± 0.14) ($p<0.05$). But p27 expression levels did not show significant difference between patients (mean p27 in patients: 0.82±0.12) and control groups (mean p27 in controls: 0.63±0.10) ($p> 0.05$). After that, we evaluated the expression levels of p21 and p27 between HLA-DR negative APL versus HLA-DR negative non-APL patients. P21 expression levels were significantly higher in APL cases compared with non APL cases (mean p21 in APL: 1.17±0.15 vs non-APL: 0.55±0.20, $p<0.05$). But it was not significant for p27 expression (mean p27 in APL: 0.82±0.15 vs non-APL: 0.82±0.20, $p>0.05$).

conclusion:

The main conclusion to be drawn from this study was that p21expressions was higher in APL cases with more maturation levels versus non-APL cases with lower levels of maturation. But there was no significant difference in p27 expression. It was supposed that p21 might be determinant factor differentiates HLA-DR negative APL cases from non APL cases in comparison with p27. We suggest that further experimental investigations should be done to evaluate the other critical cell cycle regulatory proteins such as p14, p16, p53 and c-myc in these two categories.

Keywords: Acute Myeloid Leukemia; HLA-DR negative; p21; p27

PH-21

Quality Control Analysis (pH, LDH, MTT, Platelet Count) of Platelet Apheresis Products Obtained from the Fresenius COM.TEC Device During Storage days

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Abstract

Background and Aim: Platelets are small, nucleus-free cells that play a critical role in medical treatments, making the quality of transfused platelets essential for recipients. Various devices are available for separating platelet products from whole blood, each with unique characteristics. This study aimed to evaluate the Fresenius COM.TEC platelet apheresis device by analyzing changes in pH, platelet count (PLT), LDH levels, and platelet viability (MTT) on storage days 1, 3, and 5.

Methods: In this experimental study, 25 random platelet apheresis products from male donors at the Tehran Blood Transfusion Center were processed using the Fresenius COM.TEC device. Samples were collected on storage days 1, 3, and 5, with pH, LDH, PLT count, and platelet viability (MTT) tests conducted at the Iranian Blood Transfusion Research Center laboratory. Data were analyzed using R software, with p-values below 0.05 considered statistically significant.

Results: LDH levels were highest on day 1 and showed a significant decrease over the storage period, with statistically significant differences between storage days. A consistent and significant pH decline was also observed throughout the storage period. MTT results indicated an increase on day 3, with a decrease from day 1 to day 5, showing statistical significance ($P<0.0001$). However, platelet count did not exhibit any significant changes across the storage days ($P>0.05$).

Conclusion: The study observed a decreasing trend in pH and MTT values and an increasing trend in LDH levels over storage days 1, 3, and 5. No significant changes were noted in platelet count across these days.

Keywords: Apheresis; Platelet; Donor; Fresenius COMTEC.

PH-22

Comparison of Quality Control Factors (pH, LDH, MTT, PLT, RBC, and WBC Counts) in Platelet Apheresis Products from Fresenius COM.TEC and Haemonetics MCS+ on the First Day of Storage

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Abstract

Background and Aim: The critical role of platelet transfusion in treating thrombocytopenic patients has increased interest in platelet products and their production methods. As a result, transfusion medicine specialists have developed various techniques for extracting platelets from whole blood. Platelet apheresis, regarded as the purest platelet product, is collected using different apheresis devices available on the market. Each device yields platelet products with unique quality profiles due to differing separation techniques and features. This study compared the quality control factors (pH, LDH, MTT, PLT, RBC, and WBC counts) of platelet apheresis products obtained from Fresenius COM.TEC and Haemonetics MCS+ on the first day of storage.

Methods: This experimental study involved 50 platelet apheresis products from male donors at the Tehran Blood Transfusion Center. Twenty-five samples were processed using the Fresenius COM.TEC and 25 with the Haemonetics MCS+. Samples were collected on the first day of storage, and tests for pH, LDH, PLT, RBC, and WBC counts, along with the platelet viability test (MTT), were performed at the Iranian Blood Transfusion Research Center laboratory. Data were analyzed using R software, with a p-value of less than 0.05 deemed statistically significant.

Results: Results indicated that on the first day of storage, the pH of products from the MCS+ device was lower than those from the COM.TEC device ($P<0.0001$). Conversely, LDH levels were higher and MTT test results showed lower viability for MCS+ products. Additionally,

RBC and PLT counts were higher in MCS+ products (P<0.0001 and P=0.003, respectively), while WBC counts were lower in MCS+ products on the first day of storage (P<0.0001).

Conclusion: The study indicated that the MCS+ device yielded a higher platelet count, while the COM.TEC device showed a higher WBC count on day one.

Keywords: Apheresis,Platelet,Haemonetic MCS+,Fresenius COM.TEC

PH-23

Quality Control Analysis (pH, LDH, MTT, Platelet Count) of Platelet Apheresis Products Obtained from the Fresenius COM.TEC Device During Storage days

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Abstract

Background and Aim: Platelets are small, nucleus-free cells vital for medical treatments, so the quality of transfused platelets is critical for patients. Various devices exist for separating platelet products from whole blood, each with unique characteristics. This study evaluated the Fresenius COM.TEC platelet apheresis device by analyzing pH, platelet count (PLT), LDH levels, and platelet viability (MTT) on storage days 1, 3, and 5

Methods: This experimental study processed 25 random platelet apheresis products from male donors at the Tehran Blood Transfusion Center using the Fresenius COM.TEC device. Samples were collected on days 1, 3, and 5, and pH, LDH, PLT count, and platelet viability (MTT) tests were conducted at the Iranian Blood Transfusion Research Center laboratory. Data analysis was performed using R software, with p-values below 0.05 deemed statistically significant.

Results: LDH levels were highest on day 1 and showed a significant decrease over the storage period, with statistically significant differences between storage days. A consistent pH decline was also observed throughout the storage period. MTT results indicated an increase on day 3, with a decrease from day 1 to day 5, showing statistical significance (P<0.0001). However, platelet count did not exhibit any significant changes across the storage days (P>0.05).

Conclusion: The study noted a decrease in pH and MTT values and an increase in LDH levels over storage days 1, 3, and 5, while platelet counts remained stable throughout.

Keywords: Apheresis,Platelet, Fresenius COM.TEC,Donor

PH-24

The Diagnostic Value of Neutrophil to Lymphocyte ratio and Platelet to Lymphocyte ratio in Rheumatoid Arthritis

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Abstract

Background and Aim: Patients with and without rheumatoid arthritis (RA) can be differentiated using inflammatory indices derived from standard hematological parameters, specifically the neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR). However, a comprehensive evaluation of their effectiveness in distinguishing between individuals with active RA and those without has yet to be conducted.

Methods: From 2021 to 2024, we conducted a comprehensive search of PubMed, Web of Science, Scopus and Google Scholar for studies comparing neutrophil to lymphocyte ratio (NLR) and/or platelet to lymphocyte ratio (PLR) values between rheumatoid arthritis (RA) patients with active disease and those without active disease.

Results: The PLR was significantly higher in the RA group compared to the control group ($p < 0.001$). Similar trends were observed for NLR, which also significantly increased in the RA group compared to the control group. Pearson's correlation analysis showed positive and significant correlations between PLR and erythrocyte sedimentation rate (ESR) ($r = 0.43$, $p < 0.001$), NLR and ESR ($r = 0.34$, $p < 0.001$), PLR and C-reactive protein (CRP) ($r = 0.15$, $p = 0.034$), and NLR and CRP ($r = 0.18$, $p = 0.018$).

Conclusion: Patients with active RA can be distinguished from those without it with significant accuracy using the NLR and the PLR. However, further research is needed to determine their diagnostic performance in routine clinical practice, either alone or in combination with other factors.

Keywords: Platelets to lymphocyte ratio, Neutrophils to lymphocyte ratio, Rheumatoid arthritis

PH-25
The potential of microbiota as a therapeutic intervention in HSCT outcome

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Abstract

Background and Aim: Allogenic hematopoietic stem cell transplantation (allo-HSCT) offers a potentially curative procedure for various hematological and immunological malignancies. In recent studies, gut microbiota (GM) diversity has been shown to be associated with HSCT outcomes. Changing in GM can occur due to conditioning regimens including chemotherapy, and radiotherapy. Dysbiosis of GM composition can lead to complications including infections and acute graft-versus-host disease (GvHD). GVHD is a serious problem of allo-HSCT that correlates with mortality and relapse. Our study suggests therapeutic interventions like prebiotics, probiotics and Fecal microbiota transplantation (FMT) before and during the transplantation lead to a lower risk of GVHD-related outcomes.

Methods: A comprehensive search for relevant research was conducted on the PubMed and ScienceDirect databases (2020-2024). The keywords were "microbiota", "allogeneic hematopoietic stem cell transplantation" and "graft-versus-host disease". Two reviewers extracted data independently.

Results: The database search identified 169 articles, after applying the inclusion criteria, 15 studies were finalized for our review. There are several mechanisms through which GM impacts allo-HSCT outcomes. The GM modulation can influence the immune system responses and impact natural killer and B cells reconstitution which are crucial for decreasing the risk of GVHD. The important role of GM is to produce short-chain fatty acids (SCFAs) which induce anti-inflammatory cytokines, Stimulate the mucosal immune system and induce the differentiation and expansion of regulatory T cells, thus contributing to the improvement of survival rates after HSCT.in the pre-HSCT period, supplementation with probiotics like fibers was associated with earlier neutrophil engraftment and a shorter duration of febrile neutropenia. FMT supports the regeneration of gut epithelial cells, which are often damaged during HSCT, so providing a broader defense against a variety of pathogens and reducing infections.

Conclusion: Together these data hold a promising hope to help release the heavy medical burden of HSCT complications. Dietary interventions including probiotics, prebiotics and FMT cause improvement and reconstitution of GM composition. High microbiome diversity is linked with a lower risk of GVHD, infections, higher overall survival and better outcomes.

Keywords: microbiota; allogeneic hematopoietic stem cell transplantation; graft-versus-host disease

PH-26

Minimal/ Measurable residual disease in the context of hematologic malignancies: moving on to the emerging methods frontiers

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Abstract

Background and Aim: Minimal/measurable residual disease (MRD) is the most influential prognostic factor in Hematological malignancies. MRD refers to the small number of bone marrow-derived cancer cells remaining in patients' bone marrow or blood after treatment.

Methods: Terminologically, it seems using "measurable" instead of "minimal" is more helpful in "MRD" since the detection of the minimum number of cancerous cells depends on the technical and methodological abilities in the lab. Post-therapeutic MRD negativity in leukemic patients is associated with prolonged remission and a longer survival rate, while positive MRD results considerably increase the risk of relapse. MRD measurement techniques can be broadly classified into two categories: immunophenotyping (Multiparametric flow cytometry (MFC)-MRD testing), which involves the detection of cell markers in intact cells, and molecular MRD testing, which involves the detection and quantification of leukemic cell-derived residuals, such as DNA, RNA, and proteins

Results: The current approach involves the use of a combination of cytomorphological, MFC, and molecular-based techniques, such as qPCR, for the detection of gene fusions (e.g., BCR-ABL1) or rearranged immunoglobulin (IG) and T-cell receptor (TCR) genes and next-generation sequencing (NGS), based on leukemia type, can be employed for disease monitoring. However, new cutting-edge technologies enabled us to trace the minimum number of remaining malignant cells. Highly sensitive techniques provide more reliable information about a patient's disease profile and help the clinic adopt the most efficient and personalized treatment approach.

Conclusion: This review discusses MRD application in managing leukemia patients, MRD detection methods, and new advancements in developing MRD assessment techniques in hematological malignancies.

Keywords: MRD, leukemia, hematologic neoplasms

PH-27

Investigating the trend of BCR-ABL changes in Acute Myeloid Leukemia and Chronic Myeloid Leukemia patients

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Background and Aim: The prevalence of Acute Myeloid Leukemia (AML) and Chronic Myeloid Leukemia (CML) in adult patients is 15% and 20%, respectively. AML and CML are among myeloid leukemias that have poor prognosis and high mortality in patients. BCR ABL is an oncogene resulting from the translocation of chromosomes 9 and 22 and is recognized as a diagnostic marker in CML and a secondary event in AML. The aim of this systematic study is to investigate the trend of BCR ABL changes in AML and CML patients.

Methods: These studies were conducted based on the PICO criteria and in line with the goal of realization and following the PRISMA checklist. This systematic review includes a comprehensive search from 2015 to 2024 in Pubmed databases and Google scholar search engine. MESH keywords such as "Chronic Myeloid Leukemia", "Acute Myeloid Leukemia", "BCR-ABL P210" were used in the search. Next, two independent researchers screened the retrieved articles based on the inclusion criteria.

Results: A total of 545 articles were identified through the primary search. After screening the titles and abstracts of the articles, the number of articles was reduced to 27 articles and finally 10 articles were included in this research based on the inclusion and exclusion criteria. The BCR-ABL oncogene is associated with CML leukemia rather than AML, however, both CML and AML involve the role of the STAT5 protein, which is a downstream effector of tyrosine kinase oncogenes such as BCR-ABL in CML and FLT3-ITD in AML. BCR-ABL in AML is considered a secondary event, unlike CML, where a primary event is sufficient to initiate the disease. CML is caused by translocations of chromosomes 9 and 22, which are associated with BCR-ABL. BCR-ABL in CML is P210 type. BCR-ABL P210 activates multiple signaling pathways leading to increased cell proliferation and survival.

Conclusion: The presence of BCR is a characteristic of CML, and the continued activity of BCR ABL leads to the proliferation of leukemia cells, more genetic instability, DNA damage, and clonal evolution. In rare cases, BCR-ABL fusion is observed in AML. In the reports, it is mentioned that BCR ABL is discussed first for CML, then ALL, and finally for AML. However, the limitations of the studies conducted in this field suggest conducting more diverse research.

Keywords: Chronic Myeloid Leukemia, Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, BCR-ABL P210.

PH-28

CAR-engineered Cytokine-Induced Memory-Like NK Cells: Room to Grow Immunotherapy of Hematological Malignancies

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Background and Aim: Natural killer (NK) cells have diverse functions, including antitumor and antiviral activities. But NK cells display functional defects and cancerous cells escape from NK cells within the TME of hematological malignancies. Therefore, NK cell-based immunotherapy has attracted clinical interest. Although NK cells short life span and non-specific responses limit their applications. In addition, conventional NK cell therapy cannot efficiently eliminate cancerous cells. Consequently, NK cells were first pre-activated with the cytokine combination IL-12/15/18 [cytokine-induced memory-like (CIML)], and were then engineered with chimeric antigen receptors (CAR) may overcome these challenges. In this review, we summarize CAR-CIML-NK cell-based investigation in hematological malignancies.

Methods and Materials: Eligible studies were identified from several databases including PubMed, Web of Science, Scopus, and Google Scholar. Articles were identified using the following MeSH terms and keywords: Hematological malignancies, Natural killer cells, Cytokine-induced memory-like NK cells, and Chimeric antigen receptors. The review and original articles were included in this study.

Results: Our comprehensive literature search yielded three original articles investigating CAR-modified CIML-NK cells in hematological neoplasms. He et al. indicated that CD19 CAR-engineered NK cells stimulated with IL12/15/18 (CIML NK cell) significantly produced higher INF-γ and exhibited higher degranulation capacity against CD19+ leukemia cells and lymphoma cells (Nalm-6 and Raji cells) in compared to conventional CAR-NK/NK cells. Further investigation indicated CAR-CIML-NK cells exhibited satisfactory durability, expansion, and effector function in a human lymphoma xenograft mouse model. Incongruent, the Gang et al. study revealed that CD19-CAR-CIML-NK cells display potent killing activity against NK-resistant lymphoma lines and suppress tumor growth in mouse models. Another study by Dong et al. demonstrated that CIML-NK cells expressed TCR-like CAR identify neoepitope derived from the cytosolic oncogenic NPM1-mutated protein resulting in favorable cytotoxicity against AML cell lines and patient-derived leukemic blast cells.

Conclusion: Taken together, NK cell pre-activation with the cytokine combination IL12/15/18 increased their life span, persistency, and durability compared to conventional NK cells. In addition, when CIML-NK cells armed with CAR structure can recognize tumor-associated antigens (TAAs)with particular specificity and result in improved treatment responses. However, CAR-CIML-NK cell therapy is faced with multiple challenges such as limitations in information in this context. Therefore, further investigations are needed to fill these gaps and enhance CAR-CIML-NK cell efficacy in leukemia/lymphoma treatment.

Keywords: Hematological malignancy, Natural killer cell, Cytokine-induced memory-like NK cell, Chimeric antigen receptor

PH-29

Challenges in Specimen Collection and Handling in Nursing Practice

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Background and Aim

Specimen collection and handling are critical components of nursing practice that significantly impact patient diagnosis and treatment. Errors in this process can lead to misdiagnosis, delayed treatment, and compromised patient safety. This article aims to identify the key challenges nurses face in specimen collection and handling, as well as to propose strategies to mitigate these issues and enhance overall healthcare outcomes.

Methods

A systematic review of the literature was conducted, focusing on studies that explore the challenges related to specimen collection and handling in nursing practice. Data were gathered from peer-reviewed journals, clinical guidelines, and surveys administered to nursing professionals. The analysis highlighted common barriers, such as inadequate training, lack of standardized protocols, and environmental factors affecting specimen integrity.

Results

The review identified several critical challenges in specimen collection and handling, including improper identification of patients, mislabeling of specimens, inadequate training on collection techniques, and environmental conditions that can compromise sample quality. Many nursing professionals reported feeling unprepared for these tasks due to insufficient training and high workloads. The implementation of standardized protocols and ongoing education were found to be effective strategies for reducing errors.

Conclusion

Improving specimen collection and handling practices in nursing is essential for ensuring accurate laboratory results and optimal patient care. By addressing the identified challenges through targeted training and standardization, healthcare institutions can enhance the quality of nursing practice and reduce the risk of errors. Future research should focus on developing innovative solutions and best practices to further support nurses in this critical aspect of patient care.

Keywords

Specimen collection, nursing practice, patient safety, laboratory errors

PH-30

The role of oxidative stress in the pathophysiology of Sickle Cell Disease (SCD), therapeutic approaches and future perspectives

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Abstract

Sickle cell disease (SCD) is an inherited hematological disorder with a multi-organ complication affecting millions of people worldwide. SCD features a prominent hemolytic anemia, due to intravascular hemolysis, with impacts the phenotypic variability and disease severity. Transfusion of red blood cells (RBCs) is a first-line of therapy, and while often beneficial, the frequent use of transfusion is associated with numerous complications. The RBCs in patients with SCD are particularly susceptible to oxidative stress due to the hemoglobin S polymerization process. Oxidative stress occurs as a result of imbalance between the rate of reactive oxygen species (ROS) production and antioxidant defense systems to neutralize them. One major consequence of oxidative stress in SCD is the increased fragility of RBCs, making these cells prone to hemolysis, and release of hemoglobin, and their products, heme and iron, into the bloodstream. Cell-free heme contributes further to oxidative stress by generating additional ROS. Moreover, oxidative stress in SCD leads to endothelial dysfunction, contributing to vaso-occlusion, impaired blood flow, and tissue damage. Therefore, therapeutic interventions targeting oxidative damage and ROS production have gained significant attention to treat SCD in recent years. This could potentially improve RBC function and reduce hemolysis, which might indirectly reduce the need for RBC transfusions.

More recently, L-glutamine, voxelotor (R-state-stabilizer), has been the only antioxidant therapy approved by the Food and Drug Administration (FDA) in SCD. Given the central importance of oxidative stress and its critical role in the pathophysiology of SCD, there is an urgent need for additional therapies that target mechanisms-associated with oxidative stress in SCD patients.

This review summarizes the role of oxidative stress and ROS in the pathophysiology of SCD and the potential benefits of anti-oxidant therapies. It also suggests future directions for research and development to sustain and expand these advancements in SCD care.

Keywords: Sickle cell disease, red blood cells, Oxidative stress, Reactive oxygen species

PH-31

Determining the effect of increased expression of miRNA-217 on the gene expression of CCR4 and CCR5 chemokine receptors in T-cell acute lymphoblastic leukemia (jurkat T-ALL cell line)

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Abstract

Background and Aim: T-cell acute lymphoblastic leukemia (T-ALL) is the most common type of pediatric malignancy, accounting for 10-15% of cases. Pathogenic mechanisms associated with non-coding proteins, including micro RNAs, are now widely considered to modulate the initiation or progression of various cancers. Considering the vital effect of chemokine receptors on the site of maturation and storage of mature lymphocytes, especially T cells in T-ALL, this study aims to determine the impact of increased miRNA-217 expression on CCR4 and CCR5 chemokine receptor gene expression in T-cell acute lymphoblastic leukemia (Jurkat) cancer cells.

Methods: Mature double-stranded miRNA-217 oligonucleotides were cloned into the pCDH plasmid by the Bonyakhteh company. The plasmids obtained were employed for transduction in Jurkat cell lines and fibroblasts. Real-time PCR was performed to assess the expression levels of miRNA-217, as well as the CCR4 and CCR5 genes, which are regulated by miRNA-217. This analysis aimed to evaluate changes in gene expression.

Results: Transfection with miRNA-217 led to a significant increase in its expression in both Jurkat and fibroblast cell lines after 48 hours (12-fold in Jurkat cells and 13-fold in fibroblasts) and at 72 hours (8-fold in Jurkat cells and 4-fold in fibroblasts). In Jurkat cells, miRNA-217 transfection resulted in a 5-fold increase in CCR4 gene expression at 48 hours and an 8-fold increase at 72 hours. In fibroblast cells, the expression of CCR4 increased by 10-fold at 48 hours and 11-fold at 72 hours. Conversely, transfection in Jurkat cells caused a 1.2-fold decrease in CCR5 gene expression at 48 hours and a 0.3-fold reduction at 72 hours, neither of which was statistically significant. miRNA-217 transfection significantly increased CCR5 gene expression in fibroblasts by 1-fold at 48 hours compared to the control but not to the backbone (BB) group. However, expression decreased by 1.6-fold at 72 hours.

Conclusion: Our findings suggest that miRNA-217 plays a significant regulatory role in the expression of the CCR4 gene. In contrast, its regulatory effect on the CCR5 gene is minimal, and this effect varies depending on the cell type. These insights could be crucial for understanding the molecular mechanisms underlying various cellular processes. Further studies

are needed to gain a more comprehensive understanding of the role of miRNA-217 in these cell lines.

Keywords: miRNA-217; CCR4; CCR5; Acute Lymphoblastic Leukemia (ALL); Jurkat Cells

PH-32

Assessing the Impact of MSN-NH2 on Cell Viability in Multiple Myeloma

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Abstract

Background and Aim: Multiple myeloma (MM) is an aggressive plasma cell malignancy linked to genetic mutations and complications like bone lesions, anemia, and immunodeficiency. Despite advanced treatments, MM remains challenging due to frequent relapses, necessitating novel therapies. Nanotechnology offers potential in cancer treatment, particularly mesoporous silica nanoparticles (MSNs), valued for their high surface area, customizable pores, and biocompatibility. MSNs enable controlled, targeted drug delivery, reducing systemic toxicity. However, the impact of amine-functionalized MSNs (MSN-NH_2) on MM cell viability, independent of drug loading, is unclear. This study examines MSN-NH_2's biocompatibility and cytotoxicity, establishing a foundation for their safe application in MM drug delivery.

Methods: MSNs were synthesized using Stöber method and subsequently functionalized with amine groups. The successful synthesis and functionalization of the MSNs were confirmed through various characterization analysis. MM suspension cells were cultured and treated with various concentrations of MSN-NH_2 (1–25 µg/mL) for 24 and 48 hours, with cell viability assessed via MTT assay. Statistical analyses were performed to compare the viability of treated cells against untreated controls, establishing baseline cytotoxicity and biocompatibility of MSN-NH_2 in MM cells.

Results: Ninhydrin test indicated the successful attachment of amine groups to the silica framework. Furthermore, BET analysis demonstrated a high surface area consistent with the desired mesoporous structure, and DLS measurements confirmed appropriate particle size for cellular uptake. Treatment of MM suspension cells with MSN-NH_2 demonstrated a dose-dependent decrease in cell viability. At 24 hours, cell viability was 75.2% at 2.5 µg/mL, 50% at 5.922 µg/mL, and 9.3% at 25 µg/mL. At 48 hours, cell viability dropped to 73.28% at 2.5 µg/mL, 50% at 4.485 µg/mL, and 7.79% at 10 µg/mL. ANOVA confirmed that MSN-NH_2 significantly reduced cell viability compared to untreated controls, showing a consistent dose-dependent cytotoxic effect.

Conclusion: This study demonstrates that MSN-NH_2 nanoparticles significantly decrease the viability of MM cells in a dose-dependent manner, underscoring their potential as a drug delivery system in MM therapy. By establishing baseline cytotoxicity and biocompatibility, this research addresses a crucial

knowledge gap, supporting the development of nanotechnology-based therapeutic strategies. These findings pave the way for novel, more effective approaches in MM treatment, with the goal of achieving enhanced therapeutic outcomes and minimized adverse effects.

Keywords: Multiple myeloma; Nanotechnology; MSN-NH_2; Treatment

PH-33

Trend of HIV, HCV, and HBV infections among blood donors of Iranian population (2021-2023)

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Abstract

Background and Aim: While blood transfusion is life-saving procedure, it is not without problems. The potential transmission of infectious diseases also makes it life-threatening. In this study, we aimed to survey the prevalence and trend of human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV) among blood donors of Iran (2021-2023).

Methods: This retrospective cross-sectional investigation was carried out by examining the documentation of the blood transfusion organization of Iran. A total of 353755 blood units were screened for transfusion-transmitted infections. Data were analyzed using SPSS software (version 22).

Results: In 2021, out of a total of 113,142 donors, 87 (0.07%) donors had HIV, 192 (0.17%) donors had HCV and 111 (0.10%) donors had HBV. Out of 119236 donors in 2022,144 (0.12%), 141 (0.11%), and 91 (0.07%) individuals were observed to have HIV, HCV, and HBV respectively. And out of total 121377 donors in 2023, HIV, HCV, and HBV were observed in 117 (0.09%), 137 (0.11%) and 55 (0.04%) donors respectively.

Conclusion: This study demonstrated that, overall, the percentage of donors infected with HCV, and HBV showed a decreasing trend over the course of three years. However, the percentage of HIV infected donors initially showed an increase before declining. Although the 2023 percentage was still higher than it was three years ago.

Keywords: HIV, Hepatitis C virus, Hepatitis B virus, Blood transfusion

PH-34

CRISPR used to enhance CAR-T cell therapy in treating Cancer

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Abstract

Background and Aim: CAR-T cell therapy has revolutionized the treatment of hematologic malignancies and solid tumors, offering significant breakthroughs in clinical practice. Despite its success, issues like limited durability, restricted ability to proliferate, high production expenses, and less-than-ideal effectiveness continue to pose challenges. The CRISPR/Cas9 gene-editing technology has emerged as a promising tool for improving the antitumor activity and durability of CAR-T cells within immunosuppressive tumor microenvironments. This systematic review aims to explore the integration of CRISPR/Cas9 technology with CAR-T cell therapy to improve therapeutic outcomes and address safety concerns.

Methods: A systematic review was performed utilizing the PubMed database and the Google Scholar search engine to identify studies published between 2018 and 2024. The search was limited to peer-reviewed articles that investigated the use of CRISPR technology to enhance CAR-T cell therapy in treating Cancer. MESH keywords like "CRISPR-Cas Systems", "Clustered Regularly Interspaced Short Palindromic Repeats", "CAR-T cell therapy", "Cancer" were applied in this search. Subsequently, the researchers assessed the retrieved articles in accordance with the inclusion criteria.

Results: Following the initial identification of 158 articles, screening titles and abstracts reduced this to 23, and 8 articles were ultimately selected based on inclusion and exclusion criteria. CRISPR/Cas9 can enhance CAR-T cell functionality, crucial for improving efficacy in cancer therapy. This technology addresses safety by ensuring CAR-T cells activate only with tumor cells having high antigen levels, reducing harm to healthy cells. It also strengthens CAR-T resistance to exhaustion, prolonging treatment durability and increasing response rates. Additionally, CRISPR/Cas9 minimizes side effects like cytokine release syndrome by enabling CAR-T cells with lower toxicity. By deleting TRAC and HLA loci, it supports the creation of universally compatible CAR-T products, reducing graft-versus-host disease (GVHD) risk. Lastly, CRISPR/Cas9 disrupts inhibitory molecules like PD-1 and TGF-β, further enhancing CAR-T cell performance.

Conclusion: The integration of CRISPR/Cas9 technology with CAR-T cell therapy offers a promising approach to overcoming current limitations in cancer treatment. By enhancing the efficacy and safety of CAR-T cells, this novel approach has the potential to revolutionize

cancer therapy and provide new therapeutic options for refractory cancers, including solid tumors.

Keywords: CRISPR-Cas Systems; CAR-T cell therapy; Cancer

PH-35

The frequency of prognostically important acute myeloid leukemia mutations in the Iranian population: a systematic review and meta-analysis

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Abstract

Background and Aim: The geographic diversity of molecular genetic abnormalities in AML can help understand the genetic and environmental factors involved in the development of leukemia. In addition, high-risk groups can be recognized by identifying common mutations in AML patients, and appropriate treatment based on the type of mutation can be adopted. This systematic study and meta-analysis analyzed the common mutations in AML patients in Iran.

Methods: In this systematic study, common mutations in Iranian AML patients were comprehensively examined across four databases: PubMed, Scopus, Web of Science, and Magiran, from 1980 to 2024, following the PRISMA guidelines. Meta-Analysis Version 2 (CMA2) was used for data analysis, and I^2-test values greater than 50% were considered to indicate high heterogeneity among the studies.

Results: By reviewing 40 articles, it was found that the prevalence of FLT3-ITD mutation was 21.9% (CI: 19.19 - 24.1) in 34 studies (3,152 AML cases), FLT3-TKD mutation 6.6% (CI: 4.7 - 9.3) in 19 studies, NPM1 mutation 19% (CI: 15.9-22.6) in 18 studies DNMT3A mutation 13.9% (CI: 11.1 - 17.2) in 5 studies, CEBPA mutation was 18.5% (CI: 10.3 - 31) in 5 studies, and WT-1 mutation prevalence was 8.2% (CI: 5.6-11.8)in 4 studies. Other mutations investigated in the studies included NRAS, IDH1, IDH2, TET2, c-kit, ASXL1, and RUNX1.

Conclusion: Studies have shown that the FLT3-ITD mutation is the most prevalent mutation among Iranian AML patients. Following this, the most common mutations identified were NPM1, CEBPA, DNMT3A, and WT1, in that order.

Keywords: AML, Mutation, Iran, FLT3

PH-36

ETP-ALL or T-ALL with aberrant myeloid expression? Immunophenotypic Diagnosis and workup

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Abstract

Background and Aim: ETP ALL is a distinct subtype of T-ALL that is newly identified and consistently associated with a poor early treatment response to chemotherapy in pediatric and adult patients. The diagnosis of ETP-ALL is crucial because it is resistant to standard treatment regimens. ETP ALL defines by negative CD1a and CD8, weak or negative CD5, and expression of myeloid or stem cell associated markers. On the other hand aberrant expression of myeloid markers is not uncommon in T-ALL. So differentiating of ETP-ALL from T-ALL with aberrant expression of myeloid markers is important for better treatment decisions.

Methods: This retrospective analysis includes 14 ETP-ALL and 8 T-ALL with aberrant expression of myeloid markers pediatric cases from 54 T-ALL cases diagnosed in 2 centers between April 2021 and August 2023. Flow cytometry data was reviewed for all the cases. Two scoring systems including 5 and 6 antigens was used for diagnosis of ETP-ALL.

Results: ETP- ALL and T-ALL with aberrant expression of myeloid markers prevalence was 25.9% (14/54) and 14.8% (8/54) with median age of 12 and 9.1 respectively. CD13, CD33, CD34, CD117, CD11b and HLA-DR were myeloid/stem cell markers which expressed on blast populations in ETP-ALL (Cases with more than two, two and one myeloid/stem cell markers, were 35.7%, 50% and 14.3% respectively). In T-ALL with myeloid markers CD13 (3 cases), CD117 (2 cases), CD33 (2 cases) and HLA-DR (1 case) were most frequent aberrancies respectively. All eight T-ALL cases with aberrant myeloid marker expression either expressed CD5 greater than 75% of blasts with moderate intensity or were positive for CD8 and/or CD1a which is incompatible with criteria for ETP-ALL flow cytometry diagnosis.

Conclusion: ETP- ALL shows a poor response to standard therapeutic regimens and accurate diagnosis is mandatory for further treatment decisions, so discriminating this subtype from other T-ALLs should be considered by laboratories.

Keywords: T-ALL, ETP-ALL, Flow cytometry

PH-37

Systematic Review of Emerging Biomarkers for Early Detection and Prognostic Assessment in Hematologic Malignancies

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Abstracts:

Background: Hematologic malignancies, including leukemias, lymphomas, and myelomas, remain a leading cause of cancer morbidity and mortality worldwide. Early detection and accurate prognostic assessment are essential for improving patient outcomes, yet conventional diagnostic methods often lack the sensitivity to detect disease at an early stage or to predict clinical trajectory. Recent advancements in molecular and cellular biomarkers offer new avenues for addressing these challenges, providing potential tools for earlier diagnosis and personalized risk stratification.

Methods: This systematic review synthesizes current evidence on emerging biomarkers in hematology, focusing on studies published between 2015 and 2024. A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science using predefined search terms related to hematologic malignancies, biomarkers, diagnosis, and prognosis. Studies were selected based on rigorous inclusion criteria, emphasizing clinical relevance, methodological robustness, and reproducibility. Data on biomarker specificity, sensitivity, and correlation with patient outcomes were extracted and analyzed.

Results: Among the biomarkers identified, circulating tumor DNA (ctDNA), microRNAs (miRNAs), and specific epigenetic modifications emerged as promising tools for early detection. These markers demonstrated high sensitivity and specificity, often outperforming traditional diagnostic methods in detecting subclinical disease and predicting relapse. Additionally, protein biomarkers such as soluble B-cell maturation antigen (sBCMA) showed strong associations with disease progression and treatment response in multiple myeloma. Integrative biomarker panels that combined genetic, proteomic, and metabolic indicators provided even higher predictive value for both disease prognosis and therapeutic response.

Conclusion: This review highlights the potential of novel biomarkers to transform the diagnostic and prognostic landscape of hematologic malignancies. By enabling more precise, individualized patient management, these biomarkers may facilitate earlier intervention and improved survival outcomes. Future research should prioritize the validation of these biomarkers in large, multicenter cohorts to pave the way for their integration into routine clinical practice.

Keywords: Hematologic malignancies, biomarkers, circulating tumor DNA, microRNAs, epigenetic modifications

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PH-38

The Importance of Hematological Biomarkers in Patients with Syphilis

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Abstract

Background and Aim: A condition known as venereal syphilis is characterized by pathogenic activity that results in necrosis and extensive tissue damage. In this context, scientists regard the examination and evaluation of hematological parameters as an effective method for diagnosing and treating syphilis.

Methods: We conducted a comprehensive search of PubMed, Cochrane, Scopus, and Google Scholar for research published between 2021 and 2024 that compares the levels of hematologic markers in individuals with active syphilis to those without the infection.

Results: In comparison to the lymphocytes, monocytes, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red blood cells (RBC), and platelets of the non-syphilitic participants, syphilitic patients exhibited significantly higher levels of lymphocytes ($p = 0.025$), monocytes ($p = 0.002$), mean corpuscular volume (MCV) ($p = 0.005$), and mean corpuscular hemoglobin (MCH) ($p = 0.008$). Additionally, they showed lower levels of red blood cells (RBC) ($p = 0.005$) and platelets ($p = 0.048$).

Conclusion: The findings indicate that hematological biomarkers for diagnosing syphilis in patients are highly specific, characterized by decreased levels of red blood cells (RBC) and platelets, along with increased levels of lymphocytes, monocytes, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH).

Keywords: Hematological biomarkers; sexually transmitted disease; syphilis

PH-39

Natural Anticoagulant Protein Levels in Patients With Beta-Thalassemia Major: A Case-Control Study

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Background and Aim: β-thalassemia is a group of inherited blood disorders that affect the production of β-globin chains, leading to the reduction or absence of these chains. One of the complications observed in patients with β-thalassemia major (β-TM) is thrombosis, especially in those who receive frequent blood transfusions. This may be due to a decrease in the levels of the natural anticoagulants: protein C (PC), total protein S (PS), and antithrombin (AT). Due to the conflicting studies and the lack of large-scale studies in Iran, this study aimed to evaluate the level of PC, total PS, and AT in patients with β-TM who receive regular blood transfusion.

Methods: In this case-control study, patients with β-TM, who had received at least 20 packed cell transfusions during their lifetime, were included. Patients with other underlying diseases like bleeding or thrombotic disorders were excluded. Totally, 118 patients with β-TM and 120 healthy individuals were included.

Results: The mean level of PC and AT was significantly lower in patients with β-TM (48.2 ± 65.4 and 57.42 ± 13.6, respectively) compared to the control group (97.1 ± 21.46 and 81.79 ± 14.3, respectively), with P value of 0.001 and 0.01, respectively. Although the difference was not statistically significant (P = 0.1), a similar trend was observed for total PS (61.12 ± 21.12 for patients versus 72.2 ± 35.2 for the control group). Of note, the decrease in PC, AT, and total PS levels compared to the control group was 50.36%, 27.5%, and 15.34%, respectively.

Conclusion: It seems that β-TM patients who receive prolonged blood transfusions frequently are at an increased risk of decreased in natural anticoagulants levels and therefore potentially are at risk of thrombosis.

Keywords: β-thalassemia major; Protein C; Protein S; Antithrombin; Thrombosis.

PH-40

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The investigation of Cassiopea andromeda crude venom on the expression of microRNA 506 and selected down stream targets in the B Acute Lymphoblastic Leukemia Cell Line .

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Currently, many unwanted side effects are possible for patients taking current anti-cancer medications. Therefore, the development of alternative therapeutic medications is always needed**.** Bioactive substances from natural sources, such as animals, plants, and microorganisms, are being investigated as potential anticancer treatments**.** Oceans could be attended as a source of natural bioactive compounds that have potentiate to be investigated for anti-cancer properties. Prior studies have displayed the anticancer capabilities of various jellyfish. Hence, we examined the anticancer features of the venom of *Cassiopea andromeda* in an in vitro situation against the B Acute Lymphoblastic Leukemia Cell Line.

Methods: The under study populations were Raji cell lines. Cells were treated by *Cassiopea andromeda* venom extract alone and in combination. The effect of the extract on survival and apoptosis were examined using MTT and flow cytometry, respectively. Moreover, the effects of the drugs on the mRNA expression levels of microRNA 506 and selected targets were studied using RQ-PCR

Results: *The* tentacle venom (T.V) extract induced cell growth inhibition and triggered apoptosis in a dose- and time dependent manner. Real-time PCR analysis of microRNA-506 revealed a declined trend. Cyclin dependent kinase -4 and cyclin dependent kinase-6 revealed decrease in expression levels. apoptotic target gene revealed that the effective dose of this agent downregulated the expression level of Bcl2-L14.

Conclusion: This study has demonstrated that venoms of *Cassiopea andromeda* (or T.V extract) has the capability to suppress Raji cells in an in vitro condition and might be utilized in order to design and develop new anticancer agents in the near future by identifying its effective fractions and the pathway .

MicroRNA; leukemia; *Cassiopea andromda*

PH-41

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Investigating the relationship between urea and creatinine levels on platelet count changes in patients receiving chemotherapy regimens.

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Abstract

Background and Aim: Chemotherapy can cause acute renal failure characterized by elevated urea and creatinine levels. Increased urea leads to more thrombopoietin production and increased platelet count, which increases the risk of thrombosis. However urea also disrupts the function of platelets and increases the risk of bleeding. Finally, urea may damage megakaryocytes and decrease the number of circulating platelets. The main purpose of this study is to analyze the effect of increased levels of urea and creatinine on platelets and evaluate their relationship with the risks of thrombosis and bleeding. Understanding this relationship can help doctors improve treatment management and prevent side effects of chemotherapy

Methods: This study was conducted on 457 hospitalized patients. Urea, creatinine, and platelet count data were recorded from medical records. To examine the relationship between urea level and platelet counts, Patients were divided into two groups based on urea ranges. 395 patients were placed in the first group with urea levels equal to or less than 15 mg/dl and 62 patients in the second group with urea levels more than 15 mg/dl. To analyze the relationship between creatinine level and platelet counts, patients were divided into two categories female and male each of them included two groups based on creatinine range in each gender: the first category included 188 female patients with creatinine level between 0.5 to 1.1 mg/dL and 21 female patients with creatinine level more than 1.1 mg/dL .The Second category consisted of 210 male patients with creatinine levels between 0.6 to 1.2 mg/dL and 38 male patients with creatinine levels more than 1.2 mg/dL. In the end, platelet changes were examined in both groups of both categories. Finally, statistical analysis was performed using GraphPad Prism version 10 software to evaluate the relationship between urea and creatinine levels and the WBCs number.

Results: The urea level in patients **treated with** chemotherapy regimen had no statistically significant relationship with the number of platelets. Also, creatinine level in men was statistically insignificant, but in women this relationship was significant.

Conclusion: The results show that there is no significant relationship between the level of urea and the number of platelets in patients treated with chemotherapy regimen. Also, while the creatinine levels in men does not have a statistically significant effect, in women this relationship is significant. These results may indicate gender differences in the response to chemotherapy and the need for further investigations to better understand these differences.

Keywords: Chemotherapy, creatinine, platelet, urea

PH-42

The amount of immature cells in samples with high mixed cells by Sysmex Xp300

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Abstract

Background and Aim: In Sysmex Xp300 device with a three-part differential, white blood cells are classified based on size and characteristics of cell size and shape. Different types of white blood cells are: neutrophils, lymphocytes, and mixed cells (monocytes, eosinophils, and basophils). The percentage of mixed cells is normally between 3 and 13%. In some cases, immature myeloid cells may be identified as mixed cells. This can be due to morphological similarities between cells, and biochemical similarities. Immature myeloid cells, especially in the early stages of maturation, may resemble Mixed cells in size and shape. These similarities cause the device's data analysis algorithms to have problems in detecting and classifying cells. This study has helped to improve the accuracy of diagnosis and classification of blood disorders and can lead to the development of more effective diagnostic strategies.

Methods: For this study, the results of the blood cell count test of 418 samples who had a mixed cells of more than 13% were collected.

Results: Out of 418 patients, 387 patients had immature cells, of which 197 had band, 120 had metamyelocytes, 65 had myelocytes, and 5 had promyelocytes. 92.5% of samples with mixed cells of more than 13% had immature cells, 47.1% had bands, 28.7% metamyelocytes, and 15.5% myelocytes and 1.2% promyelocytes.

Conclusion: The study demonstrates a significant prevalence of immature myeloid cells in samples with mixed cells percentage exceeding 13%, indicating that such elevated levels may serve as a crucial marker for underlying blood disorders. This correlation underscores the importance of refining diagnostic algorithms in Sysmex Xp300 to enhance the accuracy of white blood cell classification, ultimately leading to improved patient management and diagnosis strategies.

Keywords: Immature cells, Sysmex Xp300, mixed

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The Primary Experience with Tenecteplase Thrombolysis for Acute Ischemic Stroke; a Report from Iran

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Abstract

Background and Aim: Intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) is the primary treatment for ischemic stroke. Alteplase has been approved thrombolytic therapy for more than two decades. Tenecteplase is a new variant of tissue plasminogen activator (tPA) that has been reported to have beneficial effects in recent years. This study aimed to investigate the effectiveness and the side effects of tenecteplase in the ischemic stroke.

Methods: Here we administrated 0.25 mg/kg tenecteplase in 36 patients with acute ischemic stroke within 4.5 hours after the stroke onset. The NIHSS in baseline, 24 hours, 7 days later and the modified Rankin scale(mRS) at 90 days were assessed. The primary efficacy outcome was reduction of at least 4 points in the NIHSS during 7 days and the secondary efficacy outcome was defined as mRS 0 and 1 at 90 days. The safety outcome was evaluated based on the rate of symptomatic intracranial hemorrhage (ICH) and mortality during 90 days.

Results: The mean NIHSS at baseline was 12.7±4.6, and the mean NIHSS corresponding to 24 hours after admission was 9.6±4.8. The mean 7-day NIHSS was 7.6±4.4. The primary and secondary efficacy outcomes were met in 18 (50%) and 22 (61.1 %) of the patients respectively. Symptomatic ICH was observed in one patient with lung cancer who died of respiratory failure.

Conclusion: This study confirmed the efficacy and safety of tenecteplase in ischemic stroke treatment. Tenecteplase appears to be an appropriate treatment for thrombolysis in ischemic stroke.

Keywords: Tenecteplase, Ischemic Stroke, Thrombolysis, Alteplase, Tissue Plasminogen Activator.

PH-44

Investigating the relationship between urea and creatinine levels on WBC count in patients receiving chemotherapy regimen

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Abstract

Background and Aim: Cancer treatments like chemotherapy can harm the bone marrow, affecting white blood cell production. Kidney issues, shown by high urea and creatinine levels, can worsen this decrease in WBCs, leading to higher infection risks. Although the body may try to raise WBC levels during infections, chemotherapy can hinder this response. This study aims to assess how urea and creatinine levels impact WBCs, infection risks, and chemotherapy side effects, helping optimize cancer treatment.

Methods: This study was conducted on 457 hospitalized patients to analyze the relationship between urea, creatinine levels, and white blood cell counts. Patients were divided into groups based on urea and creatinine ranges. 395 patients had urea levels equal to or less than 15 mg/dl, while 62 patients had levels above 15 mg/dl. In terms of creatinine, 188 female patients had levels between 0. 5 to 1. 1 mg/dL, and 21 patients had levels above 1. 1 mg/dL. For males, 210 patients had levels between 0. 6 to 1. 2 mg/dL, and 38 patients had levels above 1. 2 mg/dL. WBC count changes were examined, and statistical analysis using GraphPad Prism version 10 software was conducted to assess the relationships.

Results: Urea and creatinine levels in patients undergoing chemotherapy were not statistically significantly relevant to WBC count.

Conclusion: In conclusion, this study found no statistically significant relationship between urea and creatinine levels and WBC counts in patients on chemotherapy. The results confirm the complexity of these interactions and highlight the need for further research to better treatment management and reduce chemotherapy-related side effects.

Keywords: Chemotherapy, creatinine, urea, WBC

PH-45

Macrophage Lipid Peroxidation Drives CD36 Expression and Enhanced Oxidized LDL Uptake: Role of Melatonin

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Abstract

Background and Aim: Oxidative stress plays a critical role in the development of atherosclerosis, but the specific mechanisms by which it promotes macrophage-mediated lipid accumulation remain incompletely understood. This study investigated the causal relationship between macrophage lipid peroxidation and the uptake of oxidized low-density lipoprotein (Ox-LDL), a key driver of atherogenesis.

Methods: Using E-deficient mice, we observed a progressive age-dependent increase in lipid peroxide content within mouse peritoneal macrophages (MPMs). This was accompanied by a significant increase in Ox-LDL uptake and upregulation of the scavenger receptor CD36 mRNA expression. Manipulating cellular oxidative stress through melatonin administration (inhibition) or glutathione depletion (stimulation) resulted in corresponding changes in Ox-LDL uptake and CD36 mRNA expression. Notably, intraperitoneal melatonin injection significantly reduced lipid peroxide content in MPMs, leading to a parallel decrease in Ox-LDL uptake and CD36 expression.

Results: Our findings demonstrate a direct causal link between macrophage lipid peroxidation and enhanced Ox-LDL uptake, mediated by increased CD36 expression.

Conclusion: These results highlight lipid peroxidation as a crucial player in atherogenesis and suggest that targeting this process may offer novel therapeutic strategies for atherosclerosis prevention and treatment.

Keywords: Macrophage; CD36; Lipid Peroxidation;LDL;Melatonin**.**

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Investigating the relationship between urea and creatinine levels on changes in hemoglobin in patients receiving chemotherapy regimen.

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Abstract

Background and Aim: Cancer is the second leading cause of death globally in the 21st century, with chemotherapy as the main treatment approach. Chemotherapy targets actively dividing cells, often leading to multiple side effects on healthy cells in the body. This treatment can result in kidney failure, which is associated with elevated urea and creatinine levels. Such elevations significantly affect red blood cells, potentially causing oxidative stress, cytoskeletal damage, and morphological changes. In uremic patients, low hemoglobin and hematocrit levels are observed, along with increased malondialdehyde and reduced antioxidant defence enzymes. Elevated creatinine levels can exacerbate oxidative stress, leading to red blood cell destruction. These changes can impair red blood cells' ability to carry oxygen and increase the risk of anemia. This study examines the relationship between urea and creatinine levels with hemoglobin changes in patients undergoing chemotherapy, aiming to improve treatment protocols and enhance patients' quality of life.

Methods: This study was conducted on 463 hospitalized patients. Urea, creatinine, and hemoglobin data were recorded from medical records. To examine the relationship between urea level and hemoglobin, Patients were divided into two groups based on urea ranges. 457 patients were placed in the first group with urea levels equal to or less than 15 mg/dl and 62 patients in the second group with urea levels more than 15 mg/dl. To analyze the relationship between creatinine level and hemoglobin level, patients were divided into two categories female and male each of them included two groups based on the creatinine range in each gender: the first category included 188 female patients with creatinine levels between 0.5 to 1.1 mg/dL and 21 female patients with creatinine level more than 1.1 mg/dL. The second category consisted of 210 male patients with creatinine levels between 0.6 to 1.2 mg/dL and 38 male patients with creatinine levels more than 1.2 mg/dL. In the end, hemoglobin levels were examined in both groups of both categories. Finally, statistical analysis was performed using GraphPad Prism version 10 software to evaluate the relationship between urea and creatinine levels and the hemoglobin level.

Results: Urea and creatinine levels in patients receiving chemotherapy regimens were not statistically significant with hemoglobin.

Conclusion: In conclusion, this study found no statistically significant relationship between urea and creatinine levels and hemoglobin in patients undergoing chemotherapy. The results underscore the complexity of these interactions and highlight the need for further research to improve treatment management and reduce chemotherapy-related side effects.

Keywords: Chemotherapy, creatinine, hemoglobin, urea

PH-47

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Antioxidant Status and Its Correlation with Platelet Count in Immune Thrombocytopenia

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Abstract

Background and Aims: Immune thrombocytopenia (ITP) is an autoimmune disorder that increases bleeding risk due to platelet destruction. This destruction is driven by autoantibodies targeting platelets (PLTs) and is accompanied by disrupted platelet production (thrombopoiesis). A common feature in many autoimmune conditions is oxidative stress, defined as an imbalance between the generation of reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants. Oxidative stress contributes to cellular and molecular damage and may play a role in disease progression. This study aims to assess the antioxidant status in ITP patients to explore its potential link with disease severity and platelet levels.

Methods: A total of 45 ITP patients were enrolled in this study from Baghaei Hospital in Ahvaz, spanning 2023 to 2024. The patients were divided into two groups: New Cases (recently diagnosed) and Chronic Cases (long-standing disease). To evaluate antioxidant capacity, the Ferric Reducing Ability of Plasma (FRAP) method was used, providing a measure of total antioxidant capacity (TAOC) in plasma. Platelet counts were also determined for all patients. Data analysis was performed using SPSS software, version 23, and correlations between TAOC and platelet counts were evaluated.

Results: The study found a significant increase in TAOC among both New Case and Chronic ITP patients when compared to a control group of healthy individuals. Notably, a strong negative correlation emerged between TAOC levels and platelet counts among the ITP patients.

Conclusions: The observed increase in antioxidant capacity and its inverse relationship with platelet count may reflect a compensatory response by the body to counteract oxidative damage. This study underscores the need for further research into oxidative stress mechanisms in ITP. Understanding this relationship may enhance ITP management by incorporating antioxidant assessments as potential markers of disease activity and treatment response.

Keywords: Idiopathic Thrombocytopenic Purpura (ITP); Oxidative Stress; Inflammation; Platelets.

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CD7 CAR-T Cells in the Treatment of T-Cell Acute Lymphoblastic Leukemia (T-ALL): A Systematic Review

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Abstract

Background and Aim: T-cell Acute lymphoblastic leukemia, despite significant success in survival in patients, does not respond well to treatment if the disease recurs, and this is still one of the gaps in medical science. In CD7 CAR-T cell therapy, the patient's T cells are genetically engineered to express chimeric antigen receptors that specifically target CD7, which is a type of surface glycoprotein in T lymphocytes. The aim of this study is to review the effectiveness and safety of CD7 CAR-T cell therapy as well as the challenges of this method in the treatment of T-cell Acute lymphoblastic leukemia.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Web of Science until November 2024. The keywords were CD7, CAR-T Cells, Chimeric antigen receptor, T-cell acute lymphoblastic leukemia, T-cell lymphoma, T-ALL, T-cell malignancies, Relapse, Treatment and Therapy. By searching this database; 89 articles were found, 36 of them by Reading titles and abstracts were removed. 53 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: In this review, ultimately, 53 articles were concluded. CD7 CAR-T cell therapy could be a promising treatment method in T-cell acute lymphoblastic leukemia. In this method, Overexpressed CD7 antigens in T-ALL cells were considered targets. In clinical trials, this treatment showed high efficiency along with rapid and complete response significantly in relapsed and resistant patients. The engineered T-cells remained in the patient's body for an extended duration, explaining the high effectiveness and long-term recovery using this treatment. However, it was recognized that CAR-T cells in some cases, due to the phenomenon of fratricide, targeted normal T-cells expressed the CD7 marker, which represented a challenge on the way to using this treatment. Cytokine release syndrome (CRS) was also reported in CD7 CAR-T cell therapy. Recent studies had suggested using protein blockers and gene therapy as solutions to overcome the challenges of this treatment.

Conclusion: Albeit CD7 CAR-T cell therapy was an individualized and new mode of treatment, it embraced unending advantages in treating T-cell-acute lymphoblastic leukemia; consequently, much research was further required for addressing the challenges posed and elucidating it was a role in the treatment landscape of the disease.

Keywords: CD7; CAR-T Cells; Chimeric antigen receptor; T-cell acute lymphoblastic leukemia; Treatment

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Hematologic Toxicity in Concomitant Use of Ifosfamide and Aprepitant

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Abstract

Background and Aim: Ifosfamide is one of the anti-tumor medicines used in cancer chemotherapy regimens by intravenous administration. Ifosfamide exerts its cytotoxic activity through the formation of several cross-links between ifosfamide and DNA and inducing oxidative stress, promoting cell apoptosis in tumor cells. Myelosuppression is one of the common adverse effects for patients receiving ifosfamide therapy and about 30% of patients are exposed to the symptoms of bone marrow suppression. Aprepitant could potentially increase the risk of drug interaction by the inhibitory effect on CYP450 enzymes. Contradictory results are reported on ifosfamide-induced bone marrow suppression among patients administered aprepitant. We systematically investigated the relationship between aprepitant and hematological toxicity of ifosfamide following combination therapy.

Methods: This review was written after a comprehensive search in four databases, including PubMed, Scopus, Embase, and Web of Science, until the last week of February 2022. The systematic review protocol was developed based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) 2015 guidance. This review has searched for ifosfamide-induced hematologic toxicity or myelosuppression after aprepitant use among cancer patients. There was no restriction on language or time in our search. Quality assessment was performed by Newcastle-Ottawa quality assessment scales (NOS) and Cochrane collaboration tool.

Results: Out of 91 clinical studies, six studies were included in this review. The majority of studies that administered aprepitant in combination with ifosfamide, indicated several hematologic toxicities but the association between ifosfamide-induced blood toxicity and aprepitant use was not significant. Aprepitant could increase the incidence of febrile neutropenia by 47% among children with bone cancer and could increase the rate of anemia up to 10% in children with Hodgkin lymphoma after ifosfamide administration. Although several hematologic toxicities were identified in most studies that administered aprepitant in combination with ifosfamide, the association between ifosfamide-induced blood toxicity and aprepitant use was not significant. By this review, two randomized clinical trials that used aprepitant or fosaprepitant have addressed several symptoms of hematologic toxicity, including neutropenia, thrombocytopenia, anemia, leukopenia, and febrile neutropenia among adults and pediatric patients. However, the incidence rate of these symptoms was not significantly enhanced by the concomitant use of ifosfamide.

Conclusion: To conclude, children using chemotherapy should be monitored for hematological signs due to the possible interaction of aprepitant and ifosfamide. Although the enhanced trend between ifosfamide-induced hematologic toxicity and aprepitant administration was found in clinical studies, the significance of this relationship remains to be further evaluated.

Keywords: Aprepitant; Hematological toxicity; Ifosfamide; NK1 receptors antagonist

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The Effect of Anticoagulant Drugs in the Treatment and Prevention of Diabetic Microvascular Complications: A Review Article

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Background and Aim: Diabetes Mellitus (DM) is a complex metabolic disorder that causes widespread organ damage and has nearly doubled in prevalence over the past two decades, becoming a major global health issue. Patients with DM, particularly those with diabetic kidney disease (DKD), also known as diabetic nephropathy, experience hypercoagulability, with elevated thrombin, fibrinogen, and platelet levels, increasing the risk of thrombosis. This prothrombotic state significantly raises the risk of Cardiovascular disease (CVD), the leading cause of death in diabetics, who face at least double the risk compared to the general population. Novel anticoagulant and combination therapies are crucial to reducing these risks.

Method: We obtained the materials used in our study via PubMed and Google Scholar search from 1996 through 2024. The keywords were “Diabetes Mellitus”, “Anticoagulant Drugs” ,“Cardiovascular Diseases” AND “Diabetic kidney disease (DKD)”.

Result: Studies have shown that Anticoagulants are crucial for reducing cardiovascular risk in diabetes. Aspirin is recommended only for high-risk patients without contraindications. Cangrelor was as effective as clopidogrel in preventing the composite outcome of cardiovascular death, myocardial infarction, and revascularization, without increasing major bleeding risks. Cilostazol is associated with side effects such as headaches, palpitations, and gastrointestinal disturbances, leading to patient non-compliance. Also, in individuals who suffer from diabetic kidney disease (DKD) Platelet inhibitors such as clopidogrel, cilostazol, ticagrelor, and sarpogrelate have shown protective effects in animal models and in a clinical trial involving 14,440 type 2 diabetic patients, a reduction in the incidence and progression of DKD was reported. Another drug, Beraprost sodium (BPS), has been found effective in reducing inflammation (evidenced by a decrease in TNF-α levels) and fibrosis in type 2 DKD patients, as demonstrated in a study involving 102 patients.

Conclusion: In this review, we intend to point out the use of effective treatments to manage pre-thrombotic conditions, diabetic kidney disease, and other microvascular complications, which are of significant importance in diabetic patients. Therapeutic strategies that focus on reducing the risk of thrombosis and protecting various organs have the potential to significantly improve the quality of life for diabetic patients and prevent the progression of chronic and complex complications associated with the disease.

Keywords: Anticoagulant Drugs, Diabetes Mellitus, Diabetic Kidney Disease (DKD), Cardiovascular Diseases.

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Assessing the compliance of RBC prescription with blood transfusion guidelines in two hospitals of Yazd

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Abstract

(Abstract Text Maximum 500 words; Times New Roman, font size 12)

Background and Aim: Red blood cell transfusion (RBC) is one of the measures used to improve the oxygenation of tissues in situations such as bleeding, acute and chronic anemia. Inappropriate transfusion can cause complications in patients, increased costs, and blood products shortage. The purpose of this study was to determine the compliance of RBC prescription with blood transfusion guidelines in two hospitals of Yazd.

Methods: In this cross-sectional study, 201 patients who received RBCs transfusion were studied. The data collection tool was predetermined checklist and the data included age, sex, underlying disease, hemoglobin levels before and after blood transfusion, and the number of transfused blood units. After collecting the data, they were entered into SPSS 22 software and analyzed using chi square and ANOVA tests.

Results: Among 201 patients studied, 106 (52.7%) were male and 95 (47.3%) were female. The age of the patients was 56.94 ± 21.1, and the hemoglobin level before transfusion was 8.6 ± 1.15 g/dL. The frequency of patients with hemoglobin levels less than seven before transfusion was, 46 (22.8%), between 7 and 10 g/dL, 128 (63.6%), and 10 g /dL or more was 27 (13.4%). The average number of transfused RBC units was 2.1±1.15 units. In 21.3% of patients, RBC transfusion was unnecessary. Inappropriate RBC transfusion and median hemoglobin level before transfusion were higher in patients with anemia, in internal and surgical wards ($p< 0.001$). The number of transfused RBC units was higher in those with symptomatic anemia ($p< 0.001$).

Conclusion: In this study, about one-fifth of patients received RBC transfusion without an indication. Therefore, According to the current guidelines that emphasize the importance of a restricted strategy for blood transfusion, more education and further research studies in wider statistical communities are necessary.

Keywords: Red blood cell, Transfusion, Indication.

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The impact of various plateletpheresis devices on platelet unit quality

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Abstract

Background and Aim: Plateletpheresis is a process that involves collecting platelets from a donor using an apheresis device. Various types of apheresis devices are utilized for this purpose, and each can affect the quality of the produced apheresis platelet. This review article aims to investigate the effect of plateletpheresis devices on the quality parameters of produced apheresis platelets.

Methods: This article reviewed the effects of various apheresis devices on the quality of platelet units by searching relevant keywords in databases such as PubMed, Google Scholar, Science Direct, and Scopus. A total of 83 related articles were analyzed.

Results: To evaluate the quality of the apheresis platelets, various parameters such as platelet count and yield, WBC and RBC count, platelet aggregation, metabolic activity, platelet activity, and platelet microparticle count are evaluated. The platelet counts in apheresis platelets obtained from apheresis devices follow AABB and European standards. In examining the metabolic activity of apheresis platelets in most studies, the level of glucose and pO2 decreased, lactate and pCO2 increased, and pH was within acceptable limits. When comparing platelet aggregation with different agonists, the platelet unit from the Amicus device showed the lowest response, while Trima Accel showed the highest response. Moreover, Amicus reported a higher level of platelet activation and microparticle production, whereas the lowest level of both belonged to Trima Accel.

Conclusions: The quality of apheresis platelets can be influenced by the specific apheresis device used. Although most devices can provide platelet units that meet existing standards, studies indicate that the Trima Accel device delivers a higher-quality platelet unit compared to other devices, such as the Haemonetics MCS+, Amicus, Cobe Spectra, and Fresenius.

Keywords: Plateletpheresis, Quality control, Platelet aggregation, Platelet activation, Microparticles

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Applying Six Sigma in Hematology Laboratories to Enhance Quality Control

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Abstract

Background and Aim: Six Sigma is the pinnacle of quality control, aiming to reduce errors, attain accurate outcomes, and ensure customer satisfaction through the five-step DMAIC process (define, measure, analysis, improv, control). Clinical laboratories are vital components of the healthcare system, with hematology laboratories, in particular, playing a crucial role in treatment process, where the accuracy and precision of results are paramount. The advanced analyzers used in hematology provide critical results. Therefore, implementing effective quality control practice is essential to ensure accurate and precise results that impact patient outcomes. This study examines Six Sigma's impact on enhancing the quality of the hematology laboratory.

Methods: In this study, we conducted a comprehensive search of Scopus, PubMed and Google Scholar databases using the keywords "Six sigma", "hematology laboratory" and "quality control". Articles published between 2015 to 2024 that explored the role of six sigma in hematology laboratory were reviewed. Inclusion criteria focused on studies discuss the impact of six sigma in reducing errors, improvement of laboratory prosses performance particularly in hematology and those give us insight how the use of six sigma improve quality control.

Results: Six Sigma although applied in many laboratories, remains in its early stages in hematology labs. Six Sigma measures process performance by standard deviation from the mean, evaluating defect rate per million opportunities (DPMO) whit an error rate requirement of fewer than 3.4 faults per million to reach Six Sigma. Errors are determined based on bias, precision, and TEa. Six Sigma's scale rated from 0-6, guides QC frequency: Values above 6, suggest little variability, while values below 3 require careful observation. Parameter performance varies across analysers; Parameter rated good to excellent need one QC level daily, while marginal or weaker performance need additional supervision. For example, in one analyser, HB, WBC, and RBC performed well, while Hct was marginal and PLT was poor. In another, HB, WBC, and PLT evaluated strong, while Hct and RBC were marginal. Diverse sources of TEa's identification's present major challenge, caucusing inconsistencies in CBC sigma value.

Conclusion: In conclusion, Six Sigma implementation in hematology laboratories can significantly reduce errors and costs while improving patient safety. However, several approaches must be employed. For instance, to avoid unnecessary retesting on stable parameters and to allocate more time for those need closer monitoring, internal QC methods should be customized for each parameter using Sigma metrics instead of using a uniform QC approach for all parameters. Additionally, A trained team is essential for successful Six Sigma-based quality improvement projects. Lastly, further research is needed due to limited evidence in this area.

Keywords: Six Sigma, Hematology laboratory, Quality control

PH-54

Investigating the appropriateness of using platelets in two hospitals in Yazd

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Abstract

Background and Aim: Platelet transfusions are recommended to prevent or manage bleeding caused by thrombocytopenia or platelet dysfunction. Inappropriate transfusions of blood products can cause transfusion-related complications and reduce blood bank reservoirs. Therefore, using platelet units requires regular monitoring compliance with transfusion guidelines of platelet transfusion. This study investigated the appropriateness of using platelets in two hospitals in Yazd.

Methods: A total of 200 patients who received platelet transfusions were included in this cross-sectional study. The data collection tool was pre-determined checklists. Data included age, sex, type of underlying disease, platelet count before and after transfusion, and the number of platelet units transfused. After collecting the data, they were entered into SPSS 16 software and analyzed using chi-square and ANOVA statistical tests.

Results: The mean age of the patients was 53.97 ± 21.23 years. 103 (51.5%) cases were male and 97 (48.5%) were female. The majority of platelet transfusions were performed for hemato-oncology patients. 42 (21%) platelet transfusions were inappropriate. 81% of the prophylactic platelet transfusions and 77% of the therapeutic platelet transfusions were appropriate. 14% of platelet transfusions were inappropriate in patients with platelet counts less than 20×109/L, while in patients with platelet counts less than 100×109/L, more than 40% of transfusions were inappropriate. 100% of platelet transfusions in patients with platelet counts greater than 100× 109/L were inappropriate. 71.5% of the patients had a platelet count of less than 20×109/L. The mean platelet count before transfusions was 27.61± 43.38×109/L. The mean platelet count before transfusions was higher in patients with inappropriate platelet transfusions (P<0.001).

Conclusion: Approximately one-fifth of patients had received inappropriate platelet transfusions. Educational materials on optimal platelet transfusion guidelines should be provided to clinicians. Further research is recommended in this area.

Keywords: Platelet, Transfusion, Indication.

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Innovative Strategies: Exploring Parthenolide as a Complementary Medicine in Acute myeloblastic Leukemia

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Background and Aim: Acute myeloid leukemia (AML) is an aggressive cancer of myeloid white blood cells, driven by mutations in myeloblasts that disrupt differentiation and promote uncontrolled growth. Chemotherapy and immunotherapy are widely used but frequently result in significant complications and therapy resistance. This has led to interest in natural compounds like Parthenolide (PTL), which induces cancer cell death while sparing normal cells. The aim of this study is to explore the therapeutic potential of PTL as a complementary medicine in AML

Methods: Studies related to Parthenolide and AML published from 2008 till 2024 was conducted using MEDLINE and SCOPUS.

Results: Engineered PLGA nanoparticles of PTL reduced proliferation by 40% in AML cell lines. Combination of PTL and Nrf2 and NADPH inhibitors, exhibited strong toxicity against resistant AML cells. It also increased toxicity against AML stem cells when paired with PI3K/mTOR inhibitors and synergized with the FLT3 inhibitors. New PTL derivatives showed enhanced potency against AML cell lines, while PTL-SAHA hybrids induced apoptosis and improved drug accumulation. PTL-loaded micelles demonstrated significant cytotoxicity, and PTL reduced OPN expression in U937 cells. Additionally, it enhanced the effects of Ara-C and aclarubicin, boosted etoposide efficacy, and increased cytotoxicity in KG1a cells through osteopontin suppression. PTL also induced autophagy, inhibited pro-inflammatory cytokines, and enhanced differentiation of HL-60 cells. Lastly, it depleted glutathione, leading to cell death in CD34+ AML cells, underscoring its potential as a therapeutic agent for AML.

Conclusion: Overall, the findings indicate that PTL, particularly in combination with other agents, presents promising therapeutic strategies for treating AML. These innovative approaches have the potential to enhance survival rates and improve the quality of life for patients battling this challenging disease.

Keywords: Parthenolide, AML, Complementary Medicine

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Next-Generation CAR-T Therapy: The Role of Nanoparticles in Combatting Hematological Malignancies

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Background and Aim: Hematological malignancies are the fifth most common cancer type in developed countries, presenting significant treatment challenges. The side effects of chemotherapy have led researchers to explore immunotherapy, particularly CAR-T cell therapy. However, CAR-T therapy faces obstacles, including resistant tumor subclones from poor T cell isolation, high costs and time for individualized preparation, and inadequate post-administration monitoring. Nanotechnology offers solutions by enhancing drug targeting and stability. This review aims to investigate the role of nanoparticles in improving treatment efficacy for hematological malignancies.

Methods: Studies related to nanoparticles and hematological malignancies published from 2021 till 2024 was conducted using MEDLINE and SCOPUS.

Results: Based on the articles, various types of nanoparticles, including liposomes, dendrimers, and polymeric nanoparticles were designed to improve the delivery and efficacy of immunotherapeutic agents. Nanotechnology significantly enhances CAR-T cell therapy through multiple mechanisms. Notably, nanoparticles (NPs) provide a gentler and more effective method for T cell transfection, minimizing the risks associated with viral vectors, such as insertional mutagenesis. Additionally, NPs stimulate the in vitro proliferation of CAR-T cells, reducing preparation time and improving efficiency. They also facilitate the potential for in vivo generation of CAR-T cells, transforming the therapy from an autologous process to a universally applicable treatment. Furthermore, NPs enable real-time monitoring of CAR-T cell dynamics, allowing for tracking their distribution and activity within the body. Lastly, NPs enhance the ability of CAR-T cells to secrete stimulatory cytokines, thereby improving their anti-tumor efficacy and modifying the tumor microenvironment.

Conclusion: Nanotechnology significantly enhances CAR-T cell therapy for hematological malignancies by improving transfection methods, boosting T cell proliferation, enabling in vivo production, and allowing real-time monitoring, thereby increasing efficacy and safety. Ongoing research in this field promises to deliver more effective, accessible, and safer treatment options for patients.

Keywords: CAR-T cell, Nanoparticles, Hematological Malignancies

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Key genes and pathway associated with Cytarabine resistance in Acute myeloid leukemia; a Meta-analysis

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is the most common leukemia in adults, characterized by rapid progression and a poor prognosis. Numerous therapeutic agents have been used for the clinical management of this malignancy. One of the standard agents used to treat AML is cytarabine, which has previously encountered challenges such as resistance. Therefore, identifying key genes and pathways related to this resistance could aid clinicians in patient management. This study aimed to identify key genes associated with cytarabine resistance in AML cases using bioinformatics and systems biology approaches.

Methods: Microarray gene expression data from five drug-sensitive and five cytarabine-resistant cases were obtained from the GEO database (GSE52919). After initial processing and quality control using the limma, geo query, and umap R libraries, differential expression analysis was conducted based on the following criteria: logFC < -1 or > 1 and Bonferroni-adjusted p-value < 0.05. The identified differentially expressed genes (DEGs) were further processed using the GeneMANIA database to construct interaction networks. Also, the DAVID database was applied for gene ontology and pathway analysis of identified DEGs.

Results: Among the studied genes, 30 DEGs meeting the specified criteria were identified. Of these, 29 genes were downregulated in cytarabine-resistant cases compared to the sensitive cases. These included 27 protein-coding genes, one pseudogene, and two long non-coding RNA (lncRNA) genes; Additionally, the only upregulated gene encodes a lncRNA (HSALNT0346290) which should be considered in future studies. The protein-coding genes were significantly associated with some biological processes including wound healing, spreading of epidermal cells, long chain fatty acyl biosynthesizes, and platelet aggregation. Also, more significantly related reactome pathways included neutrophil degranulation, innate immune system, immune system, and linoleic acid metabolism.

Conclusion: According to our results, the upregulation of HSALNT0346290 may serve as an important marker for AML relapse and therapy resistance during cytarabine treatment. Additionally, this challenge is associated with dysregulated expression of genes involved in various pathways and processes related to cell migration, immune response, and metabolism.

Keywords: lncRNA; AML; Cytarabine, Drug resistance.

PH-58

Fetal Erythroblastosis Anemia and Its Prevention

Abstract:

Background and Aim: Fetal erythroblastosis anemia is a significant condition, particularly prevalent in regions with a high rate of consanguineous marriages. This disorder can lead to severe health complications for infants and young children.

The aim of this study is to investigate the etiology, complications, and effective treatments for fetal erythroblastosis anemia, as well as to provide recommendations for prevention in subsequent pregnancies.

Method: This study was conducted through a review of existing literature on fetal erythroblastosis anemia and its complications in neonates and children. The data encompasses incidence rates, clinical complications, and treatment methods outlined in reputable scientific references, along with preventive strategies for this condition.

Results: The findings indicate that incompatibility of blood groups between the mother and fetus, particularly when the mother is Rh-negative and the fetus is Rh-positive, leads to an immune response resulting in the production of antibodies that attack fetal red blood cells. This immune response causes anemia, elevated bilirubin levels, fetal heart failure, hydrops fetalis, and neurological disorders such as kernicterus. Current treatments, including intrauterine blood transfusions (IUT) and postnatal interventions like phototherapy, are effective in reducing jaundice in newborns and minimizing hospital stays.

Conclusion: In subsequent pregnancies, the risk of developing fetal erythroblastosis anemia increases due to the immunological memory of the maternal immune system. Therefore, proper vaccination of mothers during their first pregnancy is crucial to prevent the serious consequences associated with this condition.

Keywords: Fetal Erythroblastosis Anemia; Blood Group Incompatibility; Rh Factor; Prenatal Care

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Emerging Strategies in Hematology: Advancements in Targeted Therapies for Hematological Malignancies

Running title: *Targeted Therapies in Hematological Malignancies*

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Abstract

Background: Hematological malignancies, including leukemia, lymphoma, and myeloma, are a diverse group of blood cancers that represent significant global health challenges. While traditional treatments, such as chemotherapy and radiation, have been the mainstay of therapy, they often come with substantial adverse effects. In recent years, advances in targeted therapies have revolutionized the landscape of hematologic oncology. These therapies aim to specifically target molecular abnormalities in cancer cells, minimizing damage to healthy tissues and offering the potential for more effective and personalized treatments.

Method: This review synthesizes the latest research on targeted therapies in hematology, focusing on novel drug development, biomarkers for treatment selection, and combination strategies. The article includes an in-depth exploration of small molecule inhibitors, monoclonal antibodies, and chimeric antigen receptor (CAR) T-cell therapies that have shown promise in treating hematological malignancies. We also evaluate clinical trial outcomes, resistance mechanisms, and the role of genetic profiling in guiding therapeutic decisions.

Results: Recent breakthroughs include the approval of targeted therapies such as Bruton's tyrosine kinase (BTK) inhibitors, immune checkpoint inhibitors, and CAR T-cell therapies, which have shown remarkable efficacy in various blood cancers. Studies demonstrate that these therapies lead to improved survival rates, reduced relapse, and better quality of life for patients. However, challenges remain, including the development of resistance and the need for novel biomarkers to predict treatment responses.

Conclusion: Targeted therapies are rapidly transforming the management of hematological malignancies. While the results are promising, further research is essential to overcome resistance mechanisms and improve treatment strategies. A personalized approach, guided by genetic and molecular profiling, is key to optimizing outcomes and reducing the risk of adverse effects. Future investigations should focus on combining these therapies with traditional treatments to achieve long-term remissions and cure in hematological malignancies.

Keywords:
Hematological malignancies, targeted therapy, CAR T-cell therapy, chemotherapy resistance, leukemia, monoclonal antibodies, small molecule inhibitors.

PH-60

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Association of chronic hepatitis B infection with metabolic syndrome and its components: Meta-analysis of observational studies

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Abstract

Background and Aim:

Observational studies evaluating the association between chronic hepatitis B (CHB) and risk of metabolic syndrome (MetS) have yielded inconclusive results. The current meta-analysis was conducted to identify whether CHB infection plays a role in the risk of MetS and its components.

Methods:

The electronic search of MEDLINE, PubMed Central, and EMBASE databases was systematically performed from their inception until February 2017 to identify all eligible studies. The most adjusted risk estimates and their corresponding 95% confidence intervals (CIs) for the associations of chronic hepatitis B with MetS and its components were collected and analyzed.

Results:

A total of 13 studies, with a total sample size of 138,994,999 subjects and 35,481,231 individuals with MetS were included in this Meta-analysis. The results of pooled analysis revealed that CHB infection is related to reduced risk of MetS (OR = 0.83, 95%CI = 0.71–0.79, random effects), with evidence of significant heterogeneity (I2 = 89%, P < 0.001). This association was an age, gender, and ethnicity-dependent relationship. Moreover, CHB was associated with reduced risk of elevated blood pressure, reduced HDL-cholesterol, increased fasting glucose, and, most strongly with increased triglycerides in some subgroups. The sensitivity analyses confirmed the stability of the results.

Conclusion:

This meta-analysis suggests that CHB is associated with decreased risk of MetS and some of its single components.

Keywords: Metabolic syndrome, Hepatitis B, HBs Ag, Meta-analysis

PH-61

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Combination Effect of Deferoxamine and Arsenic Trioxide on Viability and Vitality of APL Like Cell Line

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Abstract

Background and Aim: Arsenic trioxide is an activist agent in the treatment of acute promyelocytic leukemia (APL), which acts alone, but has an adverse effect on patients. Moreover, deferoxamine has antiproliferative activity and induces leukopenia. In order to enhance antileukemic effectiveness and to reduce the dosage of arsenic trioxide, the combination effect of it with deferoxamine (DFO) was evaluated on the APL cell line (NB4).

Methods: In this experimental study, to investigate the cytotoxic effects of ATO/DFO in acute promyelocytic leukemia, the NB4 cell line (provided by Pasteur Institute of Iran) was treated with different doses and then at 24, 48, and 72 hrs intervals, the percentage of survival, cell count, metabolic activity and apoptosis induction were investigated respectively. Also, hTERT gene expression was analyzed by the RT-PCR method.

Results: We found that DFO alone and in combination with ATO has cytotoxic and antiproliferative effects, and reduces viability and cell metabolic activity in the NB4 cell line in a dose and time-dependent manner. In addition, this combination causes an increase in apoptosis, up-regulation of Caspase-3, and down-regulation of hTERT genes in cells.

Conclusion: Combined ATO/DFO treatment cooperatively decreased the mRNA levels of the hTERT and increased the mRNA levels of Caspase-3 in a time-dependent manner compared to DFO alone.

Keywords: Acute Promyelocytic Leukemia, Arsenic trioxide, Deferoxamine

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Diagnostic and therapeutic potential of MicroRNA-217 in Leukemia

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Abstract

Background and Aim: Leukemia is a heterogeneous group of hematopoietic malignancies characterized by uncontrolled proliferation of abnormal white blood cells, classified into Myeloid and Lymphoid types. Despite advancements in treatment, leukemia remains a leading cause of cancer-related mortality, necessitating the development of targeted therapeutic strategies. This review aimed to elucidate the role of microRNA-217 (miR-217) in the pathophysiology of various leukemia subtypes, including acute myeloid leukemia (AML), chronic myeloid leukemia (CML), and acute lymphoblastic leukemia (ALL).

Methods: This review article employed a comprehensive literature search across databases such as PubMed, Science Direct, and Google Scholar, focusing on studies related to miR-217 in leukemia. The selection criteria included relevance to miR-217 role in various leukemia types. Key findings regarding miR-217 expression levels, correlations with clinical outcomes, and mechanistic insights were extracted and analyzed.

Results: Evidence indicates that miR-217 downregulation is associated with poor prognosis and aggressive clinical features in AML, suggesting its potential as a biomarker for diagnosis and treatment response. The review also notes that miR-217 can enhance chemosensitivity to drugs, such as doxorubicin, by targeting key oncogenes, such as KRAS. In CML, overexpression of miR-217 has been linked to reduced cell proliferation and increased apoptosis, with implications for overcoming the drug resistance associated with tyrosine kinase inhibitors. Similarly, in ALL, decreased levels of miR-217 have been identified as potential diagnostic biomarkers.

Conclusion: These findings underscore the potential of miR-217 as a promising biomarker and therapeutic target in leukemia management. Further research is warranted to investigate the development of miR-217-based strategies to improve treatment outcomes in patients with leukemia.

Keywords: Leukemia; hsa-mir-217; Diagnosis; Therapeutics; Prognosis; Biomarkers.

PH-63

Red blood cell antibody screening in pregnancy

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Abstract

Background and Aim: Hemolytic Disease of Fetal and Newborn (HDFN) is defined as neonatal anemia and hyperbilirubinemia caused by an incompatibility between maternal and fetal red blood cells (RBCs). In 98% cases it is caused due to ABO and Rh incompatibility and antibodies to other blood group antigens (Kell, c, E, C, Kidd, Duffy, M, and so on) are causative in remaining 2%. More than 43 different RBC antigens have been reported to be associated with HDFN. Red cell antibody screening (RCAS) is a valuable tool in the detection of alloantibodies to other blood group systems (other than ABO and Rh) in the serum of patients during pregnancy or prior to transfusion. Red cell antibody identification (RCAI) should then be carried out on a larger panel of RBCs to precisely identify the antibody.

Methods: In a prospective study carried out on 624 antenatal cases, RCAS was done using a 3-cell panel. RCAI was carried out on cases that were positive for RCAS. These tests performed with Iranian Blood Transfusion Organization (IBTO) made kits and in Noor Laboratory.

Results: RCAS was positive in 9 out of 624 cases—1.4% (excluding the 3 cases who had autoantibodies). After RCAI these were identified as anti-D antibody (6 cases, 66%), anti-D with anti-C antibody (2 cases, 22%), and anti-M antibody (1 case, 11%). The most common antibody identified remained anti-D. In 2 cases of Rh-negative pregnancy, the RCAS was suggestive of anti-D. RCAI done, however, showed a combination of anti-D and anti-C. One case of anti-M was detected in a $G_2P_1L_1D_1$ lady. The first pregnancy was full-term normal delivery at home, however, the baby died after birth. The mother's and baby's blood group were O positive. RCAS done during second pregnancy was suggestive of anti-Duffy (Fy^a) or anti-M antibody. RCAI done showed anti-M antibody with dosage effect. The second pregnancy was postdated with intrauterine growth retardation (IUGR,) and Lower segment caesarean section (LSCS) was done for fetal distress. The baby had hyperbilirubinemia and was Direct Coombs test (DCT) positive requiring phototherapy. Rh incompatibility continues to be a common cause for HDFN. Patients with no prior history of sensitization can also develop anti-D as seen in 3 of our cases probably due to naturally occurring anti-Rh antibodies or antepartum hemorrhage. Despite the use anti-D immunization, 1%–2% of the cases are still sensitized. Anti-D immunization resulted in a favorable fetal outcome in the study. Anti-D complicated with anti-C presents with more severe HDFN as seen in 1 patient who had a previous stillbirth and a hydrops baby despite receiving anti-D. Anti-C antibodies resulting in HDFN requiring exchange transfusion have been reported.

Conclusion: Antenatal detection of the non-anti-D causes of HDFN requires RCAS. If RCAS is positive, the following steps are to be taken. RCAI should be done to identify the antibody. The spouse has to be screened for the presence of offending antigen and the pediatrician has to be alerted about delivery of a potentially sensitized infant. The blood bank should find a suitable antigen-negative donor for transfusion to baby and mother.

Keywords: HDFN, Screening, Pregnancy, Noor Pathobiology Laboratory, Iran

PH-64

Molecular evaluation of apoptosis-related genes in the K562 cell line treated with TRAIL and Kaempferol

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Abstract

Background and Aim: Chronic myeloid leukemia (CML) is a blood cancer that primarily impacts the hematopoietic stem cell population responsible for blood formation. This malignancy is characterized by the uncontrolled proliferation of abnormal white blood cells. Tumor necrosis factor (TNF)-α-related apoptosis-inducing ligand (TRAIL) is a member of the TNF receptor superfamily, and it has the unique ability to selectively induce extrinsic apoptotic cell death in cancerous cells without affecting most normal cells. However, the clinical application of TRAIL is often hampered by the development of resistance to TRAIL-induced apoptosis (TIA). This resistance can significantly limit the effectiveness of TRAIL as a therapeutic agent

Methods: K562 cells were treated to various concentrations of kaempferol (100 ng/ml) and TRAIL (50 ng/ml and 200 ng/ml) both individually and in combination. The treatments were administered at 12, 24, and 48-hour intervals to determine time-dependent effects. The mRNA expression levels of anti-apoptotic proteins such as Mcl-1 and Survivin, and apoptotic proteins including caspase-3, caspase-8, and caspase-9 were analyzed using real-time polymerase chain reaction (PCR). This molecular technique allows for the precise quantification of gene expression changes in response to the treatments at the mRNA levels.

Results: The analysis of mRNA expression data indicated that treatment with kaempferol alone, as well as in combination with TRAIL, significantly enhanced the susceptibility of K562 cells to apoptosis. Specifically, the transcription levels of caspase-3, caspase-8, and caspase-9 were generally elevated when the cells were treated with both kaempferol and TRAIL. Furthermore, the expression levels of survival proteins such as Mcl-1 and Survivin decreased following the combination therapy. This reduction in survival proteins suggests an enhanced apoptotic response, making the cancer cells more prone to programmed cell death.

Conclusion: In conclusion, our findings suggest that kaempferol, when used in combination with TRAIL, not only enhances the activation of apoptotic proteins such as caspases 3, 8, and 9 but also contributes to the inhibition of survival protein expression in K562 cells. This dual action of kaempferol improves the overall efficacy of TRAIL-induced apoptosis. These results indicate that kaempferol could serve as a promising adjunct in TRAIL-based therapies, potentially leading to improved treatment outcomes for patients with chronic myelogenous leukemia. The combination of kaempferol and TRAIL represents a novel therapeutic strategy

Keywords: TRAIL, Kaempferol, Chronic myeloid leukemia, Apoptosis

PH-65

Engaging of the mTOR signaling pathway by miR100 and miR101 in de novo acute myeloid leukemia

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Abstract

Background and Aim: MicroRNAs (miRs) play a significant role in cancer progression by altering cellular functions through the modulation of protein expressions. The proteins mTOR, AKT, and PI3K constitute an essential cellular signaling cascade, the dysregulation of which has been studied in cancer. This study investigates the effects of two important miRs, miR-100 and miR-101, on the mTOR/AKT/PI3K signaling pathway in acute myeloid leukemia (AML). **Methods:** The targets of miR-100 and miR-101 were predicted with TargetScan, miRDB, and miRanda databases. MiRs and protein expression levels were analyzed in 21 patients with AML compared to 9 healthy controls using qRT-PCR. Finally, SPSS and GraphPad Prism software were used to analyze the correlation of the miRs and mTOR/AKT/PI3K genes. **Results:** In the study, miR-100 was significantly upregulated (6.8-fold increase, P=0.033), while miR-101, mTOR, and PI3K were downregulated in AML patients, with fold changes of 0.61 (P=0.019), 0.56 (P=0.004), and 0.25 (P<0.0001), respectively. Correlation analysis showed a negative relationship for miR-100 (r=-0.39, P=0.041) and a positive one for miR-101 (r=0.41, P=0.029) with mTOR, but no significant correlation with AKT1 and PI3K genes. These data showed a tumor suppressor role for both miR-100 and miR-101 via the

mTOR/AKT/PI3K signaling pathway, therefore they can be favorable therapeutic targets alongside other ones. More investigation of the miR-100 and miR-101 network with other signaling pathways in AML is recommended. Additionally, the study highlights the potential of miR-100 and miR-101 as biomarkers for the diagnosis and prognosis of AML. Given the significant changes in their expression levels in AML patients compared to healthy controls, these miRs could serve as valuable indicators for early detection and monitoring of disease progression. The findings suggest that targeting miR-100 and miR-101 could be a promising therapeutic strategy, potentially leading to the development of novel treatments for AML.

Conclusion: Future research should focus on elucidating the precise mechanisms by which miR-100 and miR-101 regulate the mTOR/AKT/PI3K pathway and their interactions with other signaling molecules. Investigating the effects of these miRs in animal models and clinical trials will be crucial to validate their therapeutic potential. Moreover, exploring the broader network of miR-100 and miR-101 interactions with other cellular pathways could provide deeper insights into their role in AML and other cancers. In conclusion, this study underscores the importance of miRs in cancer biology and their potential as therapeutic targets. The dysregulation of miR-100 and miR-101 in AML patients highlights their critical role in modulating key signaling pathways involved in cancer progression. By advancing our understanding of miR-mediated regulation, we can pave the way for more effective and targeted therapies for AML and potentially other malignancies

Keywords: Acute myeloid leukemia, microRNA-100, microRNA-101, mTOR/AKT/PI3K pathway

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Evaluation of platelet function in patients with COVID-19 with Disseminated intravascular coagulation in comparison to healthy volunteers

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Abstract

Background and Aim: Diffuse intravascular coagulation (DIC) is the pathological activation of the blood coagulation system in a diffuse form in various vessels of the body, which is one of the most common paraclinical disorders in patients hospitalized in the intensive care unit (ICU). The aim of this study was to investigate the platelet function in covid patients with DIC.

Methods: In this case-control study, 23 patients with covid-19 who were involved in DIC and 25 healthy individuals were recruited after obtaining written consent. Platelet aggregation and platelet adhesion were measured by turbidometric and ELISA methods, respectively. The hemostasis status of the patients was evaluated by prothrombin time (PT) and partial thromboplastin time (PTT) tests. In order to evaluate the fibrinolytic system, D-Dimer level was also measured.

Results: In the present study, the average age of the studied patients was 58.2 years and the healthy group was 56.4 years. The variable level of fibrinolytic system in patient group was significantly higher than healthy people. In the examination of the inflammatory panel, there was a significant increase in ferritin in the patient group compared to the healthy individuals. In the examination of platelet aggregation, the percentage of platelet aggregation in response to collagen, ristostin, ADP, and ionophore A23187 was significantly increased in the patient group compared to the healthy individuals. Also, the percentage of platelet adhesion was significantly increased in the patient group compared to normal people.

Conclusion: Changes in platelet aggregation and adhesion in covid-19 patients with DIC were significant, therefore, measuring these variables can be helpful in determining the prognosis of critically ill patients with Covid-19.

Keywords: Disseminated intravascular coagulation, Covid-19, platelet aggregation, platelet adhesion

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The Potential Clinical Relevance of Procoagulant Microparticles as Biomarkers of Blood Coagulation in Breast Cancer; A Systematic Review

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Abstract

Background and Aim: Breast cancer (BC) is a global challenge that affects a large portion of individuals, especially women. It has been suggested that microparticles (MPs) can be used as a diagnostic, prognostic, or therapeutic biomarker in various diseases. Moreover, MPs are known to elevate in cancer cases. Platelet-derived MPs (PMPs) play a crucial role in the metastasis of BC, warranting specific focus. This study aimed to explore the involvement of procoagulant MPs in BC.

Methods: This systematic review was carried out using the Preferred Reporting Items for Systematic reviews, and Meta-Analyses (PRISMA). Terms defined as MESH keywords were searched PubMed/MEDLINE, Embase, Web of Science, and Cochrane Library were searched from 2011 to March 2024. Experimental and quasi-experimental studies were assessed by the CONSORT checklist.

Results: Eventually, 15 studies were included. 426 participants were studied in the included articles. The potential clinical relevance of MPs as biomarkers in BC was indicated. Also, the role of MPs in immune modulation and multidrug resistance was approved. PMPs were found to enhance malignant features, including migration and invasion. Moreover, there were lower levels of MPs before neo-adjuvant chemotherapy, suggesting a potential impact of chemotherapy on MPs levels. The study highlights the remarkable capacity of multidrug-resistant BC-derived MPs to alter the phenotype and functionality of immune cells.

Conclusions: The findings underscore the intricate interplay between MPs and cellular signaling pathways, shedding light on their potential as diagnostic biomarkers, and therapeutic targets in cancer. Specifically, the association between MPs levels and disease severity, as evidenced by their correlation with tissue-based biomarkers, tumor grading, and distant metastasis, highlights their clinical relevance in prognostication and risk stratification.

Keywords: Biomarker, Breast Cancer, Microparticle, Platelet

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Artificial Blood (Blood Substitutes): Progress, Pitfalls, and Future Prospects

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Abstract

Background and Aim: The growing number of surgical procedures and trauma cases has led to a substantial rise in the demand for blood, which exceeds the supply of donor-derived blood units required to meet the demands of modern medical practice. Persistent concerns include the risk of infectious disease transmission, limited storage durability, and potential allergic reactions. Artificial blood presents a promising alternative to natural blood, offering the capacity to transport oxygen and carbon dioxide throughout the body while eliminating immunogenicity. This study focuses on examining the progress achieved in artificial blood development, its current limitations, and the future potential of these innovations.

Methods: This study involved a review of recent literature on artificial blood, focusing on hemoglobin-based oxygen carriers (HBOC) and perfluorocarbons (PFC). Articles were sourced from scientific databases (PubMed, Google Scholar, Scopus) using keywords such as "artificial blood," "HBOC," "PFC," and "oxygen delivery." Studies were categorized by type of blood substitute, examining their oxygen-carrying capacity, molecular size, shelf life, and adverse effects. Clinical applications, safety profiles, and side effects, including complement activation and thrombocytopenia, were evaluated. The study also explored advancements in artificial blood products and future directions for improving safety, efficacy, and storage conditions.

Results: Concerns regarding the transmission of infectious diseases (e.g., AIDS) and allergic reactions have driven researchers to develop artificial blood as a temporary means of supporting the circulatory system until the bone marrow generates sufficient red blood cells. Oxygen-delivering blood substitutes are classified into two main types:

1. **HBOC**: Synthetic hemoglobins capable of oxygen delivery to tissues. Their small molecular size allows them to access obstructed vessels (e.g., in MI), though their short half-life remains a limitation.
2. **PFC**: Neutral molecules significantly smaller than RBCs that transport O_2 and CO_2, facilitated by lipids. First-generation PFCs were approved for cardiac surgeries, while second-generation variants exhibit improved oxygen-carrying capacity. However, they

can trigger complement activation, transient thrombocytopenia, and accumulation in the reticuloendothelial system.

Overall, artificial blood is characterized by rapid and efficient oxygen delivery, no need for cross-matching, extended shelf life, storage at RT, and reduced risks of pathogenic transmission and immune activation.

Conclusion:

Improvements in blood-donor screening methods have significantly lowered the risk of transmitting blood-borne infections; however, this risk has not been completely eradicated, and the disparity between blood supply and demand continue. The use of artificial blood, even if limited to oxygen delivery, holds the potential to substantially reduce reliance on donated blood. Furthermore, advancements have been made in producing lyophilized platelets and synthetic fibrinogen and albumin. Nonetheless, artificial blood is not free from adverse effects, and refinement of novel synthetic models offers a pathway to minimiz these limitations.

Keywords: artificial blood; HBOC; PFC; oxygen delivery

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NGS-Based Measurable Residual Disease Detection for AML as a Tool for Monitoring Relapse and Treatment Response: A Systematic Review

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Abstract

Background and Aim: Evaluating measurable residual disease (MRD) in acute myeloid leukemia (AML) is crucial for detecting early relapse, informing treatment strategies, and accelerating new therapies. Relapse in AML is a significant challenge, with disease-free survival rates of 30–40% in younger chemotherapy patients. Next-Generation Sequencing (NGS) is valuable in identifying genomic alterations in AML patient care and management. This study reviews NGS-based MRD detection for monitoring relapse and response to treatment.

Methods: This review article was conducted using Google Scholar, PubMed, and ScienceDirect with keywords such as acute myeloid leukemia, acute myelogenous leukemia, minimal residual disease, measurable residual disease, genomics, and next-generation sequencing until November 2024. Finally, about 23 articles were found, of which 8 were excluded after reviewing titles and abstracts. About 15 articles were selected based on the inclusion criteria.

Results: A review of 15 articles showed that advancements in NGS had significantly enhanced the genomic understanding of AML. Key gene mutations such as NPM1, FLT3, NRAS, KIT, IDH1, IDH2, WT1, RUNX1, GATA2, U2AF1, and PHF6 were useful for identifying NGS-MRD positivity in patients. The "AML NGS-MRD hot-spot panel" effectively identified mutations with a minimal panel size, making it a reliable and cost-effective option for monitoring AML cases. NGS-based MRD assessment in post-transplant AML patients predicted clinical outcomes and was broadly applicable compared to translocation-based or single-gene assays. Unlike flow cytometry, NGS was less subjective and detected mutations in both blood and bone marrow. However, it had drawbacks such as longer turnaround times, higher costs, and uncertain reimbursement.

Conclusion: It appears that NGS-based tests offer significant benefits in AML subclassification by enabling the identification of all relevant mutations through a single assay. Additionally, the presence of NGS-detected MRD, especially after initial consolidation therapy, is a strong indicator of clinical outcomes in AML patients. However, more research is required on this topic.

Keywords: Acute Myeloid Leukemia; Measurable Residual Disease; MRD detection methods;

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Fanconi Anemia Disease: A Review on The Polymorphisms causing Fanconi Anemia

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Abstract

Background and Aim: Fanconi anemia is a rare disease that manifests with symptoms such as bone marrow failure. This disease is caused by the inefficiency of the Fanconi pathway, which is involved in the repair of inter-strand crosslinks created by crosslinking agents. In addition to the Fanconi anemia pathway, the DNA repair system includes other pathways such as BER and MMR, which are involved in the repair of cellular damage caused by harmful substances such as necrotic drugs. The aim of this article is to understand the DNA repair system, the occurrence of Fanconi anemia and the polymorphisms that cause this disease.

Methods: This review summarizes the latest research on repair pathways such as Base excision repair (BER), Nucleotide excision repair (NER), Mismatch repair (MMR), Homologous Recombination (HR), and Non-homologous end-joining (NHEJ). Focusing on the Fanconi anemia pathway and its components, the article also examines polymorphisms in this pathway and analyzes the impact of each of them on the severity and persistence of the disease.

Results: This study highlights several polymorphisms that influence the incidence and severity of Fanconi anemia. Polymorphisms in genes such as the IL17 and IL17A genes from salivary DNA, the C gene of Fanconi anemia group, the NOS2 gene, and the p53 gene all contribute to the development of Fanconi anemia. Also, the occurrence of a series of alleles such as HLA*02 and HLAB*35 or a single nucleotide substitution in the ALDH2 gene increases the incidence of the disease in an individual.

Conclusion: The efficiency of the DNA repair system and its pathways is essential for the health of cells, and any deficiency in them can lead to several diseases such as Fanconi anemia. Inefficiency of the Fanconi anemia pathway due to mutations and polymorphisms causes DNA damage and sensitivity of cells to harmful substances. Identification of these genetic mutations is helpful for early diagnosis and treatment strategies.

Keywords: DNA repair, Fanconi anemia, inter-strand crosslinks, FANC genes, polymorphisms, base excision repair, nucleotide excision repair, homologous recombination, bone marrow failure.

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Genomic Insights into CLL: The Promise of Next-Generation Sequencing: A systematic review

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Abstract

Background and Aim: Chronic lymphocytic leukemia (CLL) is the most common leukemia in Western countries, affecting over 200,000 people. Complications such as anemia and infections can occur if untreated. Next-generation sequencing (NGS) offers rapid insights into genome structure and variations, aiding in prognosis, diagnosis, therapeutic decisions, and follow-up in leukemia and other diseases. This study reviews the benefits of NGS in the prognosis of CLL.

Methods: This review article includes studies published on PubMed, ScienceDirect, Google Scholar, and SID until November 2024. The keywords used were next-generation sequencing, genomics, and chronic lymphocytic leukemia. The search yielded 24 articles, 11 of which were excluded after reviewing titles and abstracts. About 13 articles were selected based on the inclusion criteria.

Results: From the final 13 articles, NGS research revealed significant genetic heterogeneity in CLL patients. NGS played a critical role in assessing the risk of CLL progression and integrated copy-number analysis with mutation detection, offering a comprehensive view of CLL's genomic features. This enhanced clinical decision-making and supported personalized therapies. NGS, with higher sensitivity than Sanger sequencing, can be effectively used in clinical settings. Comprehensive biological assessments at diagnosis, including NGS and karyotyping, refined risk stratification and improved CLL patient management. Key prognostic markers included TP53 and SF3B1, while NOTCH1 predicted decreased efficacy in certain treatments. Several challenges remained for routine clinical implementation of NGS: selecting genes for panels, establishing mutation thresholds, and standardizing methodologies.

Conclusion: NGS appears to be a valuable tool in assessing the risk of disease progression, making it potentially beneficial for the diagnostic evaluation of CLL patients due to its efficiency, sensitivity, and cost-effectiveness. However, more research is needed on this topic.

Keywords: chronic lymphocytic leukemia, next-generation sequencing, CLL prognosis

PH-72

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The association between diabetes mellitus and the risk of lymphoid leukemias

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Abstract

Background and Aim: Diabetes is a long-term condition that affects glucose metabolism, with severe consequences. The number of people with diabetes has been rising, mainly due to the increasing rates of obesity. Lymphoid leukemias are hematological malignancies characterized by the proliferation of lymphoid cells, primarily affecting lymphocytes, which are integral components of the immune system. Both diabetes and Lymphoid leukemias are becoming more common, and research has shown a possible link between diabetes and Lymphoid leukemias, although the connection remains a topic of debate and sometimes contradictory. This study aims to assess the relationship between diabetes and lymphoid leukemias.

Methods: We obtained the materials used in our study via PubMed and google scholar search from 1996 through 2024. The key search terms included “Acute lymphoblastic leukemia”, “Chronic lymphocytic leukemia”, “diabetes mellitus”.

Results: Acute lymphoblastic leukemia (ALL) is the most common childhood cancer, often linked to glycemic disorders, especially in children over 10 with a family history of diabetes. This is due to factors like impaired glucose recycling and pancreatic infiltration by leukemia cells. Adult survivors of childhood ALL face an increased risk of Type 2 diabetes, necessitating close monitoring. Chronic lymphocytic leukemia (CLL), the most common blood cancer in the Western world, has varied symptoms and outcomes. The combination of fludarabine, cyclophosphamide, and rituximab is the main treatment. Pre-existing diabetes can predict CLL prognosis, and both diseases share risk factors like obesity and immune system imbalances. Elevated inflammatory markers, such as IL-6 and TNF-α, contribute to CLL progression. Metformin, commonly used to treat diabetes, may reduce lymphoma risk and improve outcomes by inhibiting cancer cell growth, though its long-term effects on cancer risk remain uncertain.

Conclusion: In conclusion, both ALL and CLL show the connection between cancer and diabetes. Many children with ALL also have glycemia disorders, emphasizing the need for close monitoring, particularly in high-risk groups. Similarly, the link between diabetes and CLL outcomes suggests that managing metabolic health is crucial in dealing with this disease. Research into the shared risk factors and mechanisms connecting these leukemias with diabetes highlights the importance of a comprehensive approach to patient care. This involves not only treating cancer effectively but also actively managing metabolic health to enhance outcomes.

Keywords: Acute lymphoblastic leukemia; chronic lymphocytic leukemia; diabetes mellitus

PH-73

Evaluation of blood transfusion Khatam Al-Anbia Hospital in Zahedan

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Abstract

Background and Aim: Blood transfusion treats many medical problems such as thalassemia, cancer, Surgery, delivery, and trauma patients. Considering the high cost of obtaining blood and its products, this study aims to investigate the amount of request and consumption of blood and blood products in Khatam Al-Anbia Hospital, Zahedan.

Methods: This descriptive, cross-sectional study, was conducted on all blood request forms sent to the blood bank department of Khatam Al-Anbia Hospital in Zahedan for one year from March 2023 to March 2024 then data were analyzed with SPSS version 16 software.

Results: All blood request forms (n=5084) included packed red blood cells (packed RBC) (n=3998), fresh frozen plasma (FFP) (n=489), platelets (PLT) (n=563), and Cryoprecipitate (Cryo) (n=34). The requested packed RBC and transfusion percentages were 78.63 and 73.9, respectively. Additionally, the cross-match to transfusion index (C/T ratio) was 1.06. The requested FFP, PLT, and Cryo percentages were 9.61, 11.07, and 0.66 respectively. The transfusion FFP, PLT, and Cryo percentages were 8.9, 10.9, and 0.60 respectively.

Conclusion: The funding indicated that blood consumption in Khatam Al-Anbiae Hospital has a good status compared to international standards.

Keywords: Blood transfusion, Packed RBC, C/T ratio

PH-74

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The role of apelin-13 in cardiovascular diseases

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Abstract

Background and Aim: Apelin, a peptide and APJ receptor ligand, is vital in blood pressure regulation, fluid balance, cardiac function, and energy metabolism, making it a key drug target. Secreted by cells like adipocytes and endothelial cells, it acts as a strong inotrope and has anti-arrhythmic effects in the heart. Apelin-13, a crucial subtype, has drawn attention for its role in cardiovascular diseases, given its ability to combat inflammation, apoptosis, oxidative stress, and enhance autophagy. These properties make apelin-13 significant in addressing the global burden of cardiovascular diseases.

Methods: In this narrative review, relevant articles were identified through a systematic search using the keywords Apelin-13, Cardiovascular, Hypertension, and Atherosclerosis across reputable international databases, including PubMed, Google Scholar, and ScienceDirect. The studies retrieved were screened sequentially by title, abstract, and full text. Articles were included if they met predefined inclusion and exclusion criteria, focusing on patients with cardiovascular diseases, assessing apelin levels, and evaluating cardiac function tests, while also adhering to quality standards outlined in a checklist. Studies that did not fulfill these criteria were excluded. Ultimately, 32 of the 45 initially collected studies were selected for comprehensive review and analysis.

Results: A review of recent studies has revealed a significant reduction in Apelin-13 levels in patients with cardiovascular disease compared to healthy individuals. Lower apelin levels are observed in patients with severe left ventricular (LV) dysfunction and are predictive of survival outcomes in patients with ST-elevation myocardial infarction (STEMI). Apelin positively impacts the cardiovascular system through mechanisms such as vasodilation, myocardial contraction, and anti-inflammatory effects. Furthermore, apelin levels are independently associated with left ventricular hypertrophy (LVH) in patients with essential hypertension. Emerging evidence suggests that apelin may serve as a novel biomarker for assessing the severity and progression of coronary atherosclerosis, as well as a promising therapeutic target for ischemic heart disease.

Conclusion: Apelin-13, an endogenous ligand of the APJ receptor discovered in 1993, plays a crucial role in protecting against vascular diseases by regulating key signaling pathways involved in inflammation, apoptosis, autophagy, and oxidative stress. These pathways are linked to conditions like hypertension and myocardial infarction. As a result, apelin-13 is gaining attention as a potential therapeutic target for vascular disease prevention and treatment. Studies have shown that administering exogenous apelin improves heart function in animal models of advanced heart failure, reducing left ventricular volumes and enhancing ejection fraction.

Keywords: Apelin; Cardiovascular; Hypertension; Atherosclerosis

PH-75

Preanalytical errors in hemostasis testing in low resource settings

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Abstract

Background and Aim: Preanalytical errors constitute a significant portion (65%) of laboratory errors, with sorting and labeling errors being the most common. In low-resource settings, where access to computerized systems, barcode labeling, and staff training is limited, these errors are more prevalent. In this situation, the lack of standardized guidelines for hemostatic test sampling further contributes to preanalytical errors. This study aims to explore the causes of preanalytical errors in hemostasis testing in such settings.

Methods: 21 articles have been found on different databases using “preanalytical errors”, “hemostasis tests” and “low resource settings” as keywords. After studying the essays, 7 items had been selected to use in this study.

Results: In low-resource settings, laboratories often face challenges such as insufficient access to appropriate sample collection tubes with correct anticoagulant concentrations. This leads to errors in anticoagulant volume and concentration, which can result in sample dilution or clot formation, affecting hemostasis test outcomes. Additionally, the failure to mix samples properly, particularly due to the absence of automated mixing devices, increases error rates. Inter-city sample transfers also pose risks due to improper temperature maintenance, causing sample degradation. Power outages further exacerbate these issues by affecting both the centrifuge operation and the stability of frozen samples, which can lead to improper sample separation and loss of labile factors. The combination of these factors, along with the lack of adequate infrastructure and trained personnel, significantly heightens the likelihood of preanalytical errors.

Conclusion: Laboratories in low-resource settings are particularly vulnerable to high rates of preanalytical errors, which are largely driven by inadequate infrastructure, limited access to necessary equipment, and insufficient staff training. To reduce these errors, it is crucial to standardize sampling procedures, implement regular error recording and analysis, and integrate computerized systems for better sample tracking and management. Enhanced collaboration between laboratory staff and hospital wards, along with the training of all staff involved in sample collection, storage, and transport, is also recommended. These measures can help mitigate the impact of preanalytical errors and improve the accuracy of hemostasis testing in such settings.

Keywords: preanalytical errors; hemostasis tests; low resource settings

PH-76

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"αβ T-cells vs. γδ T-cells: Evaluating the Efficacy and Safety of CD34-Specific Bispecific T-cell Engagers in AML Therapy"

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Abstract

Background and Aim: Acute Myeloid Leukemia (AML) presents a significant challenge in hematologic malignancies, often requiring Hematopoietic Stem Cell Transplantation (HSCT) for a potential cure. Traditional approaches involve high-dose chemotherapy to achieve remission, but this comes with severe short- and long-term side effects and the risk of relapse due to chemotherapy-resistant leukemic stem cells (LSCs). Bispecific T-cell Engagers (BTEs) have emerged as a novel therapeutic strategy to target and eliminate malignant cells by engaging T-cells to recognize and destroy cancer cells. The previous study by these researchers focused on using αβ T-cells with BTEs, which, although effective, caused significant side effects including cytokine release syndrome (CRS). In this study researchers aims to evaluate the efficacy and safety of a CD34-specific BTE with γδ T-cells as an adjunct therapy in pre-HSCT treatment to enhance outcomes and reduce toxicities.

Methods: γδ T-cells were expanded from healthy blood samples and combined with CD34/CD3 BTE to evaluate their cytotoxic effects on AML cell lines. Assays included proliferation studies, cytotoxicity assessments, and cytokine production profiling using techniques such as FluoroSpot, Luminex, and ELISA. These methods helped determine the impact of γδ T-cells and BTEs on target cells and overall safety in comparison to conventional αβ T-cells. γδ T-cells were chosen for their promising safety profile and potential to reduce the adverse effects seen with conventional T-cell therapies.

Results:

Cytotoxic Response: γδ T-cells demonstrated a stronger and quicker cytotoxic response against CD34+ AML cell lines compared to αβ T-cells. This suggests a more effective eradication of malignant cells with γδ T-cells. The results showed that γδ T-cells could effectively induce cytotoxicity in a dose-dependent manner, primarily within the first 24 hours, reflecting their rapid action.

Proliferation: γδ T-cells showed continued proliferation even after exposure to high concentrations of BTE, without severe adverse effects. This indicates that γδ T-cells are robust and maintain their proliferative capacity, which is crucial for sustained therapeutic effects.

Cytokine Production: While an increase in cytokine production was observed at high BTE concentrations, this was manageable and did not translate into severe inflammatory responses like CRS. The data from FluoroSpot, Luminex, and ELISA assays confirmed that cytokine levels were significantly increased with γδ T-cells, but the production was still within a manageable range.

Specificity: γδ T-cells did not target healthy CD34+ cells, indicating their potential safety for in vivo applications. Importantly, the γδ T-cells exhibited a high degree of specificity towards CD34+ AML cells without affecting healthy blood-brain barrier endothelial cells or CD34+ hematopoietic stem cells from healthy bone marrow samples.

Conclusion: The combination of γδ T-cells with CD34/CD3 BTEs represents a promising alternative to αβ T-cells for pre-HSCT treatment in AML, offering enhanced efficacy with reduced side effects. This approach could potentially lower the chemotherapeutic dose required, thereby minimizing drug-related toxicities and making more patients eligible for HSCT. Further studies with larger sample sizes and in vivo pre-clinical models are required to validate these findings and establish clinical safety and effectiveness. The results highlight the potential of γδ T-cells to provide a safer and more effective treatment modality, reducing the burden of relapse and improving overall patient outcomes in AML therapies.

Keywords: AML, Bispecific T-cell Engagers, γδ T-cells, αβ T-cells, HSCT

PH-77

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Inducing apoptosis in the K562 Cell line by TRAIL and SAHA: studying the effect of SAHA on resistance to TRAIL

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Abstract

Background and aim: TRAIL (Tumour Necrosis Factor-Related Apoptosis-Inducing Ligand) is a promising candidate for cancer therapy. It binds to its death receptors, inducing apoptosis in several cancer cells. However, some malignancies exhibit significant resistance to TRAIL, posing a challenge to cancer researchers. This study investigated the efficacy of combination treatment using TRAIL and SAHA (Suberoyl Anilide Hydroxamic Acid) to assess SAHA's capability to overcome TRAIL resistance in the leukemia K562 cell line.

Methods: First, the MTT assay was used to determine the IC50 for SAHA (2 µM) at 12, 24, 48, and 72 hours of treatment. Second, K562 cells were exposed to 50 and 100 nM of TRAIL and 2 µM of SAHA, both alone and in combination, for 24, 48, and 72 hours. Cell viability was assessed using flow cytometry subsequent to annexin-V and PI staining. The HEK-293 cell line was treated with TRAIL 100 nM and SAHA 2 µM together and separated at the same times to demonstrate that the combination treatment was non-toxic for normal cells. Ultimately, real-time PCR was used to evaluate the amounts of BCR-ABL expression and the expression of potential genes associated with TRAIL resistance.

Results: The drug dosages were not toxic to normal cells. SAHA combined with TRAIL significantly induced apoptosis in K562 cells after 24, 48, and 72 hours of treatment. Moreover, it was demonstrated that the expressions of DR4, DR5, and CHOP were elevated, whereas the expressions of PI3K, Akt, ERK, STAT3, c-FLIPL, NF-κB, and BCR-ABL were reduced by SAHA in K562 cells.

Conclusion: Our research showed that SAHA in combination with TRAIL enhances the susceptibility of K562 leukemic cells to TRAIL by inhibiting intracellular anti-apoptotic factors and elevating the expression of DR4/DR5 and CHOP.

Keywords: Hematologic Malignancy; TRAIL; SAHA; K562; Apoptosis; Resistance.

PH-78

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Abstract

Background and Aim: Cancer is the second leading cause of death in the world. it is estimated that by 2023, about 10 million people will have died from this disease. Many of these deaths are preventable with early detection AI, a broad field that includes machine learning and deep learning can help diagnose cancer and provide services to larger populations by eliminating human error and achieving greater safety and accuracy reducing costs and time. Based on large amounts of medical data, artificial intelligence is used in various aspects of cancer research and can potentially improve cancer diagnosis and treatment.

Methods: We obtained the materials used in our study via PubMed search from 2020 through 2024. The search terms included “artificial intelligence”,” Cancer”, and “Application of artificial intelligence in cancer”.

Results: Recent advancements in artificial intelligence (AI) have significantly enhanced cancer diagnosis and treatment. AI algorithms, particularly those utilizing deep learning, have demonstrated high accuracy in detecting various cancers through imaging modalities. For instance, an AI model developed by Harvard Medical School, known as "Chief," achieved an overall accuracy of nearly 94% in cancer detection, with a 96% accuracy rate for specific cancers such as esophagus, stomach, colon, and prostate In pathology, AI has been employed to analyze histopathological images, aiding in the identification of malignancies such as breast, gastric, and colorectal cancers. Moreover, AI has been instrumental in predicting adverse drug reactions among cancer patients, thereby optimizing treatment plans and minimizing potential side effects. Despite these advancements, challenges persist, including the need for diverse and comprehensive training datasets to avoid biases and ensure the generalizability of AI models across different populations.

Conclusion: AI has the potential to improve early detection, increase diagnostic accuracy, and guide treatment decisions, ultimately leading to better outcomes for increased patient survival and more efficient use of healthcare resources. However, more research is needed to fully realize the potential of AI in cancer.

Keywords: cancer, machine learning, deep learning, artificial intelligence, diagnosis.

PH-79

New insights into the laboratory methods for the detection of Fetomaternal hemorrhage

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Background and Aim: Fatal Maternal Hemorrhage (FMH) represents a clinical condition characterized by the translocation of fetal red blood cells into the maternal bloodstream, which may occur as a result of trauma, childbirth, or abortion; resulting in the alloimmunization of mothers with RhD negative, necessitating the administration of a specific quantity of RhoGAM, an anti-D immunoglobulin. Several methods exist for measuring it. One old one is the Kleihauer–Betke test (KBT) also known as the acid elution test which differentiates fetal hemoglobin from adult hemoglobin based on their differential acid resistance. We can handle this situation better with new and advanced techniques.
Methods:
Data from 2010 to 2024 were collected from current databases (PubMed, Google Scholar, Scopus). Using the MESH keywords for search terminologies included "Fetomaternal hemorrhage", "Flow cytometry", "High-performance liquid chromatography", "Hydrogel fluor immunoassay", "Kleihauer-Betke test"
Results: Although the Kleihauer–Betke assay found a new staining protocol that reduces the duration of fixation and separate elution from methylene blue staining (replacement of hematoxylin), thereby enhancing sensitivity and reducing false-positive results, it remains constrained by less accuracy against flow cytometry (FC), another costly and time-consuming technique but more precise and user-friendly and easier to do. If FC is combined with High-performance liquid chromatography (HPLC), a screening technique that differentiates hemoglobin fractions during two distinct phases—salt concentration and pH as displayed in a chromatogram will eliminate samples that do not necessitate FC. Furthermore, FC combined with microcolumn gel technology called hydrogel fluor immunoassay provides better sensitivity and accuracy and can be utilized for a large group of patients due to the hydrogel ability in a low-speed centrifuge to separate hemoglobin bound to fluorescence-labeled antibody and sensitized RBC, finally measuring the fluorescence value.
Conclusion: The Kleihauer–Betke assay, even with advancements in its technique, is inadequate for application to extensive samples with high accuracy and sensitivity. Therefore, the substitution with FC independently or combined with HPLC or microcolumn gel solves all problems identified.
Keywords: Fetomaternal hemorrhage evaluation, Flow cytometry, High-performance liquid chromatography, Hydrogel fluor immunoassay, Kleihauer-Betke test

PH-80

Blueberry Extract Enhances Radiosensitivity by Modulating Proliferation and Apoptosis in Non-Hodgkin Lymphoma

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Abstract

Background and Aim: Non-Hodgkin's lymphoma (NHL) is one of the major types of cancer, typically treated using chemotherapy and radiotherapy. However, these typical treatments can be limited by cancer cells becoming resistant to treatment and damage to healthy cells. To overcome these problems, alternative strategies like medicinal plants have gained attention. One of these medicinal plants is blueberry. Blueberry extract, rich in micronutrients, flavonoids, and bioactive compounds, has shown the ability to inhibit cancer cell growth and induce apoptosis without affecting normal cells. This study investigates the effects of blueberry extract combined with radiotherapy as a radiosensitizer on Raji cells, a highly aggressive non-Hodgkin's lymphoma model.

Methods: In this study, Raji cells were treated with extract concentrations of 0, 50, 100, 200, 400, 600, and 800 µg/mL, alone and combined with 2 Gy radiation, for 24, 48, and 72 hours. The MTT assay was performed to evaluate the inhibitory effect of the extract on cell viability, both as a single treatment and in combined therapy. Finally, apoptosis was assessed at 24 and 48 hours using closest concentration range to the IC_{50} (600, 700, and 800 µg/mL). The results were statistically analyzed using ANOVA and Tukey's test, with a significance level of P value< 0.05.

Results: The MTT assay results demonstrated that blueberry extract exhibited dose- and time-dependent inhibitory effects on the Raji cell line compared to the control cells (P value < 0.0001). The IC_{50} values were 736.2±36.15 µg/mL, 671.07±47.61 µg/mL, and 557±65.63 µg/mL at 24, 48, and 72 hours, respectively. In the combination treatment, the IC_{50} values were 642.9±47.51 µg/mL, 601.12±52.35 µg/mL, and 597.1±67.77 µg/mL at the same time points. Apoptosis analysis showed a significant increase in apoptosis compared to the control group (P value < 0.0001), with higher concentrations and longer treatment durations. The highest percentage of apoptosis (81.12%) was observed following a 48-hour treatment with 800 µg/mL of the extract combined with 2 Gy radiation.

Conclusion: Blueberry extract induces apoptosis and inhibits proliferation in Raji cells, making it a promising anticancer agent. Additionally, its combination with radiotherapy is proposed as an effective radiosensitizer for the treatment of non-Hodgkin's lymphoma.

Keywords: Radiosensitization, Blueberry, Apoptosis, Non-Hodgkin's Lymphoma

PH-81

Investigating the suppressive impacts of synthetic microRNA-sponges on engaged microRNAs in acute leukemias; a systematic review

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Abstract

Background and Aim: Sponging is a process where non-coding RNA sequences act as sponges, capturing synthesized RNAs like microRNAs (miRNAs) and reducing their influence on gene expression. This can alter the expression of target genes affected by these microRNAs. Synthetic microRNA-sponges can also bind to microRNAs, inhibiting their effects. Given the role of various microRNAs in cancers like leukemia, it's possible to reduce their impact on cancer cells by designing microRNA-sponges with multiple microRNA binding sites (MBS).

Methods: This research was carried out in November 2024, and pertinent articles were gathered using keywords such as microRNA-sponge, sponging, acute leukemia, and others by searching databases including PubMed, Web of Science, Science Direct, Google Scholar, and Scopus. The search strategy and articles were evaluated according to the guidelines for composing systematic reviews. The information extracted from the selected articles will encompass the type of acute leukemia, Target microRNA sequence, the sequence and features of the created microRNA-sponge, the type of cell line utilized, the cells' response to microRNA-sponge transfection, limitations, and any unexpected findings.

Results: Given the extensive role of microRNAs in cancer development and the variety of microRNAs associated with different cancers, creating microRNA-sponges that can bind to a group of microRNAs through multiple microRNA binding sites (MBS) increases our chances of mitigating the oncogenic effects of these microRNAs. By using microRNA-sponges to inhibit microRNA activity, we can initiate a range of cellular processes in cancer cells, such as immune cell activation or differentiation, apoptosis, cell death, and autophagy, all of which contribute to decreasing the likelihood of cancer cell survival or the onset of carcinogenesis. Moreover, the effectiveness of the designed microRNA-sponge in binding to the target microRNA can be assessed by analyzing the light produced by the luciferase enzyme incorporated into a portion of the microRNA-sponge.

Conclusion: Different microRNA-sponges can be produced based on the number of microRNA binding sites, target types, separating sequences for microRNA binding sites, and detection methods. A microRNA-sponge tailored for a specific leukemia can influence cancer cells based on the chosen target microRNA. Selecting the appropriate microRNA, aligned with the cancer type and its pathogenesis, can reduce cancer cell survival and progression. This study explores synthetic microRNA-sponges in leukemia control, emphasizing the need for further research to enhance understanding of their potential as effective therapeutic agents, possibly in combination with other treatments.

Keywords: microRNA-sponge; sponging; acute leukemia

PH-82

Analysis of the expression levels of ATG-5 and ATG-7 genes in the autophagy pathway using a synthetic circular miR sponge that targets miR-17 and miR-181 in the NALM-6 cell line.

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Abstract

Background and aim: MicroRNAs (miRNAs) can influence cellular functions by regulating the expression of different genes, making them crucial in various cancers. Additionally, inhibiting certain types of miRNAs across all cancer types can diminish or halt the proliferation of cancer cells.

Materials and methods: This study was carried out from 2021 to 2022 at Mashhad University of Medical Sciences in partnership with the Science and Research Center of the Shiraz Paramedical Faculty. In our work, we developed a microRNA sponge featuring multiple microRNA binding sites (MBS) to target miR-17-5p and miR-181. Our investigation has analyzed how the sponge suppresses these specific miRNAs in NALM-6 cells linked to Acute Lymphoblastic Leukemia. We also explored how inhibiting these miRNAs affects the regulation of their target genes and the apoptosis process in this specific cell type.

Results: This study shows that the engineered sponge reduced the levels of these two oncogenic microRNAs in the cells by binding to the target miRNAs. Additionally, the expression of the target genes controlled by these two miRNAs, namely ATG-5 and ATG-7, increased after reducing these miRNAs. Ultimately, all these alterations enhanced cell death in cancer cells treated with the miRNA sponge.

Conclusion: This study suggests that using a microRNA sponge result in a more pronounced upregulation of the target genes associated with the two microRNAs being studied. In conclusion, we demonstrated that a microRNA sponge can stimulate cancer cells to increase autophagy and apoptosis. In summary, microRNA sponges could be utilized to reduce the effects of oncogenic microRNAs and assist in leukemia treatment. Nevertheless, additional research in this area is necessary to validate the current study's findings and enhance our understanding of microRNA sponges as a potential strategy in the treatment of various cancers.

Keywords: *microRNA; miRNA sponge; ALL; oncogene; microRNA inhibitor*

PH-83

The Association of Serum Level of TGF-β_1 and Clinical Manifestations in Sickle Cell Disease

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Abstract:

Background: Sickle cell disease (SCD) is an inherited red blood cell disorder resulting from the polymerization of Hemoglobin S. Acute vaso-occlusive crisis and multiple organ damage are the most common complications of SCD. Because of its multifunctional role in inflammation, endothelial dysfunction, and fibrosis, TGF-β1 could be involved in SCD development, which may explain a variety of symptoms associated with this disease. This study aimed to investigate the role of TGF-β1 as a non-invasive biomarker for predicting the types of SCD clinical manifestations.

Method: The level of TGF-β1 in serum was measured using the ELISA method in 98 SCD patients and 98 healthy individuals without any history of hemoglobinopathies, who served as the control group. Moreover, a questionnaire was completed for each patient to determine the type of clinical symptoms they experienced.

Results: The laboratory parameters including hemoglobin, RBC, HCT, MCV, and MCH were lower in SCD patients compared to the control group, and WBC, RDW-CV, platelet count, MPV, and LDH were higher in these patients. No significant correlation was observed between laboratory parameters and TGF-β level ($p>0.05$). The serum TGF-β1 level was higher in patients but there was no significant correlation between TGF-β_1 level and type of clinical symptoms in these patients.

Conclusion: We observed a higher prevalence of certain complications in SCD patients in the Arab population of Khuzestan Province. There was no significant correlation between the clinical manifestation of SCD and TGF-β_1.

keywords: Sickle Cell Disease, Clinical Manifestation, Hematological Biomarkers, Transforming Growth Factor

PH-84

Mesenchymal Stromal Cell-Derived Extracellular Vesicles: Novel Approach in Hematopoietic Stem Cell Transplantation

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Abstract

Background and Aim: Bone marrow mesenchymal stromal cells (MSCs) play a crucial role in the regulation of hematopoiesis. These cells affect the process through direct cell-cell contact, as well as releasing extracellular vehicles (EVs) into the bone marrow microenvironment (BMM). MSC-derived EVs are prominent intercellular communication tolls enriched with broad-spectrum bioactive factors. They mimic some effects of MSCs by direct fusion with hematopoietic stem cells (HSC) membranes in the BM, thereby affecting HSC destiny. Due to the capacity of these vesicles in proliferation and differentiation of HSCs, MSC-EVs have been considered as a useful and efficient tool in hematopoietic stem cell transplantation (HSCT).

Methods: In the present review study, the authors investigated numerous articles over the past two decades which have been published in terms of the roles of MSC-derived EVs in the biology of HSCs.

Results: The review of various articles showed that MSCs exert their paracrine impacts through secreting different types of vesicles. MSC-derived EVs support HSCs homing, proliferation, self-renewal, and differentiation in the bone marrow, whereas suppress HSCs apoptosis.

Conclusion: Recent studies have demonstrated that MSC-derived EVs play an influential role in the BMM because of their unprecedented capacity to regulate HSC fate; therefore, the existing paper intends to speculate upon the preconditioned MSC-derived EVs as a novel approach in HSCT.

Keywords: Mesenchymal Stem Cells, Hematopoietic Stem Cells, Extracellular Vesicles

PH-85
CAR-T Cell Therapy and Oncolytic Virotherapy: A Combination Strategy for Hematological Malignancies

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Abstract

Background and Aim: Innovative approaches such as CAR-T cell therapy and oncolytic virotherapy are currently being tested for treating hematological malignancies. Treating these diseases with these methods has its pros and cons. This review aims to investigate the potential and challenges of these approaches and the combination of them.

Methods: Data were collected from multiple databases, including PubMed, Scopus, and Web of Science using specific keywords, including CAR therapy, hematological malignancies, and Oncolytic viruses. A total of 2840 articles was collected and 120 of them were selected using expert panels. Studies evaluating the use of CAR therapy and virotherapy with oncolytic viruses in hematologic malignancies were investigated.

Results: Multiple studies indicated that both techniques indicated promising results in tests on mice with normal and weakened immune systems as well as in human trials. CAR-T cell products targeting CD19 have shown significant success in treating B cell lymphomas and leukemias, while the use of oncolytic viruses has led to strong outcomes in melanoma and nasopharyngeal carcinoma patients. Despite that, the efficacy of using virotherapy is limited due to the immune response against viral antigens, especially in cancer patients undergoing therapies, who typically have weakened immune systems. In addition, the primary obstacles encountered by the existing CAR-T cell therapy configurations encompass the absence of targetable surface antigens specific to tumors, the heterogeneity of tumor cells, and the immunosuppressive tumor environment, along with the high expenses. It seems some challenges can be solved by merging the two methods.

Conclusion: There were reports of success in the combination of CAR-T cell therapy and oncolytic virotherapy. In case of a local inflammatory response from the virus, immune suppression in tumors could be reversed, following CAR-expressing lymphocytes to penetrate easily into the tumor. The combination of viral and CAR-induced cytotoxicity can present tumor neoantigens effectively and stimulate the patient's immune cells to target tumor cells. Yet, more investigations about the combinations of CAR-based and virolytic approaches in hematology malignancies are needed.

Keywords: CAR-T cell therapy, Hematological malignancies, Oncolytic viruses, Oncolytic virotherapy

PH-86
Treatment of the Hemophilia B using CRISPR-Cas9 technology: A review

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Background and Aim: Hemophilia B (HB) is a genetic blood clotting disorder caused by mutations in coagulation factor IX (FIX). There are approximately 815,100 cases of hemophilia worldwide, with a prevalence of 1 in 25,000 in males. Although innovative treatments such as rebalancing therapy and biospecific antibody therapy have been introduced, hemophilia treatment still encounters two challenging limitations: The inability to achieve long-lasting therapeutic effects and the development of neutralizing antibodies against clotting factors. Advances in clustered regularly interspaced short palindromic repeat (CRISPR)-CRISPR-associated protein 9 (Cas9), which modifies target genes, have allowed lasting treatment. Therefore, we have reviewed and summarized relevant studies.

Methods: Multiple databases were searched, including PubMed, Google Scholar, Web of Science, Scopus, etc. Using the terms “CRISPR-Cas9”, “Hemophilia B” and “treatment”, relevant articles published since 2020 were selected and reviewed.

Results: According to one research conducted on the CRISPR-Cas9 technology, optimized CRISPR-Cas9 is a human F9 cassette that could be integrated into the ribosomal DNA (rDNA) region of mouse embryonic stem cells *ex vivo*. However, systemic delivery of the donor templates using CRISPR-Cas9 faces off-target effects, such as the lack of repair templates for a majority of the 3000 different types of aberrant F9 mutations leading to HB pathology. Another study was constructed on the CRISPR-Cas9 combined with single-stranded oligodeoxynucleotides (ssODNs) in a model of human induced pluripotent stem cells (hiPSCs) containing the F9-Padua mutation. After off-target screening, clones were differentiated into hepatocytes capable of secreting FIX with a higher activity. Engineered Cas9 (SpCas9-NG) recognizing NGN (single guanine) can modify various mutations. After the transplantation of hepatocyte-like differentiated cells into immunodeficient mice, SpCas9-NG corrected the mutation and production of FIX. Nonetheless, the clinical use of the mentioned methods requires further investigation.

Conclusion: HB is an X-linked, recessive disorder primarily affecting males. Besides, 30% of HB patients suffer from severe hemophilia, meaning the concentration of coagulation proteins in the blood is less than 1% of normal levels. Thus, to achieve an efficient treatment, hiPSCs modified with CRISPR-Cas9 are used to produce differentiated hepatocytes capable of secreting FIX with ameliorated function. These studies confirm that gene therapy using CRISPR-Cas9 can ease the way to reach the clinical treatment of HB.

Keywords: HB treatment, CRISPR-Cas9, gene therapy

PH-87

Emerging Blood-Based Biomarkers for the Diagnosis and Management of Rheumatoid Arthritis: A Systematic Review

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that leads to joint inflammation, pain, and function loss. While traditional biomarkers like rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) are commonly used, recent advances have identified novel blood-based biomarkers that offer improved diagnostic accuracy and potential for personalized treatment. This systematic review evaluates the emerging biomarkers in RA, focusing on their diagnostic and prognostic potential.

Methods: A comprehensive search of PubMed, Scopus, and Web of Science was conducted for studies published between 2000 and 2024. Studies were included if they evaluated blood-based biomarkers like 14-3-3η, S100A8/A9, fibronectin-aggrecan complex (FAC), and anti-PAD4 in RA. A total of 42 studies were included in the final analysis.

Results: 14-3-3η Protein: Elevated levels are linked to early RA diagnosis, joint erosion, and aggressive disease progression.

S100A8/A9 (Calprotectin): A reliable marker of synovial inflammation, it correlates with ultrasound findings and predicts disease flares.

Fibronectin-Aggrecan Complex (FAC): Found in early RA, FAC indicates cartilage degradation and is associated with joint matrix breakdown.

Anti-PAD4 Antibodies: Linked to severe disease courses and increased joint damage, they provide potential for RA stratification.

Conclusion: Emerging blood-based biomarkers like 14-3-3η, S100A8/A9, FAC, and anti-PAD4 offer more precise tools for diagnosing and monitoring RA. When combined with traditional markers, these biomarkers enable earlier diagnosis, better disease management, and personalized treatment strategies.

Keywords:

Rheumatoid arthritis, 14-3-3η, S100A8/A9, fibronectin-aggrecan complex, anti-PAD4, blood biomarkers, personalized medicine, disease progression

PH-88

The role of Dendritic cells in infertility and failed In Vitro Fertilization (IVF)

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Abstract

Background and Aims: Infertility and the low success rates of in vitro fertilization (IVF) are prominent concerns worldwide. Dendritic cells (DCs), as critical mediators between innate and adaptive immunity, function as antigen-presenting cells that either activate immune responses or promote immune tolerance. While their role in the pathogenesis of endometriosis—a major cause of infertility—has been well-documented, the mechanisms by which DCs influence fetal tolerance and successful pregnancy outcomes remain inadequately understood. This study aims to investigate these mechanisms.

Methods: A comprehensive literature review was conducted using PubMed and Google Scholar to identify relevant studies published between 2016 and 2024. The search included terms such as "endometriosis," "infertility," "in vitro fertilization (IVF)," "macrophages," "dendritic cells (DCs)," "B cells," and "T cells."

Results: The analysis revealed that DCs play a crucial role in establishing immune tolerance toward the fetus. An increase in dendritic tubercles correlates with higher rates of recurrent miscarriage. In endometriosis, the ratio of mature DCs to immature ones is reduced in endometrial tissue, significantly influencing lesion progression and prognosis. Furthermore, DC dysfunction disrupts regulatory T-cell activity and compromises immune system balance, contributing to adverse reproductive outcomes.

Conclusion: Given the central role of dendritic cells in regulating immune responses, further research into their functions and therapeutic modulation may provide new insights into improving infertility treatment and IVF success rates.

Keywords: endometriosis, infertility, In Vitro Fertilization, macrophages, dendritic cells (DC), B cells and T cells.

PH-89

The role of autoimmune-related genetic risk factors in the inhibitor development in patients with hemophilia: prognostic approach

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Abstract

Background and Aim: Hemophilia A and B are two of the most common bleeding disorders. Genetic risk factors are associated with the development of autoantibodies released in hemophilia patients, against alternative factors, and are the most important problems associated with the care of these patients. in this manuscript, we reviewed genetic risk factors that are related to autoimmunity in patients with hemophilia A and B who develop inhibitors against alternative factors, that increase the coherent in patients' management.

Methods: This study is based on PubMed database information (2016–2024) in English-language using the terms' inhibitor hemophilia', 'autoimmunity', and 'hemophilia'.

Results: Studies showed that multiple genetic factors (CTLA-4, *PTPN22, Cytokine polymorphisms,…)* increase the risk of producing an inhibitor against the alternative factors (8 and 9)in patients with severe hemophilia.

Conclusion: The presence of inhibitory antibodies in patients with severe hemophilia can be associated with autoimmune-related genetic risk factors, but several studies showed that in most cases, autoimmune disease-related polymorphisms (rs2476601 PTPN22, rs2069812 IL5, rs1800629 TNF-α), produce autoimmune antibodies or exacerbate them.

Keywords: Hemophilia, Autoimmune Antibody, Genetic, Inhibitor hemophilia, autoimmunity

PH-90

Plasma Calprotectin Level as a Potential Biomarker in Different Stages of Pediatric Hemato-Oncologic Malignancies

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Abstract

Background and Aim: Calprotectin has been known as a biomarker for systemic inflammation for many years, especially in autoimmune disorders. Inflammation is a process associated with malignant progression, and calprotectin is a potential prognostic biomarker in some hematologic malignancies. Our pilot study aimed to evaluate the plasma calprotectin level as a promising biomarker in the relapsed/refractory phase of pediatric hemato-oncologic malignancies.

Methods: This pilot research was a case-control study. A total of 168 individuals were included in the study. The analyses were conducted on 73 pediatric patients diagnosed with acute leukemia and 60 others with solid tumor cancers who had been referred to Ahvaz Shafa Hospital in Iran. The patients were subdivided based on the three phases of the disease, including on-treatment, relapsed/refractory, and remission phases. Also, 35 healthy children were considered as the control group. After consent was received from all the participants, their blood samples were collected in ethylene diamine tetra acetate (EDTA) tubes to measure plasma calprotectin levels by the enzyme-linked immunosorbent assay (ELISA) method.

Results: There was no statistically significant difference between plasma calprotectin levels in different stages of acute leukemia (P=0.099); however, the mean levels of studied groups were higher compared to healthy controls. This increase in the average calprotectin level was also observed in different stages of solid tumor cancers compared to the control group. Besides, a significant difference was also seen between the on-treatment and remission groups compared to the control group, respectively (p=0.011, p=0.016).

Conclusion: The mean plasma calprotectin levels increase in different phases of some pediatric hemato-oncologic malignancies, but it cannot be used as a specific biomarker for the relapsed/refractory phase. Further investigations with a larger sample size are needed to decisively speak on this issue.

Keywords: Calprotectin, S100A8, S100A9, Biomarker, Relapse, Acute Lymphoblastic Leukemia, ALL.

PH-91

The significant effect of vitamin D on myeloid malignancy

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Abstract

Background and Aim: Vitamin D, a fat-soluble vitamin synthesized in the skin through sun exposure, is essential for numerous physiological processes, including bone health. Recent research links vitamin D deficiency to increased risks of autoimmune diseases and cancers. This study focuses on its role in myeloid disorders diseases affecting bone marrow and blood characterized by abnormal blood cell production. Researchers examined the relationship

between vitamin D levels and the severity, treatment response, and survival outcomes in patients with these disorders. Findings aim to shed light on how vitamin D influences the pathogenesis and progression of myeloid disorders, offering potential insights for improved management strategies.

Methods: A comprehensive literature search was conducted using PubMed and Google Scholar to identify relevant articles published in the past five years. The search terms included "AML" "Vit D" " acute myeloid leukemia" and " calcitriol".

Results: In vitro, calcitriol promoted differentiation of myeloid cells into mature phenotypes and increased apoptotic rates in leukemic blasts. Clinically, higher serum vitamin D levels were associated with improved overall survival and reduced progression rates in patients with AML. These findings were significant after adjusting for disease severity and treatment regimens.

Conclusion: This study will provide valuable insights into the role of vitamin D in the pathogenesis and progression of myeloid disorders. Understanding the impact of vitamin D deficiency on these diseases may lead to the development of novel therapeutic strategies, such as vitamin D supplementation, to improve patient outcomes. Further research is needed to elucidate the underlying mechanisms and to establish optimal vitamin D dosing and treatment duration for patients with myeloid disorders.

Keywords: AML; acute myeloid leukemia; Vit D; calcitriol.

PH-92

Proteomic Analysis in Identifying New Therapeutic Targets for Blood Cancer: a key to the locked doors.

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Background and Aim: Hematological malignancies, such as Leukemia, lymphoma, and multiple myeloma, show A wide range of complex molecular changes. These changes make it

challenging to find an effective therapy, and some new methods seem to be needed in this situation. As proven by many studies, Proteomics looks to be the missing key in identifying biomarkers and therapeutic targets. Insights into disease mechanisms can be provided by This powerful tool, which enables the advancement of personalized medicine. This review is meant to review the role of proteomic analyses in order to discover therapeutic targets for blood cancers.

Methods: This study conducted a comprehensive literature search in PubMed for articles published between 2000 and 2024 using keywords such as “proteomics,” “mass spectrometry,” “phosphoproteomics,” and “hematological malignancies.” Of the 185 studies retrieved first, 62 were selected based on their relevance to proteomic applications in therapeutic target identification. In order to extract key findings, Open-access articles with available full texts were reviewed with an emphasis on translational and clinical relevance to this subject. Prioritizing studies with advanced techniques such as tandem mass spectrometry and reverse-phase protein arrays (RPPA) was the other technique to prepare an on-point review of this topic.

Results: NF-κB and JAK/STAT, and other Critical dysregulated pathways are highlighted by reviewing Proteomic studies. These signaling pathways often are involved in blood cancer pathogenesis. According to biomarker analyses, Proteins such as S100A4 and IDH2 are possible candidates for therapeutic targets. By summing up the proteomic information with genomics and transcriptomic data, a better understanding of post-translational modifications and their roles in disease progression can be achieved. Many of these findings focus on the proteomics potential to guide combination therapies and develop accurate strategies to fight cancers. A noticeable sensitivity and specificity in detecting molecular targets are detected from Advanced proteomic technologies, leading the way into clinical implementation.

Conclusion: Identification of novel therapeutic targets and biomarkers in blood cancers by using Proteomic analyses seems to be highly promising. This review investigates the remarkable potential of proteomics in developing precision medicine by using molecular stratification and targeted therapies. However, turning these findings into clinical practice needs detailed confirmation in different patient cases and the standardizing proteomic workflows. Ongoing technological advancements are expected to enhance the clinical utility of proteomic approaches further, ultimately improving patient outcomes in hematological malignancies.

Keywords: Proteomics, Hematological malignancies, Therapeutic targets, Mass spectrometry, Precision oncology.

PH-93

The significant effect of vitamin D on lymphoma malignancy

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Abstract

Background and Aim: Vitamin D, known for its role in calcium metabolism, has been increasingly recognized for its immunomodulatory properties. Evidence suggests that vitamin D deficiency may contribute to immune dysregulation and influence the pathophysiology of

lymphoid disorders, including lymphoma and chronic lymphocytic leukemia (CLL). However, the mechanisms underlying these effects and their clinical implications remain inadequately understood. This study aimed to investigate the impact of vitamin D on lymphoid cell function and disease progression in lymphoid disorders, exploring its potential as a therapeutic adjunct.

Methods: A comprehensive literature search was conducted using PubMed and Google Scholar to identify relevant articles published in the past five years. The search terms included "CLL" "Vit D" " chronic lymphocytic leukemia" and " calcitriol".

Results: Vitamin D treatment resulted in a dose-dependent decrease in lymphoid cell proliferation and an increase in apoptosis. Cytokine profiling revealed a shift toward an anti-inflammatory phenotype. In the animal model, vitamin D supplementation delayed disease progression and improved survival. The retrospective clinical analysis demonstrated that patients with sufficient serum vitamin D levels had better overall survival and reduced disease-related complications compared to those with deficiency.

Conclusion: The findings suggest that vitamin D exerts beneficial effects in lymphoid disorders by modulating immune responses and inhibiting malignant cell proliferation. These results underscore the potential of vitamin D as a cost-effective, non-invasive therapeutic adjunct. Further prospective clinical trials are warranted to validate these findings and establish optimal supplementation strategies.

Keywords: CLL; chronic lymphocytic leukemia; Vit D; calcitriol.

PH-94

The effect of microcytic red blood cells on platelet count in a thalassemia patient

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Abstract

Background and Aim: As platelet count is one of the valuable laboratory tests for disease diagnosis, its errors, such as the upper discrimination for the platelet volume distribution (PU) flag, could cause problems and misdiagnosis. Blood cell histogram evaluation can come close to overcoming the limitations of the platelet counting test.

Methods: In this study, a 36-year-old thalassemia minor male presented with the symptoms of fever and myalgia. Petechiae and purpura were observed in the patient's lower extremities in the physical examination. Nihon Kohden Celltac G and Sysmex XP-300 cell counters were used to report the platelet count, which was reported to be 10000/µL and 129000/µL, respectively. However, the peripheral blood smear (PBS) assessment confirmed that the result of the Sysmex XP-300 cell counter was wrong, and a platelet flag was seen. This situation can be corrected by the complete blood count (CBC) histogram and PBS evaluation.

Results: Sysmex XP-300 cell counter's inability to differentiate severely microcytic cells from platelets can cause the PU error, which means the severe microcytic red blood cells (RBCs) were counted as platelets, causing the platelet count to be reported higher than the actual number for this patient. The PU flag means the platelet histogram intersects the PU line without touching the zero baselines, which occur in conditions such as platelet clumps, giant platelets, microcytic, and fragmented or dysplastic RBCs. In the Nihon Kohden Celltac G cell counter, this error was prevented due to the change in the PU line, and the patient's actual platelet count was reported. To avoid such errors, abnormal platelet counts should always be confirmed with the findings of PBS.

Conclusion: Poikilocytosis, such as microcytic RBCs and, can cause the PU flag, so platelet and erythrocyte histograms and PBS evaluation should be assessed.

Keywords: Sysmex XP-300, Nihon Kohden Celltac G cell counter, Platelet count

PH-95

The Role of MicroRNAs in Cancer Progression and Metastasis

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Abstract

Background and Aim: MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression and have emerged as critical players in cancer biology, particularly in progression and metastasis. This systematic review aims to consolidate current knowledge regarding the specific miRNAs involved in cancer cell migration and metastasis. To identify and summarize the role of specific miRNAs in cancer progression and metastatic processes across various cancer types.

Methods: A comprehensive literature search was performed across several major scientific databases, including PubMed, Scopus, and Web of Science. The search utilized a range of keywords focused on "miRNA," "cancer progression," and "metastasis" to identify relevant research articles. After an initial review, a larger pool of articles was screened, which included both primary research and review articles. Studies were then meticulously selected based on rigorous empirical evidence demonstrating the association of specific microRNAs with key processes involved in cancer cell migration, invasion, and metastatic behavior. Inclusion criteria were established to ensure relevance and quality, focusing on studies published between 2010 and 2023. After applying these criteria, a total of 45 pertinent studies were identified for in-depth analysis, providing a robust foundation for examining the critical roles of miRNAs in cancer metastasis.

Results: The findings indicate that among the specifically highlighted miRNAs in this review are **miR-200, miR-21,** and **miR-34**, which have been selected due to their critical roles in processes such as epithelial-mesenchymal transition (EMT), cell migration, and invasion, significantly influencing metastatic behavior in various cancer types. Dysregulation of these miRNAs has been consistently associated with enhanced migratory and invasive capabilities in multiple cancer types, including breast, lung, and colorectal cancers.

Conclusion: This review underscores the pivotal role of miRNAs in cancer metastasis, highlighting their potential as therapeutic targets and diagnostic biomarkers. Further investigations are necessary to explore their therapeutic implications and the mechanisms through which they modulate metastatic behavior in cancer cells.

Keywords: miRNA, cancer progression, metastasis, epithelial-mesenchymal transition, therapeutic targets.

PH-96

The potential of piRNAs as a predicting and prognostic biomarker in Multiple Myeloma

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Abstract

Background and Aim: Among hematological malignancies, multiple myeloma(MM) is the second most prevalent disease. The rise in medication resistance calls for more research into

the pathophysiology of MM. PiWI-interacting RNAs(piRNAs) are a recently identified class of short non-coding RNAs (ncRNAs) and are composed of 26–30 nucleotides with a 2′-O-methyl at the 3′-terminal and a uridine base at the 5′-terminal or an adenosine base at the tenth position. The function of piRNA in MM and endothelial cell intercellular communication is poorly understood. In this study, we discuss the role of piRNAs in multiple myeloma progression and metastasis as well as its molecular mechanisms.

Methods: In this review, articles were collected from PubMed, Scopus and web of science databases, published between 2010 to 2024. These databases were searched using the keywords of multiple myeloma, piRNA, piwi RNA, Epigenetic regulations.

Results: According to the findings of earlier studies, piRNA-823 plays a part in MM and is primarily found in EVs formed from MM cells (MM-derived-EVs) and the peripheral blood of MM patients. Increased piRNA-823 expression was associated with late stages and poor prognosis of MM. The piRNA-823 mimic and inhibitor were designed to upregulate or to suppress the endogenous function of piRNA-823.

piRNA-823 up-regulates the expression of glucose-6-phosphate dehydrogenase (G6PD) and inhibits the amount of intracellular reactive oxygen species (ROS). This prevents the ubiquitination of hypoxia-inducible factor-1 alpha (HIF-1α).

Additionally, PIWI-interacting RNA-004800 (piR-004800) is another piRNA implicated in MM and is overexpressed in early MM cells as well as exosomes from bone marrow supernatant from MM patients. There is a positive correlation between the phases of MM and the expression level of piR-004800. According to earlier research, the sphingosine-1-phosphate receptor (S1PR) signaling pathway is essential for the growth of MM cells.

Conclusion: Taken together, our data point to piR-004800 and piRNA-823 playing an oncogenic role in MM, providing insight into a novel mechanism that could lead to therapeutic approaches for MM.

Keywords: multiple myeloma; piRNA; piwi RNA; Epigenetic regulations.

PH-97

The potential roles of ncRNA encoded peptides in hematological malignancies

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Abstract

Background and Aim: Hematologic malignancies are a very diverse group of disorders related to the blood and bone marrow. The pathophysiology of hematologic malignancies has been linked to the aberrant expression of several non-coding RNAs (ncRNAs). Meanwhile, it has been found that some ncRNAs can encode small peptides or micropeptides due to the

development of proteomics and translation technology. They are involved in several aspects of cancer. The aim of this study was to review the all ncRNA-encoded peptide in hematological malignancies and their potential roles in progression and protection.

Methods: At the present review, articles in PubMed, Scopus and web of science were searched with the following terms: leukemia, hematological malignancy, noncoding RNA, encode, peptide either alone or in a combination form. The search was without time limitation and all English articles which was relevant to our aims, were selected.

Results: After reviewing the published articles in the mentioned databases, we found 4 ncRNA with peptide secretion potential. APPLE is a kind of lncRNA transcript in acute myeloid leukemia (AML); this peptide can regulate the initiation step of translation by promoting PABPC1-eIF4G interaction, mRNA circularization, and eIF4F initiation complex. In addition, circHNRNPU_603aa and circCHEK1_246aa are peptides which secrete from circRNA involved in Multiple Myeloma; circHNRNPU_603aa encoded by circHNRNPU could significantly increase the growth rate of tumor cells. circHNRNPU-603aa mediates SKP2 selective splicing and competitively inhibits c-Myc ubiquitination, thereby up-regulating the splicing isomers of circHNRNPU603aa and SKP2-NM_001243120. CircCHEK1_246aa interacts with CEP170, and by upregulate NFATc1 expression, leading to MM cell proliferation, drug resistance, and bone disease formation. Recent research has found that CLLU1, a lncRNA, can encode a short peptide similar to interleukin-4. Its abnormally elevated expression is only found in chronic lymphoid leukemia, indicating malignant pathological features and poor prognosis.

Conclusion: In conclusion, the present understanding of proteins encoded by circRNAs and lncRNAs in hematologic malignancies is comprehensively summarized in this review. In addition to discussing their diverse functions in controlling RNA and protein metabolism, this review emphasizes their potential for targeted therapy, disease prediction, and cancer diagnostics. In order to further study in this area, this review attempts to provide new insights and perspectives.

Keywords: leukemia; hematological malignancy; noncoding RNA; encode; peptide.

PH-98

Analysis of acute myeloid leukemia using cytogenetics and CRISPR; from diagnosis to treatment

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Abstract

Background and Aim: Acute myeloid leukemia (AML) is characterized by uncontrolled proliferation of myeloid progenitor cells in the bone marrow. Genetic analysis plays a crucial role in the understanding, diagnosis and treatment of acute myeloid leukemia (AML). Among the various methods used, cytogenetics and CRISPR technology stand out for their contributions to the elucidation of the genetic basis of AML. This review article summarizes

the findings on the application of these techniques, focusing on their diagnostic relevance and therapeutic potential.

Methods: Articles available in Scopus, PubMed and Web of Science from 2000 to 2024 with the keywords Acute Myeloid Leukemia, Cytogenetics, , CRISPR/Cas9, Genome Editing in the title/abstract for the main topics were used for this study. The study was conducted according to PRISMA guidelines. Articles were selected based on the exclusion criteria and included in the study after review.

Results:

Following the removal of duplicate articles, 374 results were accepted for screening, and a certain number of studies were included in the final analysis. The flexibility of CRISPR technology has inspired research into targeted therapies, particularly in acute myeloid leukemia (AML). Researchers focus on enhancing the sensitivity of AML cells to existing treatments by modifying genes associated with drug resistance and poor prognosis. Notably, targeting the RUNX1-RUNX1T1 fusion gene in AML patients with the t(8;21) mutation has demonstrated significant potential in experimental models, leading to reduced cell growth and tumor volume in vivo. Cytogenetic studies serve as a cornerstone in diagnosing AML, with karyotyping enabling the detection of chromosomal abnormalities. In contrast, CRISPR technology provides new insights into the genetic underpinnings of AML, facilitating precise genomic modifications that enhance modeling of the disease and identification of potential therapeutic targets.

Conclusion: Genetic analysis of AML using cytogenetics and CRISPR technology is a promising approach for the diagnosis and treatment of this complex disease. By harnessing the power of both modalities, physicians can improve patient outcomes through precision medicine approaches by customizing therapies based on genetic profiles. Ongoing research and ethical considerations will shape the future landscape of AML treatment, ultimately leading to more targeted therapies and better survival rates for patients.

This review highlights the need to combine cytogenetic insights with advanced genome editing technologies to advance in the fight against AML.

Keywords: Acute Myeloid Leukemia, Cytogenetics, , CRISPR/Cas9, Genome Editing

PH-99

Proteomic Analysis in Identifying New Therapeutic Targets for Blood Cancer: a key to the locked doors.

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Abstract

Background and Aim: Hematological malignancies, such as Leukemia, lymphoma, and multiple myeloma, show A wide range of complex molecular changes. These changes make it challenging to find an effective therapy, and some new methods seem to be needed in this situation. As proven by many studies, Proteomics looks to be the missing key in identifying biomarkers and therapeutic targets. Insights into disease mechanisms can be provided by This powerful tool, which enables the advancement of personalized medicine. This review is meant to review the role of proteomic analyses in order to discover therapeutic targets for blood cancers.

Methods: This study conducted a comprehensive literature search in PubMed for articles published between 2000 and 2024 using keywords such as "proteomics," "mass spectrometry," "phosphoproteomics," and "hematological malignancies." Of the 185 studies retrieved first, 62 were selected based on their relevance to proteomic applications in therapeutic target identification. In order to extract key findings, Open-access articles with available full texts were reviewed with an emphasis on translational and clinical relevance to this subject. Prioritizing studies with advanced techniques such as tandem mass spectrometry and reverse-phase protein arrays (RPPA) was the other technique to prepare an on-point review of this topic.

Results: NF-κB and JAK/STAT, and other Critical dysregulated pathways are highlighted by reviewing Proteomic studies. These signaling pathways often are involved in blood cancer pathogenesis. According to biomarker analyses, Proteins such as S100A4 and IDH2 are possible candidates for therapeutic targets. By summing up the proteomic information with genomics and transcriptomic data, a better understanding of post-translational modifications and their roles in disease progression can be achieved. Many of these findings focus on the proteomics potential to guide combination therapies and develop accurate strategies to fight cancers. A noticeable sensitivity and specificity in detecting molecular targets are detected from Advanced proteomic technologies, leading the way into clinical implementation.

Conclusion: Identification of novel therapeutic targets and biomarkers in blood cancers by using Proteomic analyses seems to be highly promising. This review investigates the remarkable potential of proteomics in developing precision medicine by using molecular stratification and targeted therapies. However, turning these findings into clinical practice needs detailed confirmation in different patient cases and the standardizing proteomic workflows. Ongoing technological advancements are expected to enhance the clinical utility of proteomic approaches further, ultimately improving patient outcomes in hematological malignancies.

Keywords: Proteomics, Hematological malignancies, Therapeutic targets, Mass spectrometry, Precision oncology.

PH-100

Aptamers: Potential Diagnostic and Therapeutic Agents for Blood Diseases: A systematic review

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Abstract

Background and Aim: Aptamers, synthetic molecules which had been reported playing pivotal role as an important tool in medical management approaches in recent decade, have more scalability, stability, the capacity of binding to different functional groups, and cost-efficient mass production in comparison to monoclonal Abs. Similar to all cancers, early detection of hematologic malignancies is crucial in survival prediction. The aforementioned superiority of aptamers, make them incredible for application in diagnostic, treatment, and complication of leukemia, lymphoma and multiple myeloma. Therefore, the aim of this study was to review the potential applications of aptamers in managing hematologic malignancies.

Methods: The focus of this systematic review was on human participants randomized controlled trials (RCTs). Articles were identified through PubMed, Google Scholar, and ScienceDirect databases using keywords such as Aptamers, blood disorders, Acute Lymphoid Leukemia, Multiple Myeloma, and Lymphoma. Studies published between January 2020 and November 2024 were considered in the review. In the first step of the search 204 articles were found; 196 of them were eliminated after screening of titles and abstracts for review format or irrelevantness. Finally, eight published studies ultimately satisfied the requirements for inclusion.

Results: Eight articles were included in the study. Aptamers showed significant potential in diagnosing and treating hematologic disorders. For example, CD38 and Anti-CXCL12 Spiegelmer (NOX-A12) were reported to be beneficial for early-stage MM diagnosis, while AS1411 and CD117 help detecting AML in patients. ZW25 aptamer played role in prevention of tumor development and delivers doxorubicin to CD123+ AML cells. Tb3+-aptamer was effective in managing acute lymphoblastic leukemia. Aptamers targeting lymphoma markers like CD30, CD19, and CD20 were accurate and effective. Moreover, aptamers reduced chemotherapy's adverse effects by enabling targeted drug delivery.

Conclusion: Aptamers offer a path toward individualized molecular therapy and are a potential developmental strategy for the diagnosis and treatment of blood-related diseases. However, more cellular, preclinical, and large population-based clinical trials are needed to investigate the most appropriate and efficient aptamers in each stage of different hematologic malignancies.

Keywords: Aptamers; Blood Disorders; Acute Lymphoid Leukemia; Multiple Myeloma; Lymphoma

PH-101

Pseudo Thrombocytopenia Due to Platelet Cold Agglutination

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Abstract

Background and Aim: Platelet cold agglutination (PCA) is a rare in-vitro phenomenon caused by Immunoglobulin M (IgM) autoantibodies, resulting in pseudo thrombocytopenia (PTCP). The aim of this case report is to highlight the importance of correctly diagnosing PCA to prevent unnecessary medical interventions.

Methods: The diagnosis was made based on peripheral blood smear (PBS) examination and pre-test warming of the blood sample. The patient's blood was tested using EDTA and sodium citrate anticoagulants, and the sample was warmed to 37°C before retesting with a Mindray BC-6000 automated cell counter. Rheumatologic tests were also performed.

Results: A 26-year-old male undergoing pre-surgical tests initially presented with a low platelet count of 23 × 109/L. PBS examination revealed extensive platelet aggregates. After warming the blood sample to 37°C, the platelet count increased dramatically to 216 × 109/L. Rheumatologic tests were mostly negative, with only HLA-B27 showing positive results.

Conclusion: The patient was diagnosed with PCA, which is caused by a clinically insignificant cold antibody. This case emphasizes that, PCA-associated antibodies cannot function at body temperature and are therefore clinically insignificant. Proper diagnosis involves careful examination of peripheral blood smears (PBS) and pre-warming blood samples to obtain accurate platelet counts. This case underscores the critical need to differentiate between genuine thrombocytopenia and pseudo thrombocytopenia to prevent unnecessary medical procedures such as platelet transfusions, splenectomy, or invasive diagnostic tests.

Keywords: Platelet cold agglutination (PCA), Pseudo thrombocytopenia (PTCP), Peripheral, Immunoglobulin M

PH-102

CRISPR/Cas9 and Beta-Thalassemia: Could it be a promising treatment for beta-thalassemia?

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ABSTRACT

Background and Aim: Beta thalassemia is the most prevalent inherited anemia, resulting from reduced or absent beta globin production. The primary clinical forms are beta thalassemia major and intermedia, with patients typically showing symptoms like pallor and growth issues between 6 to 24 months of age. Treatment usually involves regular blood transfusions. The advent of CRISPR-Cas9, a bacterial immune system tool, has revolutionized genetic research by enabling precise DNA editing. This technique allows for quick and cost-effective modifications in living organisms, significantly speeding up experiments compared to traditional methods that could take years.

Methods: This review article was conducted using articles published in PubMed, ScienceDirect, Google Scholar, SID, and Web of Science until October 2024. The keywords were CRISPR-Cas9 AND gene editing AND beta thalassemia. All articles were chosen from English and Persian sources.

Results: CRISPR-Cas9 technique, by impacting BCL11A, led to gene editing and improvement in transfusion-dependent thalassemia (TDT) patients and demonstrated promising results in the treatment of these patients. One study reported two patients with TDT, after targeting BCL11A and CD34 gene by CRISPR-Cas9, exhibited significant allele editing in bone marrow and an increase in fetal hemoglobin (HbF) levels after one year. Another investigation involving two TDT patients by modulation of BCL11A gene, revealed notable clinical improvements 18 months post-treatment. Furthermore, a broader study involving 12-35 years TDT patients; indicated that 91% of participants no longer required blood transfusions following CRISPR-Cas9 intervention. In another study, researchers investigated the results of gene editing by hemoglobin electrophoresis; they targeting the BCL11A and HBG1/2 genes, resulted in highest levels of hemoglobin, respectively 39.5% and 41.5%. These findings highlighted the CRISPR-Cas9 as a therapeutic approach for more effective treatment options in severe hemoglobinopathies.

Conclusion: In conclusion, it was found that CRISPR-Cas9, by targeting the BCL11A and HBG1/2 genes, has been identified as the most promising option for increasing fetal hemoglobin (HbF). However, recent studies have shown that HBG1/2 is a relatively more promising genetic target for managing beta thalassemia compared to BCL11A.

Keywords: CRISPR-Cas9, Gene Editing, Beta Thalassemia

PH-103

Title of Abstract: *"Clinical Significance of Erythrocyte Sedimentation Rate (ESR): A Review"*

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Abstract

The erythrocyte sedimentation rate (ESR) is a commonly used hematologic test that quantifies the rate at which red blood cells are deposited within a vertical column of blood over a period of time. The article discusses the underlying physiological processes that govern ESR and provides insights into its utility as an inflammatory marker that helps physicians detect and treat various diseases, including infections, autoimmune diseases and malignancies. This article provides an overview of erythrocyte sedimentation rate (ESR), including a discussion of the limitations associated with the methods used to measure ESR and an examination of the various causes of elevated and decreased ESR levels. In addition, the performance and interpretation of erythrocyte sedimentation rate (ESR) tests at the bedside and the various elements that can lead to bias in the results are explained.

Background and Aim

This review article looks at the erythrocyte sedimentation rate in modern medicine and its importance as an essential inflammatory marker for diagnosing various diseases and inflammations. The study also discusses the limitations of this marker and the progress made with it.

The aim of our study is to compare different ESR methods and their different clinical applications.

Result

This article provides an overview of erythrocyte sedimentation rate (ESR), including a discussion of the limitations associated with the methods used to measure ESR and an examination of the various causes of elevated and decreased ESR levels. In addition, the performance and interpretation of erythrocyte sedimentation rate (ESR) tests at the bedside and the various elements that can lead to bias in the results are explained.

CONCLUSION

Erythrocyte sedimentation rate (ESR) remains a widely used, cost-effective, and non-invasive diagnostic tool in clinical practice. Despite being a century-old test, its utility persists due to its simplicity and broad applicability in detecting inflammation and monitoring disease progression. This review highlights the clinical significance of ESR in a wide array of conditions, including infectious, autoimmune, and malignant diseases. However, ESR is not without limitations; it is influenced by numerous physiological and pathological factors, necessitating its interpretation in conjunction with clinical findings and other diagnostic markers.

Advancements in molecular and imaging technologies have led to the development of more specific and sensitive diagnostic tools, yet ESR continues to serve as a valuable initial screening and monitoring tool, particularly in resource-limited settings. Future research should focus on improving the specificity of ESR, exploring its integration with modern biomarkers, and better defining its role in personalized medicine. By doing so, ESR can continue to provide significant insights into patient care while adapting to the evolving landscape of modern diagnostics.

Keyword: ESR, erythrocyte sedimentation rate, laboratory test, inflammatory diseases, diagnostic marker

PH-104
The Application of Liquid Biopsy in Diagnostic and Treatment of Hematological Malignancy

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Abstract

Background and Aim: Hematologic malignancies, including leukemia, lymphoma, and myeloma, are the most common cancers in children and young adults. A liquid biopsy is a non-invasive method for diagnosing and monitoring diseases by analyzing body fluids, primarily blood. It detects genetic mutations, cell-free DNA (cfDNA), circulating tumor DNA (ctDNA),

and circulating tumor cells (CTCs). Liquid biopsies offer real-time disease monitoring, treatment response tracking, and early cancer detection, making them essential for personalized medicine and minimal residual disease (MRD) assessment.

Methods: This review was conducted through a comprehensive literature search of PubMed, Google Scholar, and Web of Science databases for all studies on Liquid Biopsy in Hematologic Malignancy published from December 2019 to June 2024. These databases were searched using the keywords of Liquid Biopsy, circulating tumor DNA, and cell free DNA.

Results: Tumor biopsy is the gold standard for assessing somatic mutations but is invasive and limited in addressing tumor heterogeneity. Liquid biopsies, in contrast, are non-invasive, rapid, and provide real-time insights. Circulating Tumor DNA analysis in liquid biopsy reflects the mutational profile of tissue biopsy and can detect mutations absent in tissue samples. Methods for detecting ctDNA/cfDNA include droplet digital PCR (ddPCR), BEAMing, TAm-Seq, CAPP-Seq, WGBS-Seq, WES, and WGS, which are used for genotyping and monitoring treatment responses. Techniques like immunogenicity-based methods and biophysical property-based enrichment are employed for circulating tumor cell (CTC) detection. Circulating Tumor DNA analysis, especially from plasma, is widely used for monitoring hematological malignancies and assessing minimal residual disease (MRD). In healthy individuals, cfDNA concentrations in plasma range from 1 to 16.8 ng/ml, with levels rising in conditions like exercise, trauma, or infection. In cancer patients, cfDNA levels increase due to the release of tumor cell fragments.

Conclusion: Circulating Tumor DNA analysis from liquid biopsies is increasingly used in hematological malignancies for tumor genotyping, outcome prediction, and monitoring therapy. Technological advancements have integrated standard molecular profiling with liquid biopsy, enhancing biomarker detection. Ongoing clinical trials are using ctDNA to tailor treatments, marking a significant step toward precision medicine. Liquid biopsy offers a less invasive, dynamic approach to monitoring and treating hematological cancers.

Keywords: Liquid Biopsy; Hematologic Malignancy; ctDNA; cfDNA; CTC.

PH-105

Microbiota and hematologic malignancies: a complex relationship.

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Abstract

Background and Aim: This comprehensive review explores the latest insights into the importance of microbiomes in hematological malignancies. Recent developments show a noticeable association

between gut microbiome and the development, prognosis, and treatment of leukemia, lymphoma, and multiple myeloma. Changing microbiota(dysbiosis) can happen because of these malignancies' pathological conditions and chemotherapies. The gut microbiome plays an important role in hematopoiesis and sends signals to hematopoietic stem cells and the bone marrow microenvironment, influencing various aspects of hematopoiesis. Dysbiosis may lead to potential tumor promotions and immune efficacies. Our analysis is meant to examine changes in gut microbiota in different types of hematologic cancers.

Methods: We performed a comprehensive literature search using major biomedical databases, mainly PubMed. We prioritized articles published in English within the past five years, with specific attention to recent advancements in understanding the cause-and-effect relationship between gut microbiota and leukemia and emerging microbiota-based approaches for reducing chemotherapy complications.

Results: The gut microbiome likely affects the incidence and development of leukemia through regulation of the immune system, stimulation of inflammation, infection by pathogenic bacteria, influence on overall metabolites and metabolism, and gene mutation. Bile acids and other Gut microbiome metabolites play a crucial mediating role in these relationships. Each type of leukemia shows a unique pattern of microbiome changes. For instance, patients with acute myeloid leukemia (AML) often show less diversity in their gut microbiota. At the same time, patients with AML undergoing induction chemotherapy lose diversity in their gut microbiome. On the other hand, chronic lymphocytic leukemia (CLL) patients may have increased levels of certain bacterial species. The gut microbiome affects the behavior of cancer cells through the production of different metabolites. These metabolites can be divided into two categories: promoters and inhibitors. Understanding these metabolites and their effects on cancer cells is crucial for developing new therapeutic approaches.

Conclusion: Overall, there is a complex and multifaceted association between the microbiome and hematologic malignancies. We can modify the gut microbiome by using microbiome-based treatments, such as prebiotics, probiotics, antibiotics, and fecal transplants, which can also affect leukemia. Understanding these mechanisms can reveal new ways to prevent or treat hematologic cancers. Recent studies have shown promising ways to diagnose, treat, and prevent leukemia by using the composition and diversity of the microbiome. However, there are still many significant challenges in converting this information into clinical practice.

Keywords: gut microbiome, dysbiosis, hematological malignancies

PH-106

LncRNA UCA1 as a biomarker for multiple myeloma: A systematic review

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Abstract

Background and Aim: Long non-coding RNAs (lncRNAs) are transcripts longer than 200 nucleotides that regulate proliferation and apoptosis by influencing oncogene and tumor suppressor gene expression. LncRNA UCA1, initially found in bladder cancer, is now a biomarker for multiple cancers like multiple myeloma (MM). MM is a hematologic cancer

marked by uncontrolled plasma cell proliferation. LncRNAs are therapeutic targets for understanding cancer biology and developing diagnostic and treatment strategies. Several studies have investigated the connection between lncRNA UCA1 and MM, but no definitive conclusions have emerged. A systematic review will be conducted on the relationship between lncRNA UCA1 and prognosis in MM patients.

Methods: This systematic review was conducted in the PubMed, Web of Science, Scopus databases, and Bentham Science using the keywords "Multiple Myeloma OR Plasma Cell Myeloma OR Kahler Disease OR Myelomatosis" AND "urothelial carcinoma associated 1 OR UCA1" AND "long Noncoding RNA OR lncRNA OR Long non-protein-coding RNA OR Long Non-Translated RNA" AND "prognostic OR prognosis OR outcome OR recurrence OR clinicopathological OR diagnosis OR survival". Human studies investigating the relationship between LncRNA UCA1 and prognosis in MM patients were included. The animal studies, meta-analyses, case reports, clinical trials, reviews, and non-English articles were excluded.

Results: Out of 55 articles reviewed, ٤ articles were included. Sedlarikova (2016) discovered reduced lncRNA UCA1 expression in 6 MM patients compared to 6 healthy donors (HD). Sedlarikova (2018) in another study measured lncRNA UCA1 Expression in serum exosomes 56 MM and 49 MGUS patients, and 36 HD. Unlike BM biopsies, liquid biopsies capture from all tumor sites. However, they found that lncRNA UCA1 wasn't released into the serum of any group. Yang (2019) found lncRNA UCA1 was up-regulation in 15 MM patients compared to 15 HD. lncRNA UCA1 Promotes proliferation and Suppresses apoptosis in MM by targeting lncRNA UCA1/miR-1271-5p/HGF axis. Li (2019) found up-regulation of lncRNA UCA1 in 35 MM patients compared to 20 HD. UCA1 enhances Proliferation and reduces Apoptosis by activating the JAK2/STAT3 pathway through the lncRNA UCA1/miR-331-3p/IL6R axis. Low UCA1 levels were linked to higher survival rates, while high levels indicated lower survival rates.

Conclusion: This study finds that lncRNA UCA1 is overexpressed in MM patients than healthy individuals, while one study shows reduced expression possibly due to a smaller sample size. UCA1 is associated with lower survival rates, promotes proliferation, and reduces apoptosis. These findings highlight UCA1's complex role in MM and its potential as a prognostic biomarker. However, further studies are required to confirm these results.

Keywords: Multiple myeloma; lncRNA UCA1; Biomarker; Diagnosis**,** Prognosis.

PH-107

A systematic review of gene therapy for hemophilia A and B

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Abstract

Background and Aim: Hemophilia is a blood disorder whose main characteristic is a deficiency in coagulation factor VIII or IX which cause hemophilia A and B. Unlike other treatment, gene therapy with a special method shows a bright future in the treatment of these patients. In this method, by

introducing a functional version of the defective gene in these patients using viral vectors, a long-term or even permanent treatment solution can be achieved. Our effort in this study is to show the effect of this method in the treatment of hemophilia and the future that this method has in front of these patients.

Methods: the data were sourced from PubMed, Scopus, and ClinicalTrials.gov using the search terms "hemophilia A," "hemophilia B" and "gene therapy". Out of the 20 studies identified in the initial search, 18 were included in the analysist that published from 2014 to 2024. The inclusion criteria mandated that studies involve human subjects, report clinical outcomes related to bleeding rates or factor expression levels, and provide safety information. Studies were excluded if they were not in English, were preclinical in nature, or lacked adequate follow-up (≥6 months).

Results: In investigations assessing gene therapies for hemophilia, significant and sustained efficacy was noted, characterized by marked reductions in annual bleeding rates and the utilization of factor concentrates. Fidanacogene elaparvovec led to a 71% decrease in bleeding episodes, with a mean factor IX activity recorded at 26.9% after 15 months. FLT180a exhibited dose-dependent enhancements in factor IX levels, with five patients reaching normal levels during a median follow-up period of 27.2 months. Valoctocogene roxaparvovec resulted in increased factor VIII activity, significantly lowering both bleeding incidents and the need for factor VIII concentrates. The safety profiles of these therapies included manageable adverse effects, such as temporary elevations in liver enzymes and immune responses, with serious adverse events being rare. Factor expression remained stable in the majority of participants; however, some individuals required immunosuppressive treatment or resumed prophylactic measures due to immune reactions.

Conclusion: The findings showed that gene therapy, leads to a significant increase in the level of coagulation factor VIII or IX, which leads to a decrease in annual bleeding in patients. this treatment shows stable hemostatic effectiveness. It is noteworthy that this method has been found to have challenges such as immune responses, variation in the expression of factors, and the spontaneous need to suppress the immune system in some cases, while the immune factors are generally favorable. This issue can be further investigated in future studies.

Keywords: hemophilia A ; hemophilia B ; gene therapy.

PH-108

Review on the efficacy and performance of different coagulometers

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Background and Aim: Coagulometers are vital tools in the medical and laboratory fields used for diagnosing and monitoring bleeding and coagulation disorders. Owing to their critical importance among laboratory instruments, present review was aimed to compare the efficiency of various coagulometers investigated in different studies.

Methods: We explored the internet in Google Scholar, Pubmed, Pubmed Central and Bing search engines using main key words including Coagulometer, accuracy, efficiency, diagnosis, PT, aPTT and fibrinogen. All the manuscripts after 2018 were included in the present review.

Results: Coagulometers vary in efficiency based on brand, power, and technology. The CP300 is versatile for lab use but needs optimization for aPTT and TT, while the CA-200 provides excellent accuracy in hypocoagulable conditions. High-end models like the Diagon Coag XL perform well overall but requires refinement in aPTT tests, and systems like QCM-D are highly accurate for fibrinogen. Portable models like Biolabo Solea 100 offer reliable results for PT, aPTT and fibrinogen for smaller labs.

Conclusion: Portable coagulometers can satisfy the diagnostic demands of most of the medical laboratories in contrary of high-end models for central labs. However, more advances technologies are warranted to address their calibrations challenges caused by environmental factors.

Keywords: Coagulometer, accuracy, efficiency, diagnosis

PH-109

Investigation of p21 Gene Expression in Acute Lymphoblastic Cells After Coculture with Platelet-Rich Plasma (PRP)

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Abstract

Background and Aim: T cell- Acute lymphoblastic leukemia is an aggressive hematological malignancy that arises from the transformation of T-cell progenitors. It accounts for 10–15% of pediatric and 25% of adult ALL cases. The P21 gene is a critical regulator of cell cycle progression and its expression can be indicative of cellular response to various stimuli, including regenerative factors found in platelet-rich plasma (PRP). Platelets are small discoid blood cells that are responsible for maintaining homeostasis and are derived from the cytoplasm of megakaryocytes. Platelets play a wide

range of roles in both health and disease. The quantity and quality of platelets are important in patients with acute leukemia and can predispose these patients to bleeding. Platelets are also associated with tumor metastasis, inflammation, and immune responses. Acute leukemia cells and platelets are found in common anatomical structures, and recent studies have shown that not only can acute leukemia cells affect platelets, but platelets can also affect these cells.

This study explores the effects of PRP on P21 gene expression in ALL cells (Jurkat cell line) to elucidate the potential impact of PRP on leukemia cell biology and its possible implications in therapeutic strategies.

Methods: This is an original study. Using a co-culture system, ALL (Jurkat cell line) cells were cultured and then exposed to PRP derived from healthy donors at doses of 10% and 20%, and subsequent changes in P21 expression were quantitatively assessed by real-time polymerase chain reaction (PCR).

Results: Our findings showed a significant decrease in p21 gene expression after interaction with PRP at a dose of 20% compared to the control group, indicating a link between PRP components and the regulation of cell cycle and apoptosis pathways in ALL cells.

Conclusion: In conclusion, the investigation into the expression of the p21 gene in acute lymphoblastic leukemia (ALL) cells following coculture with platelet-rich plasma (PRP) has provided promising insights into the potential role of PRP in modulating cancer cell behavior. Our results indicate that the addition of PRP to cultures of ALL cells results in a significant downregulation of the p21 gene at dose of 20%, a well-known cyclin-dependent kinase inhibitor implicated in the regulation of the cell cycle and tumor suppression. The observed downregulation suggests that components within PRP may influence cell cycle checkpoints and potentially induce a state of growth in leukemic cells. The specific pathways through which PRP affects p21 expression remain not to be fully elucidated. However, these findings raise important considerations for the development of novel therapeutic strategies. By harnessing the growth-regulatory properties of PRP, it may be possible to enhance the efficacy of existing treatments or devise new approaches to control the proliferation of ALL cells.

Keywords: Acute lymphoblastic leukemia; P21 gene expression; Platelet rich plasma (PRP)

PH-110

CRISPR-Cas9 Gene Therapy: Revolutionizing Treatment for Hemophilia A

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Abstract

Background and Aim:

Hemophilia A (HA) is an X-linked recessive disorder caused by mutations in the F8 gene, expressed in liver sinusoidal endothelial cells (LSECs), with an incidence of 1 in 5000 male births. HA patients experience spontaneous bleeding episodes, particularly in joints, internal organs, and intracranially, as well as excessive bleeding during surgery or trauma. Current treatments like FVIII protein injections and AAV-delivered F8 transgene therapies are costly and temporary. Genome editing offers a promising alternative by restoring endogenous

clotting factor production. This study reviews the CRISPR-Cas9-based in vivo genome editing method as a potential treatment for HA.

Methods: Using the terms “CRISPR-Cas9” and “hemophilia A”, relevant articles published up o 2023 were searched in databases including PubMed, Scopus, and Google Scholar.

Results: In the studies conducted, the researchers aimed to develop a gene therapy process for hemophilia A using CRISPR-Cas9 for precise modification of the F8 gene in mouse models, and with the successful restoration of F8 gene expression, it was determined that site-specific genome editing leading to permanent replacement of F8 in in vivo tests are efficient. Also, with long-term benefits of at least seven months, no evidence of hepatotoxicity or significant off-target effects was observed.

Conclusion: These findings indicate the potential of CRISPR-Cas9; the gene-editing method capable of producing a long-term expression of the F8 gene, minimal bleeding periods and increasing the quality of life of patients. This approach has been confirmed to replace the previous strategies without having their side effects and limitations. However, further experiments are needed to evaluate the effectiveness of CRISPR-Cas9.

Keywords: Hemophilia A(HA) , factor 8 (F8), The clustered regulatory interspaced short palindromic repeats (CRISPR)-Cas9

PH-111
Integrated Single-cell Sequencing Analysis revealed Different Transcriptional Pattern in Relapsed Acute Myeloid Leukemia

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Abstract

Background and Aim: Acute Myeloid Leukemia (AML) is an aggressive hematological malignancy characterized by the clonal expansion of immature myeloid cells in the bone marrow. Despite advances in treatment, relapse remains a significant challenge in AML management. Identifying and characterizing the cellular and molecular features of these relapse-driving populations is crucial for improving therapeutic strategies. Single-cell RNA sequencing (scRNA-seq) has emerged as a transformative technology for dissecting the complexity of AML and its relapse mechanisms. In this study, we aimed to explore the critical mechanisms in relapsed CD8+ NKT-like cells compared to these cells in patients with AML using an integrated scRNA-seq analysis.

Methods: Single-cell RNA sequencing (scRNA-seq) generates a wealth of transcriptomic data, offering insights into cell-specific gene expression patterns and heterogeneity. In this study, analysis was performed on bone marrow samples from healthy control, relapsed, and AML patients. GSE116256 and GSE227903 serve as primary resources. A subset of these datasets, including 26 AML samples, 11 relapsed samples, and 5 control samples underwent quality control and integration using the Seurat and Harmony R packages. Cell population annotation was performed using SCType and SingleR packages. Finally, FindMarkers function of Seurat was used to analyze the DEGs between the AML/ relapse and control clusters ($\log 2\ FC \geq \left|1\right|$, P. adjusted value ≤ 0.05, test.use = "Wilcox").

Results: The clustering of all cells identified 16 clusters, including progenitor, CD8+ NKT−like cells, classical monocytes, endothelial cells, cancer cells, erythroid−like and erythroid precursor, common myeloid progenitor (CMP), basophils, pro−B cells, neutrophils, hematopoietic stem cells/ multipotent progenitors (HSC/MPP), granulocyte monocyte progenitor (GMP), plasmacytoid dendritic cells, naive B cell, platelets, and memory B cells. After identifying the differentially expressed genes (DEG) in CD8+ NKT−like cells of the relapsed-control and AML-control, the unique DEG in the relapsed-control group were determined. Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis showed that these genes were mainly enriched in antigen processing and presentation, allograft rejection, and graft-versus-host disease.

Conclusion: In AML relapse, **CD8+ NKT-like cells** exhibit changes in genes related to antigen presentation and immune responses, particularly through **HLA class I** downregulation. This reduction impairs their ability to effectively present antigens and mount immune responses, allowing tumor cells to evade immune surveillance. These alterations also play a role in **graft-versus-host** responses, where immune tolerance mechanisms in the tumor microenvironment and post-transplantation settings may promote relapse. Understanding these immune changes offers potential therapeutic targets to restore immune function and prevent relapse in AML patients.

Keywords: Single-cell RNA sequencing; Acute Myeloid Leukemia; Relapse.

PH- 112

"Platelet Microparticles Regulate Biological Activities of Acute Lymphoblastic Leukemia Cells: Insights into Gene Expression and Proliferation"

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Abstract

Background and Aim: In recent years, there has been increasing interest in the role of extracellular vesicles in intercellular communication. Studies have demonstrated that these vesicles influence target cells by transporting signaling complexes, ligands, miRNA, and transcription factors, thereby inducing epigenetic changes. Platelet-derived microparticles (PMPs) are particularly important in mediating intercellular communication, significantly impacting the complexity of cancer pathology and treatment outcomes. The focus of this study was to examine the effects of PMPs on cell proliferation and the expression of key genes, such as P53 and P21, in the context of an Acute Lymphoblastic Leukemia (ALL) cell line (Nalm-6).

Methods: Platelet microparticles were collected by centrifuging at different speeds, and their concentration was measured using the BCA assay. Both dynamic light scattering (DLS) and flow cytometry were used to study the size and immunophenotypic characteristics of the PMPs. Cell proliferation was evaluated using the MTT assay, and cell cycle analysis was performed by assessing DNA content. Real-time PCR was used to analyze the gene expression of P53 and P21..

Results: The research findings demonstrated that Platelet-derived microparticles can inhibit the growth of Nalm-6 cells, while not influencing the progression of the cell cycle. Additionally, the analysis conducted using real-time PCR revealed an upregulation in the gene expression of P53 and P21.

Conclusion: This investigation highlights the complex relationship between Acute Lymphoblastic Leukemia (ALL)and its microenvironment, specifically focusing on the role of platelet-derived microparticles (PMPs). The study emphasizes the potential of PMPs to impact cell behavior and gene expression, offering a deeper understanding of their significance in ALL and its therapeutic implications.

Keywords: Platelet-derived Microparticle, Gene expression, Acute Lymphoblastic Leukemia

PH-113

Cause and treatment of chronic myeloid leukemia cancers resistant to medical treatments

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Abstract

Introduction: Chronic myeloid leukemia cancer is one of the cancers that can be caused somatically or hereditary in the cells of the reproductive line. One of the main causes is a change in chromosomes 22 and 9, called the Philadelphia chromosome. Various causes of this malignancy have made it resistant to treatment.

Method: In this research, we have used data from the past in treatments that experts have reviewed. Articles and research by pharmacists in collaboration with geneticists were also reviewed.

Result: One cause is new mutations in the BCR ABL gene. These mutations usually occur in certain areas of the BCR-ABL protein called the drug-binding site.

Primary Resistance, in which the patient does not respond to treatment with TKIs from the beginning. This type of resistance can be due to the presence of primary resistant mutations in the BCR ABL gene, which makes the drug unable to bind to the BCR-ABL protein effectively.

Acquired Resistance, in this case, the patient becomes resistant to drugs after a time that has responded positively to the treatment, due to new mutations in the BCR ABL gene or other changes in the cancer cells.

Mutations in the ATP binding site of the BCR ABL protein make the drug unable to effectively inhibit the BCR-ABL protein.

Resistance is due to problems in signaling pathways, including activation of alternative signaling pathways, which may include mTOR, PI3K / Akt, or Ras / Raf pathways. Another cause of resistance to CML treatment can be the increased activity of drug efflux pumps (such as ABC pumps), which remove anticancer drugs from inside cancer cells and keep them in the cell at lower doses, so the cells become resistant to the drug.

In some cases, changes in microRNAs or other gene-regulating molecules may help cancer cells become resistant to treatment.

Allogeneic Stem Cell Transplantation is usually recommended to treat CML in advanced stages or when the disease has become resistant to drug treatments.

Graft-versus-host disease - GVHD One of the important complications of allogeneic transplantation is that the transplanted cells can attack the tissues of the patient's body.

Conclusion: To concluded, these resistances can reduce the effect of the treatment and the progress of the disease, and due to the potential complications of the treatments available in this leukemia, the doctor, taking into account the conditions of the special conditions and the recovery results of the lack of recovery in the patients, appropriate treatments such as bone marrow transplantation or Chemotherapy with Imatinib.

PH-114

Investigation of the Effect of Time on Factor VIII Activity in FFP from Plasma Separation to Freezing

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Abstract

Background and Aim: Factor VIII is a crucial protein in the blood coagulation process, and its deficiency can lead to coagulation disorders such as Haemophilia A. Fresh frozen plasma (FFP) serves as a rich source of Factor VIII and is effective in managing and controlling

coagulation disorders. Due to the instability of this factor, the conditions under which plasma is separated and frozen are critical for preserving its activity. This study aims to evaluate the impact of the time interval between plasma separation and freezing on Factor VIII activity and to propose strategies for optimizing the production process of fresh frozen plasma.

Methods: This cross-sectional analytical study collected 60 whole blood samples from healthy male donors with a mean age of 38 ± 5 years and various blood groups. After separating the plasma from red blood cells and other blood components, the samples were divided into three groups. In the first group, the plasma was frozen immediately after separation. In the second and third groups, the plasma was stored at room temperature (20-24°C) for 90 and 180 minutes in the same order, before being frozen at -20°C. After freezing, the activity of Factor VIII was measured using the clot formation method with Diagnostica Stago kits (France) in duplicate samples. The results for each blood group and storage duration were analyzed using ANOVA in SPSS version 16.

Results: The study showed that Factor VIII activity in plasma frozen immediately after separation was at its highest level while increasing storage time decreased activity. The mean Factor VIII activity at 0, 90, and 180 minutes was 91.75 ± 5, 90.2 ± 5, and 88.75 ± 5 percent, respectively. Although no significant differences were observed among blood groups, group B showed the highest activity, while group O exhibited the lowest. These findings demonstrated the importance of rapid plasma freezing for preserving Factor VIII activity and we observed even short delays can lead to reduced product quality. Further studies are encouraged to ensure the findings can be extended to a more diverse population, particularly women.

Conclusion: Given the importance of Factor VIII as a quality indicator for fresh frozen plasma (FFP) and cryoprecipitate, optimizing plasma production conditions to preserve its activity is essential. This study displayed that immediate freezing of plasma after separation is one of the effective methods for preserving Factor VIII activity. As a result, these findings can contribute to improving the quality of blood products in blood transfusion centers.

Keywords: Factor VIII; Fresh Frozen Plasma (FFP); Haemophilia A**,** Plasma Freezing)

Production and Investigating Spleen-Cell-Conditioned Medium Treated With Different Concentrations of Adenosine

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ارائه دهنده [1]
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-

Medical Immunology

Background and aim: Breast cancer is the most common cancer among women, and according to the World Health Organization, one out of every ten women suffers from breast cancer. The immune system plays a significant role in controlling malignant cells. One of the tumor-mediated immunosuppression mechanisms which have been considered as a potential therapeutic target is the purinergic signaling pathway. With the activation of this pathway, purine nucleoside adenosine increases in the tumor microenvironment and can potentially suppress the function of T and NK cells. In this study, we investigated the effects of the supernatant (conditioned medium) obtained from adenosine-treated splenocytes on the

Methods: : Splenocytes were isolated from the mouse spleen under sterile conditions and transferred to RPMI 10% medium for subsequent culture. Then we added 100, 50, and 25 µM concentrations of adenosine to splenocytes. After 72 hours, the supernatant obtained from adenosine-treated splenocytes was separated and added to 4T1 cells. After 24 hours, survival and growth rate of supernatant-treated 4T1 cells were evaluated using Trypan Blue assay

Results: The results show that adding the conditioned medium of splenocytes treated with 25 µM adenosine concentration to 4T1 cells decreases the survival and growth rate along with increased apoptosis and necrosis of the 4T1 cell line

Conclusion: It seems that low concentrations of adenosine can have beneficial effects on the anti-tumor function of immune cells, but at increased concentrations, the anti-tumor function of immune cells decreases.

keywords: Adenosine1, Survival2, Conditioned Medium3, Splenocytes4

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The Relationship Between Serum and Tissue Levels of IL-13 and TYK2 in Colorectal Cancer Patients

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Medical Immunology

Background and aim: Colorectal cancer (CRC) is a third cause of death worldwide. The immune system plays a significant role in the tumor microenvironment and identifying its components involved in cancer development can aid in finding new biomarkers for prognosis, treatment monitoring, and immune-based therapies. Interleukin 13 (IL-13) is a cytokine produced by immune cells that has been implicated in tumor invasion, proliferation, and metastasis. Previous studies have shown that IL-13 causes the phosphorylation of Tyrosine kinase 2 (TYK2), which may contribute to the development and progression of cancer. This study investigated the levels expression of IL-13 and TYK2 in the tissue and

Methods: 105 patients with CRC and 105 healthy individuals were involved in the study. Tissue and blood samples were collected. The quantitative Real-Time PCR (qRT-PCR) technique was used to assess the expression levels of the IL-13 and TYK2 CRC tissue samples in comparison with the adjacent control tissue.

Results: The expression levels of IL-13 were lower and TYK2 were found to be higher in CRC tissue compared to normal tissue. Additionally, serum levels of IL-13 were decreased in CRC patients while TYK2 levels were elevated. A significant negative correlation was found between the expression levels of IL-13 in both serum and tissue and the cancer stage.

Conclusion: These results suggest that IL-13 and TYKMay 2 play essential roles in CRC development and progression and may serve as potential biomarkers for early detection and treatment.

keywords: Colorectal cancer (CRC), IL-13 , tyrosine kinase 2

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Assessing the Potential of Hematological Markers as Diagnostic Tools for Evaluating Disease Activity in Rheumatoid Arthritis Patients

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Medical Immunology

Background and aim: This study aimed to evaluate hematological markers as predictive tools for assessing disease activity in rheumatoid arthritis (RA) patients.

Methods: 305 RA patients were assessed for disease activity according to the American College of Rheumatology (ACR) eular 2010 rheumatoid arthritis classification criteria. A range of laboratory tests were conducted including white blood cells (WBC) count, red blood cells (RBC) count, platelets, neutrophils, lymphocytes, monocytes count, hemoglobin (Hb) concentration, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), red cell distribution width (RDW), rheumatoid factor (RF), anticyclic citrullinated peptide antibodies (anti-CCP), anti-nuclear antibodies (ANA), and C-reactive protein (CRP).

Results: Results indicated that CRP and erythrocyte sedimentation rate (ESR) showed significant difference among RA groups. Platelet-lymphocyte ratio (PLR), lymphocyte-monocyte ratio (LMR), and neutrophil-lymphocyte ratio (NLR) were assessed as potential markers of inflammation. Results showed that NLR, PLR, LMR, ESR, and CRP were important markers to differentiate active form of RA from remission form of RA. The AUC for the ESR marker was 0.80, 70% specificity, 75% sensitivity with a cutoff value of 19.5. The AUC for the CRP marker was 0.63, 72% specificity, 52% sensitivity with a cutoff value of 5.4. The AUC for NLR marker was 0.66, 81% sensitivity, 49% specificity with a cutoff value of 1.85. The AUC for PLR marker was 0.64, 68% specificity, 61% sensitivity with a cutoff value of 10.9.

Conclusion: These results suggest that NLR, PLR, LMR, ESR, and CRP can be potential biomarkers for assessing disease activity and inflammation in RA patients.

keywords: Rheumatoid arthritis (RA), Inflammation, Hematological marker

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Evaluation of IL35 levels in male seminal plasma of couples with unexplained recurrent spontaneous abortion

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Medical Immunology

Background and aim: Recurrent spontaneous abortion (RSA) is defined as the loss of two or more pregnancies before 24 weeks gestation. Although multiple factors are involved in RSA pathogenesis, but in some RSA cases no known causes can be found. Seminal plasma contains factors that protect and nourish sperm, as well as cytokines and chemokines that affect the male and female reproductive tract. Interleukin 35 belongs to interleukin12 family and has anti-inflammatory properties. IL-35 is produced by a variety of regulatory lymphocytes. The aim of this study was to evaluate IL-35 levels in seminal plasma of couples suffering from idiopathic RSA.

Methods: In this case control study , 21 male partners of couples with unexplained RSA (uRSA group) and 21 fertile men who had one or more child and referred to Royan institute for sex selection of next child (control group), were enrolled. RSA couples with known causes were not enrolled Men with anamnestic symptoms of genital tract infection, hypogonadism, history of chemotherapy, venereal diseases or using any immune-modifying medications were not enrolled. After 48-72 h of sexual abstinence, semen samples were collected by masturbation. beyond liquefaction of semen, to remove sperm and cellular debris, semen samples were centrifuged at 6000 rpm for 10 minute . IL-

35 was detected using an enzyme-linked immunosorbent assay (ELISA) kit (Zell BIO , Germany). SPSS was used for data analyses. Results are presented as mean and standard deviation(SD). T test was used for statistical analysis . P value less than 0.05 was considered statistically significant.

Results: The mean concentration of seminal IL35 level was significantly higher in uRSA group (6.28 ± 0.94 ng/ml) than control group (5.11±1.05 ng/ml) (p-value: 0.001). No significant differences were found between the two groups in regard to body mass index (BMI), smoking and alcohol consumption (p-value 0.05). The mean age of control group (39.45±3.80years) was higher than uRSA group (37.13±3.53years) (p-value: 0.45).

Conclusion: This study showed that seminal IL-35 levels were significantly increased in uRSA group compared to fertile men. An increase in anti-inflammatory cytokines level such as IL-35 in semen can reduce the phagocytic activities to clear the male genital tract of nonejaculated/stored sperms and increase the antigenicity of the sperm cells and impair female tract tolerance against embryo. Also, the quality of sperms decrease.

keywords: (Interluekin35, RSA, Seminal plasma)

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Toll-Like Receptor-Mediated Exosome Biogenesis: Implications for Cancer Development and Progression

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Medical Immunology

Background and aim: Exosomes are small extracellular vesicles involved in cell-to-cell communication and play an important role in various physiological processes, including immune regulation and cancer progression. Toll-like receptors (TLRs), are known to influence exosome biogenesis. TLR signaling and exosome production may be provided to how cancer cells manipulate immune responses for tumor growth.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Toll-Like Receptor, Exosome, Cancer, 79 articles were extracted and analyzed.

Results: TLR activation, particularly by TLR3 and TLR4, has been shown to regulate exosome biogenesis by influencing intracellular trafficking mechanisms. In cancer cells, TLR-mediated exosome release often leads to the promotion of the immune response and enhances the suppressive effect of the tumor microenvironment. Studies have also demonstrated that these exosomes contain cancer-related signaling molecules that can promote metastasis and resistance to therapy.

Conclusion: The link between TLR signaling and exosome biogenesis suggests a possible mechanism by which tumors exploit immune pathways to promote their growth and spread. Targeting TLR-mediated exosome production may offer new therapeutic strategies to prevent cancer progression. However, further research is needed to elucidate the molecular mechanisms and to translate these findings into clinical applications. Understanding the dual role of TLRs in both cancer

progression and immune activation is key to development of new therapeutic strategies.

keywords: Toll-Like Receptor, Exosome, Cancer.

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NLRP3 inflammasome activation in dendritic cells: A strategic therapeutic target for managing autoimmune diseases, cancer, and infectious conditions

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Medical Immunology

Background and aim: The NLRP3 inflammasome, a key component of the innate immune response, is essential in activating inflammatory responses and the regulation of cytokine release. In dendritic cells (DCs), the NLRP3 inflammasome plays a role in sensing cellular stress and promoting inflammation. Its dysregulation is associated with various pathological conditions, including autoimmune diseases, cancer, and infectious diseases. Targeting the NLRP3 inflammasome in DCs offers a potential therapeutic approach to treat these diseases.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords NLRP3, dendritic cells, autoimmune diseases, cancer, infection, 57 articles related to inclusion criteria were extracted and then analyzed.

Results: Researches indicate that NLRP3 activation in dendritic cells promotes the production of pro-inflammatory cytokines like IL-1β and IL-18 as, factor related to chronic inflammation in autoimmune diseases, facilitating tumor growth and metastasis in cancer. Additionally, certain infectious pathogens exploit the NLRP3 pathway to enhance their survival and replication. Therapeutic approach such as specific NLRP3 inhibitors, showed that effective in reducing inflammation in autoimmune disorders and inhibition of tumor progression in cancer models.

Conclusion: Targeting the NLRP3 inflammasome in dendritic cells represents a promising therapeutic strategy for autoimmune diseases, cancer, and infectious conditions. Further research is needed to optimize these treatments for therapeutic approach. NLRP3 modulators could offer new and, effective therapies to control chronic inflammation and immune dysregulation due to diverse pathological conditions.

keywords: NLRP3, Dendritic cells, Autoimmune diseases, Cancer, Infection.

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Gene editing approaches to overcome the current challenges of CAR-T cell therapy in solid tumors

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Medical Immunology

Background and aim: Chimeric Antigen Receptor T (CAR-T) cell therapy has shown remarkable success in hematological malignancies, but its efficacy in solid tumors remains limited due to various barriers. These obstacles include the immunosuppressive tumor microenvironment, poor CAR-T cell infiltration, and antigen heterogeneity within solid tumors. Gene editing strategies are being explored to enhance CAR-T cell effectiveness in overcoming these challenges.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords CAR-T cell, Solid tumors, Gene editing, 73 articles related to inclusion criteria were extracted and then analyzed.

Results: Gene editing has shown promising results in overcoming several challenges associated with CAR-T cell therapy in solid tumors. For example, CRISPR-mediated knockout of inhibitory checkpoint molecules (like PD-1) has improved CAR-T cell persistence and activity within the tumor. Additionally, gene editing has enabled CAR-T cells to express chemokine receptors, enhancing their ability to traffic into solid tumors. Multi-targeting strategies have also been developed to address tumor antigen heterogeneity, leading to more durable responses in preclinical models.

Conclusion: While gene editing strategies hold significant promise for improving CAR-T cell efficacy in solid tumors, several challenges remain. Off-target effects, potential toxicity, and manufacturing scalability are areas that need further investigation before widespread clinical adoption. Ongoing advancements in

gene editing technologies, coupled with robust clinical trials, are crucial to harnessing the full therapeutic potential of CAR-T cells in solid tumors.

keywords: CAR-T cell, Solid tumors, Gene editing.

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Evaluation of IL-41level in seminal plasma of couples with unexplained recurrent pregnancy loss

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Medical Immunology

Background and aim: Recurrent pregnancy loss (RPL) is defined as the loss of two or more pregnancies before the 24th week of pregnancy (ESHRE 2022) . A successful pregnancy is Secondry to the tolerance of the semi-foreign fetus by the mother's immune system, so one of the factors that can play a role in the mother's tolerance of the fetus is paternal seminal plasma. Seminal plasma contains several molecules, cytokines, chemokines and growth factors. Interleukin 41 as a novel cytokine is found in seminal plasma. In this study, the level of expression of IL-41 in the seminal plasma of men whose wives had

Methods: In this case-control study, seminal plasma samples were obtained from 20 men in the RPL group whose wives had at least 2 abortions and 20 men in the control group who were referred to Royan Institute for sex selection of future child. After seminal plasma collection the IL 41 cytokine level was measured using the ELISA method (Zell Bio GmbH, Germany). SPSS version 24 was used for data analyses and the result are presented as mean and standard deviation (SD). T-test was used for statistical analysis and P value less than 0.05 was considered statistically significant.

Results: The mean age of men was significantly higher in the control group (39.45 ± 3.80 years) than RPL group (37.13 ± 3.53 years) (P value=0.045) The mean of BMI was 27.93 ± 5.47 kg/m2 and 26.86 ± 3.40 kg/m2 in the RPL and control groups respectively which was not statistically significant. The concentration of IL41 cytokine was significantly higher in the seminal plasma of the RPL group (1.16 ± 0.174795 ng/ml) than in the control group (1.01ng/ml ± 0.129371) (P0.002)

Conclusion: in this study, for the first time it was shown that the level of interleukin 41 is increased in the semen of men whose wives had recurrent pregnancy loss. Considering the role of interleukin 41 in the balance of Th1, Th2 and Th17, it can play a role in the pathogenesis of RPL.

keywords: Recurrent pregnancy loss (RPL), Cytokine, Interleukin 41, Seminal Plasma

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Mesenchymal Stem cells and new therapies related to them

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Medical Immunology

Background and aim: So far, 344 clinical plans to investigate copper-based cell therapy are being implemented. With the advancement of preclinical studies, MSCs are effective in the treatment of many diseases, including both immune diseases and non-immune diseases

Methods: Our article search databases were two databases, PubMed and Google Scholar, and their inclusion criteria were articles related to mesenchymal stem cells and cell therapy. The selection of articles was based on the up-to-dateness of its information by year and its relationship with the subject of cell therapy by mesenchymal cells, and finally, the information of the selected articles was extracted and their data was analyzed and arranged systematically in the order of information progress during the year.

Results: Clinical applications of MSCs, for several diseases, have been registered at the National Institutes of Health ClinicalTrials.gov website (https://www.clinicaltrials.gov/)as clinical trials in different phases. When this study was being written, the approximate percentages of studies about cardiovascular disorders (15%), neuro degenerative diseases (12%), bone and cartilage diseases (6%), malignancies (5%), liver problems (3%), kidney problems, and other conditions were autoimmune diseases (25%) [including: graft versus-host diseases (GvHD, 9%), multiple sclerosis (MS, 4%), Crohn's disease (3%), type1 diabetes (T1D, 5%), systemic lupus erythematous (SLE, 2%), rheumatoid arthritis (RA, 2%)] andother diseases (31%).

Conclusion: To enhance MSC therapy's therapeutic efficacy, new guidelines are proposed. Combining strategies could be intriguing and helpful in improving understanding of the potential, roles, and clinical viewpoints of MSCs. These tactics include preconditioning, manipulating, and examining possible or unanticipated dangers. Most likely, the hazards would be the development of

tumors, unfavorable immunological reactions, and accidental agent transmission.

keywords: Mesenchymal stem cells (MSCs) , Cell Therapy , Therapy,

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Brain microstructural changes is associated with the reduction of sleep quality in individuals with chronic insomnia disorder

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Medical Immunology

Background and aim: Insomnia is the most common sleep disorder, affecting one's daily activities negatively. Despite the importance of sleep on human health, the exact mechanism of insomnia pathogenesis and risk-inducement has not yet been identified. The aim of the study was to identify the relationships between sleep-related information (Pittsburgh Sleep Quality Index (PSQI) score, REM sleep duration, non-REM sleep duration) and brain microstructural changes. In this regard, we examined different brain regions using diffusion-weighted magnetic resonance imaging (MRI) in CID individuals compared to control group.

Methods: Blood samples were collected from 24 individuals diagnosed with CID (18 females, mean age 41.7 y, range 19-65) based on PSQI and full-night video-polysomnography (V-PSG) and 24 healthy individuals (16 females, mean age 42.3 y, range 19-65) based on PSQI. MRI scans were obtained on a Siemens Magnetom Avanto 1.5 T MRI whole body scanner with an 8-channel head coil. The whole-brain diffusion weighed imaging data were collected using a single-shot spin-echo

EPI sequence. A total of 68 slices were used to cover the entire brain. All diffusion tensor images were concatenated and corrected for eddy current, subject movement and EPI distortions through Eddy-FSL. DTIFIT (part of FMRIB Software library, Oxford) tensor model was applied to corrected DTI data to generate fractional anisotropy (FA) and mean diffusivity (MD (maps from eigenvalues.

Results: Diffusion MRI analysis revealed significantly increased right-cerebellum-cortex and lateral ventricle MD bilaterally in individuals with CID compared to control group (p 0.05). However, the individuals with CID and controls did not display any significant differences in FA values. The Spearman correlation analysis indicated that left lateral ventricle MD had high positive correlation with PSQI scores (correlation coefficient 0.941, p 0.01) in individuals with CID.

Conclusion: We speculate that increased lateral ventricles and cerebellum cortex MD in individuals with CID may be an evidence for impaired BBB integrity which cause further infiltration of inflammatory factors and macrophages into the brain.

keywords: Chronic insomnia, Brain microstructure, Diffusion-weighted magnetic resonance imaging

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Changes of peripheral blood NKT cells during ovulation stimulation cycles in women with endometriosis undergoing ART cycles

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Medical Immunology

Background and aim: Endometriosis is a chronic estrogen-dependent and inflammatory disease that affects 10% of women in reproductive age. Endometriosis could cause infertility and chronic pelvic pain. Various factors including immunological factors are involved in its pathogenesis. Changes in Natural killer T cells (NKT) in women with endometriosis have been observed. As the use of gonadotropin-releasing hormone (GnRH) agonist and antagonist drugs in six months is effective in the treatment of endometriosis, this study aimed to investigate the effect of these hormonal drugs used in ovarian stimulation cycles on peripheral blood NKT cells (pNKT)in women with endometriosis during assisted reproductive technology (ART) cycles.

Methods: In this cohort study, 40 infertile women with endometriosis will be enrolled during the ovarian stimulation cycle at Royan infertility clinic. Whole blood sample (3 cc) was collected from studied women at least 2 time points: 1. second or three day of menstrual cycle 2. oocyte puncture day (OPU): At first, blood samples were stained with PerCP anti-humanCD3 antibody (T cell marker), APC anti-human CD56 antibody (NK cell marker), FITC anti-human CD16 antibody (another NK surface marker) and PE anti-human CD107a antibody (NK activity marker) for 30 minutes in 4° C. Lysis buffer was added to each tube for red blood cells lyses. In the next step, phosphate buffer saline (PBS) was added for washing, and after that samples were centrifuged for 5 minutes (1500 RPM). The flow cytometry method was done using BD FACS Calibur. Data analysis was done using Prism software.

Results: Up to now, 18 women with endometriosis were enrolled. The mean age of the studied women was 25.02 years old and the mean body mass index (BMI) was 32.61 Kg/m2. The frequency and activity of pNKT cells were compared between these two time points (at the start and end of the ovarian stimulation cycle). The percentage of pNKT cells (CD3+CD56+) has decreased between these two time points but that isn't significant. Also, the percentage of cytotoxicity markers on CD3+ cells (CD3+CD16+CD107a) is not significantly different between these two days.

Conclusion: According to this sample size, we didn't find any significant changes. Although a conclusion will be drawn after the enrollment of 40 women in this study.

keywords: Endometriosis, Natural killer T cells, GnRH agonist, GnRH antagonist, ART

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Impaired immune homeostasis through increased IL-1β and reduced anti-inflammatory cytokines IL-10 and TGF-β is associated with decreased sleep quality in chronic insomnia disorder

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Medical Immunology

Background and aim: Nearly one-third of the general population experiences symptoms of insomnia, with approximately 10% of those individuals classified as having chronic insomnia disorder (CID). Although sleep is crucial for overall health, the exact mechanisms underlying the development of insomnia remain unclear. A growing body of evidence highlights inflammation as a significant element in the development and progression of insomnia. However, despite extensive investigations, the exact relationship between insomnia and inflammation remains unclear. The present study aim to evaluate the

relationship between immune system homeostasis, reflected by cytokines serum levels, and sleep quality in individuals with CID.

Methods: Blood samples were collected from 24 individuals diagnosed with CID (18 females, mean age 41.7 y, range 19-65) based on Pittsburgh Sleep Quality Index (PSQI) and full-night video-polysomnography (V-PSG) and 24 healthy individuals (16 females, mean age 42.3 y, range 19-65) based on PSQI. The serum levels of interleukin-1β (IL-1β), interleukin-18 (IL-18), interleukin-10 (IL-10) and transforming growth factor beta (TGF-β) was evaluated using enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed using the SPSS®, version 26.0 (IBM Corporation, Armonk NY; USA).

Results: Serum concentrations of cytokines IL-1β and IL-18 were found to be significantly higher in CID group compared to controls. In addition, significant decreases in IL-10 and TGF-β were observed in individuals with CID compared with controls. The correlation analysis indicated that serum levels of IL-1β have a significant negative correlation with IL-10 and TGF-β (r=0.456 and r= 0.532, respectively, P0.05) in individuals with CID.

Conclusion: According to these results, a significant reduction in circulating levels of IL-10 and TGF-β in individuals with CID could maintain a chronic inflammatory. Consequently, impaired maintenance of immune homeostasis following uncontrolled pro-inflammatory cytokines signaling can be considered as one of main underlying mechanisms of the etiopathogenesis of CID.

keywords: Chronic insomnia, Interleukin- 1β, Interleukin 10, TGF-β

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Detection of immunodominant antigens in symptomatic and asymptomatic clinical forms of canine Leishmaniasis caused by Leishmania infantum using immunoblotting technique: A preliminary study.

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Medical Immunology

Background and aim: Domestic dogs (Canis familiaris) are the main reservoirs of leishmaniasis caused by Leishmania infantum, which occurs in two symptomatic and asymptomatic forms. Accurate and early detection of canine leishmaniasis (CanL) caused by Leishmania infantum can be decreased the transmission rate from the infected dogs to humans. . The aim of the present study was to identify markers and prognostic factors for the detection of symptomatic and asymptomatic forms of L.infantum infection.

Methods: This study was performed on 15 dog serum samples divided into three groups containing 5 dogs/group as follows: Group 1 included 5 seropositive (antibody titer≥1:320) infected dogs with symptomatic leishmaniasis; Group II included 5 seropositive (1:160≤ antibody titer ≥1:80) infected dogs with asymptomatic leishmaniasis, and; Group III included 5 seronegative asymptomatic dogs as negative controls based on DAT results. In order to confirm the DAT results; indirect immunofluorescent antibody (IFA) test was also carried out on each serum sample. Then, purified proteins of standard strain L. infantum (Iranian strain MCAN/IR/07/Moheb-gh) were exposed to diluted canine sera in all three groups using the immunoblotting technique.

Results: A total of 11 bands were observed in sera of group I, with various frequencies and severities. Western blotting bands were within the range of 11-100 kDa with immunodominant bands at 14, 33, 59, and 63kDa were found in all samples from group I (frequency 100%). In the group I, 80% of the samples recognized a strong band at 11, 25, 35 and 45 kDa. Moreover, bands with molecular weights of 19, 20, and 100 kDa were observed in three serum samples from group I (frequency 60%). In the sera of dogs belonging to group II, a total of five weak immunodominant bands were observed within the range of 14-75 kDa. In the group II, 60% of the samples recognized a weak band at 33, 63, and 75 kDa. Moreover, bands with molecular weights of 41 kDa were observed in two serum samples from group II (frequency 40%). Strongest reactions

Conclusion: The preliminary data from the current study indicate the potential of several VL immunodominant antigens in the serodiagnosis of specific antibodies against L. infantum in dogs.

keywords: Leishmania infantum; canine leishmaniasis; western blotting; immunodominant antigen; Iran.

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The Role of MicroRNA Dysregulation in Modulating Bortezomib Sensitivity in Multiple Myeloma Patients

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Medical Immunology

Background and aim: MicroRNA (miRNA) dysregulation plays a crucial role in the development and progression of multiple myeloma (MM). Recent studies suggest that miRNA expression profiles can influence the sensitivity of MM patients to bortezomib, a proteasome inhibitor widely used in MM treatment. Understanding the connection between miRNA dysregulation and bortezomib response could help optimize therapeutic strategies and improve patient outcomes.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords MicroRNA, Multiple Myeloma, Bortezomib 69 articles related to inclusion criteria were extracted and then analyzed.

Results: Findings indicate that certain miRNAs, such as miR-29b and miR-221, are significantly dysregulated in bortezomib-resistant MM cells. These miRNAs have been shown to regulate apoptotic pathways and influence the expression of genes associated with drug resistance. Downregulation of miR-29b was correlated with enhanced survival of MM cells under bortezomib treatment, while overexpression of miR-221 was linked to reduced drug efficacy. Additionally, manipulating miRNA levels in experimental models has restored bortezomib sensitivity, suggesting potential therapeutic benefits.

Conclusion: miRNA dysregulation plays a pivotal role in modulating bortezomib sensitivity in multiple myeloma. Targeting specific miRNAs may offer new avenues to overcome drug resistance and improve treatment outcomes.

However, further clinical trials are required to validate these findings and determine the best therapeutic strategies for incorporating miRNA-based interventions in MM treatment protocols.

keywords: MicroRNA; Multiple Myeloma; Bortezomib.

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Cytokine-Induced Killer Cells: Emerging Perspectives in the Treatment of Hematologic Cancers

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Medical Immunology

Background and aim: Cytokine-Induced Killer (CIK) cells represent a promising immunotherapeutic approach for treating hematologic malignancies. CIK cells, derived from peripheral blood mononuclear cells (PBMCs), are expanded in vitro with a combination of cytokines. They exhibit both NK cell and T cell-like properties, making them effective against a wide range of cancer cells. This review aims to provide insights into the therapeutic potential of CIK cells in hematologic cancers.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Cytokine-Induced Killer Cells, Hematologic Cancers, Immunotherapy, 66 articles related to inclusion criteria were extracted and then analyzed.

Results: CIK cells have demonstrated significant cytotoxic activity against a range of hematologic malignancies, including leukemia, lymphoma, and multiple myeloma. Clinical trials reported positive responses in patients, with minimal toxicity compared to other immune-based therapies. The ability of CIK cells to target both tumor cells and leukemic stem cells suggests their broad therapeutic potential. Some studies also reported enhanced efficacy when combined with other therapies such as chemotherapy or monoclonal antibodies.

Conclusion: CIK cell therapy offers a novel and promising approach for treating hematologic cancers, especially in relapsed or refractory cases. Their dual NK-like and T cell-like activity enhances their cytotoxic potential while minimizing off-target effects. However, challenges remain, including optimizing their expansion,

improving persistence in vivo, and overcoming immune evasion mechanisms in tumors. Future studies should focus on combination therapies and personalized approaches to maximize the clinical efficacy of CIK cells in hematologic malignancies.

keywords: Cytokine-Induced Killer Cells, Hematologic Cancers, Immunotherapy.

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Survivin in Hematological Malignancies: Implications for Therapy and Future Directions

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Medical Immunology

Background and aim: Survivin is a unique member of the inhibitor-of-apoptosis proteins (IAPs) family; its roles have been demonstrated to occur in different hematological cancers. One of the critical roles of Survivin is its pro-mitotic and anti-apoptotic functions. Survivin expression in hematological malignancies is almost always associated with poor prognosis, illness progression, short survival rates, and drug resistance. These properties make Survivin a potentially attractive therapeutic target for various hematologic malignancies. Therefore, in this study, we review the role of this molecule in various hematologic malignancies and introduce it as a therapeutic target in these disorders.

Methods: According to the Preferred Reporting Items, this narrative review was conducted in August 2024. This study used a comprehensive literature search in PubMed, Scopus, and Google Scholar to identify relevant articles. The search strategy included the following MeSH terms and keywords: Survivin, Leukemia, Lymphoma, Multiple myeloma, and Therapy. The language of the reviewed articles was limited to English, and review and original articles were included in this study.

Results: Most preclinical and clinical studies have shown an increase in Survivin expression at both the gene and protein levels in leukemia, lymphoma, and multiple myeloma. This increase in expression has explained the defect in cell

apoptosis and disease progression. It has also been proposed as a factor associated with inferior overall survival and a poor prognostic marker in patients with hematological malignancies. Evidence has also shown that the use of Survivin inhibitors alone or in combination with other cancer treatment methods is an attractive treatment strategy for hematological cancers.

Conclusion: Nowadays, the resistance of cancer cells to anti-cancer drugs, chemotherapy, and radiotherapy has increased. Eliminating the effects of molecules associated with this increase in resistance led to the sensitization of cancer cells to chemical and physical agents. One of these critical molecules is Survivin. According to the experiments studied in this review, most results reported an increase in Survivin expression in hematologic malignancies. The evidence suggested that specific Survivin inhibitors and their combination with other cancer inhibitors greatly enhance their therapeutic effects in treating hematologic malignancies.

keywords: Survivin; Apoptosis; Hematological malignancies; Targeted therapy

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Identification of DEGs Associated with Cetuximab Response in Colon Cancer: an in silico analysis

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Medical Immunology

Background and aim: Globally, colorectal cancer (CRC) is the third most common cancer. Approximately 25% of patients with colorectal cancer are diagnosed with metastatic disease, and 40 to 50% of newly diagnosed patients will eventually develop metastatic disease. Standard chemotherapy treatments for CRC, which include monoclonal antibodies and cytotoxic agents, have become well-established in clinical practice. Notably, epidermal growth factor receptor (EGFR)-targeting agents have demonstrated significant clinical benefits. Cetuximab is a chimeric monoclonal antibody that specifically targets the EGFR, a receptor that is found in excess in 25-80% of colorectal cancer tumors and linked to advanced disease. However, mutations are associated with resistance

Methods: In the current study, two microarray datasets (GSE56386, GSE140973) were downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual gene levels were calculated; differentially expressed genes (DEGs) with |FC| 1 and P-value 0.05 were considered to be significant. The Venn diagram was carried out for the overlapped part via Funrich software.

Results: A total of 974 overlapped upregulated genes and 62 downregulated genes were identified. To identify the most influential genes in each group, we calculated the Degree for all upregulated and downregulated genes and selected the top 20 genes with the highest Degree values. Analysis showed that up-regulated genes involve in ErbB receptor signaling, CDC42 signaling, S1P1

pathway, and Arf6 signaling events. Down-regulated genes mainly associate with viral RNP complexes in Host Cell Nucleus, HIF-1-alpha transcription factor network, mesenchymal-to-epithelial transition, and Hypoxic and oxygen homeostasis regulation of HIF-1-alpha.

Conclusion: This in silico prediction identified differentially expressed genes in the sensitive versus resistant states to the drug cetuximab in colorectal cancer patients, which can be used as predictive and therapeutic biomarkers.

keywords: colorectal cancer; cetuximab; EGFR; microarray datasets; gene expression

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The relationship between future cancer metastases and fibroblast activation protein-α (FAP-α)

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Medical Immunology

Background and aim: Fibroblast activation protein-α (FAP-α) has been implicated in cancer progression and metastasis. As a cell-surface serine protease expressed in cancer-associated fibroblasts (CAFs), FAP-α contributes to tumor invasion and metastasis. Understanding its relationship with future cancer metastases may offer insights into prognosis and therapeutic targets.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Cancer, Metastasis, Fibroblast Activation Protein-α, 63 articles related to inclusion criteria were extracted and then analyzed.

Results: : The results revealed that high levels of FAP-α expression in tumors correlate with increased likelihood of future metastasis. The most significant associations were observed in cancers such as colorectal, breast, and pancreatic cancers. FAP-α overexpression also correlated with poorer overall survival and increased invasiveness, confirming its role as a potential predictor of metastatic behavior.

Conclusion: This analysis highlights the crucial role of FAP-α in cancer metastasis. Its overexpression in CAFs appears to facilitate tumor invasion by remodeling the extracellular matrix and promoting tumor-stroma interactions. Targeting FAP-α could offer new therapeutic strategies to prevent metastasis, especially in cancers where it is highly expressed. However, further research is needed to clarify its exact mechanisms and potential as a prognostic biomarker across different cancer types.

keywords: Cancer, Metastasis, Fibroblast Activation Protein-α.

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Nanobodies; natures tiny weapons against infection disease

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Medical Immunology

Background and aim: Nanobodies are the smallest known antigen-binding molecules so far. Their small size, tissue penetration, stability, and solubility are superior to conventional antibodies, which make them promising candidates for various medical and biotechnology applications. The aim of this study is to review their role in the fight against infectious diseases as a new method.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Infectious disease, Nanobodies, Diagnosis, Treatment, 78 articles related to inclusion criteria were extracted and then analyzed.

Results: The results of studies indicate that nanobodies have a special application, including neutralizing viruses and bacterial toxins and fighting against bacteria that are resistant to antibiotics.

Conclusion: Nanobodies are a very promising tool for a wide range of biomedical applications due to their superiority in terms of small molecular size and physical and chemical properties. It is also necessary to conduct more extensive studies in this field for a better understanding of the treatment process and their impact.

keywords: Infectious disease, Nanobodies, Diagnosis, Treatment.

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The Role of Extracellular Heat Shock Protein 90 Alpha (eHsp90α) in Cancer Progression and Therapeutic Strategy Development

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Medical Immunology

Background and aim: Extracellular Heat Shock Protein 90 Alpha (eHsp90α) has emerged as a critical player in cancer biology, influencing tumor progression and immune evasion. This study investigates the role of eHsp90α in cancer progression and its potential as a therapeutic target.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Extracellular heat shock protein 90 alpha, Cancer biomarker, Cancer target, 78 articles related to inclusion criteria were extracted and then analyzed.

Results: Our findings demonstrate that elevated levels of eHsp90α correlate with increased tumor aggressiveness and poor patient prognosis across multiple cancer types. Functional assays revealed that inhibition of eHsp90α significantly reduced cell migration and invasion, while promoting apoptosis. Mechanistically, eHsp90α was found to modulate key oncogenic pathways, including PI3K/Akt and MAPK signaling, leading to enhanced tumor cell survival and proliferation.

Conclusion: This study highlights the pivotal role of eHsp90α in cancer progression, suggesting it as a promising biomarker for tumor aggressiveness and a potential therapeutic target. Targeting eHsp90α may offer a novel strategy for cancer treatment, particularly in cases resistant to conventional therapies. Further research is warranted to explore eHsp90α inhibitors in clinical settings and their potential synergistic effects with existing treatment modalities.

keywords: Extracellular heat shock protein 90 alpha, Cancer biomarker, Cancer target.

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Advancements in CAR-T Cell Therapy: Insights into precision Targeting for Hematologic Malignancies

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Medical Immunology

Background and aim: Immunotherapy is a powerful clinical strategy for cancer treatment. This treatment has been widely targeted for hematological cancers. Chimeric Antigen Receptor T (CAR-T) cell therapy has revolutionized the landscape of hematologic malignancies, offering hope where traditional treatments have faltered. Recent advancements in this field underscore a paradigm shift towards precision targeting, enhancing therapeutic efficacy while minimizing off-target effects. The evolution of CAR constructs has seen the incorporation of novel antigen targets, including CD19, BCMA, and CD22, which are pivotal in the pathogenesis of various blood cancers such as acute lymphoblastic leukemia (ALL) and multiple myeloma.

Methods: The research used the keywords immunotherapy, Hematologic Malignancies, CAR-T cell, and cancer prognosis in databases including Google Scholar, PubMed, and Science Direct. According to the articles' period and English language, the articles were selected and the information from at least 10 articles was extracted.

Results: Innovations in genetic engineering techniques, including CRISPR-Cas9 and transposon-based systems, have facilitated the development of next-generation CAR-T cells with improved persistence and functionality. These engineered T cells not only exhibit enhanced cytotoxicity against malignant cells but also possess the ability to evade tumor-induced immunosuppression. Furthermore, the advent of dual-targeted CAR-T therapies aims to circumvent antigen escape mechanisms, providing a robust strategy for addressing heterogeneity in tumor expression profiles. Recent clinical trials have demonstrated promising outcomes, with significant response rates and durable remissions observed in heavily pre-treated patient populations. However,

challenges remain, particularly concerning cytokine release syndrome (CRS) and neurotoxicity. Ongoing research is focused on refining safety profiles through the implementation of "on-switch" technologies that allow for controlled activation of CAR-T cells.

Conclusion: As we continue to unravel the complexities of hematologic malignancies, the future of CAR-T cell therapy lies in its ability to integrate precision medicine principles. By tailoring therapies to individual tumor characteristics and patient profiles, we stand on the brink of a new era in cancer treatment one that holds the promise of improved outcomes and enhanced quality of life for patients worldwide.

keywords: HematologicMalignancies_Immunetherapy_CAR-TCell _Therapy CAR-T Cell Therapy

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STATs signaling pathways in dendritic cells: As potential therapeutic targets?

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Medical Immunology

Background and aim: Dendritic cells (DCs) are professional antigen-presenting cells (APCs) that encompass heterogeneous populations, effectively bridging innate and adaptive immunity. While Signal Transducers and Activators of Transcription (STAT) factors are pivotal in cytokine signaling, their specific roles in DC maturation, antigen presentation, and the modulation of immune responses—such as the differentiation of T cells into T helper (Th)1, Th2, or regulatory T (Treg) cells—are not fully elucidated. This review aims to clarify the significance of STAT transcription factor signaling pathways across various DC subtypes and to explore their potential as targets for enhancing DC-based immunotherapies in cancer and autoimmune diseases.

Methods: In the current study, we review recent studies on the roles of STAT transcription factors in different dendritic cell subtypes. Based on recent findings, we investigate how specific STAT proteins influence DC maturation, antigen presentation, and the subsequent differentiation of T cells into Th1, Th2, or Treg subsets. Additionally, we evaluate the therapeutic potential of targeting STAT factors with specific activating or inhibitory agents to improve the efficacy of DC-based immunotherapies for cancer and autoimmune conditions.

Results: Our review indicates that distinct STAT factors play unique roles in the functional differentiation of DCs and their ability to influence T cell responses; for example, STAT1 and STAT2 enhance antigen presentation and T-cell responses, whereas STAT3 inhibits certain immune functions. GM-CSF-mediated STAT5 induction influences DC differentiation, offering targets for therapy. Moreover, it has been indicated that STAT6 upregulation decreases DC maturation. Generally, dysregulation of STAT signaling pathways in DCs is associated with impaired immune responses and the progression of various cancers and autoimmune

disorders. Targeting specific STAT pathways in DCs has shown potential in preclinical studies to boost anti-tumor immunity and restore immune balance in autoimmune diseases.

Conclusion: STAT transcription factors are essential regulators of dendritic cell functions and the orchestration of immune responses. By delineating the distinct roles of various STAT proteins in different DC subtypes, this review highlights the potential of targeting STAT signaling pathways as a therapeutic strategy. Modulating these pathways offers promising avenues for enhancing DC-based immunotherapies, providing significant benefits for patients with cancer and autoimmune diseases through the precise activation or inhibition of specific STAT factors.

keywords: Dendritic cell, STAT signaling, T cell, Cancer, Autoimmune disease

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The Effect of IV Anti-CD20 Treatment On Multiple Sclerosis Patients

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Medical Immunology

Background and aim: Multiple sclerosis is a chronic neurological disorder that affects the central nervous system is characterized by immune-mediated myelin loss and neurodegeneration. Historically, multiple sclerosis (MS) was considered primarily a T-cell- mediated autoimmune disease; however, it is now well established that B cells play a crucial role in the pathophysiology of MS. This is particularly evident given the repeated and significant success of B-cell–depleting anti-CD20 therapies in mitigating the disease. Ublituximab, a novel monoclonal antibody that targets a unique epitope on the CD20 antigen, is glycoengineered to enhance B-cell targeting through antibody-dependent cellular cytotoxicity. In this article, we provide an overview

Methods: In this review, we searched Pubmed Scientific Information Database (SID;Iran), and Google Scholar for the years 2020 to 2024. The search conducted Keywords were anti-CD20 treatment and multiple sclerosis. In this review, we analyzed 22 studies.

Results: According to the studies we reviewed, the drugs used in this treatment are rituximab and ocrelizumab. The mean treatment duration for ublituximab was 47 weeks. At week 48, a significant percentage of patients had undergone all assessments to evaluate for any evidence of disease activity. CD19+ B-cells were effectively depleted during the treatment. IgM and IgG levels in patients receiving B-cell depleting therapies significantly decreased at 6 months and 30 months, respectively. An increase in CD8 T regulatory cells was observed at 6 months, with no change in the level of cytotoxic T lymphocytes (CTL), indicating that this is a gradual change rather than a rise in all CD8 cells. There were no significant differences in the depletion kinetics between rituximab and ocrelizumab.

Ublituximab was generally well tolerated; no patients discontinued the study due to drug- related adverse events, no serious infections were reported, and no deaths occurred.

Conclusion: The success of Phase II and III clinical trials utilizing selective intravenous B-cell depleting therapies have transformed the treatment landscape for not only relapsing MS but also active progressive MS. In clinical trials, anti-CD20 therapies, including rituximab and ocrelizumab, have proven to be effective and well-tolerated in patients with MS, thereby expanding the therapeutic options available to them.

keywords: Multiple Sclerosis, Ublituximab, Rituximab, Ocrelizumab

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Designing a Multi-Epitope Vaccine Against the Monkeypox Virus Using Immunoinformatics Approaches

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Medical Immunology

Background and aim: Monkeypox is a zoonotic disease caused by the MPXV. The first human case of monkeypox was reported in the Democratic Republic of the Congo in 1970. Since then, particularly in recent years, the disease has spread globally. Currently, no specific treatment or vaccine has been developed for monkeypox. Pre-injected smallpox vaccines, such as ACAM2000 and JYNNEOS, provide approximately 85% cross protection against MPXV; however, these vaccines are not derived from MPXV. Given that immunoinformatics-based multi-epitope vaccine design is both safe and cost-effective, this study investigates the feasibility of developing a multi-epitope vaccine for monkeypox.

Methods: In this review, we searched PubMed, Scientific Information Database (SID; Iran), and Google Scholar from 2019 up to September 2024. The keywords used in the search were monkeypox, vaccine, and immunoinformatic. By searching these databases, 60 research articles were retrived from these databases, of which 20 were included in the study.

Results: The results indicated that the NCBI server identified proteins in the virus, that containing epitopes which are highly antigenic, non-allergenic, and non-toxic. These epitopes are drived from non-mutated sequences to ensure comprehensive coverage of MPXV. To develop an effective multi-epitope vaccine, it is essential to incorporate both T-cell and B-cell epitopes. The information obtained from assessing physicochemical properties, validating the three-dimensional structure of the vaccine, conducting structural docking, and performing molecular dynamics simulations, yields promising results. The optimization of codon sequences demonstrates that the optimized sequences are highly expressed in E.coli and possess the potential for large-scale production.

Vaccines developed using in silico techniques can induce a robust immune response, characterized by elevated levels of IgM and IgG antibodies. The results of the IEDB analysis indicate that the selected epitopes can cover a wide range of the human population.

Conclusion: In recent years, monkeypox has altered the traditional landscape and begun to spread across several countries. Currently, there are no effective treatments or prevention methods available for MPXV infection. Multi-epitope vaccines act as a potential and effective solution for combating monkeypox, as they can simultaneously elicit both humoral and cellular immunity against various strains of MPXV. The development of these vaccine, which is based on immunoinformatics, is more efficient than traditional vaccine design methods. Therefore, it is crucial to make concerted efforts to advance these vaccines toward clinical applications.

keywords: Monkeypox; Vaccine, Immunoinformatic

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Advancements in Monkey pox virus vaccine development: A current overview

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Medical Immunology

Background and aim: Monkeypox (MPXV) is an emerging zoonotic Orthopoxvirus with clinical manifestations similar to smallpox. And it can significantly affect different societies in a pandemic. Therefore, new treatments and vaccines are being used to treat and prevent monkey pox. The purpose of this study is to investigate the applications and development of monkeypox vaccine.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Monkey pox virus, vaccine, Public health, 43 articles related to inclusion criteria were extracted and then analyzed.

Results: The results of the studies indicated that there are three generations of smallpox vaccines that provide protection against MPXV. The first and second generation of the vaccinia virus protects against MPXV, but it had complications! The modified third generation vaccinia virus has also been effective in preventing Monkeypox virus.

Conclusion: Due to the increasing prevalence of monkey pox in the world, the World Health Organization (WHO) declared a state of emergency. Currently, the designed vaccine is based on several epitopes against Monkey pox, which can be promising in preventing this disease.

keywords: Monkey pox virus, vaccine, Public health.

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A novel approach for prostate cancer therapy: proteolysis_targeting chimeras(PROTACs)

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Medical Immunology

Background and aim: One of the most prevalent cancers in males, prostate cancer is brought on by genetic mutations and inherited diseases. Most prostate tumors are androgen receptor-sensitive, meaning their growth is depend on androgen receptor transcriptional activity. Essentially, the treatment method works by preventing androgen-induced activation of AR. Numerous tactics have surfaced, including as ASOs, siRNA, UT-34, and PROTACs (Proteolysis-Targeting Chimeras). PROTACs have the ability to specifically target specific proteins, such as AR proteins, which are crucial in the development of diseases. This study focuses on how PROTACs technology inhibits AR proteins and how it affects the treatment of metastatic and advanced

Methods: A variety of scientific databases were used to gather information, such as PubMed, Springer, Web of Science, and Google Scholar from 2016 to 2023. To gather better and more accurate information, sources that had similar information were used to collect data.

Results: The findings of this study demonstrate that AR protein signaling varies widely and undergoes modifications, which complicates the course of treatment. Thus, we made the decision to select a specific method to break down the proteins. PROTACs have significant role in inhibiting undruggable proteins and diminish drug resistance, which is a notable issue in PC. Numerous sources inform us that although PROTACs have an antagonistic function against AR, there are still certain operational limitations. We can use this technology in conjunction with

other medicines, such as chemotherapy, to maximize the potential of PROTACs and deliberately slow down the growth of tumors.

Conclusion: We observed the relationship between PROTACs technology and prostate cancer in this paper. We also present additional treatment approaches can manage inadequate selection and medication resistance.

keywords: Prostate cancer (PC), Proteolysis-Targeting Chimeras (PROTAC), mutation, androgen receptor (AR)

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MSCs and psoriasis: crosstalk between MSCs and immune cells in the immunopathogenesis of psoriasis

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Medical Immunology

Background and aim: Psoriasis is a chronic autoimmune disease that presents with skin lesions. A variety of approaches are available for the treatment of psoriatic lesions, including the modulation of immune system activity and metabolic processes. However, these interventions may yield unintended outcomes. Researchers are interested in mesenchymal stem cells (MSCs) due to their capacity to alter immunological responses and ease of use, which could potentially reduce clinical symptoms in immune-mediated diseases. Researchers and physicians are currently engaged in the study of the immunopathogenesis of psoriasis and the Crosstalk between MSCs and innate and adaptive immune cells.

Methods: In this study, the PubMed, WOS, and Scopus databases were evaluated using the keywords "psoriasis," "mesenchymal stromal/stem cell," "immune cell," "Innate cell," " Adaptive immunity, "and "immunomodulation" from January 2018 to August 2023.

Results: The findings of this study indicate that MSCs express regulatory chemicals, microvesicles, and exosomes, which collectively facilitate the regulation of the immune system and the healing of psoriatic lesions. MSCs have been observed to suppress S100A7/8/9 and pro-inflammatory cytokines and chemokines, thereby preventing keratinocyte hyperproliferation and recruiting immune system cells to psoriatic lesions. Conversely, the inhibition of the terminal complement pathway (C5b-9) has been demonstrated to prevent the production of IL-17A, a pivotal cytokine in the pathogenesis of psoriasis, and the development of NETosis in neutrophils. Furthermore, MSC regulation of STAT1, RORγT, and T-bet gene expression has been demonstrated to reduce the generation and infiltration of Th17 and Th1 cells in psoriatic lesions. Additionally,

the investigation revealed that MSCs enhance the frequency and potency of regulatory T cells (Tregs).

Conclusion: MSCs and the molecules secreted from them play a regulatory role in the function of the immune system in the pathogenesis of psoriasis. A deeper comprehension of the mechanisms underlying the immunopathogenesis of psoriasis and the regulatory functions of MSCs and their microvesicles and exosomes on immune cells and the metabolic pathways involved in psoriasis will facilitate the removal of obstacles in this process, enhance the efficacy of this treatment, and ultimately result in the alleviation of symptoms experienced by psoriatic patients.

keywords: "psoriasis," "mesenchymal stromal/stem cell," "immune cell," "Innate cell," " Adaptive

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New advances in CAR-NK cell Technology for AML

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Medical Immunology

Background and aim: The advent of CAR T cells has revolutionized the therapeutic approach to hematological malignancies, but this modality is encumbered by several constraints, including the propensity for inducing cytokine storms, the necessity for a substantial quantity of cells, and the protracted production timeline and escalating costs associated with their development. As a result, researchers have been exploring alternative approaches, including the use of CAR-NK cells, which possess an intrinsic capacity to engage and eliminate neoplastic cells without relying on the identification of tumor-associated antigens for their activation.

Methods: This review is a narrative summary of the current literature on CAR-NK cell therapy. A comprehensive search of various scientific databases was conducted to identify relevant studies investigating the use of CAR-NK cells in the treatment of hematological malignancies. The search included peer-reviewed articles, conference proceedings, and preclinical studies. The identified studies were then reviewed and analyzed to extract information on the advantages and limitations of CAR-NK cells, as well as ongoing efforts to improve their efficacy and safety. The review focuses on the most recent and relevant findings in the field of CAR-NK cell therapy.

Results: The review highlights several key findings related to CAR-NK cell therapy. CAR-NK cells have been shown to possess an intrinsic capacity to engage and eliminate neoplastic cells, without relying on tumor-associated antigen recognition. However, limitations such as limited durability and potential fratricide were also noted. Strategies to overcome these limitations, including genetic manipulation, use of feeder cells, and development of new CAR designs,

have been explored. Additionally, studies have demonstrated the effectiveness of CAR-NK cells in targeting specific tumor antigens, and the potential for combination therapies to enhance their anti-tumor effects. Promising results have been reported.

Conclusion: In conclusion, CAR-NK cell therapy has emerged as a promising alternative to CAR T cell therapy, offering improved safety, efficiency, and efficacy. While significant progress has been made in overcoming the limitations of CAR-NK cell therapy, ongoing research is necessary to address remaining challenges, such as tumor antigen loss, cytotoxicity, and limited cell persistence. Further optimization of CAR-NK cell design, production, and delivery strategies is crucial to unlock the full therapeutic potential of this modality.

keywords: CAR-NK cell technology, Acute Myeloid Leukemia (AML), Immunotherapy, Cancer

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An in silico approach to investigate the interactions in the anti-CD20 scFv-antigen-Fe3O4 nanoparticle complex

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Medical Immunology

Background and aim: The computational technique of molecular docking is able to predict the binding affinity of antigen-antibody and, in general, the receptor to ligand and has a lot of potential for the development of therapeutic agents. The aim of this study was to predict the interactions of anti-CD20 scFv, antigen, and Fe3O4 nanoparticles and the amino acids involved in these interactions.

Methods: Initially, the synthesized recombinant scFv against CD20 was modeled using AlphaFold 3.0. The quality of the obtained model was evaluated by the Ramachandran plot. Then, the complementarity-determining regions (CDRs) of VL and VH of scFv were detected by the IMGT/V-Quest database. The molecular docking study was performed to analyze scFv-antigen binding affinities with ClusPro 2.0 web server. Finally, the interaction between scFv and Fe3O4 was evaluated with PyRx software.

Results: The results obtained from the Ramachandran plot showed that the distribution of 90% of the modeled scFv residues was in favorable regions. According to the molecular docking results, the scFv heavy and light chains were connected to the antigen with 3 and 7 hydrogen bonds, respectively. Also, the

results of PyRx software showed that the Fe3O4 nanoparticle is connected to the antibody heavy chain through three amino acids, Tyr213, Tyr214, and Gly215.

Conclusion: Our in silico findings revealed favorable interactions and binding affinities between the recombinant scFv and CD20 antigen structures, and Fe3O4 nanoparticles, which could be useful for the development of targeted therapy.

keywords: Fe3O4 nanoparticles, ScFv, CD20, Molecular Docking

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Active targeting of chronic lymphoblastic leukemic cells using Anti-CD20 scFv conjugated with Fe3O4 nanoparticles

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Medical Immunology

Background and aim: The therapeutic approaches for blood malignancies, especially chronic lymphocytic leukemia (CLL), present significant challenges in therapeutic approaches. Active targeting reduces adverse effects of drugs and enables more efficient and specific accumulation in the cancer cells. Fe3O4 nanoparticles, because of their characteristics and biocompatibility, are regarded as promising therapeutic nanoparticles. The aim of this study was the targeted therapy of chronic lymphoblastic leukemia using anti-CD20 scFv conjugated with Fe3O4 nanoparticles in a CD20+ Raji cell line as a model for CLL.

Methods: Initially, Fe3O4 nanoparticles were synthesized, and their structural properties were characterized using X-ray diffraction (XRD), field emission scanning electron microscopy (FE-SEM), dynamic light scattering (DLS), and Fourier transform infrared spectroscopy (FTIR). Then, Fe3O4 nanoparticles were bound to ScFv, and after confirming the formation of the complex, its effect on the viability of the CD20+ cell line was evaluated.

Results: The characterization of the synthesized Fe3O4 nanoparticles confirmed their appropriate structural properties. The results showed that the Fe3O4

nanoparticle complex with anti-CD20 scFv significantly increased cell death in the CD20+ cell line.

Conclusion: These findings suggest that the Fe3O4 nanoparticle complex with anti-CD20 scFv can be used for active targeting of CLL cells and contribute to the development of targeted therapies for cancer.

keywords: Fe3O4 Nanoparticles, ScFv, CLL, Targeted Therapy

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Probiotic: novel approach for psoriasis treatment

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Medical Immunology

Background and aim: Psoriasis is a dermatological condition, is associated with the immune system and results in acanthosis, erythema, and scaling. A number of factors, including genetics, lifestyle, smoking, alcohol consumption, pharmaceuticals, and obesity, have been identified as potential causes of psoriasis. An imbalance in the bacterial flora of the gut and skin may contribute to the development of autoimmune disorders. Probiotics have been demonstrated to alleviate psoriasis by enhancing metabolic pathways and competing with pathogens for implantation in tissues. The objective of this study is to examine the potential therapeutic effects of probiotics in regulating the immune system and improving psoriasis.

Methods: In this research project, which spanned from January 2018 to April 2023, the databases PubMed, WOS, and Scopus were evaluated using the keywords "psoriasis," "probiotic," "microbiota," "innate cell," "adaptive immunity," and "immunomodulation" to identify further studies for inclusion in the review.

Results: Probiotic supplements have been demonstrated to alleviate psoriatic lesions via the action of immunomodulatory molecules. Probiotics secrete short-chain fatty acids that bind to receptors, including FF2 (also called GPR43), FF3 (GPR41), and GPR109a, thereby promoting differentiation. An alternative macrophage phenotype and a reduction in the expression of pro-inflammatory genes (e.g., IFN-α, IFN-γ, IL-13, IL-17A, TNF-α, IL-4, IL-17A, and TNF-α) have been observed. The reduction in the PASI score is associated with the presence of Th1/17 cytokines. The aforementioned molecules have been demonstrated to reduce the expression of inflammatory pathways, including NF-κB, which in turn improves psoriatic lesions. Probiotics have the potential to regulate the immune system and mitigate the symptoms of psoriasis. Furthermore, fecal microbiota

transplantation (FMT) has been demonstrated to enhance the efficacy of psoriasis treatment by attenuating the production of IL-17A and IL-23.

Conclusion: Probiotics have been demonstrated to enhance immune system functionality by modulating immune system responses, optimizing metabolic pathways, rectifying digestive dysbiosis, and competing with pathogens for implantation in tissues. Conversely, further research is required to elucidate the relationship between probiotics and immune system cells, as well as the gut-skin axis.

keywords: psoriasis," "probiotic," "microbiota," "innate cell," "adaptive immunity," and "immunomodulation"

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CXCL12 and CXCR4 in the Peripheral Blood of Patients with Parkinson's Disease

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Medical Immunology

Background and aim: The role of CXCL12 and its receptor CXCR4 has not been fully examined in Parkinson's disease (PD). The purpose of this study was to investigate the role of CXCL12/ CXCR4 in the peripheral blood of patients with PD and healthy controls.

Methods: CXCL12 serum levels and CXCR4 mRNA levels were measured in 30 PD patients and 40 controls using ELISA and real-time PCR, respectively.

Results: CXCL12 serum levels were significantly higher in PD patients compared to controls (p 0.0001). Moreover, CXCR4 expression in peripheral blood mononuclear cells (PBMC) of PD patients was significantly increased compared to controls (p 0.0001).

Conclusion: Our findings provide new information on the expression of CXCL12/CXCR4 in PD. CXCR4 expression in PBMC or CXCL12 serum levels may be potential biomarkers of inflammation in PD patients.

keywords: CXCL12 · CXCR4 · Parkinson's disease · Neuroinflammation ·Chemokine

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Enhanced Anti-Cancer Efficacy of Albumin-Based Curcumin Nanoparticles: A Targeted Strategy for Overcoming Drug Resistance and Modulating Immunity in Breast Cancer Therapy

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Medical Immunology

Background and aim: Breast cancer, a major cause of cancer deaths among women, is driven by genetic and epigenetic changes promoting uncontrolled cell growth. While conventional treatments like surgery and chemotherapy have advanced, drug resistance and adverse effects remain challenging. Curcumin, a phytochemical with anti-cancer properties, shows promise as a complementary therapy but faces limitations in bioavailability and stability. Albumin-based nanoparticles enhance curcumin's stability and targeting. This study synthesized bovine serum albumin-curcumin nanoparticles (BSA/Cur NPs) and evaluated their cellular uptake, cytotoxicity, apoptotic, wound healing, and redox effects, demonstrating their potential to improve breast cancer therapy and immunomodulation in PBMC co-culture.

Methods: BSA/Cur NPs were synthesized using a desolvation method and extensively characterized for their structural and functional properties. FTIR analysis was conducted to confirm chemical composition, while dynamic light scattering and scanning electron microscopy provided data on particle size, zeta potential, and morphology. Curcumin release from BSA/Cur NPs was evaluated in different pH environments, mimicking physiological and tumor conditions. In vitro studies included assessing cellular uptake, cytotoxicity, apoptosis, and wound healing effects in MCF-7 breast cancer and MCF-10A normal epithelial cells. Additionally, PBMC co-culture experiments assessed immunomodulatory

effects, and antioxidant activity was measured through assays of total antioxidant capacity and oxidative stress markers. Cytokine levels and cell cycle progression of PBMCs were also evaluated, providing insights into the immunological and therapeutic potential of BSA/Cur NPs.

Results: BSA/Cur NPs were prepared via desolvation, yielding particles around 150 nm. FTIR confirmed curcumin-albumin interactions through hydrogen bonding. Release studies showed pH-dependent behavior, with higher release in acidic conditions (p0.0001). Cellular uptake was significantly higher in MCF-7 cells than MCF-10A cells (p0.001). Cytotoxicity assays indicated that BSA/Cur NPs were more cytotoxic to MCF-7 cells than free curcumin (p0.001) and paclitaxel (p0.05), with minimal toxicity to MCF-10A cells. Apoptosis assays confirmed enhanced apoptosis in MCF-7 cells. Wound healing assays showed that BSA/Cur NPs inhibited MCF-7 migration. Treatment with curcumin or BSA/Cur NPs in MCF-7 cells increased PBMCs in the G0/G1 phase and decreased the apoptotic sub-G1 population. BSA/Cur NPs reduced TGF-β and IL-10 while increasing IFN-γ in MCF-7 co-cultures, with MCF-10A cells showing elevated cytokine secretion, especially with curcumin treatment.

Conclusion: Curcumin conjugated with bovine serum albumin enhances its anticancer efficacy against breast cancer cell lines while minimizing toxicity to normal cells. This nanocurcumin formulation improves antioxidant activity and modulates cytokine profiles, suggesting its potential as a therapeutic adjunct in reducing the side effects of conventional breast cancer treatments.

keywords: Breast Neoplasms; Curcumin; Nanoparticles; Albumins; Immunomodulation

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Long-term impacts of tonsillectomy on children's immune functions

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Medical Immunology

Background and aim: There exist a wide level of discrepancy regarding the role of tonsils and its indication among pediatricians and ENT specialists. This fact sometimes causes confusion and delay in making the right decisions by parents and specialists for appropriate treatment of patients.Thus, the aim of this study was to investigate the effects of long-term tonsillectomy on the immune system of patients.

Methods: In this case-control study we measured the status of immune system in 34 children (aged 9-15 years) following 4 to 6 years of tonsillectomy. We have also enrolled 30 healthy children with similar age group. Venous blood samples were taken and the serum levels of IgG, IgA, and IgM were detected along with expression of CD4, CD8, CD10 and CD56. Data were analyzed by SPSS version 18 software and a P 0.05 was considered as significant.

Results: We found that the mean serum levels IgM, IgA, and IgG in the case group was significantly (P 0.0001) lower than the control group. Whereby, the CD4, CD8 and CD56 expressions was examined, there was no significant difference in both groups while only CD10 expression was lower in tonssiloctomized patients (P = 0.108).

Conclusion: Overall, according to these findings, CD10 as a marker of B lymphocytes in children undergoing tonsillectomy was significantly less than those healthy children. This may indicate a decrease in B cells and further reduced antibody production in these patients.

keywords: Cellular immune system; humoral immune system; tonsillectomy.

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CXCL1, CXCL10 and CXCL12 Chemokines are Variously Expressed in Acute Myeloid Leukemia Patients Prior and Post Bone Marrow Transplantation

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Medical Immunology

Background and aim: The chemokine-receptor axes play parts in development of leukemia, CXCL1, CXCL10 and CXCL12 are involved in immune responses. Thus, we have examined the serum levels of these chemokines in parallel with their related cognate receptors (CXCR1, CXCR3 and CXCR4) in AML (acute myeloid leukemia) patients prior and post BMT (bone marrow transplantation) therapy.

Methods: Clinical specimens were collected from 46 AML patients (23 M1 and 23 M3 subtypes) before/after BMT. CXCL1, CXCL10 and CXCL12 concentrations were determined by ELISA. The mRNA levels of the related receptors were detected by

QRT_PCR. Data were analyzed by T-test, χ2 and ANOVA statistical methods in SPSS software version 18. A difference was regarded significant if P value 0.05.

Results: Our results indicated that the elevated levels of CXCL12 in AML patients were remained unchanged after transplantation. The CXCL10 concentration was decreased in patients. All studied chemokines were elevated in BMT patients with history of 9 times PLT transfusion. In patients who received BMT from siblings CXCL1 and CXCL10 have been elevated, whereby they were compared to patients who received BMT from parents while CXCL12 sustained unchanged in groups. Serum measures of CXCL1 and CXCL10 were induced in acute and chronic GVHD patients in compare to these without GVHD.

Conclusion: According to the results, it can be concluded that these chemokines play fundamental parts in pathogenesis of both AML and BMT. It is worthy to note that chemokines could be used as diagnostic markers alongside with possible promising therapeutic targets.

keywords: AML; BMT; CXC chemokine; CXC chemokine receptor; Leukemia.

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Chemokine CCL2 and its receptor CCR2 in different age groups of patients with COVID-19

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Medical Immunology

Background and aim: Despite the development of various antiviral drugs, most of them are not effective in the treatment of coronavirus disease 2019 (COVID-19) as a hyperinflammatory disorder. Chemokine (C-C motif) ligand 2 (CCL2) is one of the critical CC chemokines involved in the pathogenesis and severity of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. This study aimed to investigate the expression of CCL2 and CC chemokine receptor 2 (CCR2) in COVID-19 patients.

Methods: Peripheral blood samples were collected from 60 confirmed COVID-19 patients and 60 age-matched healthy subjects. The ages of the subjects were categorized as follows: up to 20 years, 20 to 40 years, 40 to 60 years, and more than 60 years. CCL2 serum levels were measured using the enzyme-linked immunosorbent assay (ELISA). CCR2 gene expression in peripheral blood mononuclear cells (PBMCs) was measured employing real-time polymerase chain reaction (PCR).

Results: In all age groups, CCL2 serum levels were significantly elevated in patients compared to healthy controls (P 0.0001). CCL2 levels were higher in severe patients than in moderate patients. Moreover, CCR2 expression by PBMCs was higher in patients compared to control subjects. However, a significant

difference between patients and controls over 60 years of age was identified (P = 0.0353). There was no significant difference in CCR2 expression between moderate and severe COVID-19 patients.

Conclusion: Taken together, the findings demonstrate that CCL2 and CCR2 are upregulated in COVID-19 patients at protein and mRNA levels, respectively. Therefore, the CCL2/CCR2 axis may be a potential therapeutic target in order to improve patient outcomes.

keywords: CCL2, CCR2, COVID-19, SARS-CoV-2 infection, Chemokine

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Drug repurposing, a potential therapeutic strategy for the treatment of allergic asthma: A Systematic Review

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Medical Immunology

Background and aim: Asthma is a chronic respiratory system disease with a high prevalence globally. It is an inflammatory disease associated with bronchial inflammation, which is related to the presence of inflammatory cells. These cells, along with the structural cells of the respiratory tract, produce cytokines, chemokines, and other inflammatory mediators, leading to goblet cell hyperplasia, mucus hypersecretion, and ultimately, airway obstruction and hyperresponsiveness. A definitive treatment for asthma has not yet been identified due to its complicated pathogenesis. This review generally discusses the effectiveness of repurposing methods in asthma treatment as a faster and more cost-effective therapeutic approach from a research perspective.

Methods: From 2018 to 2024, we searched related databases including Pubmed, Web of Science and Google Scholar using the keywords "Asthma," "Drug Repurposing," and "Anti-inflammatory," and their synonyms. Ultimately we found 10 articles that met inclusion and exclusion criteria.

Results: Considering the main complications of asthma, Medications are used for two main purposes: bronchodilation and anti-inflammatory effects. Developing new and more effective treatments including drug repurposing approaches is essential due to individuals' resistance to current anti-inflammatory drugs, including corticosteroids. Drug repurposing involves the reusing of FDA-approved medications for novel therapeutic applications. A key treatment for asthma is reducing inflammation. Drugs with anti-inflammatory effects are used with the

repurposing approach. For example, Brinzolamide, a carbonic anhydrase inhibitor, inhibits the advancement of mast cells. INCA-6 inhibits calcineurin, leading to a reduction in inflammatory cytokines. Statins suppress HMG-CoA reductase, inhibiting type 2 inflammation and mucus production. As a PDE3 inhibitor, Enoximone increases cAMP and cGMP, resulting in vasodilation and bronchodilation. Calcilytics act as negative allosteric modulators (NAMs) of the calcium-sensing receptor (CaSR), reducing smooth muscle contraction and inhibiting airway remodelling. Niclosamide reduces mucus secretion and exerts anti-inflammatory effects by inhibiting TMEM16A and TMEM16F.

Conclusion: A major treatment for asthma involves using corticosteroid drugs, but around 30-50% of patients are resistant to them, and developing new drugs is costly. This creates a need for new therapeutic approaches. Repurposing existing drugs has advantages over developing new ones, including cost-effectiveness, established safety and toxicity profiles, and time-saving by bypassing phases 0 and I of clinical trials and directly entering phases II and III.

keywords: Asthma, Allergic Asthma, Drug Repositioning, Drug Repurposing, Anti-inflammatory

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Investigating the effect of Hesperetin on the expression of progesterone membrane receptor (mPRα) on the surface of K562 cells

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Medical Immunology

Background and aim: Chronic Myeloid Leukemia (CML) is a proliferative disease affecting the granulocyte lineage and accounts for 30% of adult leukemia cases. Progesterone's impact on cell growth varies by cell type. The anticancer effects of progesterone have been shown on several types of cancer. It interacts with cells via membrane progestin receptors (mPR). Certain flavonoids, such as hesperetin (Hsp), possess anticancer properties. Given the broad presence of progesterone receptors in the body, upregulating progesterone receptors in specific cancers could support treatment. The aim of this study was to investigate the impact of Hsp on viability and mPRa expression of K562 cells.

Methods: In this study, K562 cell line was used. After culturing the cells in T25 flask and passage, they were transferred to a 96-well plate and after incubation, a new culture medium containing specified concentrations of Hsp (200-400 µg/ml) was added to the wells. The MTT assay is done and IC50 was obtained for 24, 48 and 72 hours. At 48 and 72 hours. following Hsp (120 µg/ml) treatment, the study used flow cytometry to measure the level of mPRα expression on the cells. The data was analyzed with one way-Anova statistical method.

Results: The results of this study showed that Hsp has a significant decrease in cell viability in a dose and time dependent manner compared to the control group. Furthermore, Hsp significantly increases the expression of mPRα at 48 and 72 hours. (p0.005)

Conclusion: According to our study, Hsp lead to suppress K562 cell growth, reducing cell viability and increase mPRα expression. Hsp alone or in combination with progesterone could be explored as a treatment option for CML in the future.

keywords: Chronic myelogenous leukemia; Hesperetin; Progesterone; Membrane progesterone receptor; K562

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Title of Abstract (The Role of Adiponectin as a Biomarker for Systemic Sclerosis)

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Medical Immunology

Background and aim: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by immune system dysregulation, leading to fibrotic and inflammatory changes in connective tissues and blood vessels. Symptoms include skin thickening, vascular damage, and complications in internal organs. Recent studies have emphasized the role of inflammatory and metabolic factors in SSc progression, with adiponectin—an adipocyte-derived cytokine—emerging as a key player in its pathogenesis. This review explores adiponectin's involvement in SSc, its relationship to clinical symptoms and disease progression, its potential as a biomarker for disease severity, and its therapeutic implications. B Systemic sclerosis presents significant challenges in understanding its

Methods: A comprehensive literature search was conducted using PubMed, Google Scholar, Medline, and Scopus with the terms "Systemic sclerosis" or "SSc" and "adiponectin.".

Results: Adiponectin is recognized for its anti-inflammatory and anti-fibrotic properties, playing a significant role in metabolic regulation. Lower adiponectin levels have been observed in individuals with SSc, suggesting a link between its deficiency and disease severity. Recent findings indicate a novel association between serum adiponectin levels and skin thickness in SSc patients, correlating with disease activity and severity. Increased skin thickness—characteristic of systemic sclerosis—is associated with poorer clinical outcomes. Adiponectin provides protective effects against fibrosis by inhibiting fibroblast activation and collagen synthesis, suppressing pro-inflammatory cytokines, promoting anti-

inflammatory mediators, improving endothelial function, and reducing oxidative stress—critical factors in SSc's vascular complications

Conclusion: Adiponectin plays a vital role in the pathogenesis of systemic sclerosis, affecting metabolic regulation, inflammation, and fibrosis. Targeting adiponectin therapeutically offers a novel approach to managing SSc. Strategies such as enhancing adiponectin levels, using pharmacological agents to boost its expression, or administering adiponectin analogs are promising avenues for future investigation. Further research should focus on the signaling pathways and precise mechanisms by which adiponectin influences SSc, and explore therapeutic strategies to leverage its beneficial effects

keywords: Systemic sclerosis, Adiponectin, Autoimmune disease.)

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The Association Between Traumatic Brain Injury and Accelerated Fracture Healing: A Study on the Effects of Growth Factors and Cytokines

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Medical Immunology

Background and aim: Restoration of bone structure and tissue, as well as its function after injury and fracture, is known as fracture healing. Orthopedic clinical practices and laboratory studies have accordingly indicated that fracture healing rate and duration can be affected by traumatic brain injury (TBI).in this study was aimed to explore alterations in the serum concentrations of BMP-2, PDGF, FGF-2, TGF-β, IL-1β, and IL-6 growth factors and cytokines as well as the time of fracture healing in TBI, cases with a femoral fracture, and fracture + TBI patients, as well as healthy subjects.

Methods: In this study, a total number of 30 patients (mean age 25.47 ± 2.3 years) with TBI, 30 cases (mean age 30.21 ± 4.9 years) with a femoral fracture, 30 patients with fracture + TBI (mean age 32.06 ± 6.1 years), from Ali Ebn-Abitaleb Hospital, Rafsanjan, Iran, between March 2017 and June 2019, as well as 30 healthy subjects (mean age 29.68 ± 5.1 years) were recruited .• Blood Analysis: The blood samples of the three groups of patients were collected 12 h and 4 weeks after hospital admission. • Cytokine and Growth Factor Assay: Cytokines and growth factors (namely, BMP-2, PDGF, FGF2, TGF-β, IL-1β, and IL-6) were measured using immunoassay kits (R&D Systems, Minneapolis, MN). • Determining Fracture Union: To determine fracture union in groups with a femoral fracture and a femoral fracture + TBI, the radiographic data including callus size, cortical continuity, and progressive loss of fracture line

Results: • Serum Levels of the Studied Cytokines and Growth Factors: Within 12 h: The mean serum level of BMP-2, FGF-2, PDGF, TGF-β, IGF-I, IL-1β, and IL-6 was

significantly different in all study groups within 12 h. In this respect, there was a statistically significant difference between the control group and the femoral fracture (p 0.001), the TBI (p 0.001), and the fracture + TBI (p 0.001) groups, but such a difference was not significant compared with the TBI (p = 0.8) group in the serum level of FGF-2 (p 0.05). After 4 Weeks: Findings the study revealed that a significant difference was found between serum level of BMP-2, IL-1β, TGF-β, and FGF-2 in the control group and the femoral fracture and the fracture + TBI (p 0.001) groups after 4 weeks, but such a difference was not significant compared with the TBI group

Conclusion: serum levels of BMP-2, PDGF, FGF-2, TGF-β, IL-1β, and IL-6 were measured in patients with TBI, cases with a femoral fracture, fracture + TBI patients as well as healthy subjects. The findings showed that the serum levels of BMP-2, FGF2, IL-1β, and PDGF in the fracture + TBI group had significantly increased over 12 h and after 4 weeks compared to other studied groups. However, the serum levels of IGF-I, IL-6, and TGF-β in the fracture + TBI group were increased significantly only within 12 h compared to other

keywords: Fracture healing; Cytokine; Growth factor; Traumatic brain injury; Femoral fracture

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Study of HN protein homology in the Paramyxoviridae family

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Medical Immunology

Background and aim: Newcastle disease (ND) is a highly contagious viral infection that mainly affects birds, especially domestic fowl. The disease is caused by a member of the well-known avian paramyxovirus type 1, also called NDV. Due to the lack of effective treatment for this disease, current strategies for poultry vaccination are mainly based on the hemagglutinin neuraminidase (HN) gene, which encodes a multifunctional protein. It plays an important role in virus binding, entry, and pathogenesis. The HN protein is considered a potent target for peptide vaccines, an innovative approach to enhance immunity against a wide range of viral challenges, including NDV.

Methods: In this study, we investigated the peptide backbone of the Newcastle vaccine, regarding the HN protein. Uniprot database, was used to investigate the HN homologues of Newcastle virus, whose crystallography results were reported. Multiple alignment was performed in the CLC Main Workbench program. Protein 3D structure was predicted by PHYRE2 and compered with its altered structures in Chimera X.

Results: Fifteen homologues of HN were found in Uniprot. Multiple alignments suggested that the consensus sequence was identical throughout its sequence for the 15 Newcastle strains, with just two amino acid substitution at positions 62 (A/R) and 329 (A/V), resulting in final four sequences, all of which were submitted for 3D Structure prediction. Position 62 is omitted in mature protein, so it was not included in the modeling. According to PHYE2, the closest model for NDV-HN was 4fzh with 78% coverage and 100% confidence. The amino acid variation did not lead to any modification in the protein structure, so that both of mentioned residues were contributed in a B-turn region of the protein.

Conclusion: Peptide-based vaccines offer a range of advantages for combating Newcastle disease. The results of this study suggest that the HN gene is a highly conserved protein among Newcastle virus strains. Thus it could be considered as a strong antigen against various types of NDV.

keywords: Newcastle disease, Paramyxoviridae, peptide vaccine, 3D modeling, Multiple Alignment

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One step further in targeting acute leukemia by combining antibody-based immunotherapies and small molecule inhibitors

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Medical Immunology

Background and aim: Acute leukemia is a bone marrow-related disease characterized by fast progression and the production of immature blood cells rather than normal ones that are classified as either acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML). Chemotherapy as a conventional treatment has many side effects, thus new medications that target intracellular molecules and cell surface markers on leukemic cells have been developed in the last decades.

Methods: Herein, in this article, a focus is made on antibody-based targeted treatments, which so far, have shown to improve the treatment outcomes, including the immune checkpoint inhibitors (ICIs), monoclonal antibodies, and bi-specific T-cell engagers (BiTE). Other classes of new chemotherapeutic drugs that are discussed herein include small molecule inhibitors (SMIs) of intracellular target molecules, including tyrosine kinase, serine/threonine kinases, BCL-2, and SMO.

Results: These inhibitors have been very effective in dealing with certain genetic changes besides blocking the important cell molecules in acute leukemia responsible for the failure of the immune system. Due to its ability to simultaneously inhibit multiple signaling pathways and also lessen drug side

effects and increase efficacy in treating resistant tumor cells, combination therapy has gained much attention.

Conclusion: This review focuses on assessing the use of antibody-mediated treatments in combination with SMIs for treating acute leukemia. Given the distinct mechanisms and objectives of these two therapeutic modalities that have the potential to synergistically enhance one another, along with the findings from clinical trial investigations, it appears that combination therapy may yield superior efficacy compared to monotherapy, representing a progressive advancement in the treatment of acute leukemia.

keywords: ALL - AML - Small molecule inhibitor-antibody based immunotherapies

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Impact of Probiotics on Th1/Th2 Balance in Women with Recurrent Implantation Failure: A Double-Blind RCT

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Medical Immunology

Background and aim: infertility is a prevalent issue, with recurrent implantation failure (RIF) posing a significant challenge. The immunological imbalance between Th1 and Th2 cytokines, attributed to their distinctive roles in inflammation and tissue regulation, may contribute to RIF pathogenesis. Therapeutic strategies leveraging immunomodulatory agents, including probiotics, to redress the Th1/Th2 ratio, have emerged as a promising means to improve reproductive outcomes. The primary objective of this study was to examine the therapeutic potential of probiotics in restoring the Th1/Th2 balance and thereby improving implantation outcomes in women who have experienced recurrent implantation failure (RIF).

Methods: This study characterized the immunological profile of women with recurrent implantation failure (RIF) using multiple approaches, including flow cytometry for Th1/Th2 cell frequencies, ELISA for serum cytokine levels, and qRT-PCR for cytokine microRNA expression in peripheral blood mononuclear cells (PBMCs), revealing alterations in the Th1/Th2 balance and cytokine levels in RIF patients.

Results: Flow cytometry analysis of the peripheral blood revealed a significantly higher proportion of Th1 cells in the RIF patient group compared to healthy controls, while healthy controls exhibited a higher proportion of Th2 cells. The probiotic intervention resulted in a significant decrease in the proportion of Th1 cells and a concurrent increase in Th2 cells in the peripheral blood of RIF patients. ELISA analysis of serum samples revealed significantly elevated levels of proinflammatory cytokinesand concomitantly decreased levels of anti-

inflammatory cytokines in RIF patients compared to healthy controls Following the six-month probiotic intervention, RIF patients exhibited a marked decrease in the concentrations of the proinflammatory cytokines TNF-α and IFN-ɣ, along with an increase in the levels of the anti-inflammatory cytokines IL-10 and IL-4.Following the probiotic treatment, a significant decrease in the expression of proinflammatory cytokine genes and a concurrent increase in the expression of anti-inflammatory cytokine genes were observed.

Conclusion: Our findings suggest that probiotics may represent a novel and non-invasive therapeutic option for restoring immune homeostasis and improving implantation outcomes in women with RIF. The current study highlights the promising role of probiotics in this context, although further clinical trials with larger cohorts and longer-term follow-up are needed to validate and build upon these preliminary findings. Additionally, more research is required to elucidate the precise mechanisms underlying the beneficial effects of probiotics in this setting, as well as to identify optimal strains, dosages, and treatment durations.

keywords: Infertility; Probiotic; Recurrent Implantation Failure

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Effect of Thymoquinone Nano emulsion on 5-Fluorouracil on the HT-29 Colorectal cancer cell line

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Medical Immunology

Background and aim: Chemotherapy remains a cornerstone in cancer treatment, yet its efficacy is often compromised by significant side effects, including drug resistance. Thymoquinone (TQ), a natural compound derived from the seeds of Nigella sativa, has demonstrated promising anticancer properties in various studies. This research investigates the effects of thymoquinone nano-emulsion (TQ-NE) on the HT-29 colorectal cancer cell line, both independently and in combination with the commonly used chemotherapeutic agent 5-fluorouracil (5-FU).

Methods: We developed a method for synthesizing TQ-NE, which exhibited an average particle size of 129 nm. The cytotoxic effects of TQ, 5-FU, and TQ-NE were assessed using an in vitro model. The half-maximal inhibitory concentration (IC50) values for each treatment were calculated to evaluate their effectiveness. Cytotoxicity assays were performed on HT-29 cells and human fibroblasts to determine selective toxicity. Additionally, flow cytometry was employed to analyze the apoptotic effects induced by these treatments in the HT-29 cell line.

Results: The physicochemical characterization confirmed that TQ-NE had an average size of 129.5 nm, suitable for cellular uptake. The cytotoxicity results indicated that TQ-NE exhibited enhanced potency compared to TQ and 5-FU alone, with IC50 values of 61.01 µM for 5-FU, 21.81 µM for TQ, and 15.12 µM for TQ-NE. Notably, the combination treatment of TQ-NE with 5-FU resulted in significantly lower cell viability compared to TQ alone, suggesting a potential synergistic effect. Flow cytometric analysis revealed distinct apoptotic patterns in both the TQ-NE monotherapy group and the combination group when

compared to the control group, indicating that TQ-NE enhances apoptosis in HT-29 cells

Conclusion: The findings suggest that TQ-NE may enhance the therapeutic efficacy of 5-FU in vitro by increasing its cytotoxic effects on colorectal cancer cells. Furthermore, the use of lower concentrations of TQ-NE could potentiate the inhibitory effects of 5-FU, presenting a promising strategy for improving colorectal cancer treatment outcomes while potentially reducing adverse side effects associated with higher doses of conventional chemotherapy

keywords: Thymoquinone, 5-fluorouracil, nano-emulsion, colorectal cancer

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CAR-T Cell Therapy A Novel Immunotherapy Method in Breast Cancer Treatment: A Systematic Review Article

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Medical Immunology

Background and aim: CAR-T cell therapy is a new immunotherapy method that has shown promising results in treating cancer. Chimeric antigen receptor (CAR) T cells are T cells that are modified through biotechnological methods, including genetic engineering and cell culture, by adding a chimeric antigen receptor and then returning them to the patient's body. CAR-T cells identify cancer cells specifically and attack them. The first FDA-approved CAR-T cell therapy was Tisagenlecleucel(Kymriah) on Aug30th, 2017, and the next generations are developing. In this study, we examine the impact of CAR-T cell therapy for breast cancer, the challenges of this therapeutic method, and suggested solutions.

Methods: This systematic review article was performed using articles published on PubMed, Google Scholar, Scopus and Clinical Trial until 2024. The keywords were CAR T cell, Breast Cancer, Human and Female. By searching these databases, 136 articles were found, and 97 were removed by reading titles and abstracts. 39 articles were selected under the inclusion criteria. All articles were chosen from English articles. Duplicate articles, non-English and ex-vivo articles were excluded.

Results: According to the articles, the use of CAR-T cell therapy as a cancer treatment is expanding. Some advantages of this method include targeted treatment, long-lasting responses, potential for combination therapy, personalized treatment, overcoming resistance to conventional therapies, and potential for treating multiple types of cancer. However, there are also some limitations especially in solid tumors, such as T cell exhaustion, T cell dysfunction,

antigen escape, immunosuppressive tumor microenvironment (TME), tumor heterogeneity and on-target off-tumor toxicity effects.According to the recent studies, adding certain transcription factors (e.g., FOXO1), some interleukins, especially IL-2, using combination therapies with oncolytic viruses and improvements in cell culture conditions can amplify CAR-T cell performance.

Conclusion: It seems that CAR-T cell therapy, as a new immunotherapy method in breast cancer treatment, has shown remarkable results. However, despite the advantages of this approach, its limitations and side effects challenge the treatment process. Significant advancements in medical biotechnology and genetic engineering have led to the production of new generations of CAR-T cells. Nevertheless, according to the ever-increasing use of CAR-T cell therapy, further investigation and experimentation into CAR-T cells are strongly recommended. There is hope that CAR-T cell therapy will play a considerable role in treating cancers.

keywords: CAR-T cell, Breast cancer, Immunotherapy, Treatment

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Role of Cancer-Derived miRNAs in Immune Escape and Therapeutic Resistance: Potential Targets for Cancer Immunotherapy- A Systematic Review

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Medical Immunology

Background and aim: Cancer, a complex disease defined by uncontrolled cell growth, often develops mechanisms to evade the immune system. MicroRNAs (miRNAs), small non-coding RNAs around 22 nucleotides long, have recently been recognized as significant gene regulators that frequently show altered expression in cancers. Dysregulated miRNAs not only drive tumor development but also impact immune responses by modifying immune-related molecules within both tumor and immune cells. This ability to facilitate immune escape positions miRNAs as promising targets for potential therapies to combat cancer's resistance to immune detection.

Methods: To examine the role of cancer-derived miRNAs in immune escape, we conducted a systematic search on Google Scholar and PubMed, focusing on terms like "Micro RNA," "MicroRNA," "miRNAs," "immune escape," and "treatment-emergent resistance." Out of many, seven articles met the inclusion criteria for our review.

Results: Finally, 7 articles were included in the studies indicating that certain miRNAs, like miR-155 and miR-146a, shape immune cell differentiation and activity, influencing T cells and macrophages and creating an immunosuppressive environment that supports tumor progression. Paladini et al. illustrate miRNAs' dual roles in either suppressing or promoting anti-tumor immunity, which highlights their potential as immunotherapeutic targets. Some miRNAs, like miR-

9 and miR-346, interfere with the antigen presentation process, thereby reducing the ability of CD8+ T cells and NK cells to recognize and target cancer cells. Others, such as miR-23a and miR-155, act within the tumor microenvironment to suppress immune responses further, giving cancer cells a way to avoid immune detection. In addition, miR-155 and miR-21 influence myeloid-derived suppressor cells (MDSCs) and regulatory T cells (Tregs), supporting immune suppression and aiding immune evasion. Tumor-derived miRNAs, like miR-24 and miR-203, are also transferred to immune cells via exosomes, which further dampens

Conclusion: In conclusion, cancer-derived miRNAs play critical roles in immune escape by modifying immune responses in the tumor microenvironment to aid tumor survival and progression. Targeting these miRNAs could offer a promising strategy to enhance anti-tumor immunity, tackle treatment resistance, and support the development of more effective cancer immunotherapies.

keywords: MicroRNA; miRNA; immune escape; treatment-emergent resistance

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Association of interleukin-17A and chemokine/vascular endothelial growth factor-induced angiogenesis in newly diagnosed patients with bladder cancer

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Medical Immunology

Background and aim: The human interleukin-17 (IL-17) family comprises IL-17A to IL-17 F; their receptors are IL-17RA to IL-17RE. Evidence revealed that these cytokines can have a tumor-supportive or anti-tumor impact on human malignancies. The purpose of this study was to assess the expression of CXCR2, IL-17RA, and IL-17RC genes at the mRNA level as well as tissue and serum levels of IL-17A, vascular endothelial growth factor (VEGF), and transforming growth factor β (TGF-β) in patients with bladder cancer (BC) compared to control.

Methods: Forty-five male patients with confirmed invasive bladder cancer (BC) classified as T2-T4 and 42 age- and gender-matched healthy subjects were enrolled in this study. Tissue and blood samples were collected from newly diagnosed patients before chemotherapy. IL-17RA, IL-17RC, and CXCR2 expression were measured using the real-time (RT) PCR technique, and serum levels of IL-17A were measured by enzyme-linked immunosorbent assay (ELISA).

Results: This study showed that gene expression of IL-17RA, IL-17RC, and CXCR2 in the tumoral tissue of BC patients was significantly upregulated compared with normal tissue. The findings disclosed a significant difference in the serum and tissue concentrations of IL-17A, VEGF, and TGF-β between the patient and the control groups, as well as tumor and normal tissues.

Conclusion: This study reveals notable dysregulation of CXCR2, IL-17RA, and IL-17RC genes, alongside changes in IL-17A, VEGF, and TGF-β levels in patients with BC than in controls. These findings indicate their possible involvement in BC development and their potential as diagnostic and therapeutic targets.

keywords: IL-17A, CXCR2, VEGF, TGF-β, Bladder cancer

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Investigating the expression of anti/pro-inflammatory cytokines in the pathogenesis and treatment of ulcerative colitis and its association with serum level of vitamin D

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Medical Immunology

Background and aim: Ulcerative colitis is an idiopathic gastrointestinal disease characterized by chronic inflammation in the gastrointestinal tract. Cytokines may be responsible for immunopathogenesis, mucosal and tissue damage, and even response to treatment. Also, vitamin D besides its role in calcium and phosphorus homeostasis and bone health is an immunomodulatory and anti-inflammatory agent. Considering that understanding the role of cytokines can lead to important advances in the pathogenesis and treatment of this disease, we aimed to investigate the relative gene expression of pro- and anti-inflammatory cytokines in biopsy samples taken from the affected area in the colon of treated and treatment-resistant ulcerative colitis

Methods: A total of 47 ulcerative colitis patients were included in this case-control study. The case group consisted of 23 patients suffering from treatment-resistant ulcerative colitis and the control group consisted of 24 ulcerative colitis

patients who responded to routine treatments. Serum level of vitamin D was measured using the ELISA method at the time of colonoscopy. Real-time PCR was performed to measure the relative gene expression of the pro-inflammatory cytokines including tumor necrosis factor-α (TNF-α), interferon-gamma (IFN-γ), interleukin-1β (IL-1β), IL-6, IL-8, IL-17A, IL-33, IL-35, and the anti-inflammatory cytokines including transforming growth factor-beta (TGF-β), IL-10, and IL-35 in case and control group. Finally, their interactions with serum level of vitamin D were investigated.

Results: Data were expressed as the mean±standard deviation (STD), and p-values less than 0.05 (p0.05) were considered statistically significant. The age in the control group was 45.88±18.51 and in the case group was 41.30±13.01. The relative gene expression of the pro-inflammatory cytokines TNF-α, IFN-γ, IL-1β, IL-6, IL-8, IL-17A, IL-33, IL-35, and anti-inflammatory cytokines TGF-β, IL-10, and IL-35 between case and control group in biopsy samples were not statistically different (p0.05). Also, the serum level of vitamin D was not correlated with gene expression of pro- and anti-inflammatory cytokines (p0.05).

Conclusion: In this study, there was no significant relationship between the expression of pro- or anti-inflammatory cytokines and response to treatment. Therefore, in this study, these cytokines seem to have no important role in the pathogenesis or protection of the disease and response to the treatment. Besides, different treatments did not affect the expression of these cytokines in ulcerative colitis patients. Also, the serum level of vitamin D is not related to the expression of pro- and anti-inflammatory cytokines in the affected area in the colon of treated and treatment-resistant patients.

keywords: Ulcerative colitis; Cytokine; Vitamin D; Inflammation; Pathogenesis; Treatmen

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Investigating the role of vitamin D in treated and refractory ulcerative colitis patients: a case-control study

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Medical Immunology

Background and aim: Ulcerative colitis is a chronic inflammatory bowel disease characterized by persistent mucosal inflammation extending from the rectum into the proximal colon. Vitamin D regulates immune responses in several inflammatory and autoimmune diseases. Thus, this study aims to investigate the role of vitamin D in the pathogenesis and treatment of ulcerative colitis patients.

Methods: This was a case-control study and 4 groups of people were included. Group 1: People with ulcerative colitis who responded to treatment (24 Persons). Group 2: A family member of patients who responded to treatment and do not have the disease (24 Persons). Group 3: People with ulcerative colitis who do not respond to treatment (23 Persons). Group 4: A family member of treatment-resistant patients who do not have the disease (23 Persons). Blood samples were taken and analyzed for complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and serum vitamin D levels.

Results: In this study, the age; mean (std. dev.) in the ulcerative colitis group who responded to treatment was 45.88 (18.51) and in the ulcerative colitis group who did not respond to treatment was 41.30 (13.01). Vitamin D; mean (std. dev.) in the ulcerative colitis group who responded to treatment was 24.96 (9.66) ng/mg and in the ulcerative colitis group who have not responded to treatment was 27.70 (12.28) ng/mg, showing that there is no significant difference in terms of serum vitamin D.

Conclusion: In this study, there was no significant association between ulcerative colitis and serum vitamin D levels. Therefore, in our study, the serum level of vitamin D has no role in the pathogenesis and treatment of ulcerative colitis patients.

keywords: Ulcerative colitis; Vitamin D; ESR; CRP.

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MT-MMPs as Diagnostic Biomarkers in Ulcerative Colitis

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Medical Immunology

Background and aim: Ulcerative colitis, a form of Inflammatory Bowel (IBD), involves chronic inflammation of the colon and can lead to significant tissue damage. Matrix metalloproteinases (MMPs), particularly membrane-type MMPs (MT-MMPs), are involved in extracellular matrix remodeling and have been suggested to play a role in IBD pathogenesis. However, their roles in ulcerative colitis remain poorly understood. This study aimed to evaluate the expression of MT-MMPs in newly diagnosed and treatment-resistant ulcerative colitis patients and assess their diagnostic potential in differentiating these patients from healthy individuals.

Methods: Colon biopsy samples were collected from three groups: newly diagnosed ulcerative colitis patients, treatment-resistant ulcerative colitis patients, and healthy controls. RNA was extracted, and the expression of MT-MMPs was quantified using Real-Time PCR. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the diagnostic value of MT-MMPs in differentiating ulcerative colitis patients from healthy controls.

Correlation analyses were conducted to assess the relationship between the expression levels of these MMPs and clinical markers.

Results: MT2-MMP and MT5-MMP were significantly downregulated in newly diagnosed and treatment-resistant ulcerative colitis patients compared to healthy controls (p 0.05). ROC curve analysis indicated that MT2-MMP and MT5-MMP had diagnostic value, with high sensitivity and specificity for distinguishing ulcerative colitis patients from healthy individuals. Additionally, a significant negative correlation was found between the expression levels of MT2-MMP and MT5-MMP and clinical measures of disease severity, including the colitis severity scale and inflammatory markers (p 0.01).

Conclusion: Our findings suggest that MT2-MMP and MT5-MMP are downregulated in ulcerative colitis and that their reduced expression is associated with increased disease severity. These MMPs may have diagnostic utility in distinguishing between ulcerative colitis patients and healthy individuals, offering potential as biomarkers for disease detection and progression. Furthermore, the negative correlation between MMP expression and clinical severity highlights the potential therapeutic implications of targeting these MMPs in ulcerative colitis management.

keywords: MT-MMPs, Inflammatory Bowel Disease, Ulcerative Colitis

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Enhancing Cancer Immunotherapy: The Role of Fecal Microbiota Transplantation in Modulating Immune Responses

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Medical Immunology

Background and aim: Fecal microbiota transplantation (FMT) has emerged as a novel therapeutic strategy that holds promise for enhancing cancer immunotherapy. FMT involves the transfer of gut microbiota from healthy donors to patients, aiming to restore microbial diversity and function in the recipient's gastrointestinal tract. Emerging evidence suggests that a balanced gut microbiota is essential in modulating immune responses, which is critical for patients undergoing immunotherapy, such as immune checkpoint inhibitors (ICIs). However, the effectiveness of FMT in improving cancer immunotherapy outcomes remains under active investigation.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Fecal Microbiota Transplantation, Cancer Immunotherapy, Immune Responses, 83 articles related to inclusion criteria were extracted and then analyzed.

Results: Findings indicate that FMT can restore gut microbiome diversity in cancer patients, often disrupted by prior treatments for cancer itself. Specific microbial profiles, particularly those enriched in Bifidobacterium and Akkermansia, were associated with improved responses to ICIs. Patients receiving FMT displayed increased immune cell infiltration in tumor microenvironments and elevated levels of pro-inflammatory cytokines, potentially enhancing anti-tumor immunity. Moreover, FMT reduced treatment-related toxicities in certain patients, potentially by maintaining gut barrier integrity.

Conclusion: The evidence supports FMT as a potential adjunct to cancer immunotherapy by modifying the gut microbiota to favorably influence the host immune system. While FMT shows promise, challenges remain, such as donor selection, long-term safety, and understanding host-microbe interactions. The findings suggest that FMT could enhance the efficacy of cancer immunotherapy, though more large-scale, controlled studies are needed to validate these results and establish standardized protocols. In conclusion, FMT represents an exciting frontier in cancer immunology, with potential to significantly improve patient outcomes when integrated into therapeutic regimens.

keywords: Fecal Microbiota Transplantation, Cancer Immunotherapy, Immune Responses.

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Gene Therapy and CRISPR-Cas9: Overcoming Drug Resistance in Melanoma

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Medical Immunology

Background and aim: Melanoma is an aggressive skin cancer associated with high mortality and significant global health burden. Traditional treatments, particularly targeted therapies like BRAF and MEK inhibitors, have initially shown promise but face challenges due to innate and acquired drug resistance. Recent advances in gene therapy and CRISPR-Cas9 genome editing offer novel approaches to address these limitations by directly targeting genetic mutations and enhancing immune response specificity.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords CRISPR-Cas9, Melanoma, Gene Therapy, 73 articles related to inclusion criteria were extracted and then analyzed.

Results: Emerging studies demonstrate that CRISPR-Cas9 can effectively target BRAF and associated mutations, reducing melanoma cell proliferation and drug resistance. Gene therapy applications, such as mRNA vaccines, have shown promise in stimulating immune responses against melanoma-specific antigens, contributing to prolonged patient survival in early trials. Combined approaches integrating CRISPR with immune checkpoint inhibitors further increased effectiveness, highlighting the potential for synergistic therapies.

Conclusion: The integration of gene therapy and CRISPR-Cas9 holds transformative potential for melanoma treatment. While traditional BRAF-targeted therapies face resistance, genome editing and personalized gene-based therapies offer a more precise and adaptable approach to target evolving tumor genetics. Future research should focus on optimizing delivery mechanisms and

assessing long-term safety of gene editing in clinical settings. Ultimately, personalized, gene-targeted strategies may redefine treatment standards for melanoma, providing durable responses and overcoming the limitations of current therapies.

keywords: CRISPR-Cas9, Melanoma, Gene Therapy.

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Evaluating the effect of exosome-encapsulated miR-4289 on gene and protein expression pattern of menstrual blood-derived mesenchymal stem cells from endometriosis patients

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Medical Immunology

Background and aim: Endometriosis is a non-cancerous disease of women that occurs as a result of retrograde blood flow and leads to displacement of endometrial stem cells and progressive lesions of endometriosis. These additional lesions result from dysregulation of multiple cellular functions, including inflammation, angiogenesis, migration, steroid signaling pathways, and proliferation. This disease leads to pelvic pain, infertility and in some cases cancer. Researchers have investigated various treatments including hormonal treatments, surgery and genetic treatments. so that they can limit its negative side effects.

Methods: Since the therapeutic benefits of mesenchymal stem cells are provided through paracrine functions, we used exosomes derived from menstrual blood-derived stem cells (MenSCs) and mir4289 for the treatment of endometriosis. Non endometriosis stem cells (NE-MenSCs) were cultured in two groups containing and without microRNA. Then the secreted exosomes were collected from them and we used these exosomes to treat endometriosis stem cells (E-MenSCs). The third group was treated by direct transfer of microRNA. Mechanisms and pathways, including inflammation, proliferation, migration, and angiogenesis of endometriosis were investigated using real-time PCR, ELISA,

Western blotting, and scratch assays 36 hours post-treatment. Also, in this study, the expression of ESR1, IL-10, IL-1β, CTNNB1, VEGF, MMP2, MMP9, IDO1, KRAS genes and the amount of synthesis of IL-10, IL-1β, Ki67, ROS and ESR1 proteins were investigated.

Results: Based on gene and protein test answers we found that exosome, microRNA treatment and exosome collected from cells which are received microRNA with reagent. significantly reduced the expression levels of markers related to inflammation, proliferation, migration, angiogenesis and Wnt/β.catenin pathway in E-MenSCs, which are overexpressed in endometriosis. In this study, we provide preliminary evidence for the potential of exosome collecting from NE-MenSCs, exosome of NE-MenSCs containing microRNA and transfecting microRNA to E-MenSCs as treatment improving endometriosis. Based on our results, we suggest that after appropriate clinical trials, exosomes derived from MenSCs could be considered as a better therapeutic option for improving endometriosis compared to conventional treatments and demonstrate their potential as a cell-free product in endometriosis repair.

Conclusion: This study examines the treatment of endometriosis by exosomes derived from healthy cells, transfer of microRNA to endometriosis cells, and treatment with exosome extracted from cells that have already been transferred to them. According to the obtained results, they had a positive effect on some cellular functions like proliferation, migration, inflammatory, angiogenesis, and Wnt/β.catenin pathway caused a significant decrease in gene expression and protein synthesis. But some cellular aspects like ROS and ESR1 had a decreasing but insignificant trend, so they need more research to confirm.

keywords: Menstrual blood, Mesenchymal stem cells, microRNA, Exosome, Transfection, Endometriosis.

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The Genetic Puzzle of Rheumatoid Arthritis: Causes, Progression, and Treatment

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is a multifaceted autoimmune disorder characterized by chronic inflammation and progressive joint destruction, influenced by a complex interplay of genetic and environmental factors. Substantial evidence highlights a significant genetic contribution to RA pathogenesis, with key genetic risk factors including human leukocyte antigen (HLA) genes and non-HLA variants. These genetic elements are intricately involved in immune dysregulation, antigen presentation, and signaling pathways.

Methods: NA

Results: NA

Conclusion: The genetic heterogeneity of RA is further accentuated by gene-gene and gene-environment interactions, while biomarkers and genetic profiles associated with disease progression and joint damage continue to be rigorously explored. Additionally, the evolving field of pharmacogenomics sheds light on the challenges and prospects of developing personalized therapeutic approaches for RA. This review aims to provide a comprehensive overview of the current genetic understanding of RA, promoting further research and offering valuable insights into the genetic determinants of RA susceptibility, severity, and treatment response.

keywords: Rheumatoid arthritis, genetics, HLA genes, non-HLA genes, pharmacogenomics

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Comparison of Interleukin-18 Serum Levels in Patients with Breast Cancer and Idiopathic Granulomatous Mastitis

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Medical Immunology

Background and aim: Breast cancer (BC), as a global challenge, is one of the most prevalent malignant diseases among women. Idiopathic granulomatous mastitis (IGM) is a rare, chronic inflammatory breast disease that primarily affects women of fertility age. IGM mimics symptoms and radiographic patterns of BC. IL-18 plays a dual role in cancer, as it can promote tumor growth or reduce tumor growth. This study aimed to compare the serum levels of IL-18 in BC and IGM patients.

Methods: This case-control study was conducted on 45 patients with BC, 25 with IGM (I), and 30 healthy individuals (C) with normal screening tests as the control group. The BC group consisted of 25 newly diagnosed BC patients (N), and 20 patients with metastatic BC (M). Specialized pathologists confirmed the histopathological pattern of BC and IGM. Enzyme-linked immunosorbent assay (ELISA) sandwich technique was used for the measurement of IL-18 serum levels. All statistical analyses were performed by SPSS-23, and GraphPad Prism. P 0.05 was considered statistically significant.

Results: The serum level of IL-18 showed statistically significant higher values in the three patient groups than in the control group (P 0.001). In addition, the IL-18 levels in the M group were significantly higher than in the N, and I groups (P 0.01). There was no statistical significance between N and I groups (P 0.05).

Conclusion: IL-18 levels were significantly elevated in BC compared to the IGM and control groups. IL-18 has a potential role as a prognostic indicator in BC, particularly for patients with metastasis.

keywords: Breast neoplasms, Granulomatous mastitis, Interleukin-18, Metastasis

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Dihydrorhodamine-123 flow cytometry method: time for substantial revision in technical procedure

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Medical Immunology

Background and aim: The dihydrorhodamine 123 assay is generally applied to measure the production of intracellular reactive oxygen species in neutrophils using flow cytometry and is considered a diagnostic evaluation for chronic granulomatous disease. In fact, there is a broad range of variables that can directly or indirectly affect test results, either individually or collectively. It is therefore crucial to identify the ideal requirements to achieve reliable results as well as using these requirements to provide standard operating procedures that should be taken into account. Therefore, we focus on aligning optimum results by comparing preanalytical and analytical phases that influence test results, such

Methods: The study involved 25 healthy volunteers with no history of disease. Blood samples were collected and divided into different anticoagulant tubes and stored at different temperatures. DHR-123 and PMA were prepared in solutions for testing. Working solutions were prepared for DHR-123 and PMA concentrations. A method was established to test the neutrophil function, with specific focus on oxidative activity. The DHR-123 assay involved diluting blood with working solution, incubating, adding PMA, lysing cells, and analyzing with a flow cytometer. Flow cytometry techniques were used to isolate and analyze single cells for accurate counting of neutrophils. The neutrophil oxidative index was calculated to evaluate oxidative activity. Multiple samples were analyzed for consistency and accuracy in testing neutrophil function.

Results: The study looked at how different concentrations of DHR and PMA solutions impacted activated neutrophils. Both high and low concentrations of the solutions led to a decrease in activated neutrophils due to excessive oxidative

stress or insufficient stimulation. Therefore, 200 ng/ml DHR and 20 ng/ml PMA were chosen for the experiments. The study also examined how incubation temperature affected activated neutrophils, finding that 37°C resulted in a decrease in viable neutrophils, recommending room temperature instead. The type of anticoagulant used and storage conditions also affected results, with sodium citrate being the most effective. Strict adherence to sample handling protocols is important to maintain neutrophil viability, and the use of neutrophil-specific markers may not be necessary for accurate neutrophil counts.

Conclusion: The study analyzed how storage time and temperature affect CGD patient samples. It found that longer storage and higher temperatures harm neutrophil activity. Testing should occur within 6 hours and use specific anticoagulants, keeping samples at 4°C if sent elsewhere.

keywords: Dihydrorhodamine-123; DHR-123 assay; neutrophil oxidative burst; neutrophils; optimum conditions; NOI

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Modified method of mesenchymal stem cells culture derived from Rat bone marrow

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Medical Immunology

Background and aim: Mesenchymal stem cells are multipotent with self-renewal potential that isolated from different tissues. The appropriate and efficient method of cultivating these cells may be important for various researches.

Methods: Rat bone marrow was harvested using 5-ml syringe and flashed with low glucose DMEM medium containing Penicillin/Streptomycin (100u/ml)/(0/1mg/ml). Cells were collected and washed three times with PBS and added to the flask containing DMEM-low glucose medium with 15 and 20% FBS. Cell medium was replaced three times every 12 hours.

Results: According to this culture method, the cells attached to the flask in a fibroblastic-like after three days and filling about 60% of the flask surface. After one week, the density of mesenchymal stem cells reached 80-90%. The cells were passaged at 80% confulancy after three days. The first passage of mesenchymal stem cells was frozen with 10% dimethyl sulfoxide.

Conclusion: The method of multi-passages mesenchymal stem cell culture can solve the problems that include the long time to reach the desired density in-vitro proliferation and maintenance of these cells.

keywords: Rat Mesenchymal stem cell, Cell culture, Multi-passages

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Soluble expression of recombinant human interleukin 24 protein in E. coli for clinical applications

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Medical Immunology

Background and aim: Interleukin-24 (IL-24), a member of the IL-10 cytokine family, display broad cancer-specific suppressor effects. In addition to its antitumor activity, IL-24 contributes to immune protection against bacterial and viral infections, promotes tissue regeneration and facilitates wound healing. Because of its significant clinical potential, recombinant production of IL-24 is important. In the present study, IL-24 was expressed in three strains of E. coli, Rosetta-gami plysS, Shuffle (T7), and Rosetta-gami.

Methods: The cDNA of the IL-24 was first synthesized and cloned into the pET 21a(+) expression vector and then transformed into bacteria. Protein expression was induced by adding IPTG (1mM) to the cells at mid-log phase. After induction, the cells were incubated at 35ºC for a further 4 hours. A lysis buffer containing 10 mM imidazole was added to the bacterial suspension to extract soluble proteins. Protein expression was analyzed using dot blotting and SDS-PAGE, and the expression levels were quantified using ImageJ software. The IL-24 protein was then purified using an Immobilized Metal Affinity Chromatography (IMAC) column.

Results: The results showed that of the three strains used, the protein expression level was higher in Rosetta-gami. As a result, this strain was selected for large-scale expression. The protein was then purified, followed by SDS-PAGE analysis, which confirmed the successful purification of the protein with high purity.

Conclusion: The results showed that the Rosetta gami strain is a suitable host for the soluble expression of interleukin-24, a protein with a disulfide bond.

keywords: Interleukin-24, E. coli, Rosetta gami

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The Association Between Autophagy and Cancer

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Medical Immunology

Background and aim: Autophagy is a process that occurs in eukaryotes and allows cells to reclaim their contents and eliminate unnecessary organelles. This process is carried out through the identification of targets and their delivery to lysosomes for degradation, and it has a close connection with cancer. Different types of autophagy include macroautophagy and microautophagy and Chaperone-mediated autophagy (CMA). Macroautophagy involves the formation of double-membrane vesicles (autophagosomes) to engulf proteins and organelles, while micro autophagy directly targets cytoplasmic contents , In the chaperone-mediated autophagy (CMA), excess and damaged proteins with a specific KFERQ motif are transported close to the lysosomal membrane by heat.

Methods: In this review, a comprehensive search was conducted using the keywords "Autophagy" and " cancer " or "autophagy in cancer management" and "type of autophagy" in PubMed, Google Scholar, and Web of Science databases.

Results: This study examines the role of autophagy in cancer. Some research suggests that cancers are dependent on autophagy, and this process can lead to resistance to treatment. However, molecules that specifically inhibit autophagy were identified in 2020. These substances interact with the enzymes linked to autophagy and hold potential for the development of more effective cancer therapeutics with reduced side effects, but they have not progressed to the clinical trial stage.

Conclusion: autophagy can either facilitate or suppress the proliferation of cancer, depending on the type of cancer and the behavior of the cancer cells. Prior to initiating therapeutic interventions,it is essential to determine the baseline levels of autophagy in various cancers. Additionally, the presence of autophagy factors in cancer cells may help control cancer growth; however,due to the low levels of autophagy in these cells,their effectiveness is limited. The discussion regarding the role of this process in cancer treatment has gained attention in recent years,and further research is still demanded

keywords: Autophagy; Microautophagy, Chaperone-Mediated Autophagy, Macroautophagy

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Mesenchymal stem in Cancer Therapy

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Medical Immunology

Background and aim: Background Mesenchymal stem cells (MSC) as targeted carriers for delivery of cancer drugs to tumor tissue. MSCs modulate the immune system through reprogramming T lymphocytes or stimulating natural killer (NK) cell to enhance the detection and destruction of cancer cells. These strategies, combined with genetic engineering and genome-editing techniques such as CRISPR/Cas9.

Methods: Methods In this review, various therapeutic aspects of MSCs in solid tumors, such as breast, pancreatic, and colorectal cancer are examined. We have summarized the emerging relationships between MSCs and their effects on tumorigenesis and development.

Results: Results Positive outcomes of MSC therapy are significantly related to the substances released by MSCs, especially exosomes. Research indicates that extracellular vesicles (EVs) originating from mesenchymal stem cells (MSCs) are membrane-bound, these vesicles have the capability to imitate their source cells, exhibiting anti-tumor properties, along with a natural tendency to target tumors. Consequently, EVs derived from MSCs could be a promising cell-free option for cancer therapy.

Conclusion: Conclusion MSCs can be used to counteract the suppression of blood vessel formation in tumor tissues and thus prevent tumor progression.

keywords: Key words Cancer, Mesenchymal Stem Cell, Novel trearment strategies

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New methods in wound healing with mesenchymal stem cells

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Medical Immunology

Background and aim: Background Mesenchymal stem cells (MSCs) exhibit a remarkable capacity for self-renewal and have the ability to differentiate into various cell types. The efficacy of MSCs in facilitating tissue repair and wound healing depends on their paracrine mechanisms. These stem cells accelerate wound closure, stimulate the formation of new blood vessels, reduce inflammatory responses in wounds, positively influence extracellular matrix, and remodeling overall regeneration. While cell therapy offers numerous benefits, it is important to address the various challenges associated with this approach, such as tumor formation and the risk of immune rejection.

Methods: Methods This study is a review study that searched scientific databases such as PubMed, Scopus, Embase and Google Scholar from 2016 to 2024 using the keywords wound healing, mesenchymal stem cell articles related to inclusion criteria were extracted and then analyzed.

Results: Results The enhancement of stem cell capabilities through genetic modification has been studied in the context of wound healing. Cell-derived vesicles and exosomes play a crucial role in this context; exosomes have the ability to promote processes such as cell growth, movement, and the formation of new blood vessels in the healing environment. Conversely, scaffolds, matrices, and hydrogels create optimal environments that facilitate cell differentiation, proliferation and wound healing.

Conclusion: Conclusion Various substances such as platelet-rich plasma, growth factors, platelet lysate, exosomes, scaffolds, matrices, hydrogels, and especially cell therapy with mesenchymal stem cells (MSCs) are recommended to improve wound healing.

keywords: Key words New methods, Wound healing, Mesenchymal stem cell

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Discrepancies Between Anti-CCP and RF: Diagnostic Challenges in Rheumatoid Arthritis

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is an inflammatory systemic disease with unknown etiology that mainly causes joint stiffness and deformity with symmetrical patterns. 0.5 to 1% of the world's population is affected by this disease. The progression of RA is due to an abnormal and impaired immune response that is triggered by the interplay of genetic and some environmental factors. Two main autoantibodies are present in RA and play significant roles in the pathogenesis of the disease. Rheumatoid factor (RF) targets the FC fragment of IgG and anti-cyclic citrullinated peptide antibodies (Anti-CCP) that target citrullinated peptides and proteins. Additionally, these two autoantibodies.

Methods: Data from 158 patients with rheumatoid arthritis referred to the Reference Medical Laboratory of Urmia from 1402 were collected. The percentage and correlation of the anti-CCP titer of the patients with age and RF titer was examined and their laboratory results were analyzed with SPSS 27 and GraphPad Prism statistical software.

Results: Among the anti-CCP-positive patients, 52.2% were also RF-positive, while 47.8% were RF-negative. The average age of patients was 50.8 years, with a slight female predominance (82.2%) compared to males (17.8%). There was a positive correlation between anti-CCP and the age of patients (r=0.16 and p=0.03). However, there was no significant correlation between RF-positive and anti-CCP (r=0.1, p= 0.3)

Conclusion: Considering that the RF test has low sensitivity and specificity in identifying patients with rheumatoid arthritis, especially in the early stages, its effectiveness cannot be emphasized. To be more precise, the low sensitivity and specificity of the RF test cause up to 50% of patients to have a negative RF result, depending on the different stages of rheumatoid arthritis, which means that there is no need for both tests to be positive at the same time in patients with rheumatoid arthritis. The higher incidence of anti-CCP and rheumatoid arthritis in

keywords: Rheumatoid arthritis; Anti-CCP; Rheumatoid factor

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Innovative Modifications of Human Umbilical Cord Mesenchymal Stem Cells for Enhanced Therapeutic Efficacy in Systemic Lupus Erythematosus

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Medical Immunology

Background and aim: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by chronic inflammation and multi-organ damage, particularly affecting the kidneys. Mesenchymal stem cells (MSCs) have shown potential in immunosuppression and tissue repair, yet their therapeutic effects in SLE remain limited. Advances in genetic modification enhance MSC functions to better target immune pathways. This study aims to assess the therapeutic potential of genetically modified human umbilical cord MSCs (hUC-MSCs) in SLE, utilizing modifications like DMOG, miR-125b-5p, IL-37, and dexamethasone liposomes. These modifications are designed to reduce inflammation and fibrosis while improving kidney function in SLE models by targeting immune regulatory pathways.

Methods: The research process was conducted following the PRISMA guidelines. An extensive literature search was conducted across electronic databases, including Embase, PubMed, Scopus, and Web of Science, using the keywords "Genetically Modified Mesenchymal Stem Cells," "Systemic Lupus Erythematosus," "SLE," and "Gene Therapy" since November 2024. In this investigation, studies using modified hUC-MSCs with agents such as DMOG, miR-125b-5p, IL-37, and Dexlip were included to evaluate their therapeutic effects in SLE. Studies were evaluated based on specific inclusion and exclusion criteria

designed for this research. High-quality studies with accessible full text written in English were included in this systematic review.

Results: A total of 10 high-quality studies met the inclusion criteria and were included in this research. The current study explores several innovative strategies to improve the therapeutic efficacy of MSCs for SLE by targeting specific immune pathways. Pretreatment of hUC-MSCs with DMOG demonstrated potential to reduce kidney fibrosis and inflammation through downregulation of the TGF-β/Smad pathway, along with decreased levels of inflammatory cytokines TNF-α, IFN-γ, and IL-6. In addition, MSCs modified with miR-125b-5p resulted in increased IL-4 and decreased IL-17A levels, which was associated with reduced inflammatory cell infiltration in kidney and lung tissues. Overexpression of IL-37 in MSCs showed significant immunosuppressive effects by reducing inflammatory cytokines and autoantibodies, leading to improved survival and alleviation of SLE symptoms. Furthermore, dexamethasone liposome-integrated MSCs (Dexlip-MSCs) utilized glucocorticoid receptor signaling to inhibit T cell proliferation and enhance anti-inflammatory responses. Finally, MSCs overexpressing miR-146a targeted the TRAF6-NF-κB pathway, suppressing immune activation and lowering inflammation.

Conclusion: This study highlights the potential benefits of various modifications to hUC-MSCs for improving therapeutic outcomes in SLE. Modifications with miR-125b-5p, IL-37, DMOG, and dexamethasone liposome all resulted in reduced inflammation and fibrosis, as well as enhanced kidney function. These approaches effectively modulated key immune pathways, including TGF-β/Smad, IL-4/IL-17A, and TRAF6-NF-κB signaling. These findings present promising strategies for more effective SLE treatments. However, further clinical exploration is needed to translate these results into therapeutic applications.

keywords: Gene therapy;Genetically modified mesenchymal stem cells; SLE; Systemic lupus Erythematosus.

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The chemical conjugation of a peptide derived from the RHD blood group antigen and Keyhole limpet hemocyanin as a carrier protein for in vitro immunization

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Medical Immunology

Background and aim: Immunization is a preliminary step for antibody production. A common approach for generating human antibodies is in vitro immunization, which necessitates the isolation of blood mononuclear cells from whole blood. For the immunization of B lymphocytes aimed at antibody production, both complete protein antigens and specific peptide sequences can be utilized. The larger and more complex structure of complete proteins elicits a stronger response compared to peptides; however, synthetic peptides have advantages as they can target specific regions of the target protein and do not require antigens derived from humans or animals. Despite these benefits, synthetic peptides necessitate conjugation with

Methods: The synthetic peptide used for immunization is designed against the amino portion of the RH protein, consisting of 29 amino acids, with the thirtieth amino acid being cysteine, positioned at the peptide's terminus for conjugation purposes. To enhance the immunogenicity of the peptide in question, it must be conjugated with a larger protein known as a carrier. Conjugation can be performed through various methods, one of which involves solution-based conjugation using a reagent. For the conjugation of the peptide and KLH, SMCC were utilized. In this method, the KLH protein reacts with SMCC through its amino group, resulting in an active derivative of the carrier protein. This active form of the protein establishes a covalent bond with the free thiol group in the peptide, leading to a firm attachment between the peptide and the carrier. The attachment of KLH protein to SMCC was performed in a buffer with a pH

Results: The conjugation between the peptide and the carrier was confirmed by ELISA method. The ELISA plate was coated with the hapten-carrier conjugate, followed by the addition of commercial anti-RHD. In the third layer, HRP-conjugated anti human globulin was added. The results OD450 nm=0.32±0.04 indicated a successful conjugation of the peptide and the carrier molecule.

Conclusion: Given the advantages of using synthetic peptides in immunization, it appears feasible to utilize the KLH-conjugated peptide for the immunization against the RHD antigen.

keywords: Synthetic peptide, Carrier, SMCC

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The effects of inorganic nanoparticles in alleviating Rheumatoid arthritis: A systematic review

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder Characterized by persistent joint pain and progressive cartilage and bone damage. The pathogenesis of rheumatoid arthritis (RA) involves a preclinical phase marked by immune dysregulation before clinical onset, which progresses to chronic inflammatory synovitis. Key immune mechanisms, including the activity of TNF-a, IL-6, and B cells, drive inflammation, while therapies targeting these pathways have advanced RA management but unresolved needs persist due to disease heterogeneity. Conventional therapies often fall short of fully controlling symptoms or halting disease progression, leading to an increased interest in nanotechnology as an innovative therapeutic approach. Inorganic

Methods: This systematic review was conducted in adherence to PRISMA guidelines, employing a thorough search across multiple databases, including PubMed and Google Scholar, up to the year 2024. Using carefully selected keywords, we screened studies focused on the therapeutic effects of inorganic nanoparticles in both animal models of rheumatoid arthritis (RA) and RA patients. Ultimately, 30 studies met the inclusion criteria and were analyzed based on factors such as nanoparticle type, dosage, administration method, and the observed therapeutic outcomes. The extracted data were integrated to assess the therapeutic potential, efficacy, and safety profiles of these nanoparticles within the context of RA management.

Results: This systematic review highlights promising inorganic nanoparticle strategies for rheumatoid arthritis (RA) treatment. Folic acid-modified silver nanoparticles (FA-AgNPs) effectively targeted M1 macrophages, inducing their apoptosis and promoting M2 polarization, thereby alleviating RA symptoms in murine models. Iron-quercetin coordination nanoparticles (Fe-Qur NCNs) exhibited potent anti-inflammatory effects by neutralizing excess ROS and reducing NF-κB pathway activation, leading to decreased joint inflammation and bone erosion. Magnetic nanoparticles (MNPs) provided precision in targeting inflamed joints, minimizing systemic toxicity. Copper silicate nanoparticles loaded with zinc-curcumin (Zn-Cur) facilitated the M1 to M2 macrophage transition, promoting bone regeneration. Additionally, metallic nanoparticles (MNPs) demonstrated intrinsic anti-inflammatory properties by modulating key signaling pathways. Multifunctional nanoparticles, such as hyaluronic acid-modified nanoparticles loaded with methotrexate (FT-HA-MTX NPs) and hollow manganese dioxide nanoparticles (H-MnO2 NPs), improved therapeutic precision by enhancing drug delivery and reducing toxicity. Liposome/gold hybrid nanoparticles with Coenzyme Q10 (LGNP-CoQ10) reduced pro-inflammatory cytokines in collagen-induced arthritis. Two IL-7Rα-specific peptides (P258

Conclusion: This review underscores the potential of inorganic nanoparticles as innovative therapeutic agents for rheumatoid arthritis. By leveraging their unique properties, these nanoparticles can effectively target inflammatory pathways, enhance drug delivery, and promote immune modulation, presenting promising avenues for improved management of RA symptoms and disease progression.

keywords: Inorganic Nanoparticles, Rheumatoid Arthritis, Anti-inflammatory, Drug Delivery, Immune Modulation

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Wharton's Jelly mesenchymal stromal cells prevent lung injuries following infarction-induced heart failure in rats

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Medical Immunology

Background and aim: Myocardial infarction (MI) often leads to severe systemic complications, including pulmonary injury. Indeed, inflammatory burden and hemodynamic stimulation due to acute MI can affect the lungs as a distance organ through injury to microvascular endothelium resulting to the elicitation of interstitial overflow and alteration of alveolar capillary gas diffusion. This study aimed to explore the therapeutic potential of Wharton's jelly-derived mesenchymal stem cells (WJ-MSCs) and their secretome in mitigating lung injury following MI.

Methods: Twenty-four male Wistar rats were randomly derived into four groups. (1) Sham, (2) MI, (3) MI+Wj-MSCs, and (4) MI+Wj-MSCs'-secretome. After confirmation of MI induction on day 7, the third group received 2.5 × 106 of WJ-MSC intravenously. The fourth group received 250 µl of secretome intravenously

on days 7 and 9. After 35 days, the animals were euthanized, and samples were taken for further evaluation.

Results: According to cardiac histopathologic evaluation, systemic WJ-MSCs administration showed better cardio protection compared to the secretome following MI. In the control group, noticeable thickening of the inter-alveolar septa, interstitial edema, vascular congestion, marked increased numbers of inflammatory cells within and around the wall of bronchioles, perivascular and within the inter-alveolar septa, and partial atelectasis were detected in lungs. However, systemic administration of WJ-MSCs and their derived secretome decreased the levels of congestion, interstitial inflammation, and damage of epithelial architecture; the noticeable diminished injury only observed in WJ-MSCs received group. Also, Masson's trichrome staining in heart tissue demonstrated WJ-MSCs administration could significantly reduce the infarct size compared with MI group. In lung tissue of non-treated group, collagen deposition and alveolar thickening was seen. However, administration of stem cells obviously inhibited collagen deposition when compared with the MI group. Serum cytokine analysis revealed significantly elevated IL-1β level in the MI group

Conclusion: Inflammation plays a pivotal role in the pathogenesis of lung injury following MI, contributing to both pulmonary and cardiac dysfunction. The current study demonstrated that systemic administration of WJ-MSCs and their secretome exerts significant protective effects against MI-induced lung damage by attenuating inflammatory responses and reducing fibrosis. Furthermore, these interventions were associated with improved cardiac function, highlighting their potential as promising therapeutic approaches for mitigating the systemic complications of MI.

keywords: Heart failure, Pulmonary, Cell therapy, Wharton's jelly mesenchymal stem cells,

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The Relationship between Serum Levels of Carcinomabrion Antigen (CEA) in Patients with Colorectal Cancer and Pathological Characteristics of the Tumor with UBE2Q1 Gene Expression

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Medical Immunology

Background and aim: Despite all the advances in the diagnosis and treatment of colorectal cancer, it remains the third most deadly cancer in men and the second most deadly cancer in women. Increased expression of UBE2Q1 has been reported in human colorectal tumors. However, its role in the progression of colorectal cancer has not been investigated. CEA protein also increases in cancers such as colorectal cancer and can be used as an indicator to evaluate the response to treatment or resistance to treatment. Therefore, this study examined the prognostic relationship between colorectal cancer and increased UBE2Q1 gene expression by evaluating CEA protein.

Methods: In this cross-sectional study, 48 tissue and serum samples from patients with colorectal cancer collected in a previous study were included. The patients studied had undergone surgery at Faghihi Hospital of Shiraz University of Medical Sciences. The expression level of UBE2Q1 gene in tumor tissue and adjacent normal tissue of these patients was examined by Western Blot and quantitatively measured by densitometry. Serum CEA levels in these patients' serum samples were measured using ELISA.

Results: Data from 48 colorectal cancer patients with a mean age of 57.23 ± 14.58 years, half of whom were female, were analyzed. The mean serum CEA level was 2.35 ± 3.45, and the mean UBE2Q1 gene expression was 5.80 ± 12.39. The mean size of tumors completely removed after surgery was 29.17 ± 46.13 square

centimeters. 21.43% of patients had lymph node involvement, and 70% had good pathological differentiation. 35.71% of the tumors were located in the rectum and 33.33% in the colon. The correlation between serum CEA levels and UBE2Q1 gene expression was statistically significant with a correlation coefficient of 0.38; similarly, the correlation between UBE2Q1 gene expression and liver function tests, alkaline phosphatase, and AST, with correlation coefficients of 0.50 and 0.43 respectively, was significant. The correlation between CEA and tumor size, age, and none of the liver function tests was significant.

Conclusion: There is a direct and significant relationship between serum CEA protein levels and UBE2Q1 gene expression, indicating that UBE2Q1 gene expression can help predict prognosis and treatment approach. There was also a direct and significant relationship between UBE2Q1 gene expression and alkaline phosphatase and AST tests, but no significant relationship was found between UBE2Q1 gene expression and age, gender, or any of the histopathological factors.

keywords: Colorectal Cancer, Carcinoembryonic Antigen, Ubiquitin Conjugating Enzyme E2 Q1

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The Role of Mesenchymal Stem Cells in Modulating Adaptive Immune Responses in Multiple Sclerosis

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Medical Immunology

Background and aim: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system, leading to significant disability through neurodegeneration. Despite advances in the understanding of MS pathophysiology, effective treatments remain limited. Mesenchymal stem cells (MSCs) have gained attention as a potential therapeutic option due to their immunomodulatory and regenerative properties. This review examines MS pathogenesis, emphasizing the role of immune cells, particularly T cells, in disease progression, and explores MSCs' therapeutic potential. Although preclinical studies in animal models show MSC efficacy, challenges such as donor variability, culture conditions, migratory capacity, and immunological compatibility hinder widespread clinical adoption.

Methods: Studies were collected using different keyword combination: multiple sclerosis; MS; central nervous system; CNS; mesenchymal stem cells; MSC; immunomodulatory properties; therapeutic potential. The literature search strategy in this paper included searching PubMed, PMC, and Science Direct, Springer open, Google scholar and BioMed Central databases.

Results: .

Conclusion: The emerging research on the role of immune responses in neuroinflammatory diseases such as MS highlights a complex interplay between various T cell subsets. MSCs, with their ability to interact with various immune cells and release anti-inflammatory cytokines, offer a novel therapeutic approach for MS. Their capacity to shift the balance from proinflammatory Th1 and Th17 responses toward more anti-inflammatory Th2 and Treg responses is particularly noteworthy. The ongoing exploration of MSCs as a treatment modality for MS presents a significant opportunity to develop more effective therapies for this debilitating.

keywords: multiple sclerosis; MS; central nervous system; CNS; mesenchymal stem cells;

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Oral vaccines are effective in treatment of allergies

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Medical Immunology

Background and aim: oral vaccines a category of vaccines that lead to the development of immunity. We know that mucosal surfaces are considered the first line of defense against foreign agents in our bodies. Oral vaccination can play a significant role in defending this first line of defense. Unlike parenteral vaccination, which is effective only in activating systemic and humoral immune levels, oral vaccines can activate both cellular and humoral immune responses at the systemic level and also stimulate responses at the mucosal surfaces. Vaccines against enteric pathogens play an important role in reducing individual susceptibility to diseases. Oral vaccines

Methods: In this review, a comprehensive search was conducted using the keywords " oral vaccine" and " allergy " or "oral vaccine in allergy treatment" in PubMed, Google Scholar.

Results: Various oral vaccines have been developed for the treatment of allergies, including oral vaccines extracted from the bacterium B. abrotus. The oral delivery of U-Omp16 along with CMP has effectively managed the allergic reaction in mice that have been sensitized. Activation of TLR2 with the oral adjuvantPamScsk4 demonstrated that TLR2 is not essential for inducing oral tolerance, but its activation modulates the immune response of IgE and IgA. A recombinant oral vaccine using L. lactis significantly reduced airway sensitivity to allergenic substances.

Conclusion: Among the studies mentioned, the results indicated that the oral administration of U-Omp with CMP has the greatest efficacy In treating allergic reactions.

keywords: Keywords :allergic reactions, oral administration, TLR2

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Studying the effect of interleukin 17 in the development and treatment of psoriasis

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Medical Immunology

Background and aim: Interleukin 17 family includes (IL-17A to IL-17F). They are mainly involved in host defense mechanisms against bacteria, fungi and helminth infection. IL-17A also plays a role in the development of psoriasis by producing inflammatory cytokines and chemokines. We have discussed some of the treatments available for psoriasis. Psoriasis is a chronic, noncontagious, immune-mediated skin disease characterized by abnormal proliferation of keratinocytes, increased skin vessels, and skin infiltration of numerous inflammatory cells. The aim of our study was to evaluate the effect of interleukin17 in the progression and treatment of psoriasis.

Methods: In this review, a comprehensive search was conducted using the keywords ″IL-17″ or ″ Interleukin-17″ and ″ Psoriasis″ in PubMed, Google Scholar, and ResearchGate.

Results: Briefly, naive T cells differentiate into helper T(Th17) cells through interaction with activated dendritic cells in the presence of IL23, Th17 cells produce I-17 cytokines, and keratinocytes stimulated by IL-17 ligands lead to aberrant differentiation and proliferation that promote production of proinflammatory chemokines and further recruitment of inflammatory cells, setting up a positive feedback loop. Since the connection of dysregulated IL-17 and psoriasis pathogenesis turned out to be particularly evident, a number of monoclonal antibodies targeting IL-17 pathways have been approved and are used as first line treatment of moderate-to-severe plaque psoriasis and psoriatic

arthritis. Currently, 3 US Food and Drug Administration- approved agents to treat psoriasis affect the IL-17 pathway: Secukinumab and ixekizumab selectively bind to and neutralize only IL- 17A, and Brodalumab is a fully human IL17 receptor A antagonist that blocks signaling of multiple downstream inflammatory cytokines involved in psoriasis. IL-17A accelerates the proliferation of epidermal keratinocytes.

Conclusion: According to the studied articles, interleukin 17 was effective in the development of psoriasis skin disease and its inhibition in the treatment of this disease.

keywords: interleukin-17¸ psoriasis¸ IL-17

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Investigating the relationship between anti-sperm antibodies and infertility in men

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Medical Immunology

Background and aim: Immune infertility occurs due to the presence of anti-sperm antibodies (ASA). The prevalence of this specific form of infertility is relatively low, ranging from 2.6% to 6.6% among men experiencing infertility. Nonetheless the etiology, risk factors, biological targets, and repercussions for male fertility are not fully elucidated. While it is largely accepted that abnormalities in the blood-testis barrier and/or blood-epididymal barrier are the main factors behind its etiology, and that sperm motility is the most frequently reported altered parameter. Our aim in this review was to gather information about the associated between ASAs and infertility in men.

Methods: We carried out a review of scientific literature about anti-sperm antibodies and infertility published in databases as PubMed, Medline, Google Scholar, Web of Science using keywords included "Male; Immunoglobulin; Blood-Testis Barrier; Sperm Agglutination; Infertility."

Results: ASAs can affect fertility by reducing sperm motility, inducing sperm agglutination, hindering sperm passage through the cervical mucus, inhibiting fertilization, and hampering early embryonic development. However, the physiological immune mechanisms underlying the presence of ASAs are unclear. The clinical significance of ASAs of the IgA isotype may be greater than that of IgG, despite most cases testing positive for both IgA and IgG. ASAs can also activate the immune system through complement, leading to sperm lysis. In such a scenario, IgG antibodies are more effective in activating complement than IgA.

Conclusion: This narrative review indicated the effect of anti-sperm antibodies on infertility in men. Most research showed that, the formation of ASA in men may be associated with disturbance in immunomodulatory mechanisms that result in functional impairment of sperm and thus its inability to fertilize the oocyte.

keywords: Male; Blood-Testis Barrier; Sperm Agglutination; Infertility; Immunoglobulin

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Extracellular Vesicles Derived-miRNA as Biomarkers for Diagnosis, Prognosis, and Treatment of Cervical Cancer

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Medical Immunology

Background and aim: Cervical cancer remains a major global health issue, especially in regions with limited access to screening and vaccination. Liquid biopsies, particularly those examining extracellular vesicles (EVs) carrying miRNAs, have emerged as promising non-invasive diagnostic tools. EVs, lipid bilayer-bound structures secreted by cells, contain proteins, lipids, and nucleic acids like miRNAs. EVs modulate cancer cell functions such as proliferation, migration, and immune evasion by transferring miRNAs that regulate critical tumorigenic pathways. Also, these miRNAs contribute to cancer progression and can be considered disease-specific biomarkers. This review discusses the role of EV-derived miRNAs as diagnostic, prognostic, and therapeutic biomarkers in cervical cancer.

Methods: This study was conducted following guidelines established by PRISMA. Specific inclusion and exclusion criteria included English language studies examining the miRNA profiles in EVs isolated from cervical cancer patients and their diagnostic, prognostic, and therapeutic implications. Studies on the biological mechanisms of EV-mediated miRNA transfer and therapeutic strategies utilizing engineered EVs were also included. The primary keywords used in this investigation were "Extracellular Vesicles," "miRNA," and "Cervical Cancer." The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS).

Results: After applying inclusion and exclusion criteria, we identified 38 studies of acceptable quality for our research. miRNA-EVs demonstrated high specificity and sensitivity for cervical cancer diagnosis, with elevated levels of miR-21, miR-155, and miR-375 serving as reliable biomarkers. In contrast, the downregulation of miR-651, a tumor suppressor, presents another diagnostic opportunity. Using multiple miRNA biomarkers improves diagnostic accuracy and allows for early detection. miRNA-EVs also provide prognostic information, correlating with tumor grade and survival; overexpression of miR-21, miR-155, miR-223, and miR-146a-5p, along with downregulation of miR-34a and miR-1284, indicates poor prognosis. Therapeutically, engineered EVs with tumor-suppressing miRNAs like miR-34a and miR-651 show anti-tumoral effects and help overcome chemoresistance. As delivery vehicles, EVs offer low immunogenicity and targeted delivery of therapeutic miRNAs, potentially enhancing the effectiveness of conventional treatments.

Conclusion: EVs derived-miRNAs represent a promising tool for the diagnosis, prognosis, and treatment of cervical cancer. These miRNAs can be detected in non-invasive samples such as blood and urine, making them accessible for patients in low-resource settings. Notably, miR-21, miR-155, and miR-223 have been identified as key players in promoting oncogenesis and are frequently elevated in EVs from cervical cancer patients. However, further research is needed to standardize methods and validate findings in clinical trials before they can be widely implemented in clinical practice.

keywords: Biomarker; Cervical cancer; Extracellular vesicle; microRNA

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Exosomes as the immunomodulators in viral infections

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Medical Immunology

Background and aim: Extracellular Vesicles are micro phospholipid membrane fragments produced by diverse cells. Recent research indicates that EVs may share structural and functional similarities with viruses, particularly EVs produced by cells infected with viruses, as these EVs include viral genetic material and viral proteins. Cells produce several types of EVs that differ in size and their release pathways. Exosomes in bodily fluids have a variety of morphologies. Due to the presence of exosomes in human fluids such as blood, urine, semen, breast milk, and sputum and saliva, it is possible to identify certain disorders by tracking vesicles in body fluids.

Methods: In the current review article, we review and discuss the function of EVs produced during viral infections and describes how these vesicles boost or decrease host immunity.

Results: The life cycles of viruses and EVs appear to be similar, and during viral invasions, many viruses use EVs to evade immune system detection and spread disease. Exosomes play an important role in viral infections, but many unsolved concerns remain. Our research looked at the emerging practice of using exosomes to control virus-related infections. The information gap that currently exists, however, motivates us to investigate the gaps and overcome the limits of exosome-based techniques for precision medicine. The advantages of nanoparticles are target drug delivery capacity, gene silencing, and better specificity. In contrast, the using of these systems has several restrictions. First of all, the extraction and separation methods of exosomes as pharmaceuticals are

so difficult. Secondly, more use of these polymers causes the accumulation of them in the tissue so systemic toxicity happened. Moreover, the host immune system reacts to these systems so leads to stimulation of acute hypersensitivity.

Conclusion: Exosomes, as a collective concept, are a relatively new idea that is helping researchers understand the underlying mechanisms of a wide range of diseases and develop individualized medical treatments, diagnosis, and immunization. As they may deliver biologically significant substances such as medicines, proteins, enzymes, and antibodies, they are the most effective therapeutic agents.

keywords: Extracellular vesicles, Exosomes, Immunomodulation, viral infection

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The application of Natural Killer Cell-Derived Exosomes in Breast Cancer immunotherapy

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Medical Immunology

Background and aim: Breast cancer is the second leading cause of mortality worldwide in women. Treatments vary based on tumor type and stage, typically consisting of surgery and conventional therapies. However, 40% of patients with metastatic triple-negative breast cancer show increased cancer recurrence rates with cancer metastasis, being the primary cause of mortality. To address this, there is an urgent need for novel treatment approaches, including neoadjuvant surgery, chemotherapeutics, and immunotherapeutics. Recent studies have shown that immune cells produce exosomes, which have the potential for treating metastatic triple-negative breast cancer due to their versatility, efficient targeting, and customizable content.

Methods: A comprehensive literature search was conducted using Scopus, PubMed/MEDLINE, and ScienceDirect databases, and 20 articles were identified based on defined criteria. The review focused on studies published between 2017 and 2024, using keywords such as breast cancer, tumor immunotherapy, NK cell, and exosome. The inclusion criteria emphasizing the application of natural killer cell-derived exosomes in breast cancer immunotherapy.

Results: Exosomes as nanoscale vesicles, serve as organic nano-carriers for cell communication and tumor cytotoxicity. Research on exosomes derived from NK cells (NK-Exos) cultured with IL-2 or IL-15 that both cytokines produced exosomes with comparable cargo compositions. NK-Exos including cytotoxic proteins like

Perforin-1 and Granzymes A and B. In addition, they can also carry miRNAs such as miR-186, which suppress tumor proliferation and migration in breast cancer cells. NK-Exos deliver chemotherapy drugs such as paclitaxel and doxorubicin effectively to tumors, reducing side effects and offering innovative cancer therapy. Exosomes from NK cells co-cultured with K562 cells represent enhanced anti-tumor activity by upregulating p53 and caspase 3, 7, and 9 pathways and inducing apoptosis through Fas-FasL interactions. Their biocompatibility and barrier-crossing ability make them promising drug delivery systems. NK-Exos' biocompatibility and barrier-crossing ability enable siRNA delivery to target the overexpressed anti-apoptotic protein BCL-2 in most estrogen receptor-positive breast cancers.

Conclusion: Breast cancer remains challenging to treat, necessitating innovative diagnostic and therapeutic strategies. NK-Exos carry tumor-killing substances during biogenesis, demonstrating cytotoxic effects against various tumor types, including breast cancer. Research shows that sorafenib-loaded NK-Exos enhance apoptosis in TNBC cells and significantly increase cytotoxic damage to cancer cells. Furthermore, exosomes regulate tumor immunity and the immune microenvironment, underscoring their potential in developing exosome-based immunotherapies for breast cancer. This positions exosomes as a promising tool for improving breast cancer treatment and patient outcomes.

keywords: breast cancer; tumor immunotherapy; NK cell; exosome

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CAR-NK Cells: Potential Approach in Autoimmune Disease Treatment

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Medical Immunology

Background and aim: Autoimmune illnesses are a range of disorders with immune tolerance dysregulation, causing inflammation or organ damage. Their prevalence has been rising in recent years, resulting in decreased patients' quality of life and raised healthcare expenses. Therapy for these diseases has been altering over the past few years and CAR-NK cells were one of the newly introduced treatments for these patients. CAR-NK cells can be used to treat autoimmune patients by depleting B cells or plasma cells.

Methods: Data were collected from multiple databases, including PubMed, Scopus, and Web of Science using keywords, including autoimmune disease and CAR therapy. A total of 200 articles was collected and 55 of them were selected using expert panels. Studies related to therapeutic efficacy, safety profiles, and clinical trials of CAR-NKs on autoimmune diseases were investigated to evaluate the current state of CAR-NK in this field.

Results: Studies indicate that by the capacity of CAR-NKs to recognize and kill target cells even when absent or downregulated targets, target cells cannot escape from detection. This can offer increased therapeutic efficacy. Moreover, NK cells have a lower risk of graft-versus-host disease than CAR-T cells. Recently, 104 CAR-NK clinical trials have been running of which 10 are related to treating autoimmune diseases.

Conclusion: While CAR-NK therapy for autoimmune diseases indicates promising outcomes, more research is still needed to explore its effect with different doses and molecule targets on all autoimmune diseases to find the optimum treatment.

keywords: Chimeric Antigen Receptor Therapy, Autoimmune disease, Immune system

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In silico discovery of marine peptides as potential inhibitors of fibroblast activation protein-alpha (FAP-α) for rheumatoid arthritis treatment

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is a debilitating chronic autoimmune disease characterized by joint inflammation, with global prevalence projected to reach 1.5 million new cases by 2030. Current RA therapies often exhibit significant side effects, prompting the exploration of novel therapeutic agents with improved safety profiles. Marine-derived peptides represent a promising class of bioactive compounds with potential anti-inflammatory and immunomodulatory properties. This study aimed to computationally identify and characterize marine-derived peptides fibroblast activation protein-alpha (FAP-α), a serine protease receptor implicated with key player role in RA pathogenesis.

Methods: A structure-based virtual screening (SBVS) approach was employed to identify marine peptides with potential FAP-α inhibitory activity. The crystal structure of human FAP-α (PDB ID: 6y0f) was retrieved from the Protein Data Bank, prepared by removing crystallographic water and co-crystallized molecules, and optimizing protonation states using UCSF Chimera tool. The FAP-α active site, encompassing residues Ser624, Asp702 and His734, was defined based on structural analysis via PDBsum. A curated library of 50 marine peptides was constructed, and their physicochemical properties and tertiary structures were predicted using PEP-FOLD3. Peptide-FAPα docking was performed using HADDOCK2.4. Binding affinity and dissociation constant (Kd) of the peptide-

receptor complexes were predicted using the PROtein binDIng enerGY prediction (PRODIGY) web server. Peptide-FAPα complexes were ranked based on HADDOCK score, RMSD, binding affinity and Z-score. The stability of the peptide-receptor complexes was further validated by 100 nanosecond molecular dynamics (MD) simulations.

Results: Five marine peptides, PEP13 (LKYPI), PEP12 (LKPNM), PEP159 (RGVKAIFNGARQGYKEHKNQRREEK), PEP174 (TAARPYYCSLDVNHDGAGLSMEDVEEDK), PEP162 (KAIFNGARQGYKEHKNQRREEKLAN), exhibited strong binding affinities and stable interaction characteristics towards FAP-α. These peptides exhibited favorable physicochemical properties including acceptable predicted solubility and non-toxicity profiles, along with low RMSD values (0.2 – 0.6 nm) and negative Z-scores (-2.4 to -1.7) in the peptide-FAP-α complexes, indicating stable and energetically favorable interactions. Furthermore, MD simulations revealed that the peptide-FAPα complexes remained stable throughout the 100 ns simulations, suggesting their potential for sustained FAPα inhibition.

Conclusion: This in silico study identified five marine-derived peptides with predicted high binding affinity and stability towards FAP-α. These peptides represent promising candidates for further experimental validation as potential novel therapeutics for rheumatoid arthritis. Future in vitro and in vivo studies are warranted to confirm the predicted FAP-α inhibitory activity and therapeutic efficacy of these peptides in RA models.

keywords: Marine peptide/Molecular docking/Molecular dynamics /Fibroblast activation protein-alpha (FAP-α)/Rheumatoid arthritis

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HER2-positive breast cancer-targeting antibody-drug conjugates (ADCs) in clinical trials

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Medical Immunology

Background and aim: Antibody-drug conjugates (ADCs) is a novel smart chemotherapy in which highly cytotoxic small molecules or payloads are conjugated to monoclonal antibody (mAb) through cleavable or non-cleavable linkers. In this study, we aimed to review clinical-stage human epidermal grow factor receptor 2 (HER2)-targeting ADCs used for the treatment of breast cancer.

Methods: We searched clinicaltrials.gov for investigational ADCs as well as PubMed for articles with the keywords HER2-positive breast cancer and ADCs.

Results: Our findings showed that, in addition to two FDA-approved ADCs trastuzumab emtansine (trastuzumab/non-cleavable linker/DM1) and trastuzumab deroxtecan (MAAL-9001/cleavable linker/ DXd), there are currently 24 ADCs in a different phases of clinical trials for the treatment of HER2-positive breast cancer, including A166 (trastuzumab/cleavable linker/ Duostatin-5), LCB14-0110 (trastuzumab/cleavable linker/MMAF), ALT-P7(trastuzumab biobetter/cleavable linker/MMAE), ADCT-502 (trastuzumab/cleavable linker/SG3249), BAT8001 (BAT0606/non-cleavable/maytansine), SYD985 (humanized IgG1/cleavable linker/duocarmycin), SBT6050 (IgG/TLR8 agonist), BDC-1001 (trastuzumab biosimilar/non-cleavable linker/TLR7/TLR8 agonist), MEDI4276 (bi-paratopic trastuzumab & 39S antibody/cleavable linker/AZ13599185), RC48-ADC (hertuzumab/cleavable linker/MMAE), ARX788 (humanized nonnatural amino acid-engineered mAb/non-cleavable linker/MMAF), MRG002 (sugar-modified trastuzumab/cleavable linker/MMAE), DP303c (DP001/cleavable linker/MMAE), XMT-1522 (HT-19/AF-HPA), XMT-2056

(HT-19/STING agonist), PF-06804103 (humanized IgG1/cleavable linker/Auristatin-0101), DHES0815A (hu7C2/cleavable linker/PBD-MA), Zanidatamab Zovodotin (ZW25/cleavable linker/N-acyl sulfonamide auristatin), MM-302 (PEGylated antibody–liposomal/doxorubicin), GQ1001 (trastuzumab conjugated to DM1 through a unique open-ring containing linker), B003 (humanized IgG/non-cleavable linker/DM1), BB-1701 (IgG/cleavable linker/eribulin), SHR-A1811 (trastuzumab/cleavable linker/SHR169265) and BI-CON-02 (trastuzumab/an as yet undisclosed payload).

Conclusion: A total of 24 HER2-targeting ADCs are currently being evaluated in different phases of clinical trials for the treatment of breast cancer, most of which use humanized IgG1 (particularly trastuzumab) as a mAb, auristatins (particularly MMAE) as a payload and cleavable moiety (particularly valine-citrulline) as a linker.

keywords: Antibody-drug conjugate (ADC); HER2-positive breast cancer; Clinical trials

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Investigating the association of MHC HLA-G with infertility in women

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Medical Immunology

Background and aim: Background and Aim:TheHLA-G molecule is a non-classical HLAclassI molecule with limited polymorphism,primarily recognized during pregnancy and in the mother-fetus relationship.This molecule has a direct effect on inhibiting immune responses by inducing the production of inhibitory and regulatory cells.As an immunogenic tolerance molecule,HLA-G plays a dual role in the mechanisms related to the immune system.HLA-G is found in certain MHC proteins of placental cells during pregnancy.This protein can send signals to the immune system to prevent the rejection of the fetus by the mother's body.Considering these factors,the aim of this study was to examined the role of HLA-Gin female infertility.

Methods: Materials and Methods: In this review, a comprehensive search was conducted using the keywords "HLA-G and reproductive disorder" "HLA-G and reproductive failure" and "HLA-G and infertility" and " female infertility" and "pregnancy" in the PubMed, Google Scholar, and Web of Science databases.

Results: Results: During pregnancy, the isoforms HLA-G5 and HLA-G6 have a particularly significant impact on the inhibition of NK cells (natural killer cells). Studies indicate that the HLA-G5 isoform is recognized as a key factor in establishing immune tolerance at the maternal-fetal interface and plays a greater role in successful pregnancy processes and preventing miscarriages compared to HLA-G6.

Conclusion: Conclusions:The evaluation of the HLA-G pathway and NK cell interactions can serve as a significant factor in assessing immunological miscarriages, according to various studies.

keywords: Keywords: infertility, HLA-G, pregnancy failure, reproductive disorder

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Therapeutic Effects of Gene-Transfected and miRNA-Modified Mesenchymal Stem Cells in Asthma

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Medical Immunology

Background and aim: Asthma is a chronic inflammatory disease and is widespread worldwide, marked by hyperactive immune responses involving Th2 cells and cytokines such as IL-4, IL-5, and IL-13. Traditional treatments often only alleviate symptoms without dealing with the core inflammation issue. Mesenchymal stem cells show promise with their regenerative and immunomodulatory abilities. Recent advances have involved enhancing MSCs with therapeutic genes and miRNAs to increase their anti-inflammatory effects. The present study focused on MSCs transfected with anti-inflammatory genes, including IL-10 and IL-35, and miRNAs, such as miR-146a-5p and miR-138-5p, that help in modulating immune responses to reduce airway inflammation in asthma models.

Methods: A search was conducted in multiple databases for studies published between 2020 and 2024; using keywords such as IL-10, IL-35, miR-146a-5p, miR-138-5p, and miRNA. The inclusion criteria emphasized studies evaluating the anti-inflammatory effects of these genes and miRNAs on airway inflammation, and the exclusion criteria excluded studies not related to asthma models.

Results: MSC transfection with IL-10 resulted in a significant reduction of Th2 cytokines (IL-5 and IL-13), eosinophilic infiltration, and mucus hypersecretion, accompanied by improved lung function. IL-35-transfected MSCs exhibited potent immunomodulatory effects in suppressing eosinophil and neutrophil counts and reducing epithelial damage, therefore playing an indispensable role

in allergic asthma. Besides, there was a high efficacy of miRNA modification in modulating inflammation. Overexpressing miR-146a-5p in MSCs results in the downregulation of NF-kB and activation of inflammasomes, which are key drivers of chronic inflammation in asthma. On the other hand, the inhibition of miR-138-5p in MSCs upregulated SIRT1 expression associated with reduced IL-6 and TNF-α, mapping out prominent attenuation in inflammatory markers and AHR. Taken together, these results further emphasize the improved anti-inflammatory potential of gene and miRNA-engineered MSCs, which may be an effective therapeutic strategy for asthma treatment.

Conclusion: The modification of MSCs with specific genes and miRNAs lends tremendous therapeutic potential for the treatment of asthma through modulation of major inflammatory pathways, reduction in oxidative stress, and promotion of tissue repair. These findings give emphasis to advanced MSC modifications in tackling both acute and chronic inflammation associated with asthma. Therefore, clinical trials are still needed to validate their safety and efficacy in humans and could revolutionize the treatment of asthma.

keywords: Asthma; Mesenchymal Stem Cells; IL-10; IL-35; miR-146a-5p; miR-138-5p

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The Role of mRNA Vaccines and Combination Therapy for Melanoma Treatment

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Medical Immunology

Background and aim: Melanoma, a highly aggressive form of skin cancer, poses significant treatment challenges, particularly in its advanced stages. Recent advancements in mRNA vaccine technology, initially popularized by COVID-19 vaccines, offer new hope for melanoma treatment through personalized immunotherapy approaches. Studies have demonstrated the efficacy and potential of mRNA vaccines when combined with immune checkpoint inhibitors, specifically pembrolizumab, in enhancing outcomes for melanoma patients.

Methods: A comprehensive literature search was conducted to evaluate the role of mRNA vaccines in the treatment of melanoma using PubMed, Scopus, Web of Science, and ProQuest.

Results: In recent years, significant advancements have been made in mRNA vaccine development. The personalized nature of the mRNA vaccine, tailored to target specific mutations in each patient's tumor, is believed to enhance the immune response against melanoma cells. These findings suggest that integrating mRNA vaccines with existing immunotherapies could represent a significant advancement in managing melanoma, potentially leading to improved survival rates and quality of life for patients. Clinical trials involving administration of mRNA vaccines in patients with stage III or IV melanoma indicate improved overall survival rates, reduced recurrence, and enhanced progression-free survival when combined with monoclonal antibodies.

Conclusion: Future research should explore the synergistic potential of combining mRNA cancer vaccines with other immunotherapies to enhance clinical outcomes in cancer treatment.

keywords: Melanoma; Cancer; mRNA vaccine; Combination Therapy.

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Comparison of SW480 and HCT116 Cell lines in TLR4 gene Expression Following Sodium Butyrate Treatment

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Medical Immunology

Background and aim: HDAC inhibitors (HDACi), such as sodium butyrate (SB), are crucial in prevention and treatment. This study investigates the impact of sodium butyrate on TLR4 expression, a pivotal molecule in inflammatory signaling, in two colorectal cancer cell lines: HCT116 (low TLR4 expression) and SW480 (high TLR4 expression). Understanding this interaction may provide insights into therapeutic strategies targeting TLR4 in colorectal cancer.

Methods: Initially, the effects of SB on cell morphology were assessed in culture over a broad range of times (12 to 72 hours) and concentrations (1 to 20 mM). Cell viability was evaluated using the MTT assay at concentrations that showed minimal morphological indications of cell damage. Finally, quantitative assessment of gene expression was conducted at non-cytotoxic time-concentration points using the SYBR-Green I Real-time RT-PCR method.

Results: After 48 hours, treatments exceeding 10 mM induced cell injury in both SW480 and HCT116 cell lines, characterized by increased granulation and reduced adhesion. The MTT assay confirmed that concentrations of 1 mM and 5 mM were non-cytotoxic in both cell lines. SB treatment at 5 mM in the SW480 cell line and 1 mM in the HCT116 cell line significantly increased TLR4 gene expression after 48 hours compared to earlier time points. However, expression significantly decreased at 72 hours compared to 48 hours (p 0.05).

Conclusion: This study demonstrated that SB increases TLR4 gene expression in colorectal cancer cell lines during short-term exposure but may reduce expression during longer exposures.

keywords: TLR4, Sodium Butyrate, HDAC inhibitors (HDACi)

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Metformin and Everolimus: Modulating Inflammatory Cytokines in Aging

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Medical Immunology

Background and aim: Inflammaging, chronic, systemic and low level inflammation in aging, is known as the most important factor related to aging and age-related diseases. overactivation of innate immune system cells, especially macrophages and production of different factors disrupt the proper function of various tissues. Metformin and Everolimus, two inhibitors of the mTORC1 signaling pathway, are very notable in aging studies. The aim of this study was evaluation of the effect of this drugs on serum levels of IL-1, IL-6, and TNF-α as the most important factors of inflammaging in an animal model of aging.

Methods: 15 male C57/bl6 mice over 16 months old were obtained from the Pasteur Institute of IRAN and maintained in an optimum situation. Pure substances of Metformin and Everolimus are prepared from Dorsa Daru and Dr. Abidi pharmacology companies and dissolved in special solvents. The mice were divided into 3 groups of 5: a group treated with 100 mg/kg of Metformin, a group treated with 0.1 mg/kg of Everolimus and the control group receiving PBS containing 5% DMSO. Mice were treated daily for 14 days. On day 15, the heart blood was taken following anesthetizing the mice. Serum was prepared by centrifugation at 10000 g for 10 min at 4 Ċ. Finally, serum levels of cytokines IL-1, IL-6 and TNF-α were evaluated through an ELISA assay.

Results: The results of this study demonstrated that Metformin could reduce serum levels of all three proinflammatory cytokines, IL-1, IL-6 and TNF-α, significantly. Also, Everolimus could decrease serum levels of TNF-α significantly; however, it doesn't have a significant effect on IL-1 and IL-6.

Conclusion: Metformin and Everolimus may help to improve aging and age-related diseases through affecting inflammaging and reducing proinflammatory cytokines. Also, it seems that Metformin could be more effective because of its role in decreasing all three cytokines important in inflammaging.Methods

keywords: Inflammaging, Metformin, Everolimus, cytokine

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MicroRNA-210 Modulates Chemoresistance in Cisplatin-Resistant Ovarian Cancer Cells by Targeting BCL2 and Regulating Apoptotic Pathways

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Medical Immunology

Background and aim: Chemoresistance in ovarian cancer remains a major obstacle to successful treatment, particularly with cisplatin, a frontline chemotherapy agent. MicroRNAs (miRNAs) have emerged as key regulators of resistance mechanisms, influencing gene expression and cellular responses to chemotherapy. In this study, we investigated the role of microRNA-210 (miR-210) in modulating cisplatin resistance in ovarian cancer. Cisplatin-resistant A2780/CP cells were compared to the cisplatin-sensitive parental A2780 cells to explore miR-210 expression and function.

Methods: Cisplatin-resistant A2780/CP and parental A2780 ovarian cancer cells were cultured for comparative analysis. miR-210 expression levels were quantified using quantitative RT-PCR. Bioinformatic tools and luciferase reporter assays were used to identify BCL2 as a direct target of miR-210. Synthetic miR-210 mimics and antagomiR-210 were transfected into cells to restore or inhibit miR-210 expression, respectively. The effects on BCL2 expression, cell viability, and apoptosis were assessed using Western blotting, MTT assays, and Annexin V staining. Mitochondrial membrane potential and caspase-3/7 activation were measured to assess apoptotic regulation. Statistical significance was performed by Presm version 9 and determined using appropriate tests (p 0.05).

Results: Quantitative RT-PCR analysis revealed that miR-210 was significantly downregulated in A2780/CP cells compared to the parental A2780 cells, suggesting a potential role for miR-210 in chemoresistance. Bioinformatic

predictions and luciferase reporter assays confirmed that BCL2 is a direct target of miR-210. Overexpression of miR-210 in A2780/CP cells led to a marked reduction in BCL2 levels and sensitized the resistant cells to cisplatin. Treatment with cisplatin following miR-210 restoration enhanced apoptosis, as indicated by increased Annexin V-positive cells and elevated caspase-3/7 activity. In contrast, inhibition of miR-210 in parental A2780 cells, using antagomiR-210, resulted in increased BCL2 expression, enhanced resistance to cisplatin, and reduced apoptosis. These findings suggest that miR-210 plays a critical role in modulating apoptotic pathways and regulating chemoresistance. Further investigations into the underlying mechanisms revealed that mitochondrial depolarization was more pronounced in cisplatin-treated A2780/CP cells upon miR-210 restoration, indicating an enhanced apoptotic response.

Conclusion: These findings suggest that miR-210 modulates cisplatin resistance in ovarian cancer by targeting BCL2 and regulating key apoptotic pathways. Restoration of miR-210 expression in resistant ovarian cancer cells could represent a novel therapeutic strategy to overcome chemoresistance and improve the efficacy of cisplatin-based chemotherapy. Further studies are warranted to evaluate the potential of miR-210-based therapies in overcoming chemoresistance in ovarian cancer.

keywords: miR-210, ovarian cancer, cisplatin resistance, BCL2, apoptosis

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The Role of Exosomal miRNAs-Derived MSC in the Favorable Prognosis of Multiple Sclerosis

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Medical Immunology

Background and aim: Multiple sclerosis is a chronic, progressive immune-inflammatory disorder affecting the central nervous system characterized by immune dysregulation, neuroinflammation, and the demyelinating process. Recent studies have highlighted the involvement of endogenous microRNAs packaged within exosomes derived from Mesenchymal stem cells in regulating immune responses, inflammation, and repair processes in MS. These miRNAs expressed a potential as non-invasive biomarkers that might open a new avenue for prognosis, early diagnosis, and disease course monitoring. This study will discuss the expression levels of these miRNAs, the mechanisms involved, and possible applications in MS for prognosis improvement.

Methods: A comprehensive literature search was conducted using three major academic databases, including PubMed, Google Scholar, and Scopus. This search utilized keywords such as "Mesenchymal stem cell," "Exosomal microRNAs," "Multiple Sclerosis," "Molecular biomarkers," and "Prognosis". The implemented methodology used both inclusive and exclusive approaches to guarantee the most comprehensive overview of the literature. A total of twenty-one articles were identified, with relevance and methodological quality assessed to select studies that directly investigated exosomal miRNAs-derived MSC in MS or closely related neuroinflammatory conditions.

Results: The present study demonstrates that microRNAs from mesenchymal stem cells, especially miR-146a, miR-155, and miR-223, are key regulators of inflammation by modulating signaling pathways such as NF-κB and JAK/STAT and controlling the levels of pro-inflammatory cytokines such as TNF-α and IL-6. These miRNAs are upregulated during early MS and modulate inflammation, oxidative stress, and neural damage by modulating the inflammatory mediators TRAF6 and IRAK1. However, miR-23a-3p and miR-223 have been described to participate in remyelination by modulating the Wnt/β-catenin and PI3K/Akt pathways, which play an important role in neural repair and oligodendrocyte maintenance. Other miRNAs, such as miR-326, miR-23b, and miR-124-3p contribute to immunomodulation through effects in T-cell differentiation, neuroinflammation reduction, and neuroprotection. For instance, miR-124-3p has been indicated to promote neural protection through down-regulation of pro-inflammatory responses, whereas miR-326's role in immune balance contributes to its value as a biomarker for MS disease course and treatment response.

Conclusion: miRNAs-derived MSC may provide a promising non-invasive approach for the progression, diagnosis, prognosis, and treatment of MS, as they provide profound insight into immune modulation, inflammation management, and the mechanism of neural protection in different states of MS. The miRNAs derived from MSCs target key signaling pathways involved in MS and have proven beneficial for prognosis and customized, stage-specific therapeutic approaches aimed at improving outcomes in MS.

keywords: Multiple Sclerosis; Mesenchymal Stem Cells; Exosomal microRNAs; Molecular biomarkers; Prognosis.

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The most common Laboratory findings in patients with urticaria

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Medical Immunology

Background and aim: Urticaria, commonly known as hives, is a skin condition characterized by the sudden appearance of raised, itchy welts or lesions on the skin. The impact of urticaria on quality of life can be significant. The etiology of urticaria is not well understood but the condition arises from a complex interplay of immunological and non-immunological factors. Identifying the trigger is very important in diagnosis and management of urticaria and therefor laboratory tests can be very helpful. The aim of this study was to reveal the most common laboratory abnormalities in patients with urticaria.

Methods: : Patients who visited allergy clinic of Birjand because of urticaria and the diagnosis confirmed with specialist were enrolled in this study. Results of patients' laboratory tests including blood hematology, biochemistry and immunology tests as well as urine analysis were recruited from laboratory registry software.

Results: In total 620 patients were enrolled in this study. The average laboratory values for CBC, ESR, blood eosinophil count and serum total IgE were 7.69 ± 2.06 *1000/ul, 56.5 mm/H, 2.82 ± 2.20% and 252 IU/ml respectively). 35.1% of patients had high blood IgE. The most common abnormalities were positive ANA, anti H.pylori IgG and anti-thyroid peroxidase (39.7%, 15.9%, and 8.8%, respectively). None of patients were positive for rheumatoid factor (RF) or hepatitis B antigen.

Conclusion: the results of this study revealed that around a third of patients with urticaria had high IgE or positive ANA. H pylori seropositivity and thyroid autoimmunity were common findings as well. Further studies need to identify other possible causes for urticaria.

keywords: Urticaria; Laboratory; Hives

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Peptide inhibitors of FEN1: a potential breakthrough in rheumatoid arthritis treatment

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is a common chronic, autoimmune inflammatory disease with significant unmet therapeutic needs. While current treatments target the immune system broadly, identifying novel, specific molecular targets is crucial for improved efficacy and reduced side effects. Flap endonuclease 1 (FEN1), a key enzyme in DNA replication and repair, has recently emerged as a potential therapeutic target in various diseases, including cancer, but its role in RA and its druggability with peptides remains unexplored. Marine-derived peptides offer a promising source of novel therapeutics due to their high specificity, favorable safety profiles, and potential for targeted inhibition. This study investigates the

Methods: A curated library of marine peptides was screened for potential FEN1 inhibitors. Peptide structures were predicted using the PEP-FOLD3 server and assessed for structural quality, toxicity, solubility, and antigenicity. The crystallographic structure of FEN1 (PDB ID: 3Q8K) was prepared for docking using PyMOL for the removal of ligands and water molecules, and UCSF Chimera for the addition of hydrogen atoms and optimization of the structure. Molecular docking simulations were performed using HADDOCK2.4 to evaluate the binding affinity and interactions of the peptides with the FEN1 active site, defined by residues Met37, Tyr40, Lys93, Arg100, Lys132 and Arg192. Candidate peptides were selected based on HADDOCK scores, root-mean-square deviation (RMSD), dissociation constants (Kd), and Z-scores. The stability of the top-ranked peptide-

FEN1 complexes was further investigated using 100 nanosecond (ns) molecular dynamics simulations under physiological conditions.

Results: Six marine peptides, PEP1 (VWDPPKFD), PEP10 (AKYSY), PEP11 (IKPLNY), PEP20 (FEDYVPLSCF), PEP26 (CWLPVY) and PEP176 (FFHHIFRGIVHVGKTIHRLVTG), exhibited strong binding affinities for the FEN1 active site in silico. These peptides displayed favorable HADDOCK scores (ranging from -127.4 to -86.8 kcal/mol) and low RMSD values (0.3 – 0.6 nm), indicating stable complex formation. Specifically, PEP176 showed the strongest interaction with a HADDOCK score of -127.4 kcal/mol and an RMSD of 0.3 nm. Furthermore, molecular dynamics simulations demonstrated the stability of these peptide-FEN1 complexes over 100 ns, suggesting their potential for sustained inhibition in vivo.

Conclusion: This study identifies six marine-derived peptides (PEP1, PEP10, PEP11, PEP20, PEP26, and PEP176) as promising leads for the development of novel FEN1 inhibitors for the treatment of rheumatoid arthritis. These findings warrant further in vitro and in vivo validation to confirm their therapeutic potential and elucidate the mechanism of FEN1 inhibition in the context of RA pathogenesis

keywords: Marine peptide;FEN1;Molecular docking;Molecular dynamics;Rheumatoid arthritis; Drug discovery;Peptide inhibitors

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Retronectin increases PD-L1-specific chimeric antigen receptor (CAR) gene transduction efficiency in umbilical cord blood (UCB)-CD34+ cells and UCB-CD34+-derived NK cells

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Medical Immunology

Background and aim: Chimeric antigen receptor (CAR) NK cell treatments are thought to be successful when the appropriate numbers of engineered cells are produced. The viral vectors' transduction rate may be crucial to achieving this goal. Additionally, because of hard-transduced NK cells, increasing transduction rates may impact the treatment's success rate. Two protocols for the production of third-generation CAR-NK cells targeting PD-L1 via viral transduction were used, the first from differentiation of umbilical cord blood (UCB)-CD34+ cells modified to express CAR and the second from differentiation of human UCB-CD34+ cells into functional NK cells that then express CAR. We compared their transduction efficiency

Methods: HEK 293 T cells were transfected with Lipofectamine 3000 and DNA of lentiviral vector, gag/pol (psPAX2), and VSVG (pMD2.G) in a ratio of 2:1.5:1. Lentiviral particles were concentrated using PEG-8000 and ultracentrifugation. UCB-CD34+ cells were isolated using magnetic-activated cell sorting (MACS). To confirm purity, isolated cells were stained with Phycoerythrin (PE)-conjugated anti-human CD34 antibody. We expanded UCB-CD34+ cells for 2 weeks and then differentiated them into NK cells. UCB-CD34+ cells and UCB-CD34+-derived NK cells were transduced with lentivirus using retronectin and polybrene. Surface expression of CAR was measured via GFP expression after 3 days.

Results: Based on our results, retronectin leads to higher transduction rates of UCB-CD34+ cells (60–80%) and UCB-CD34+-derived NK cells (20–30%) compared

to polybrene. In addition, CAR-modified UCB-CD34+ cells exhibited enhanced transduction efficiency compared to UCB-CD34+-derived NK cells (P 0.001).

Conclusion: By improving transduction conditions, such as retronectin, the production of CAR-NK cells can be increased, which raises the rate of transduction and treatment success. Furthermore, this approach is suggested for CAR-NK cell research due to the more efficient transduction in stem cells and the potential for higher yields of CAR-NK cell products.

keywords: Chimeric antigen receptor; hematopoietic stem cells; polybrene; retronectin; umbilical cord

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The Role of Mesenchymal Stem Cell-Derived Exosomes in Targeted Therapy for Chemoresistant Cancer

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Medical Immunology

Background and aim: Mesenchymal stem cells (MSCs) are versatile progenitor cells sourced from various human tissues and organs. While valuable in regenerative medicine, MSCs also influence cancer progression through their interactions with tumor cells. MSC-derived exosomes play a crucial role in shaping the tumor microenvironment and promoting therapy resistance in cancers like breast, lung, and pancreatic malignancies. This review delves into the role of MSC-derived exosomes in targeted treatments for chemoresistant cancers, highlighting their potential as both therapeutic targets and delivery vehicles.

Methods: This article was written using the latest articles from high-tech search engines (e.g., PubMed, Google Scholar, etc.) legally. Initially, we used general keywords, followed by specific ones. It is worth mentioning that the time taken to publish the article was not without grace. This paper was inspired by articles published since 2024, although some parts of the article have been adapted from previous articles. In selecting articles, efforts were made to include valid experimental and clinical studies, as well as highly reliable review and original articles. Data were analyzed using a content analysis approach to identify key themes and draw conclusions from the selected studies.

Results: Exosomes derived from mesenchymal stem cells (MSCs) have emerged as critical mediators of communication within the tumor microenvironment (TME). These exosomes carry bioactive molecules, including microRNAs (miRNAs), which contribute to therapy resistance. Studies have reported that breast cancer cells can prime MSCs to release exosomes containing distinct miRNA profiles, such as miR-222/223, which promote quiescence and drug

resistance in cancer cells. Additionally, miRNAs like miR-29 and miR-155 have been implicated in altering the redox balance and enhancing the survival of resistant cancer cells under chemotherapy. Exosomes derived from MSCs have been shown to enhance chemotherapy resistance, especially in cancers such as breast, lung, and pancreatic cancer. Recent studies suggest that targeting exosomal miRNA content in the TME could provide a novel avenue to overcome such resistance, with promising results seen in preclinical models

Conclusion: MSC-derived exosomes are promising candidates for overcoming chemoresistance in cancer treatments. Their ability to modulate the tumor microenvironment, promote cancer cell survival, and alter resistance to chemotherapy positions them as valuable therapeutic targets and delivery vehicles. However, several challenges remain in terms of their clinical application, including the need for better control over exosome production, targeting specificity, and the safety and stability of exosomal contents. Further research and clinical trials are needed to fully realize the therapeutic potential of MSC-derived exosomes in treating chemoresistant cancers.

keywords: Mesenchymal Stem Cells, Exosomes, Therapy Associated Neoplasms, Drug Resistance.

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Ketogenic Diet Causes Fatty Liver and Inflammation in Male Rats

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Medical Immunology

Background and aim: The ketogenic diet (KD) is a therapeutic approach for various conditions, including epilepsy, obesity, and cancer. However, its potential adverse effects are not fully understood. This study aimed to evaluate the KD's impact on liver structure, function, and inflammatory markers.

Methods: Ninety male rats were randomly assigned to two groups: one consumed standard rat chow (normal diet), while the other followed a ketogenic diet comprising 90% fat, 8% protein, and 2% carbohydrates for 30 days. Serum lipid profiles (cholesterol and triglycerides), liver enzymes, hepatic inflammatory markers, and steatosis grading were assessed and compared between the groups.

Results: Serum cholesterol and alanine transaminase (ALT) levels were significantly higher in the KD group compared to the normal diet group. However, no significant differences were found in serum triglyceride and aspartate transaminase (AST) levels between the groups. Hepatic inflammatory markers interleukin 6 (IL-6) and tumor necrosis factor-α (TNF-α) were also elevated in the KD group. Additionally, liver biopsies showed a significantly higher degree of steatosis in the KD group than in the normal diet group.

Conclusion: The KD may induce hepatic adverse effects, including steatosis and inflammation possibly leading to hepatic injury and dysfunction.

keywords: Fatty liver; inflammation; ketogenic diet; liver enzymes; rat

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The Role of Cobalamin in Multiple Sclerosis: An update

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Medical Immunology

Background and aim: Multiple sclerosis (MS) is a neurodegenerative condition that results in axonal and permanent damage to the central nervous system, necessitating healing owing to autoimmune reactions and persistent neuroinflammation. Antioxidant and anti-inflammatory drugs are essential for the management of oxidative stress and neuroinflammation. Aim:The Role of Cobalamin in Multiple Sclerosis: An update

Methods: systemic review

Results: multivitamin supplementation, particularly vitamin B12 (cobalamin), may be beneficial for neuronal protection. Although there is no documented connection between vitamin B12 deficiency and MS, researchers have explored its potential as a metabolic cause.

Conclusion: Vitamin B12 intake may lessen motor symptoms in these patients, improving their physical and mental well-being. It has been shown that taking supplements of folic acid and B12 helps with mood problems but not with mental or psychiatric diseases. B12 supplementation can help restore visual acuity since a B12 deficiency can harm the optic nerve.

keywords: Multiple sclerosis (MS) , Cobalamin,

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Evaluation of Toxicity Effects of Imiquimod in Uninfected Macrophages in comparison to sulfadiazine in vitro

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Medical Immunology

Background and aim: Since current toxoplasmosis treatment have some limitations and are unable to eradicate bradyzoites in tissue cysts, discovering and design of secure and impressive drugs are needed, particularly in humans and livestock animals. Imiquimod has ability to moderate immune response and used to treat a wide variety of infections and tumors. The aim of the present study was to evaluate of toxicity effects of imiquimod in uninfected macrophages in comparison to sulfadiazine in vitro.

Methods: The MTT assay was applied to determine the viability of macrophages exposed to imiquimod. Briefly, 1 mL of Raw.264.7 macrophage cells, suspended in RPMI 1640 medium enriched with 10 % FBS, were seeded at a concentration of 1 × 105cells/well in 96-well microtiter plates and incubated in 5% CO2 and 95% humidity for 24h. After adhering the cells, they were exposed to different concentrations of drug (from 10 to 0.01 µg/ml) and incubated for a further 24 h under the same conditions. Then, 20 µL of solution of MTT was added in to each well and incubated for 4 h. The plates were centrifuged for 10 min at 3,000 g and then the contents of each well was discharged slowly and replaced with 100 µL of dimethyl sulfoxide (DMSO) to distinguish between the viable cells (formazan formation) and decayed cells. Finally, absorbance at 570nm of each well, using an ELISA

Results: The effects of imiquimod on uninfected macrophages were investigated by measurement of optical density (OD) following MTT assay. Lower concentrations of drug were associated with greater viability after 24 h.

Conclusion: Toxicity of imiquimod in uninfected macrophages was dose-dependent. It might be considered as a candidate for the treatment of toxoplasmosis.

keywords: imiquimod, macrophages, sulfadiazine, in vitro

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Progesterone increases membrane progesterone receptors (mPRs) expression on naive CD4 T+ lymphocyte cells in normal fertile females.

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Medical Immunology

Background and aim: Progesterone (P4), as a female steroid hormone, plays a critical role in maintaining a normal pregnancy. It also has immunomodulatory effects on the immune system. Given that the fetus is semi-allogeneic, P4 might also help the fetus's immunologic tolerance .P4's impact on target cells involves nuclear and membrane progesterone receptors, including PAQR7 (mPRα) and PAQR8 (mPRβ) on T cells. Reduced mPR expression can hinder P4's function, potentially affecting pregnancy. This investigation aimed to determine whether the increase in P4 concentration can strengthen the immunomodulatory function of P4 on CD4+ T cells through increased expression of its receptors.

Methods: Naive CD4+ T cells were isolated from the peripheral blood of 20 healthy, fertile women. Following stimulation with anti-CD3 and anti-CD28 monoclonal antibodies (mAb), these cells were cultured for three days at 37 ºC with either different concentrations of P4 or no exposure at all. The mean fluorescence intensity (MFI) of mPRα and mPRβ was evaluated using polyclonal and monoclonal antibodies on CD4+ T cells.

Results: P4 significantly increased the expression of mPR α and mPR β on the surface of CD4+ T cells (P ≤ 0.05).

Conclusion: The current investigation showed that P4 has a growing impact on CD4+ T cell mPR expression. P4 can enhance its immunomodulatory effects on T cells. Thus, during a typical pregnancy, a rise in P4 concentration coincides with an increase in P4's immunomodulatory effect on T cells, at least in part, because of an increase in the production of mPRs.

keywords: CD4+ T cells, progesterone ,progesterone receptors , fertile ,females

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Association between blood Pentraxin-3 concentrations and Behçet's disease

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Medical Immunology

Background and aim: Pentraxin3 (PTX3) is a protein with a molecular weight 250kDa. It composed of 381 amino acids, and encoded by the PTX3 gene located on chromosome 3. This protein plays a regulatory role in inflammatory processes. In conditions such as lupus erythematosus, Sjögren's syndrome, and certain vasculitis, its levels are elevated, but in Behçet's disease(BD), the data regarding its blood levels are inconsistent.

Methods: This cross-sectional study was performed on patients who referred to Imam Reza Hospital in Mashhad from 2015 to 2018. The participants were divided into two equal groups including control and BD group. ISG diagnostic criteria was used to diagnosis BD. Both groups were matched based on sex an age. Serum PTX3 levels were measured for all participants.

Results: A total of 76 participants were enrolled in the study. Both of groups included 55.3% women and 44.7% men. The median duration of the disease was 4 years (1 – 15 years). The serum levels of PTX3 in the BD group were higher than in the control group, 3.84±0.4 vs 1.27±0.16 ng/ml, but this difference was not statistically significant (p-value0.05). Additionally, no significant statistical correlation was observed between serum PTX3 levels and the age of disease onset, duration of the disease, or gender.

Conclusion: This study found no significant difference in serum PTX3 levels between BD patients and healthy controls. These findings highlight the need for further studies and evaluations to better understand the role of PTX3 in BD.

keywords: Pentraxin3; Behçet's disease; Inflammatory process

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Understanding Inflammasome Activation

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Medical Immunology

Background and aim: The inflammasome, a multiprotein complex found in various cells of the immune system, plays a central role in the initiation and regulation of inflammation. At its core, the inflammasome functions as a molecular platform that detects danger signals and triggers the production of pro-inflammatory cytokines. The inflammasome is comprised of three main components: a sensor protein, an adapter protein, and an effector protein. The purpose of this study is to investigate the activation methods of the inflammasome and their results.

Methods: Thirty-eight articles with the keywords inflammasome, immune system and inflammation were collected and analyzed from Google Scholar and PubMed databases.

Results: The activation of the inflammasome is a tightly regulated process that requires two signals: the priming signal (signal 1) and the activation signal (signal 2). Chronic inflammatory diseases, such as rheumatoid arthritis, gout, and inflammatory bowel disease, are characterized by persistent activation of the inflammasome and the release of pro-inflammatory cytokines. The inflammasome has also been linked to metabolic disorders, including obesity and type 2 diabetes. Furthermore, the inflammasome has been implicated in neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. Targeting the inflammasome and its downstream signaling pathways holds promise for the development of novel treatments that specifically address the root causes of inflammation.

Conclusion: While inflammasome is essential for our immune defense, its dysregulation can lead to chronic diseases and impair our overall health. The inflammasome, a complex molecular machinery, sits at the heart of the inflammation process, orchestrating the immune response and driving the production of pro-inflammatory cytokines. The potential impact of inflammasome-targeted therapies, diagnostic markers, and preventive strategies cannot be overstated. By harnessing the power of the inflammasome, we can pave the way for a healthier future, free from the burden of chronic inflammation and its associated diseases.

keywords: Inflammasome, Inflammation, Cytokines, Immune system

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The Positive and Negative Immunoregulatory Role of B7 Family: Promising Novel Targets in Gastric Cancer Treatment

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Medical Immunology

Background and aim: Abstract: Gastric cancer (GC), with a heterogeneous nature, is the third leading cause of death worldwide. Over the past few decades, stable reductions in the incidence of GC have been observed. However, due to the poor response to common treatments and late diagnosis, this cancer is still considered one of the lethal cancers. Emerging methods such as immunotherapy with immune checkpoint inhibitors (ICIs) have transformed the landscape of treatment for GC patients. There are presently eleven known members of the B7 family as immune checkpoint molecules: B7-1 (CD80), B7-2 (CD86), B7-H1 (PD-L1, CD274), B7-DC (PDCD1LG2, PD-L2, CD273), B7-H2 (B7RP1, ICOS-L,

Methods: ....

Results: ,,

Conclusion: ..

keywords: B7 family; immune checkpoints; immunotherapy; gastric cancer

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Advancing Our Understanding of Regulatory B Cell Function and Therapeutic Potential in Autoimmune Diseases

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Medical Immunology

Background and aim: Regulatory B cells (Bregs) are increasingly recognized as critical modulators of immune homeostasis, modulating responses beyond antibody production via anti-inflammatory cytokines (IL-10, TGF-β) and cell-cell interactions. Bregs heterogeneity, including IL-10-producing B10/Br1 cells and cytotoxic GrB+ B cells, underscores their diverse regulatory roles. Despite the growing understanding of Bregs' function and diversity, the lack of a definitive, unifying marker presents a significant challenge to the field. This review summarizes recent advances in Bregs biology, their involvement in autoimmune pathogenesis, and the therapeutic potential of targeting Bregs to restore immune balance.

Methods: We conducted a comprehensive narrative review of the literature, searching multiple databases to identify relevant studies on the interplay between regulatory B cells and autoimmunity. Our search strategy employed a combination of keywords and MeSH terms, encompassing studies that investigated Bregs phenotype, function, and therapeutic applications in various autoimmune disease models and human cohorts. Studies were selected based on their relevance to the topic and their contribution to advancing knowledge in the field.

Results: Accumulating evidence highlights the significant involvement of Bregs in the pathogenesis and regulation of various immune-mediated conditions, including autoimmune diseases, allergies, and cancer. In the context of autoimmunity, alterations in Bregs frequency and function have been observed in diseases such as multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus. These alterations result from a complex interplay of genetic

factors, including MHC and CTLA-4 polymorphisms, and environmental influences. Furthermore, Bregs' differentiation and functional plasticity in response to inflammatory cytokines and the tissue microenvironment may serve as valuable prognostic biomarkers. Understanding the mechanisms governing Breg dysfunction is crucial for the development of effective Breg-based therapies. However, three major challenges hinder the advancement of such therapies: ensuring Bregs' functionality after transfer, identifying optimal stimuli for Bregs expansion, and determining the appropriate therapeutic dosage. Comparative studies evaluating the efficacy of Breg-based therapies against existing treatments for autoimmune diseases are also urgently needed.

Conclusion: Regulatory B cells hold significant promise as a novel therapeutic modality for autoimmune diseases. Further research is warranted to address current challenges, including the identification of definitive Breg markers and the development of robust and reproducible methods for Breg manipulation and expansion in laboratory settings. Despite existing hurdles, Bregs represent a potentially powerful asset in our therapeutic arsenal against immunological disorders. Continued efforts to elucidate Bregs biology and optimize Breg-based immunotherapies will pave the way for their clinical translation in the foreseeable future.

keywords: Regulatory B Cells; Bregs; Autoimmunity; Autoimmune Diseases; Immunotherapy; Immune Regulation.

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The influence of immune cells on pregnancy outcomes and the role of immunoglobulin therapy in infertility

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Medical Immunology

Background and aim: During pregnancy, the immune system is essential. They are in charge of regulating the immune system's response to invasive pathogens. Inflammation brought on by an inability to control these immune cells can lower fertility. Intravenous immunoglobulin (IVIG) is a concentrated antibody used as biological substances for the treatment of a wide range of immunodeficiencies, as well as autoimmune. The primary goal of this treatment is to repair a compromised immune system. IgGs, via attaching to specific antigens, enhance the cellular and humoral immune response of innate immunity by activating complements and binding to Fc receptors on several immune cells.

Methods: The goal of this review is to look into the immunological causes of reproductive failure, with a focus on the immunomodulatory implications of IVIG in its treatment. As a result, we analyzed literature available in the PubMed and Google Scholar databases on immune cells involved in pregnancy maintenance, as well as the effect of immunoglobulin treatment on them.

Results: Our findings indicated that IVIG is an effective treatment for pregnancy problems in women, particularly those with immune cell abnormalities. As an immunomodulator, IVIG can cause a shift towards Th2 and Treg responses, as well as cytokine production. It thus enhances the pregnancy result.

Conclusion: The primary purpose of all immune cells is to assist preserve pregnancy, and immunoglobulin-based immunotherapy is an effective way to achieve this goal.

keywords: Pregnancy failure, IVIG, NK cells, T cells, B cells.

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Modulating NF-κB signaling in rheumatoid arthritis: Computational identification of marine peptides targeting TNFAIP3

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and joint destruction, significantly impacting patient quality of life. Dysregulation of the nuclear factor-κB (NF-κB) signaling pathway is a key driver of RA pathogenesis. Tumor necrosis factor alpha-induced protein 3 (TNFAIP3), a critical regulator of NF-κB activity in pathways such as TNF and Toll-like receptor (TLR) signaling, represents a promising therapeutic target for RA. This study aims to computationally identify marine-derived peptides that exhibit strong inhibitory interactions with TNFAIP3 and may serve as novel drug candidates for RA treatment.

Methods: A library of fifty marine-derived peptides was compiled based on existing literature. Peptide three-dimensional structures were predicted using the PEP-FOLD3 web server, employing a Hidden Markov Model suboptimal sampling algorithm. Peptide toxicity and pro-inflammatory antigenicity were assessed in silico using the ToxinPred and Proinflam web servers, respectively. The crystal structure of TNFAIP3 (PDB ID: 3DKB) was retrieved from the Protein Data Bank, with the active site defined by residues Thr97, Cys103 and His256. Peptide-TNFAIP3 docking was performed using the HADDOCK 2.4 web server. The best-docked complexes were selected based on HADDOCK scores and Root Mean Square Deviation (RMSD), and their binding affinity (equilibrium dissociation

constant, Kd) were predicted by the PRODIGY web server. To evaluate the dynamic stability of the selected TNFAIP3-peptide complexes, molecular dynamics (MD) simulations were conducted for 100 ns.

Results: The modeled peptides demonstrated favorable predicted properties, including high structural quality, solubility, and low predicted toxicity and antigenicity. Six peptides, PEP1 (VWDPPKFD), PEP3 (YWVTSGPK), PEP6 (VECYGPNRPQF), PEP21 (FNVPLYEFSY), PEP178 (VRWYRNGTCR) and PEP173 (QRAKINLLSKRKPPAERWWE) exhibited promising interactions with TNFAIP3 based on HADDOCK scores, RMSD values (ranging from 0.2 to 0.3 nm), predicted binding affinities, and binding energies. MD simulations confirmed the stability of these peptide-TNFAIP3 complexes over the 100 ns timescale

Conclusion: This computational study identified six marine-derived peptides (PEP1, PEP3, PEP6, PEP21, PEP178, and PEP173) as potential inhibitors of TNFAIP3 with favorable binding characteristics and stability. These peptides represent promising lead candidates for the development of novel peptide-based therapeutics for RA. Further in vitro and in vivo studies are warranted to validate these findings and assess their therapeutic efficacy

keywords: Marine peptide;TNFAIP3;Rheumatoid arthritis;Molecular docking; Molecular dynamics simulation;Drug discovery

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Unleashing the Immune Response Against Listeria monocytogenes

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Medical Immunology

Background and aim: Listeria monocytogenes is a Gram-positive, anaerobic bacterium that can cause listeriosis in humans and animals. This bacterium can have serious consequences, especially in people with weakened immune systems, pregnant women, and newborns. Given the importance of this disease, understanding the body's immune responses to Listeria monocytogenes is of great importance. The purpose of this study is to investigate the immune responses to Listeria monocytogenes and the resulting infection.

Methods: Forty articles with keywords Listeria monocytogenes and immune response were collected and analyzed from Google Scholar and PubMed databases.

Results: The immune response against Listeria monocytogenes involves both innate and adaptive immunity to combat this bacterium. T cells and B cells are pivotal in this process. T cells, including CD8+ and CD4+ types, play crucial roles by directly killing infected cells or releasing cytokines to recruit other immune cells. CD8+ T cells kill infected cells by recognizing antigens via MHC class I, while CD4+ T cells help activate additional immune responses through MHC class II. B cells produce antibodies that bind to the bacterium, marking it for destruction and neutralizing its toxins. Activated B cells differentiate into plasma cells, which secrete antibodies and can activate the complement system. Phagocytes like

neutrophils and macrophages also play a significant role. They engulf and destroy Listeria through phagocytosis and produce reactive oxygen species and enzymes to break down the bacteria. Listeria monocytogenes can escape from phagosomes and replicate in the host cell cytoplasm.

Conclusion: Through a multi-layered defense strategy, involving innate and adaptive immunity, the immune system recognizes, neutralizes, and eliminates Listeria monocytogenes. Key players in this response include neutrophils, macrophages, T cells, B cells, and phagocytes. Listeria monocytogenes has evolved strategies to evade the immune response, such as escaping from phagosomes and manipulating immune cells.

keywords: Listeria monocytogenes, Immune system, Immune response

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Role of mesenchymal stem cells in immunosuppression

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Medical Immunology

Background and aim: Mesenchymal stem cells(MSCs) have attracted much attention in the field of immunosuppression due to their unique ability to modulate immune responses. As a result, there is a growing body of research addressing the role of MSCs in immune modulation and their potential applications in autoimmune diseases, organ transplantation and inflammatory diseases. The aim of this systematic review is to critically analyze the available evidence on the immunosuppressive properties of MSCs and to explore their therapeutic potential in relevant diseases.

Methods: This study was conducted using the collected articles in English available from2000 to2024 in Scopus, PubMed and Web of Science with the keywords MSCs, immunotherapy and regenerative medicine in the Title/Abstract field. This study was conducted on the basis of the PRISMA guideline. For this systematic review,80 studies were selected,including35 preclinical,30 clinical and15 observational studies. Inclusion criteria for the review included studies focusing on MSCs in immunosuppression of human participants, reporting outcomes related to immunomodulation and using relevant study designs, and exclusion criteria included animal studies, unrelated research topics and data.

Results: In this systematic review, a total of30 studies were identified that met the inclusion criteria, which included a wide range of study designs including randomized controlled trials, cohort studies, and case-control studies. This analysis showed consistent findings across studies that MSCs through secretion of immunomodulatory molecules, induction of regulatory T cells, inhibition of T cell proliferation, dendritic cells, B cell activity, Natural killer cells and interaction with immune cells to reduce tissue damage and inflammation and exert their suppressive effect on the immune system.

Conclusion: Clinical studies indicate that MSC-based therapies improve outcomes in graft-versus-host disease (GVHD), autoimmune, and inflammatory diseases. However, challenges such as diverse MSC sources, heterogeneous study designs, and limited duration of effects persist. Despite promising results in treating immune-related conditions, there is a critical need for the standardization of MSC sources and protocols, as well as long-term safety evaluations. Further research is essential to address these issues and facilitate the continued development of MSC-based therapies.

keywords: Immunotherapy, MSCs, regenerative medicine

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Relationship of inflammatory cytokines with leptin and adiponectin in the treatment of Covid-19 patients

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Medical Immunology

Background and aim: The SARS-CoV-2 virus caused the global outbreak of the Covid-19 disease. Considering the spread of infections and inflammations caused by this virus, it is important to know the factors and conditions of their creation in the development of treatment methods and their prevention. Obesity is a risk factor for adverse outcomes in COVID-19, potentially driven by chronic inflammatory state due to dysregulated secretion of adipokines and cytokines.

Methods: In this validity review, articles related to the topic using the determined keywords (COVID 19, Inflammations, leptin, adiponectin) in reliable and international databases (PubMed and Google scholar and Science Direct) and the World Health Organization (WHO) website were searched. After collecting the search results, first the studies were studied based on the title, abstract of the article and then the full text of the article. If the articles were related to the topic, their results were used in the review.

Results: According to various reports and records, Leptin levels were similar in critically ill COVID-19 patients and critically ill non-COVID-19 patients, with no association to the severity of COVID-19. Adiponectin levels were significantly reduced in both severe and critical COVID-19 patients, reaching similar levels to those in non-COVID-19 critical patients. The adiponectin to leptin (Adpn/Lep) ratio was also reduced in all hospitalized COVID-19 patients and non-COVID-19 critical patients. Additionally, in severe COVID-19 patients, IL-6 levels showed a positive correlation with adiponectin and visfatin levels, while they negatively correlated with leptin levels.

Conclusion: Leptin and inflammatory cytokines regulate metabolism and immune function. Adipose tissue inflammation, characterized by immune cell infiltration (macrophages and neutrophils), is stimulated by leptin, which also increases cytokine secretion. This contributes to anorexia and cachexia in inflammatory diseases. Chronic inflammation and leptin resistance lead to obesity and anorexia. Elevated leptin levels in obesity may disrupt cytokine regulation, worsening COVID-19 outcomes, which is linked to high morbidity and mortality. Further research on leptin could enhance understanding of immune responses in obese COVID-19 patients.

keywords: COVID 19; Inflammations; leptin; adiponectin

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The function of neutrophils and neutrophil extracellular traps (NETs) in phases, outcomes, and difficulties of pregnancy

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Medical Immunology

Background and aim: Neutrophils have an important part in numerous stages of the reproductive cycle, and their existence in the female reproductive system is tightly regulated, thus their function may change during pregnancy. Neutrophil extracellular traps (NETs) are extracellular strands of unfolded DNA that include histone complexes and neutrophil granule proteins. The purpose of this study was to identify and explore the role of neutrophils and neutrophil extracellular traps (NETs) during pregnancy, as well as the difficulties produced by these cells.

Methods: In this review, we will discuss the literature available in PubMed and Google Scholar databases from 2010 to 2024 on the role of neutrophils in pregnancy and the relationship between patients, pregnancy complications, and neutrophil extracellular traps.

Results: Our findings suggest that neutrophils and their components play a role in maintaining maternal-fetal tolerance, and that their dysregulation contributes to pregnancy-related complications. The discovery that the NETosis process can cause pregnancy difficulties provides the way for new biological treatments. As a result, removing NET and its components may be a viable treatment option for patients with advanced illness to minimize or avoid inflammation.

Conclusion: More research is needed to determine the precise method by which immune system neutrophils and their local increase throughout various phases of pregnancy, as well as the commencement of NET formation, contribute to pregnancy-related illnesses.

keywords: Reccurent fetal loss, Neutrophil extracellular traps, Preeclampsia, Gestational diabetes mellitus(GDM).

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Selective PI3Kδ inhibitor discovery for rheumatoid arthritis: a structure-based drug design study

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Medical Immunology

Background and aim: Peptide-based therapeutics represent a promising frontier in drug development, offering advantages over traditional small molecules, particularly those derived from marine sources. Marine-derived peptides, in particular, present unique advantages over their terrestrial counterparts. This study aimed to leverage bioinformatics approaches to identify novel marine peptides capable of selectively inhibiting the phosphoinositide 3-kinase delta (PI3Kδ) receptor, a critical target in the pathogenesis of rheumatoid arthritis (RA).

Methods: We prepared a curated library of marine peptides based on existing literature and databases. Peptide three-dimensional structures were predicted using PEP-FOLD3 web server, followed by in silico toxicity and pro-inflammatory antigenicity assessment. Molecular docking was performed using HADDOCK 2.4 with PI3Kδ protein (PDB ID: 5IS5) from the PDB database, targeting active site residues Thr750, Met752 and Trp760. The best models of each predicted docked PI3Kδ-peptide complex were selected, and their binding affinity were quantified by the PRODIGY web server. Finally, the docked PI3Kδ-peptide molecules and their conformational stability were then conducted by molecular dynamics (MD) simulations for 100 ns to evaluate conformational stability.

Results: Molecular docking and binding affinity calculations identified five peptides –PEP8 (GPLGLLGFLGPLGLS), PEP26 (CWLPVY), PEP27 (DYGLYP), PEP161 (VKAIFNGARQGYKEHKNQRREEKLA) and PEP176 (FFHHIFRGIVHVGKTIHRLVTG)–

as exhibiting strong interactions with the PI3Kδ active site. The predicted tertiary structures of the marine peptides were of high quality, and in silico analyses indicated no significant toxicity or pro-inflammatory potential, along with favorable solubility profiles. These peptides displayed low root-mean-square deviation (RMSD) values (0.1 – 0.4 nm) during MD simulations, indicating stable complex formation. The docking accuracy was supported by robust cluster sizes (45-65) and favorable Z-scores (-1.7 to -2). The HADDOCK scores for the top complexes (PEP8-PI3Kδ: -71.5 kcal/mol, PEP26-PI3Kδ: -88.6 kcal/mol, PEP27-PI3Kδ: -84.9 kcal/mol, PEP161-PI3Kδ: -80.5 kcal/mol, and PEP176-PI3Kδ: -99.5 kcal/mol) confirmed strong binding interactions. Furthermore, the 100 ns MD simulations demonstrated the sustained stability of these complexes.

Conclusion: Finally, this study identified five marine-derived peptides (PEP8, PEP26, PEP27, PEP161, and PEP176) as promising candidates for the development of novel peptide-based therapeutics against RA. These peptides exhibit strong and stable interactions with the PI3Kδ receptor in silico, suggesting their potential to modulate PI3Kδ activity and thereby mitigate RA progression. Further in vitro and in vivo experimental studies are warranted to validate these findings and explore the therapeutic efficacy of these peptides.

keywords: Marine peptide;PI3Kδ inhibitors;Molecular docking;Molecular dynamics simulation; Rheumatoid arthritis;Drug discovery

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RplL and BMEI0257 are two targets for Brucella recombinant vaccine (Structural and homology study in Brucella)

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Medical Immunology

Background and aim: Brucellosis (Malta fever) is a zoonosis caused by ingestion of unpasteurized milk from infected animals, or close contact with their secretions. It leads to serious problems in global health, especially in underdeveloped countries. Brucellosis is caused by several species of the genus Brucella; a Gram-negative, facultative intracellular pathogen, which occurs worldwide. Due to the lack of efficient treatment against brucellosis, the only strategy is vaccination, which consists of conventional approaches or next generation one, including recombinant proteins. Choosing the suitable antigen stimulating the immune system is critical in preparation of these vaccines.

Methods: The aim of this research is to pinpoint potential multi-epitope vaccine options, utilizing the genes RplL and BMEI0257, encoding Large ribosomal subunit protein bL12 and 4-hydroxyproline epimerase in B. melitensis, respectively. The CLC Protein Workbench was used to analyze physicochemical characteristics. Multiple alignment was performed by COBALT. PHYRE2 was used to predict protein 3D structures, which were then modeled and compared to homologous structures found in Uniprot.

Results: Results of this study suggest that RplL and BMEI0257 are composed of 124 amino acids and 333 amino acids, respectively. The instability indices were 18.55 and 32.83, respectively. The hydrophilicity values were 0.119 and -0.190, respectively. In the secondary structure of RplL and BMEI0257 proteins, the α-helix accounted for 47% and 17% the Beta strand was 8% and 39%, and random

coil was 23% and 1%, respectively. Multiple alignment of 8 pathogenic species indicate high conservation between homologues of both target genes among Brucella.

Conclusion: Regard to significant conservation of both RplL and BMEI0257, Proteins within the Brucella genus, characterized by their hydrophobicity and specific physicochemical properties, suggest that these two genes hold potential as promising targets for the development of recombinant vaccines. Such vaccines could confer protection against various Brucella species.

keywords: Bioinformatics; Brucella; RplL;BMEI0257

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The transformative power of Next-Generation Sequencing (NGS) in unraveling rheumatoid arthritis pathogenesis and guiding precision medicine

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Medical Immunology

Background and aim: Rheumatoid arthritis (RA) is a complex, chronic autoimmune disease characterized by persistent inflammation, joint destruction, and systemic complications. Its multifactorial etiology, involving genetic predisposition, epigenetic regulation, and environmental triggers, presents significant challenges for early diagnosis, prognosis, and treatment. Next-Generation Sequencing (NGS) has emerged as a transformative technology, offering unprecedented insights into the genetic and molecular mechanisms underlying RA. This narrative review explores the application of NGS in understanding RA pathogenesis, identifying biomarkers, and facilitating personalized treatment approaches.

Methods: This narrative review was conducted by analyzing recent studies that applied NGS technologies to investigate the pathogenesis, biomarkers, and therapeutic strategies for RA. Key databases, including PubMed, Scopus, and Web of Science, were searched using relevant keywords such as "Rheumatoid Arthritis," "Next-Generation Sequencing", "Genomics", "Epigenetics", and "Precision Medicine". The research emphasized studies employing NGS methodologies, such as whole-genome sequencing (WGS), whole-exome sequencing (WES), transcriptomics, epigenomics, and targeted gene panels. Emphasis was placed on the role of NGS in identifying genetic variants, epigenetic modifications, and dysregulated molecular pathways relevant to RA. Studies were selected based on their relevance to the topic and their contribution to

advancing knowledge in the field. Priority was given to high-quality original research, systematic reviews, and meta-analyses published in English within the last decade. The findings were synthesized to provide a comprehensive overview of NGS applications in RA research and clinical practice.

Results: NGS has revolutionized RA research by uncovering key genetic susceptibility loci, such as HLA-DRB1 alleles and non-HLA genes, providing unprecedented insights into disease risk stratification. Transcriptomic profiling has revealed distinct gene expression signatures in synovial tissues and immune cell subsets, shedding light on the complex interplay of inflammatory mediators and immune dysregulation. Epigenetic analyses using NGS have identified dynamic modifications, including DNA methylation and histone modifications, that contribute to disease initiation and perpetuation. Furthermore, NGS has enabled the discovery of promising biomarkers for early diagnosis, monitoring disease activity, and predicting treatment response, facilitating the implementation of personalized medicine approaches. By integrating genomic data with clinical parameters, clinicians can tailor therapeutic interventions to individual patients, optimizing treatment efficacy and minimizing adverse effects. Moreover, NGS has contributed to unraveling the shared genetic and molecular underpinnings of RA and its associated comorbidities, such as cardiovascular disease.

Conclusion: NGS represents a paradigm shift and groundbreaking advancement in RA research and clinical practice, providing a comprehensive understanding of the disease's complex molecular architecture. Its application has significantly enhanced diagnostic accuracy, refined therapeutic strategies, and accelerated the identification of novel drug targets. As NGS technologies continue to evolve and become more accessible, their integration into routine clinical workflows promise to revolutionize RA management, leading to improved patient outcomes and personalized care.

keywords: Rheumatoid Arthritis;Next-Generation Sequencing (NGS); Autoimmune Diseases;Genomics Transcriptomics;Personalized Medicine; Precision Medicine

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Innovative Approaches in Triple-Negative Breast Cancer (TNBC) Therapy: Mobilizing the Body's Defense Forces

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Medical Immunology

Background and aim: Breast cancer is the most common cancer in women worldwide. The international agency for research on cancer estimates that the incidence of breast cancer will increase by more than 40% and the mortality rate will increase by more than 50%. TNBC is one of the breast cancer's subtypes. Given the lack of effective treatments in this subtype of breast cancer, several efforts have been conducted in recent years to increase the therapeutic opportunities for TNBC patients. . Our study aimed to assess the effectiveness of treatment options and some promising new treatment approaches that include immunotherapy. In this case, We

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including breast cancer, TNBC, adaptive cell therapy(ACT) and immunotherapy were investigated and combined using Boolean operators (e.g., AND, OR).

Results: TNBC is extremely difficult to treat due to the absence of estrogen receptor (ERs), progesterone receptor (PRs), and human epidermal growth receptor 2 (HER2)As the special soldiers in the tumor microenvironment(TME), TILs play an important role in the process of identifying and killing target tumor cells, which has led to the development of immunotherapies. Among those immunotherapies, ACT is a new star and has achieved good results in recent years. The outstanding achievements of CAR-T cell therapy in hematological tumors and the promising effects of ACT with T-Cell receptor therapy (TCR-T) cells

in solid tumors have prompted the search for more suitable targets or combination programs for applying ACT to solid tumors. ACT approaches like TIL and CAR-T have shown promising efficacy in TNBC. Clinical trials have indicated significant improvements in survival rates and tumor reduction in some patients using these therapies. However, challenges such as antigen selection and managing

Conclusion: The biological and pathological features of TNBC provide insight into several cases, but immunotherapy research has increased in cancer biology and oncology. In general, many treatments have been used for TNBC today, such as TILs, CAR-T, etc.

keywords: Triple–negative breast cancer (TNBC); Immunotherapy; Adaptive cell therapy (ACT); Tumor-infiltrating

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Car T cell therapy

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Medical Immunology

Background and aim: Chimeric antigen receptor (CAR) T-cell therapies have revolutionised the field of haematological malignancies by achieving impressive remission rates in patients with highly refractory haematological malignancies, improving overall survival. To date, six commercial anti-CD19 and anti- BCMA CAR T cell products have been approved by the Food and Drug Administration (FDA) for the treatment of relapsed/refractory B-cell haematological malignancies and multiple myeloma. The indications for CAR T-cell therapies are gradually expanding, with these therapies being investigated in a variety of diseases, including non-malignant ones.

Methods: We conducted a preclinical assessment, including evaluation of transduction efficiency, phenotype, in vitro proliferation, cytotoxicity and cytokine production, of T cells modified to express bispecific BM38 CARs, 38BM CARs, and individual BCMA CARs and CD38 CARs. BCMA, 38BM and BM38 CARs with stronger in vitro antitumor activity were further evaluated in xenogeneic mouse models. Next, we performed a phase I clinical trial of BM38 CAR-Ts in patients with RRMM

Results: Preclinical results of BM38 CAR-Ts We constructed the bispecific BM38 CAR and 38BM CAR by connecting an anti BCMA scFv and an affinity-optimized anti-CD38 scFv in 4-1BB-containing second-generation formats (Fig. 1a). BM38, 38BM, BCMA and CD38 CARs were stably expressed on lentivirus-transduced T cells from healthy donors, and the final CAR-Ts maintained CD38+ expression (Fig. 1b). BM38 CAR-Ts composed 58.5% of CD8+ cell population and 39.5% of CD4+ cell population, and appeared to be naÃ¯ve T cells (51.5%) and central memory T cells (26.1%), consistent with the phenotypes of single-target and 38BM CAR-Ts (Fig. 1c; Additional file 1: Fig. S1 for representative staining). BM38, 38BM and CD38-directed CAR-Ts exhibited efficient in vitro expansion equivalent to those of BCMA-directed CAR-Ts and NT cells (Fig. 1d), without observable fratricide.

Conclusion: Several strategies have been developed to enhance CAR T cellexpansion, persistence and antitumor activity by introducingnovel costimulatory domains, cytokine genes, and constitutivelyactive or inverted cytokine receptors into T cells. While therearesafety concerns regarding autonomous cell growth and cytokineinduced toxicity using these approaches, encouraging efficacyand safety data from preclinical studies supports continuedpreclinical testing and evaluation in humans. Thus, we remainhopeful that optimized CAR T cells will eventually improveoutcomes and decrease toxicities for patients suffering fromsolid tumors.

keywords: CAR T-cell therapies, relapsed/refractory haematological

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The effect of ethanolic extract of wild pistachio leaf (Pistacia Khinjuk) on the expression of genes involved in the metastatic power of human breast cancer cells

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Medical Immunology

Background and aim: Breast cancer is a growing disease, with the Health Organization Worldwide predicting an increase in prevalence and death rates. Chemotherapy is effective, but drug resistance is a major issue. This study investigates the effect of the ethanolic extract of Khinjuk Pistacia leaves on gene expression in human breast cancer cells.

Methods: After calculating the 50IC effect of the extract on the expression of genes related to migration in cells Breast cancer was evaluated by the real-time PCR method. Data were collected through statistical software (SPSS) and analyzed by one-way ANOVA and student-t tests.

Results: MTT test results showed that the 50IC of the extract was 61.1078, 57.326, 85.81, and 66.28. micromolar/ml for 24, 48, 72, and 96 hours. Real-time PCR data showed that after 24 hours of treatment with a 50 IC concentration of the extract, the difference between the -2MMP and -9 genes in breast cancer cells decreased significantly (p0.05). The expression of TIMP-1 and -2 genes showed a significant increase (p0.05). uPA and uPAR gene expression showed a significant decrease (p0.05).

Conclusion: The findings of this study could help develop more effective and safe treatments for breast cancer. Wild pistachio leaf extract has anti-metastasis effects in breast cancer cells.

keywords: wild pistachio plant, ethanolic extract, Khinjuk Pistacia, gene expression, breast

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Exploring the Impact of Hypoxia-Preconditioned Hair Follicle Stem Cell Secretions on Astrocytes in Simulated Ischemic Stroke Conditions

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Medical Immunology

Background and aim: In recent years, stem cell therapy has emerged as a promising method in regenerative medicine. Given the limited survival rate of stem cells post-transplant, it is suggested that their therapeutic benefits are largely attributed to the paracrine actions of their secreted factors. Consequently, this study was designed to explore the paracrine effects of the secretome from hypoxia-preconditioned hair follicle stem cells (HFSCs) on astrocytes within an in vitro ischemic stroke model.

Methods: HFSCs were isolated from adults' rats, and then cultured in α-MEM medium with supplements. Subsequently, these cells verified by flowcytometry and immunocytochemistry. HFSCs were preconditioned under hypoxic and normoxic conditions for 24 hours before secretome extraction. Primary astrocytes were isolated from rat cortex, purified via selective shaking, and confirmed using GFAP marker. To simulate stroke, astrocytes were exposed to oxygen-glucose deprivation (OGD) for 24 hours in a hypoxia chamber. Four treatment groups were created: Control, OGD+Medium, OGD+CM-Normoxia, and OGD+CM-Hypoxia, with HFSC-conditioned media applied post-OGD. Effects on astrocyte morphology, apoptosis, and gene expression were assessed using flowcytometry and real-time PCR.

Results: Treatment with hypoxia-preconditioned secretome significantly elevated HIF-1α expression (p 0.0005) and reduced inflammatory factors IL-1β and TNF-α compared to normoxia (p 0.01).

Conclusion: These findings underscore the therapeutic potential of hypoxia-preconditioned hair follicle stem cell secretome in enhancing neuroprotection and reducing inflammation in astrocytes within a stroke model

keywords: Ischemic stroke, Hypoxia-preconditioning, Astrocytes, Hair follicle stem cell

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Development of Vaccines for Immune Response against Acinetobacter baumannii

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Medical Immunology

Background and aim: Acinetobacter baumannii, an antibiotic-resistant pathogen, is a serious challenge in the treatment of hospital infections. With the increasing resistance of this bacterium to existing treatments, it is necessary to develop vaccines that create an effective immune response. In this article, the recent progress in the development of vaccines against A.baumannii is discussed. The immune mechanisms that are activated against this bacterium, Different types of vaccines and their clinical results are reviewed and the challenges in this direction are analyzed. The aim of this article is to provide an overview of the current status and development of effective vaccines against A.baumannii.

Methods: A.baumannii surface antigens play an important role in immune responses of the body. These antigens are targets for the development of vaccines and new treatments.The identification of membrane proteins(OmpA), LPS, adhesive proteins, viral factors and the study of surface antigens of A.baumannii helps to understand pathogenic mechanisms, develop new diagnostic, therapeutic and vaccine methods.These antigens are suitable for research in the field of immunology and microbiology. A.baumannii needs a vaccine with a strong response due to its high resistance to antibiotics.Infections caused by this bacterium usually occur in immunocompromised patients, so inactivated or subunit vaccines may be more appropriate. mRNA vaccines also have great potential, but are still in the research phase and may not be ready for clinical use.The use of adjuvants to prepare subunit vaccines reduces degradation and increases immunogenicity. Immunization methods include intramuscular, subcutaneous, intraperitoneal and mucosal vaccination. This increase the safety of subunit vaccines.

Results: Despite efforts made ،No vaccine against A. baumannii has undergone clinical trials, indicating the challenges associated with creating effective vaccine against this pathogen. research on anti-A. baumannii vaccine is still in its early stages. Most studies have focused on subunit vaccines. However, there are ongoing explorations of nucleic acid vaccines, virus vectors, conjugated carriers, and co-delivery. It is worth noting that mRNA and DNA vaccine technologies have gained significant recognition due to the competition surrounding COVID-19 vaccines. Therefore, we can anticipate the increasing importance of nucleic-acid-based vaccines in treating A. baumannii and other infections in the coming years. Additionally, proteomic approaches and reverse vaccination offer the benefit of utilizing bioinformatics to systematically evaluate and select potential immunogens for vaccine candidates in silico. This method may be employed in the future to identify antigens and design vaccines that protect against A. baumannii infections.

Conclusion: Multidrug-resistant A. baumannii infections and combination therapy is a key strategy to overcome drug resistance. Antibiotic surveillance is essential to prevent the emergence of drug-resistant strains, and multivalent vaccines consisting of outer membrane vesicles (OMVs), bacterial spirits (BGs), or multiple subunit vaccines, hold promise for reducing these infections. The development of vaccines has undergone significant changes due to technological advances, especially since the development of the Covid-19 vaccine.

keywords: Acinetobacterbaumannii;Vaccinedevelopment;antigens;immune response;immunization

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Exosomes in asthma : Underappreciated contributors to the pathogenesis and novel therapeutic tools

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Medical Immunology

Background and aim: Asthma, a chronic inflammatory disease with diverse pathomechanisms, presents challenges in developing personalized diagnostic and therapeutic approaches. This review aims to provide a comprehensive overview of the role of exosomes, small extracellular vesicles, in asthma pathophysiology and explores their potential as diagnostic biomarkers and therapeutic tools.

Methods: A literature search was conducted to identify recent studies investigating the involvement of exosomes in asthma. The retrieved articles were analyzed to extract relevant information on the role of exosomes in maintaining lung microenvironment homeostasis, regulating inflammatory responses, and their diagnostic and therapeutic potential for asthma.

Results: Exosomes secreted by various cell types, have emerged as crucial mediators of intercellular communication in healthy and diseased conditions. Evidence suggest that exosomes play a significant role in maintaining lung microenvironment homeostasis and contribute to asthma pathogenesis by regulating inflammatory responses. Differential exosomal content between healthy individuals and asthmatics holds promise for the development of novel asthma biomarkers. Furthermore, exosomes secreted by immune and non immune cells, as well as those detected in biofluids, demonstrate potential in promoting or regulating immune responses, making them attractive candidatesfordesigningnewtreatmentstrategiesforinflammatoryconditions such as asthma

Conclusion: Exosomes, with their ability to modulate immune responses and deliver therapeutic cargo, offer potential as targeted therapeutic tools in asthma management. Further research and clinical trials are required to fully understand the mechanisms underlying exosome-mediated effects and translate these findings into effective diagnostic and therapeutic strategies for asthma patients.

keywords: exosome, extracellular vesicle, asthma, allergy, intercellular communication, immunotherapy

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Production of CAR T Cells by Engineered Artificial Antigen Presenting Cells and Their Effect on the Expansion of CD8+ Cells

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Medical Immunology

Background and aim: Adoptive cell therapy (ACT) with chimeric antigen receptor T (CAR T) cells is a promising approach in the field of cancer immunotherapy. Improving the production of CAR T cells is an important concern in terms of cost and product quality for access to this therapy. One strategy to improve T cell expansion is the use of genetically engineered artificial antigen-presenting cells (aAPC) that express a membrane-bound anti-CD3 to activate T cells. In this research we characterized the CAR T cells produced by aAPC-based approach in terms of expansion efficiency, CD8/CD4 T-cell ratio, and specific cytotoxicity.

Methods: In this work, we produced an aAPC cell by engineering K562 cells to express membrane-bound anti-CD3 (mOKT3) and GFP using a retroviral vector. T cells were activated by co-culturing mitomycin C-treated aAPC cells with PBMCs or by standard activation method of anti-CD3/CD28 antibodies. Not-transduced T cells and CD19-CAR T cells were characterized for expansion, activation, and immunophenotype markers. To investigate the cytotoxicity of the produced CAR T cells, they were co-cultured with the target cells and measured using a bioluminescence-based assay.

Results: Findings in this study showed that the engineered aAPC cell has the potential to expand non-transduced T and CAR T cells. It was also shown that aAPC activation method increased the proliferation of CD8+ killer cells compared to the standard method. In addition, CAR T cells produced by this method after co-culture with target cells showed specific cytotoxicity similar to antibody-based method.

Conclusion: Our findings show that regardless of immunophenotype, both aAPC and antibody-activated methods can be used to generate effective CAR T cells. These findings could be cost-effective for improving T cell expansion and future applications of aAPC-derived CAR T cells.

keywords: Artificial antigen presenting cells; CAR T cells; OKT3

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Samuel Rahbar's Legacy: How an Iranian Discovery Revolutionized Diabetes Care

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Medical Immunology

Background and aim: Glycated hemoglobin (HbA1c), a critical marker for long-term glycemic control, has revolutionized diabetes management. Originally identified in the late 1950s by Samuel Rahbar and colleagues in Iran, HbA1c's journey from a serendipitous discovery to a cornerstone of diabetes care is a testament to its clinical utility. This review aims to trace the historical trajectory of HbA1c, exploring its initial characterization in Iran, subsequent validation, and eventual global adoption as a gold standard for diabetes monitoring. Furthermore, we delve into the immunological implications of chronic hyperglycemia and HbA1c formation, highlighting the interplay between glycemic control and immune dysregulation.

Methods: We conducted a comprehensive literature review encompassing historical publications, seminal research articles, clinical guidelines, and contemporary studies focusing on HbA1c. Databases searched included PubMed, MEDLINE, Scopus, and Web of Science, using keywords such as "HbA1c", "glycated hemoglobin", "Rahbar", "diabetes mellitus", "glycemic control", "immunology", and "inflammation". Emphasis was placed on primary sources documenting the initial discovery and subsequent developments, alongside contemporary research elucidating the immunological aspects of HbA1c.

Results: The discovery of an unusual hemoglobin fraction (HbA1c) in patients with diabetes by Rahbar in Iran laid the groundwork for understanding the relationship between chronic hyperglycemia and hemoglobin modification. Subsequent research confirmed that HbA1c reflects average blood glucose levels over the preceding 2-3 months, providing a robust measure of long-term glycemic

control. The development of standardized measurement techniques, particularly through the National Glycohemoglobin Standardization Program (NGSP) and International Federation of Clinical Chemistry (IFCC), facilitated its global adoption and transforming diabetes management globally. From an immunological perspective, chronic hyperglycemia, as reflected by elevated HbA1c, is associated with increased oxidative stress, inflammation, and immune dysfunction. Glycation end products (AGEs) formed during HbA1c generation contribute to innate immune activation, impaired adaptive immunity, and increased susceptibility to infections and diabetes-related complications.

Conclusion: The discovery of HbA1c by Iranian scientists represents a pivotal moment in diabetes care, transitioning from a simple observation to a globally recognized biomarker. HbA1c not only serves as a powerful tool for monitoring glycemic control but also provides insights into the immunological consequences of chronic hyperglycemia. Understanding the interplay between HbA1c, AGEs, and immune dysregulation is crucial for developing targeted therapies to mitigate diabetes-related complications. The legacy of Rahbar's discovery underscores the importance of cross-disciplinary research and its profound impact on global health.

keywords: HbA1c; glycated hemoglobin; diabetes mellitus; Samuel Rahbar; Iranian discovery; glycemic

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Producing KSHV-CD200 and exploring its therapeutics impacts on selective chemokines in immune responses

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Medical Immunology

Background and aim: KSHV-vCD200, also known as vOX2, is crucial for host immunomodulation. We developed a humanized variant of this viral protein by fusing vCD200 with CD200 and the human γ1 Fc fragment (vCD200 hCD200c:Fcγ1) to evaluate its immunomodulatory effects on cytokine production, cell phenotype markers, lymphocyte patterns, and activities of NF-κB and AP-1, as well as in carrageenan-induced acute inflammation and collagen-induced arthritis (CII) models.

Methods: Cytokine and chemokine levels were measured using a Multiplex assay kit and quantified by the Luminex assay (Bio Plex, Bio-Rad, USA).

Results: We found that vCD200:Fcγ1 significantly reduced MCP-1 levels in primary and rIFN-γ-treated monocytes, but had not substantial effects on eotaxin, MIP-1α-1β, RANTES, GM-CSF, IL-1β, IL-6, and TNF-α. Viral chemokine antagonists that decrease chemokine production can impair leukocyte recruitment. MCP-1, a member of the CC chemokine subfamily, is primarily responsible for recruiting and activating monocyte/macrophages to inflammatory sites and plays a key role in both acute and chronic inflammation.

Conclusion: The inhibitory effect of vCD200 on IL-8 and MCP-1α may help prevent leukocyte recruitment to sites of acute inflammation during viral replication.

keywords: KSHV-vOX2, vCD200, CD200, humanised vCD200, chemokine

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Seroconversion Patterns of Islet Autoantibodies in Iranian Pediatric Type 1 Diabetes

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Medical Immunology

Background and aim: Type 1 diabetes (T1D) is an autoimmune disease marked by CD4+ and CD8+ T-cells infiltration into the islets of Langerhans and the production of autoantibodies against islet autoantigens. This study aimed to assess the prevalence of glutamic acid decarboxylase antibody (GADA), insulin autoantibody (IAA), and insulinoma-associated antigen-2 antibody (IA-2A) in Iranian children with T1D.

Methods: A total of 100 T1D patients (53 females, 47 males) were enrolled. Autoantibodies were measured using enzyme-linked immunosorbent assay (ELISA) kits (Generic Assays GmbH, Germany): sandwich ELISA for GADA and IA-2A, and indirect ELISA for IAA. Positive thresholds were defined as ≥ 5 IU/mL for GADA, 10 IU/mL for IA-2A, and ≥2.4 U/mL for IAA. All assays were performed per the manufacturer's instructions.

Results: Of the participants, 84% were positive for at least one autoantibody, while 16% were seronegative. GADA was detected alone in 18%, IA-2A in 13%, and IAA in 6%. Combined autoantibody profiles included: GADA and IA-2A (14%), GADA and IAA (11%), and IA-2A and IAA (5%). All three autoantibodies were concurrently detected in 17% of patients. No statistically significant differences in autoantibody prevalence were observed with disease duration (≤ 2, ≤ 5, and ≤ 20 years). However, trends indicated an increased prevalence of GADA and IA-2A with longer disease duration, while IAA prevalence decreased after two years.

Conclusion: GADA was the most frequently detected autoantibody among Iranian T1D children. Simultaneous seroconversion for GADA and IA-2A was common, suggesting their potential role as biomarkers for disease progression.

keywords: Type 1 Diabetes, Autoantibody, ELISA, Seropositivity

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Angiocrine functions of mesenchymal stem cell exosomes on ischemic myocardium: a systematic review.

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Medical Immunology

Background and aim: Mesenchymal stem cells (MSCs) can foster the regeneration of the ischemic myocardium in a paracrine manner via the release of several extracellular vesicles, especially exosomes. It has been indicated that exosomes are cell-free byproducts and can harbor diverse pro-angiogenic factors that are involved in the growth of blood vessels to the ischemic sites. Here, previous studies related to angiogenesis capacity of MSC exosome and restoration of ischemic myocardium are presented.

Methods: The current descriptive-analytical review study was conducted to identify relevant experiments associated with the application of MSC exosomes in the regeneration of ischemic myocardium. To this end, online search was done in databases including Google Scholar, Web of Science, and PubMed databases from 2018 until 2024. The keywords were "mesenchymal stem cells", "exosomes", "myocardium ischemia", "angiogenesis", and " Regeneration". Studies were included based in terms of relevant topic, study design, patient characteristics, therapeutic regimes, and outcomes. Data related to angiogenesis capacity of MSC exosomes in heart ischemia were extracted and included to this study.

Results: Data indicated the reparative properties of MSC exosomes via the promotion of angiogenesis within the cardiac tissue parenchyma after ischemia. The induction of vascularization into the ischemic myocardium can prevent subsequent aberrant remodeling and fibrotic changes.

Conclusion: Taken together, MSC exosomes are magic bullets and valid therapeutic options for the regulation of angiogenesis following the ischemic conditions. However, enormous experiments are mandatory to elucidate the underlying mechanisms associated with blood vessel formation within the ischemic myocardium.

keywords: Mesenchymal stem cells; exosomes; myocardium ischemia; Angiogenesis; Regeneration.

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The Potential Therapeutic Effects of Tau Interferon in pathogen-related Asthma Treatment; A comprehensive review

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Medical Immunology

Background and aim: Asthma is a multifactorial disease with high global prevalence. It is predominantly caused by a shift in immune responses toward Th2, accompanied by overproduction of cytokines such as IL-4, IL-5, and IL-13. These cytokines drive eosinophil infiltration, goblet cell hyperplasia, and bronchial smooth muscle contraction. Viral infections are a significant trigger of asthma, as they can skew immune responses toward Th2, exacerbating asthma. Considering the pathogenesis of asthma, effective therapeutic approaches are essential. In cases of pathogen-related asthma, interferon-based therapies, may offer a promising alternative. This study explores the therapeutic potential of interferons, particularly emphasizing on IFN-τ in asthma treatment.

Methods: A search was conducted in related databases including Pubmed, Web of Science and Google Scholar for studies published to the year 2024 using the keywords "Asthma," "interferon tau," and "therapeutic application," and their synonyms; The inclusion criteria emphasized studies evaluating the immunomodulatory and antiviral effects of IFN-τ. Ultimately we found 10 articles that met inclusion and exclusion criteria.

Results: Interferon tau (IFN-τ) is a type I interferon exclusively produced by the trophoblast in ruminants during days 14–21 of pregnancy. By binding to IFNAR1 and IFNAR2 receptors, IFN-τ exerts its effects similar to IFN-α and IFN-β through the activation of the JAK-STAT signaling pathway. While IFN-τ plays a critical role in establishing a successful pregnancy, it also shares the same properties of other

type I interferons, including antiviral, antitumor, immunomodulatory, antiproliferative, and anti-inflammatory. These effects help eliminate viruses, which are triggers of asthma, and restoring the Th1/Th2 immune response balance thereby contributing to asthma alleviation. These properties, along with several advantages of IFN-τ, such as cross-species reactivity in humans and mice, lower toxicity at higher concentrations compared to IFN-α and IFN-β, and fewer side effects relative to other type I interferons, position IFN-τ as a promising therapeutic candidate for the treatment of pathogen-related asthma.

Conclusion: Given the exacerbation of asthma due to respiratory viral infections, the development of effective treatment strategies is necessary and valuable. Administration of IFN-α and IFN-β can help inhibition of these infections and control asthma; however, their high toxicity limits their therapeutic use. It is hypothesized that IFN-τ, in combination with PEGylation to extend its half-life, could serve as a novel therapeutic approach. Due to its lower toxicity compared to IFN-α and IFN-β, IFN-τ offers a potentially safer alternative for treating asthma associated with viral infections.

keywords: Asthma; interferon tau; therapeutic application

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Serum CTRP1 Levels in Candidates for Coronary Artery Bypass Graft

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Medical Immunology

Background and aim: CTRP1 is an adipokine that plays crucial roles in the cardiovascular system, and its dysregulation has been reported in patients with CAD. In this study, our aim was to measure its levels in patients who were candidates for cardiac bypass surgery.

Methods: The participants consisted of 30 candidates for coronary artery bypass graft (CABG) surgery and an additional 30 controls. Inflammatory parameters were assessed using enzyme-linked immunosorbent assay (ELISA) kits. Serum CTRP1 concentration was determined using a commercially available ELISA kit.

Results: Serum CTRP1 levels significantly increased in the patient group compared to the control group (p-value 0.0001). Furthermore, CTRP1 levels positively correlated with inflammatory parameters.

Conclusion: Elevated levels of CTRP1, along with inflammation in CAD, suggest the involvement of CTRP1 in inflammatory responses. However, this hypothesis remains to be fully elucidated.

keywords: Coronary artery bypass graft; CTRP1; IL-6; TNF-α; hs-CRP

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Exosomes of 4t1 cells that are enriched with miR-34a reduce the expression of IL-6 and VEGF of 4T1 cells.

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Medical Immunology

Background and aim: : Reduction of onco-suppressor miRNAs is an important factor in many types of cancer including breast cancer. A novel type of therapy in cancer treatment is miRNA replacement therapy and the main obstacle in this field is finding the appropriate vehicle. Exosomes as intercellular carriers has become as a favorable carrier. For this purpose, we aimed to evaluate the changes of oncogenes in 4T1 cells after miRNA replacement therapy by application of exosomes as delivery vehicle.

Methods: Exosomes were purified from 4T1 cells by purification kit and characterized by dynamic light scattering, electron microscopy. Then miR-34a was loaded in exosomes by CaCl2 method. The loading efficiency confirmed by real-time PCR. Then the cultured 4T1 cells treated with free exosomes and miR-34a loaded exosomes for 48H hours. The level of IL-6 and vascular endothelial growth factor (VEGF) were evaluated by Real-time PCR.

Results: The expression level of IL-6 and VEGF significantly reduced in 4T1 cells treated with miR-34a loaded exosomes in comparison to 4T1 cells treated with exosomes or non-treated cells.

Conclusion: Application of 4T1 derived exosomes for delivery of miR-34a can effectively reduce the oncogenes expression level in 4T1 cells. In total application of tumor derived exosomes for delivery of miRNA can be beneficial for miRNA replacement therapy.

keywords: microRNA, Gene expression, IL-6, VEGF

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Investigating Factors Influencing the Level of TGF(Transforming Growth Factor) Beta Cytokine Secretion in Patients With Lung Cancer

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Medical Immunology

Background and aim: Lung cancer is a common widespread cancer which is divided in to two types: 1) non-small cell lung cancer and (NSCLC) and small cell lung cancer (SCLC).Lung cancer is caused by abnormal cells growing unchecked. Transforming Growth Factor Beta is a cytokine with three isoforms (TGF-β1, TGF-β2 , TGF-β3)which each of them have different effect.They have crucial function in controlling many cellular processes.

Methods: This review study was conducted in 2024 by searching the databases Google Scholar and PubMed, using keywords such as lung cancer,transforming growth factor,and others.out of 40,100 articles available in these databases, 14 articles were included in the final analysis after excluding duplicate papers,applying the criteria of new data,being published in English,and focusing on human samples.

Results: TGF-β reduced the level of surface protein of five NKG2DLs without altered transcription levels in lung cancer cells.In another study Galunisertib reversed the effect of TGF-β on the expression of NKG2DLs also KLF6 knockdown increases TGF-BR1 expression AMH(Anti-Mullerian hormone) and its second type receptor AMHR2,were unexpectedly indentified as potent regulators of transforming growth factor(TGF-β) in lung cancer.

Conclusion: By targeting the level of surface protein of five NKG2DLs,KLF6 and AMH ,using cell injection methods at the first stage of lung cancer for decreasing the rate of TGF-beta is recommended.

keywords: TGF Beta Cytokine,Lung Cancer,Lung Cancer Treatment

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Histopathological Evaluation of Theranekron's Therapeutic Efficacy in Experimental Crohn's Disease

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Medical Immunology

Background and aim: Crohn's disease, a chronic inflammatory bowel disease (IBD), primarily affects the distal small intestine and the proximal colon, causing severe inflammation in the intestinal wall. This inflammation often leads to complications such as strictures, abscesses, and fistulas, requiring surgical intervention. Factors like genetics, altered gut microbiota, and epithelial barrier dysfunction play roles in its pathogenesis. Current treatments face limitations in efficacy and side effects. Theranekron, with its anti-inflammatory and immune-modulatory properties, has emerged as a potential therapeutic candidate. This study evaluates Theranekron's effects on histopathological changes and intestinal mucosal barrier integrity in an experimental Crohn's disease model.

Methods: This study involved female Wistar rats (200±20 grams) divided into four groups: healthy control group, untreated diseased control group receiving normal saline, Theranekron-treated diseased group, and sulfasalazine-treated diseased group as standard treatment. Crohn's disease was induced using indomethacin (7.5 mg/kg, administered subcutaneously in two doses, spaced 24 hours apart). Theranekorn was administered as a single subcutaneous injection (1 mg/kg body weight), while sulfasalazine was given orally via oral gavage (100 mg/kg, once daily, for 10 days). Upon completion of the treatment period, the rats were humanely euthanized via intraperitoneal administration of ketamine (200 mg/kg) and xylazine (20 mg/kg). Tissue samples were then carefully collected for

subsequent analyses. The severity of inflammation, crypt structure, and mucosal damage were assessed using hematoxylin and eosin (H&E)-stained histopathological slides. All evaluations were performed in triplicate to ensure reliability and reproducibility of the results. This method ensured a comprehensive evaluation of Theranekron's therapeutic effects.

Results: Histopathological analysis revealed severe inflammation, crypt distortion, and hemorrhage in the untreated diseased control group. Treatment with Theranekron significantly (p 0.05) reduced the severity of inflammation, decreased inflammatory leukocyte infiltration, improved crypt structure, and alleviated mucosal damage. While sulfasalazine treatment also demonstrated notable improvements, Theranekron exhibited superior efficacy in specific parameters, particularly in enhancing mucosal barrier integrity. These findings underscore Theranekron's potential as a more effective therapeutic option compared to conventional treatments.

Conclusion: Theranekron demonstrated substantial anti-inflammatory and reparative effects in an experimental Crohn's disease model. By reducing inflammation, leukocyte infiltration, and histopathological damage while improving intestinal barrier integrity, it positions itself as a promising therapeutic option. Its superior performance in some measures compared to sulfasalazine emphasizes its potential advantage. However, further studies are required to validate its safety and efficacy in preclinical and clinical settings. Theranekron could potentially address the limitations of existing therapies, offering a more effective approach to managing Crohn's disease.

keywords: Crohn's disease, Theranekron, histopathology, inflammation, IBD

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Expression of Anti-PDL1 scFv-Fc in Escherichia coli Strains and HEK-293 Cells: Evaluating Binding to PDL1 Protein

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Medical Immunology

Background and aim: Programmed cell death ligand 1 (PDL1) is overexpressed in various human cancers, aiding in immune system evasion. Targeting PDL1 to interact with the programmed cell death protein 1 (PD1) has transformed cancer immunotherapy by leveraging the immune system's capabilities. Anti-PDL1 single-chain variable fragment (scFv) antibodies are particularly relevant due to their high tumor penetration, reduced immunogenicity, low production costs, and small size, making them useful for diagnostic and therapeutic applications. However, producing these antibodies is challenging due to the need for the correct formation of intrachain disulfide bonds, which do not typically form in the oxidizing environment of living cells.

Methods: The specific binding of anti-PDL1 scFv-Fc to PDL1 was demonstrated using flow cytometry and ELISA.

Results: Our study confirmed the importance of disulfide bond formation for the antigen-binding efficiency of scFv. These small antibody fragments could be valuable agents for blocking or detecting PD-L1. Notably, anti-PDL1 scFv-Fc produced in HEK-293 cells showed higher binding levels to PDL1 than those expressed in Shuffle and Rosetta strains.

Conclusion: Our findings suggest that the correct formation of disulfide bonds in HEK-293 and Shuffle and Rosetta strains significantly enhances the biological activity of anti-PDL1 scFv-Fc.

keywords: PDL1, Anti-PDL1 scFv-Fc, Shuffle and Rosetta Escherichia coli Strains, HEK-293

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Interconnections Between Gut Mycobiota and Systemic Lupus Erythematosus: Unraveling Pathogenic Mechanisms and Therapeutic Strategies

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Medical Mycology

Background and aim: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with genetic and environmental factors. Recent research underscores the crucial role of gut microbiota, including the underexplored fungal mycobiome, in SLE pathogenesis. Fungal dysbiosis disrupts immune homeostasis, contributing to disease progression and highlighting the need for targeted therapies.

Methods: We conducted a search of PubMed, Google Scholar, and Web of Science databases up until March 2024 to identify observational studies examining the relationship between systemic lupus erythematosus (SLE) and gut microbiota, with a particular focus on the underexplored fungal mycobiome in SLE pathogenesis. We included studies that investigated the association between systemic lupus erythematosus (SLE) and the gut microbiota. In this study, three reviewers independently collected summary data from published sources and evaluated both the methodological quality and the risk of bias. Disagreements about study inclusion were resolved through consultation with the corresponding author. Boolean operators were used to combine the key search terms, which included, "Systemic autoimmune diseases", "Systemic Lupus erythematosus", "SLE", "Intestinal Microbiota", "Gastrointestinal Microbiome", "Gut Microbiota", "Mycobiome", "Fungal Microbiota", "Intestinal dysbiosis", "Fungal dysbiosis", "Intestinal fungi", "Microbial imbalance", and "Microbial Interactions".

Results: Out of 3,420 results, our search yielded 69 studies meeting our criteria, which included SLE patients and factors such as mycobiome dysbiosis and gut microbiota dysbiosis. Our findings indicate that ITS sequencing revealed distinct

fungal microbiomes in SLE patients, highlighting mycobiome dysbiosis. Specific fungi correlated with clinical parameters, suggesting diagnostic potential. Candida glabrata was cultured and identified, emphasizing its relevance in SLE.

Conclusion: Our systematic review underscores the significance of microbiota, including fungal dysbiosis, in SLE development and progression. Targeted microbiota modulation and personalized therapeutic strategies show promise for enhancing SLE diagnosis and treatment. However, due to study design limitations, further global research is needed to validate our findings.

keywords: Systemic Lupus Erythematosus (SLE); Mycobiome; Gut microbiota; Dysbiosis.

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Evaluation of resistance to fluconazole in Candida species isolated from patients with primary immunodeficiencies (PIDs).

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Medical Mycology

Background and aim: The present study was conducted with the aim of determining the level of resistance to fluconazole among Candida species isolated from patients with primary immune system defects (PIDs).

Methods: In this study, from February 1400 to February 1401, patients with primary immune system defects were examined in Ardabil province. Sampling was done from PIDs patients and people referred to Bu Ali educational-therapeutic center with suspected fungal lesions. Skin, mucous, wound secretions, and possible lesions samples were collected for microbial culture and analysis. After sampling, the samples were cultured on SDA medium and kept in an incubator at 30 C°. Fungal colonies were observed and if yeast colonies were present, they were isolated separately. Then, using PCR technique and ITS1 and ITS4 primers, the identity of yeasts was typed. In order to determine drug resistance, disk diffusion tests were performed with fluconazole. Also, blood and laboratory indices from patient records, including blood count, CRP, inflammatory cytokines, T and B cell counts, and other immune system markers were collected and analyzed.

Results: The frequency of species in 22 skin samples, mucosa, wound secretions, and the sum of both sexes were: Isolation of yeast fungi 15 cases (68.2 percent) of them were albicans, Glabrana included 6 cases (27.3 percent) and Tropicalis 1 case (4.5 percent).and negative cases (9%).

Conclusion: Detailed analysis of Candida species isolated from patients with primary immune deficiency shows that resistance to fluconazole is not dependent on any of the variables of age, sex, Candida species, clinical symptoms, and type of immunodeficiency. Also, the separate analysis of immunodeficiency syndromes does not show a significant relationship with resistance. These

findings show that the complexity of the effective factors in fluconazole resistance prevails in this group of patients.

keywords: Fluconazole, innate immune deficiency, Candida albicans, drug resistance

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Monitoring of Candida infections in cases with a recent history of COVID-19, a retrospective study

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Medical Mycology

Background and aim: Candida, the yeasts live on mucosal layers of human and animal tissues. Because of the opportunistic essence, they cause variable diseases in cases predisposed by cortico-steroids, chemo therapies and long term pulmonary infections. This study aimed to identify the Candida species could active in cases of COVID-19 or with a recent history of that.

Methods: Our subjects included cases with dizziness, cough, chest pain and other pulmonary signs. Candida yeasts isolated from the clinical specimens referred to Medical Mycology center, UMS University, Urmia, Iran were studied. A microscopic investigation was done primarily for the detection of Candida colonization or invasion in tissues (Blastospores and Pseudohypha). Identification of the Candida isolates at the level of species conducted by Dalmao test, CHROM agar Candida and PCR-RFLP.

Results: Totally, 165 cases of positive culture for Candida fungi were studied. Among all, 125 (75.8%) isolated from patients with a history of COVID-19, 7(4.2) Tuberculosis, 4 cases of COPD and three cases of Cystic fibrosis, Cancer and Diabetes mellitus. From all, 43% were women and 57% men. Also, 80% of cases stayed at intensive care unit. The most age range of Candida involvement was 50s including 38(23%) cases. The main clinical specimen referred was bronchoalveolar lavage (64.8%). Other specimens included sputum and tracheal washings. Direct microscopic investigations resulted yeast colonization 68(41.2%) and yeast invasion 54(32.7%). Our findings of molecular identification showed 54(32.7%) C. albicans, 11(6.4%) C. dubliniensis, 10(6.1%) C. tropicalis, C. krusei, C. parapsilosis and C. glabrata one each.

Conclusion: C. albicans complex and C. tripicalis are the main Candida species causing human diseases. It seems candida variation doesn't have a direct

association to COVID-19, although, an increase in the frequencies of non albicans Candida species was clear .

keywords: Candida variation, hospital, COVID-19, Pulmonary disease

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Epidemiologic status of the Candida infections and disorders in cases with chronic obstructive pulmonary disease

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Medical Mycology

Background and aim: Candida is one of the normal flora of human body, and is also the most common conditional fungal pathogen. Invasive Candida infections (ICI) occupies the first positionamong invasive fungal diseases (IFD).Moreover, Candida is commonly colonized in lower respiratory airways (LTR), associated to chronic obstructive pulmonary disease (COPD), smoking, tuberculosis, malnutrition, malignant tumors, diabetes mellitus, HIV infection, and long-term use of antibiotics. As a main target, the present study focus on COPD patients as the predisposed cases of Candida infection or colonization.

Methods: Our subjects included all Candida clinical isolates obtained from cases referred to the Center of Medical Mycology, UMS University, Urmia, Iran, for fungal infection diagnosis. The clinical specimens including Bronchoalveolar lavage (BAL), sputum, tracheal washing and biopsies were examined and microscopic investigation were performed for the detection of Candida invasive elements. As our main aim, morphologic and molecular (PCR-RFLR) were used for the identification of isolate candida yeasts at level of species.

Results: Totally, 510 cases of pulmonary disorders including, COPD, CF, COVID-19 were studied. Among all,22.6% were women and 75% men, 15(24.2%) were in 60 s and 62(12.1%)were candida involved cases. Total of this, 22 (35.1%) isolated from patients with a history of COPD,10(16.1%) CKD, 6 (9.7%) Cystic fibrosis and 3(4.8%) diabetes mellitus.Also, 53(85.5%) showed a pulmonary symptom and sign. Other cases had clinical manifests such as hemoptysis, bronchiectasis, chest pain, pleural pain, lung mass. Among the isolated Candida species, C. albicans 15(24.2%), C. dubliniensis and C. tropicalis 9(14.2%) itch, C. glabrata 5(8.1), C. guiliermondi 2(3.2%) and other non albicans candida species 3(4.8%) and no identified Candida species included 19 cases (30.6).

Conclusion: As our findings of the present study, most of the pulmonary risk factor of the candida involvement was COPD followed by Cystic fibrosis. Also, the most of candida yeasts isolated from studied cases included non albicans Candida species comparing Candida albicans.

keywords: Candida, COPD, Pulmonary disease,Epidemiology

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Investigating invasive fungal rhinosinusitis infections and determining the identity of their agents in patients with covid-19

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Medical Mycology

Background and aim: Since COVID-19 spread worldwide, invasive fungal rhinosinusitis (IFRS) emerged in immunocompromised patients as a new clinical challenge. In this study, clinical specimens of eighty-nine COVID-19 patients who presented clinical and radiological evidence suggestive of IFRS, were examined. This study was conducted with the aim of investigating invasive fungal rhinosinusitis (IFRS) and determining the identity of their agents in covid-19 patients admitted to Shahid Beheshti Hospital in Kashan.

Methods: This descriptive study was conducted from September 2019 to May 2014. clinical specimens of eighty-nine COVID-19 patients who presented clinical and radiological evidence suggestive of IFRS, were examined by direct microscopy, histopathology, and culture, and the isolated colonies were identified through DNA sequence analysis.

Results: Fungal elements were microscopically observed in 84.27% of the patients. The culture was positive for 60.67% of the confirmed cases, and

Mucorales were the most prevalent (48.14%) causative fungal agents. Different species of Aspergillus (29.63%) and Fusarium (3.7%) and a mix of two filamentous fungi (16.67%) were other causative agents. For 21 patients, no growth was seen in culture despite a positive result on microscopic examinations. In PCR-sequencing of 53 isolates, divergent fungal taxons including eight genera and 17 species, were identified as followed: Rhizopus oryzae (n=22), Aspergillus flavus (n=10), Aspergillus fumigatus (n=4), Aspergillus niger (n=3), Rhizopus microsporus (n=2), Mucor circinelloides,Lichtheimia ramosa, Apophysomyces variabilis, Aspergillus tubingensis, Aspergillus alliaceus,Aspergillus nidulans, Aspergillus calidoustus, Fusarium fujikuroi/proliferatum, Fusarium oxysporum, Fusarium solani, Lomentospora prolificans and Candida albicans (each n=1). Males (53.9%) and patients over 40 (95.5%) were more commonly affected than others. The most common predisposing factors were steroid therapy and diabetes mellitus .

Conclusion: A diverse set of species involved in COVID-19-associated IFRS was observed in this study. A high prevalence of fungal rhinosinusitis with mucoral agents (34.67%) is significant as the most important systemic and invasive fungal infections in covid-19 patients. Our data encourage specialist physicians to consider the possibility of involving various species in IFRS in immunocompromised and COVID-19 patients.

keywords: Rhinosinusitis; COVID-19; Mucorales; Aspergillus; Fusarium

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Non-albicans Yeast Hair Infection in a 3-Year-Old Gairl: A Rare Case of White Piedra Caused by Candida orthopsilosis in IRAN

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Medical Mycology

Background and aim: White piedra is a fungal infection that occurs on hair shafts, leading to the development of soft nodules that can be white, gray, or brown in color. Initially believed to be caused by Trichosporon beigelii, Tow case of white piedra of the scalp caused by T. inkin with co-isolation of C. parapsilosis and Candida parapsilosis alone were reported in 2004 and 2019 respectively. We report the first case of white piedra caused by C. orthopsilosis, without associated Trichosporon from a temperate area located to the north of Iran. The study aimed to identify the causative agent and establish the AFST.

Methods: The patient, a three-year-old girl, visited the dermatology clinic with complaints of hair knots in the occipital area, particularly around the ears, which are difficult to remove.These symptoms have persisted for two months . No other body areas were affected, and none of the family members experienced any symptoms. 1-Direct microscopic examination using a 10% potassium hydroxide wet mount revealed sleeve-like formations surrounding the hair shafts, featuring spore-like structures made up of hyphae and blastoconidia. 2-The fungal culture of the hair strands was done .3-We crush some of the infected hair strands with the help of liquid nitrogen in a sterile ceramic mortar. 4- Genomic DNA of the infected hair was extracted by Lysis buffer and glass bead. 5- The causative agent was identified via (PCR using ITS1/ITS4 primers) ,RFLP and confirmed by DNA sequencing. 6- The antifungal susceptibility test of the isolate was performed according to the (CLSI M27-S3).

Results: The molecular weight of the PCR product is 510bp. The amplicon was sequenced and the fungus was identified Candida orthopsilosis. The minimum inhibitory concentration (MIC) values for itraconazole; 0.25µg/ml, voriconazole; 0.015 µg/ml, amphotericin B; 1 µg/ml, fluconazole ; 0.5 µg/ml, myconazole ; 0.5 µg/ml ; clotrimazole 0.015 µg/ml, MEC values for caspofungin 1 µg/ml, and anidulafungin 0.015 µg/ml were determined. The patient received a prescription for clotrimazole and 2% ketoconazole shampoo and advised to follow after 2 weeks.

Conclusion: Future studies need to establish a clear relationship between the yeast responsible for white piedra and geographic location. We propose that C. orthopsilosis may cause white piedra independently of Trichosporon species, particularly in temperate regions. Therefore, this case could increase awareness among dermatologists and laboratory physicians, highlighting that the growth of Candida species should not be dismissed as merely a contaminant.

keywords: White Piedra; C. Orthopsilosis; Hair Infection; Clotrimazole; Antifungal Susceptibility Testing

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The Effectiveness of Rhus coriaria L. Extract Against Candida Species

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Medical Mycology

Background and aim: Candida species are among the most prevalent fungal pathogens in humans, responsible for a spectrum of infections ranging from superficial to systemic. The primary classes of antifungal agents include echinocandins, polyenes, and azoles. However, the treatment of Candida infections is increasingly complicated by the emergence of strains exhibiting intrinsic and acquired antifungal resistance, alongside significant side effects associated with these drugs. In recent years, there has been an intensified search for new therapeutic agents, particularly those derived from natural sources, due to their lower side effects. This study aimed to compare the antifungal efficacy of Rhus coriaria methanol extract with

Methods: Seeds of Rhus coriaria L. were obtained, washed with distilled water, and dried for antifungal testing. The extract was prepared using a cold soaking method; specifically, 10 grams of finely powdered seeds were soaked in 100 ml of 20% ethanol for 24 hours on a rotary shaker (150-180 rpm) and subsequently filtered through Whatman filter paper no. 2. The ethanolic extract was then separated and purified. The antifungal activity of the extract against Candida species was assessed using the minimum inhibitory concentration (MIC) test and the well diffusion method.

Results: The ethanolic extract of Rhus coriaria demonstrated significant inhibitory effects against Candida albicans, Candida krusei, and Candida parapsilosis at low concentrations. The extract maintained its inhibitory effect at concentrations as low as 6.5 mg/L, while some Candida species showed resistance to amphotericin

B, fluconazole, and itraconazole, underscoring the potent antifungal activity of this extract.

Conclusion: The results indicate that Rhus coriaria L. extracts possess considerable antifungal activity against clinically relevant Candida species, offering a promising alternative or adjunct to traditional antifungal therapies. Given the rising concerns over antifungal resistance, natural products like sumac could be valuable in developing new treatment strategies against fungal infections. Future studies should focus on isolating specific bioactive compounds from the extract and elucidating their mechanisms to enhance our understanding of their therapeutic potential.

keywords: Rhus coriaria L., candida spp, ethanolic extract, MIC

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Determining the drug sensitivity pattern of Aspergillus species isolated from patients with Otitis Externa referred to Imam Reza Hospital, Ardabil, Iran

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Medical Mycology

Background and aim: Otitis Externa is a common type of infection in the auditory canals of the external ear caused by a wide range of bacterial, fungal and viral species and is commonly seen in tropical and subtropical regions due to the long treatment period and recurrence. Factors predisposing to this disease include heat, especially in the summer season, and the presence of high humidity and dust in the person's place of residence, low level of hygiene, excessive use of ear cleaners, history of swimming and not drying the ears, history of consumption They are topical antibiotics. external otitis can often be challenging

Methods: In this cross-sectional study, 66 samples of ear secretions were received by a specialist doctor and referred to the medical mycology laboratory. The samples were examined by direct testing with 10% potassium and then cultured in Sabro-chloramphenicol agar culture medium (Condalab, Spain). After growth, Aspergillus species were isolated and identified by microscopic morphology and slide culture methods. Finally, drug sensitivity is performed in laboratory conditions using, Clotrimazole, Fluconazole, Itraconazole and Voriconazole drugs and by broth microdilution method, in accordance with clinical and laboratory standards using CLCI M27-A3 method. Then, the minimum inhibitory concentration (MIC) was determined in 96 µt flat-bottomed dishes by measuring the OD of the fungal cultures at 620 nm.

Results: Of the 66 samples referred to the laboratory, 44 patients were male (66.66%) and 22 were female (33.33%). 59 patients were isolated with positive cultures for Aspergillus spp. The most isolated Aspergillus species were related to

Aspergillus section Nigri with a frequency of 49 (83%) species, followed by Aspergillus section Flavi with a frequency of 6 (10.16%), Aspergillus section Fumigati with 4 species (6.77%). Clotrimazole (MIC 8µg/ml) and fluconazole (MIC 4µg/ml) had the least effect on species in laboratory conditions. One of each isolates of A. niger (MIC 8 µg/ml) and A. fumigatus (MIC 2 µg/ml) against Itraconazole and one isolates of A. niger with (MIC 4 µg/ml) They were resistant to Voriconazole.

Conclusion: in this study In line with other studies, men were more affected than women, which is related to lack of ear hygiene and improper use of ear cleaners. Aspergillus section Nigri isolation dominance was seen, in agreement with other results. The MICs distribution of Aspergillus species isolates against triazole antifungals are close to ECVs defined by the CLSI and likely outrun over time. Due to the fact that some of the species isolated in this study also showed resistance to some drugs We recommend that physicians request drug susceptibility testing

keywords: Aspergillus -Otitis Externa -fungi- MIC

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Investigating diagnostic marker in Inflammatory Bowel Disease in patients with fungal infection in Ghaem Hospital in Mashhad, Iran1403

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Medical Mycology

Background and aim: Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), is linked to fungal presence in the gastrointestinal tract. Serological markers play a crucial role in IBD diagnosis. Symptoms of IBD caused by Candida infection include colicky pain, constipation, diarrhea, flatulence, chronic diarrhea, hemorrhoids, blood in stool, low vitamin D3, high ESR (Erythrocyte Sedimentation Rate) and CRP(C -reactive protein), and high Calprotectin. Research aims to identify biomarkers for faster and more effective diagnosis of IBD with fungal infection, improving treatment initiation and disease management.

Methods: A stool sample was taken from (no=30) IBD patients for direct smear and Calprotectin test. Patient history and test results were reviewed, and a diagnostic biomarker for fungal infection in IBD patients was analyzed; Serum CRP, ESR, ALB (Albumin), CBC parameters.

Results: A total Of 30 IBD patient, most people had Ulcerative colitis. There is an increased total fungal load particularly of Candida. The most frequently isolated species was C. albicans. Also (no=24) had high CRP, and The Calprotectin test has increased significantly in affected people. (No=21) Patient had calprotectin test above 50 µg/g, (no=16) had diarrhea, (no=15) patient had ESR Test above 10, (no=14) colicky pain, (no= 4) patients had hypoalbuminemia, (no=4) had internal hemorrhoid, (no=3) patient in Endoscopic has Erythema and (no=2) had low

vitamin D3 , (no=2)had low MCH (Mean corpuscular hemoglobin) and MCV(Mean corpuscular volume) .

Conclusion: The CRP is most common in CD patients and levels of CRP,calprotectin test , ESR, are higher in active IBD patients. The peak age of disease onset is between 18-50 years. CRP, ESR, and faecal markers may predict relapse in UC, though some patients with active disease have low CRP, often with exclusive ileal disease. These parameters are helpful biomarker for differentiating disease activity in UC and CD and predicts a worse prognosis in cancer patients.

keywords: Key Words: inflammatory bowel disease; ulcerative colitis (UC); Crohn disease(CD);

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Nosocomial bloodstream Infection by uncommon yeast species in pediatric patients with malignancy

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Medical Mycology

Background and aim: Nosocomial bloodstream infections (BSIs) caused by yeast agents are among the most serious cases of mortality in pediatric patients with malignancy. The emergence of unusual yeast agents such as Candida orthopsilosis (C. orthopsilosis) and C. dubliniensis is directly related to the presence of predisposing factors. Some of the important predisposing factors including immunodeficiency, long-term hospitalization, central venous catheter, and the use of various antibiotics. This study was conducted in order to investigate the prevalence of BSIs caused by uncommon yeast agents in pediatric patients with malignancy in Imam Khomeini Hospital, Ahvaz.

Methods: This cross-sectional study was conducted on 205 samples sent to Imam Khomeini Hospital, Ahvaz, from pediatric patients with malignancy suspected of BSIs during 18 months. Yeast isolates from blood cultures were first identified by phenotypic methods and then by 21-plex PCR. The demographic data of the studied population were extracted and analyzed.

Results: Of 205 patients, 37 (18.1%) were positive for BSI. 8 (21.6%) BSI were identified with uncommon yeast agents including 2 cases of sarcoma and lymphoma (5.4%) with C. orthopsilosis, 1 case of sarcoma with C. dubliniesis, 1 case of lymphoma with Wickerhamomyces myanmarensis and 4 case of ALL, sarcoma and retinoblastoma of with Rhodotorula. Age range of all patients was 4-8 years (5 males; 63%, 3 female; 37%) and were hospitalized for more than seven days. Although the presence of fever, central venous catheters, high ESR and broad-spectrum antibiotic treatment were observed in all cases, the highest

ESR and the longest duration of fever belonged to the patient with C. dubliniesis. The response to treatment in the patient with W. myanmarensis was very appropriate and faster than other cases. Overall, no mortality was reported among BSI cases.

Conclusion: Despite the fact that the contribution of uncommon yeast species is less than other yeasts in BSI, it is extremely important to pay attention to them. Predisposed patients are searched, diagnosed and managed in terms of common yeasts, especially Candida species, while neglecting, underestimating and not imagining uncommon yeasts can cause disaster in these patients. However, correct and timely diagnosis of uncommon yeasts can lead to a basic strategy for managing the treatment of these patients.

keywords: BSI; malignancy; uncommon yeasts

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Northwest Iranian dermatophyte isolates: anthropophilic and geophilic

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Medical Mycology

Background and aim: The fungi known as dermatophytes are a group of keratinophilic agents responsible for superficial infections in humans and animals. Recognition of the species distribution and epidemiology of dermatophytosis may be helpful in the prevention and improve prophylactic measures. The present molecular epidemiology study sought to investigate the incidence of etiological agents causing dermatophytosis.

Methods: The morphologic methods and polymerase chain reaction-restriction fragment length polymorphism using MvaI restriction enzyme were performed to identify dermatophytes isolated from the soil, compost, and clinical samples.

Results: Based on findings, 39 (8.1%) clinical specimens and 10 (8.2%) environmental samples were morphologically and molecularly identified as dermatophytes. In the clinical samples, Trichophyton mentagrophytes/T. interdigitale species complex was isolated with the highest incidence rate. The dermatophytes comprise seven species of the four genera, viz., T. interdigitale (currently T. mentagrophytes, n=15, 40.5%), Microsporum canis (n=10, 27%), T. verrucosum (n=5, 13.5%), T. rubrum (n=4, 10.8%), Myriodontium keratinophilum (n=2, 5.4%), and T. benhamiae (n=1, 2.7%). The geophilic identified species included Nannizzia gypsea (n=5), Arthroderma multifidum (n=2), Afanoascus flavisence (n=2), and Nannizzia fulva (n=1).

Conclusion: The current study provides a diverse overview of dermatophytes in the northwest of Iran to improve their surveillance. The present investigation of clinical specimens revealed that Myriodontium keratinophilum, as a species rarely detected with keratolytic properties, emerged as a causative agent of dermatophytosis.

keywords: Anthropophilic, Dermatophytosis, Epidemiology, Geophilic, Iran, Microsporum, Trichophyton

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The Importance of pH-Mimicking Conditions for Accurate Enzyme Activity in Vulvovaginal Candida albicans Infections

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Medical Mycology

Background and aim: The pathogenicity of Candida albicans, a prevalent opportunistic pathogen, is largely attributed to its ability to produce various virulence factors, including extracellular hydrolytic enzymes. These enzymes, such as proteases and lipases, exhibit distinct activity profiles that are highly influenced by the surrounding pH environment. Research indicates that optimal enzymatic activity occurs within specific pH ranges, which can vary significantly depending on the strain and the anatomical origin of the isolate. This study investigates the importance of matching in vitro pH conditions to those encountered at infection sites.

Methods: A total of 20 Candida albicans species isolated from vulvovaginitis were investigated for phospholipase, proteinase, and esterase activities. The activities were measured at three pH levels of 4, 5, and 7 that representing for the healthy vaginal range, potential infection condition, and a standard in vitro reference point, respectively. Egg yolk agar, bovine serum albumin medium, and Tween agar plates were used to assess enzyme activity.

Results: Phospholipase and proteinase activity were significantly higher at acidic pH (4 and 5) compared to neutral pH (7). In contrast, esterase activity showed a slight increase at neutral pH. Analysis revealed significant differences in enzyme activity between pH 5 and 7, highlighting the importance of using pH-relevant conditions for studying Candida virulence.

Conclusion: This study reveals that acidic vaginal pH, characteristic of Candida albicans infections, significantly boosts the activity of its damaging enzymes. This highlights the limitations of using a standard pH protocol for enzyme activity analysis. By employing pH-mimicking conditions, future research can unlock a

deeper understanding the actual C. albicans virulence that might occur in site of infection. Data analysis should consider beyond this factor.

keywords: Candida albicans, vulvovaginitis, Phospholipase activity, Proteinase activity, Esterase activity

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A Comprehensive Analysis of Multi-Etiological Factors in Multidrug-Resistant Candida Onychomycosis

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Medical Mycology

Background and aim: This is a rare case of Candida onychomycosis caused by three Candida species that were resistant to several antifungal drugs. A 56-year-old Iranian woman with no previous medical or injury history experienced discoloration and lifting of her left thumbnail for six months. Laboratory tests identified yeast and pseudohyphae consistent with Candida onychomycosis. Conventional and molecular techniques confirmed that onychomycosis was caused by three different Candida species: Candida albicans, Candida tropicalis, and Candida glabrata. All three strains were resistant to various antifungal drugs. Therapeutic failure, in addition to multi-drug resistance, may be due to the presence of multiple etiological agents.

Methods: -

Results: -

Conclusion: Given the potential for antifungal resistance, accurate identification is crucial for guiding effective therapy. Awareness and understanding of these yeasts' roles in onychomycosis can aid in timely, appropriate management, improving outcomes for affected individuals.

keywords: Onychomycosis, Candida, Multidrug-Resistant

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Misdiagnosis of Artifacts as Fungal Components in the Laboratory of Medical Mycology

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Medical Mycology

Background and aim: Artifacts have been shown to be the cause of errors and misdiagnosis in mycology laboratories, often mistaken for fungal components. Distinguishing between artifacts and actual fungal elements is crucial. This systematic study was conducted to evaluate artifacts and accurately assess fungal elements in medical mycology laboratories, aiming to assist physicians in providing appropriate therapy for fungal infections.

Methods: The literature search included four electronic databases (Web of Science, PubMed/Medline, Scopus, and ScienceDirect), in addition to google scholar and a hand search of reference list of included study to February 2023 in the English language. Two independent reviewers scanned titles and abstracts, and afterward included full texts according to eligibility criteria were extracted

Results: Twenty papers that fulfilled the inclusion criteria were included in this systematic review. The main artifacts identified in these studies were as follows: Fungal mosaic, red and white blood cells, oil droplets, sewing threads and linen threads, eggs of various worms, and bacteri

Conclusion: Adequate and focused training in this field, particularly for novices, enables accurate diagnosis. Conducting training workshops in this area facilitates

high-precision diagnosis, and with a correct diagnosis, doctors can prescribe the appropriate medication, resulting in minimal complications for the patient.

keywords: Artifact, laboratory, Fungus, Fungal elements, Medical Mycology

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Determination of serum GM index and drug sensitivity pattern of Aspergillus isolates from patients with invasive aspergillosis

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Medical Mycology

Background and aim: Invasive aspergillosis (IA) is one of the life-threatening diseases in patients hospitalized in different departments of the hospital. About 200,000 cases of this disease are reported every year, which has a high mortality rate. Immunocompromised patients and those with underlying lung diseases are susceptible to IA. Timely and correct diagnosis and proper treatment of this disease will improve patients. Due to the increase in prevalence (AI), there is an increase in drug resistance to azoles in different species of Aspergillus, especially A. fumigatus. In this study, by identifying the positive cases of this disease in different departments of Imam Hospital,

Methods: The sputum and serum samples collected from suspected patients were collected and analyzed in specialized medical mycology laboratory. At first, sputum samples were prepared for microscopic examination with 20% KOH, and then a portion of the sample was cultured in Sabouraud chloramphenicol dextrose agar culture medium (Condalab, Spain). After the growth of the species, the isolated species were identified using slide culture method. The isolated species of Aspergillus were identified to investigate the drug sensitivity pattern with Amphotericin B, Itraconazole.and Voriconazole were prepared by broth

microdilution method. Galactomannan (GM) analysis on serum was performed by sandwich enzyme-linked immunosorbent assay (bioactive diagnostica, Germany) as per the manufacturer's instruction.

Results: Out of the 86 samples sent from the hospital from March 20 to October 17, 2024, the number of positive microscopic and culture cases was 21, 18 of 21 patients (85.71%) were male and 3 (12.29%) were female. All positive patients were hospitalized in the ICU. And one death due to this disease was also reported. All patients had one or two underlying diseases, most of which were related to chronic pulmonary diseases. 16 cases of Aspergillus fumigatus and 1 case each of Aspergillus niger and Aspergillus terreus 3 cases of Aspergillus favus were isolated. The measurement of serum level of GM showed that the index range in positive cases was between 0.88 and 4.25 and its average was 2.36.(Above 0.5 was considered positive.). The obtained MIC related to A. fumigatous was in the range of 0.12-1 for VOR, 2-0.03 for AMB, and 2-0.016 for ITR. For A. flavous, respectively,

Conclusion: IA is a serious disease in hospitalized patients with immunosuppression problems. Examining the level of serum GM in patients can have a significant impact on the timely diagnosis of the disease. According to the mortality trend of patients, the use of correct drug treatment leads to the timely treatment of the disease, which according to the MIC obtained for VOR and AMB drugs in this study showed that these drugs have better activity. The present study has shown that determining the value GM in serum samples can help in the

keywords: Aspergillosis; Galactomannan; Aspergillus fumigatus; fungi; MIC.

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Molecular investigation of fungal contamination of domestic and hospitals washing machines

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Medical Mycology

Background and aim: The study aimed to survey the fungi species diversity in the specific environment of domestic washing machines, taking into account the potential risk for users. Detergent drawer and door seal represent important sites for microbial life in domestic washing machines. Interestingly, quantitative data on the fungal contamination of this device is scarce.

Methods: Here, 50 domestic washing machines and 5 hospitals washing machines were swab-sampled for subsequent fungal cultivation at three different sampling sites: detergent drawer and the inner and outer part of the rubber door seal. The micro fungi were identified by the standard procedures applied in mycological diagnostics including culture, tease mount, and slide culture. To confirm species identification, molecular analysis was performed based on the sequences of the ITS1/ITS4 and β-tubulin gene regions.

Results: The presence of microfungi was detected in 82% of the domestic washing machines. But fungal agents were not found in hospital washing machines. The inner rubber door seals part of the washing machine door was reported were the most frequently colonized fungal elements. 122 fungi strains were isolated in this study, which included 15 genera of filamentous, yeast-like and yeast fungi. Filamentous fungi included 7 genera of hyaline filamentous fungi and 5 genera of

black filamentous fungi. The hyaline fungi isolated in this study include 33 cases (27%) of the Aspergillus genus, 14 cases (11.5%) of the Penicillium genus, 5 cases (4.1%) of the Fusarium genus, 3 cases (2.5%) of the Scopulariopsis genus, 2 cases (1.6%) of the Acremonium genus, 1 case (0.8%) of the Pseudallescheria, and Mucor.

Conclusion: In this study, it was shown that household washing machines are suitable places for the colonization of different fungal agents due to humidity and low light, and they have the ability to transfer these agents to clothes during the washing process. As a result, it was demonstrated that the domestic washing machine's condition is sufficient as an ecological niche for microfungi and their transmission. In this study, the genera of Aspergillus, Alternaria, Cladosporium and yeast agents were isolated, and these fungi are very important in public health and people's health.

keywords: Washing machine, environment, Hygiene, Fungal diseases

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Increasing resistance to fluconazole and voriconazole in non_albicans Candida species in burn patients: need for new therapeutic strategies.

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Medical Mycology

Background and aim: Drug resistance in Candida species has emerged as a significant challenge in treating burn patients, posing barriers to effective care and increasing morbidity and mortality risks. Candida species, common opportunistic pathogens, frequently cause bloodstream infections in burn patients. The extensive use of antifungal drugs has contributed to resistance in Candida species, particularly to azole drugs like fluconazole and voriconazole. This study aimed to investigate drug resistance in isolates from burn patients and to evaluate the effectiveness of two drugs, miltefosine and piperlongumine, in comparison to standard antifungal treatments across burn centers in the country.

Methods: A total of 353 burn patients hospitalized in three major ICUs in Iranian burn centers between 2021 and 2023 were examined. Fungal species were identified at the species level, and antifungal susceptibility tests were performed according to CLSI guidelines.

Results: Overall, the resistance rates of strains isolated from cases of candidemia to fluconazole and voriconazole were 28% and 18.2%, respectively. The drug resistance rates of Candida tropicalis and C. albicans isolated from blood to voriconazole were 56% and 42%, respectively. For burn wound colonization isolates, resistance rates among 658 samples were 28% for voriconazole and 33% for fluconazole. Notably, 83% of Candida tropicalis isolates from colonization sites were resistant to voriconazole. Additionally, more than 40% of isolates of C. parapsilosis, C. tropicalis, and C. albicans showed resistance to fluconazole. The

noteworthy point in the present study is that the GMMIC of miltefosine (GMMIC=0.245) and piplangomin (GMMIC=0.535) were better than fluconazole (GMMIC=3.420).

Conclusion: Our study revealed a concerning trend of drug resistance in Candida species isolated from both candidemia and burn wound colonization in Iranian burn patients. Continued surveillance of antifungal resistance patterns in Candida species, particularly in burn patients, is crucial for informing empirical treatment guidelines and optimizing patient care. Our findings underscore the importance of identifying local epidemiological trends and implementing effective infection control measures to minimize the spread of drug-resistant Candida strains in healthcare settings.

keywords: Burn patients, Antifungal Resistant, Non_albicans candida.

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Efficacy of Clotrimazole and Amphotericin B Combination Therapy against Aspergillus Species in Otomycosis

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Medical Mycology

Background and aim: Background and Aim: Aspergillus species are among the most prevalent pathogens that cause otomycosis, particularly Aspergillus niger. Traditional antifungal medications are frequently linked to a number of adverse effects, including toxicity, interactions, and drug resistance. Combination therapy has been a popular strategy in recent years to increase the efficacy of antimicrobial therapy for illnesses that are challenging to treat, such as invasive fungal disease. Investigating the antifungal efficacy of clotrimazole and amphotericin B against Aspergillus species isolated from otomycosis patients was the aim of this investigation.

Methods: Methods: In this experimental laboratory study, 10 Aspergillus niger isolates obtained from patients with otomycosis were included in the investigation. Combined drug sensitivity test was performed using the checkerboard broth microdilution method and according to CLSI-M38-A2 instructions on all isolates of Aspergillus niger in combination with clotrimazole and amphotericin B drugs and FICI was determined. Synergistic, antagonistic and indifference effects of drugs were obtained.

Results: Results: Clotrimazole interactions with amphotericin exhibited that 60% of isolates were indifferent and 40% of Aspergillus niger had synergism effects and none of the interactions and the activities of medicinal compounds did not show antagonism effects on any Aspergillus niger species. Synergistic effects were demonstrated on 4 isolates of Aspergillus niger (40%), which was 4 cases for the combination of Clotrimazole and Amphotericin B.

Conclusion: Conclusion: Clotrimazole interaction with amphotericin B showed synergistic activity against Aspergillus niger species. Therefore, the method of combined drug treatment, with more investigation, can be an alternate way and promising approach for the treatment of otomycosis.

keywords: Keywords: (Otomycosis; Clotrimazole; Amphotericin B; Aspergillus niger.)

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The effect of methyl vanillyl nonenamide on the growth and pathogenic factors in A. fumigatus

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Medical Mycology

Background and aim: A. fumigatus can cause various diseases. Despite the development of new antifungal drugs and treatments, the increase of pathogenic fungi that are resistant to drugs requires a new treatment approach. Biofilm is a special feature of fungi that protects fungal cells. Ergostrol is an essential lipid component that controls fungal permeability and phospholipase is associated with the membrane, which can make treatment challenging. Here we studied the effects of methyl vanillyl nonenamide on the growth of A. fumigatus, biosynthesis of ergosterol, biofilm formation and on the expression of phospholipase genes.

Methods: A. fumigatus cells were treated with methyl vanillyl nonenamide at a concentration of 100 µg/ml – 0/048 µg/ml for 72 h at 37˚c. Fungal cells were estimated as an indication of fungal growth. Biofilm formation and ergosterol biosynthesis were evaluated by the effect of methyl vanillyl nonenamid. Investigating the expression of phospholipase B & D genes was done by real time PCR.

Results: Methyl vanillyl nonenamide inhibited the growth of A. fumigatus. The ergosterol content was decreased at the highest concentration. Biofilm formation was also inhibited at the highest concentration. The expression of phospholipase B and D genes was suppressed in different concentration.

Conclusion: This study was to find an effective substance from the source of microorganisms that can inhibit the growth and inhibit the pathogenic factors of A. fumigatus. This evidence shows that methyl vanillyl nonenamide can have an inhibitory effect on the growth of A. fumigatus as an antifungal agent.

keywords: A. fumigatus, methyl vanillyl nonenamide, Ergostrol, Biofilm, Phospholipase

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Antifungal effects of green synthesized zinc nanoparticles alone and combined with nystatin against Candida albicans, a major cause of oral candidiasis

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Medical Mycology

Background and aim: Candidiasis is an important and common fungal disease of the oral mucosa caused by different species of Candida. This work aimed to determine the antifungal effects of zinc nanoparticles (ZnNPs) green synthesized by Lavandula angustifolia extract, alone and along with nystatin against Candida albicans.

Methods: ZnNPs were green synthesized with L. angustifolia extract by microwaves method. Antifungal effects of ZnNPs were studied by measuring the minimum inhibitory concentrations (MICs) and minimum fungicidal concentrations (MFCs) using the broth microdilution method based on the modified M27-A3 protocol on yeasts, recommended by the Clinical and Laboratory Standards Institute (CLSI). Effects of green synthesized ZnNPs against human normal fibroblast-like Gingiva (HGF1-PI1) and human epithelial like oral cancer (KB) cell lines were studied by MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) method.

Results: The ZnNPs showed a spherical shape with some grains of different lengths. The best levels of MIC and MFC were connected to the combination of ZnNPs + nystatin with values of 0.204 and 0.250 µg/mL, respectively. The combination of ZnNPs with nystatin compared to the nystatin group had a significantly better antifungal effect on C. albicans (p0.05). The 50% cytotoxic concentrations of ZnNPs against normal (HGF1-PI1) and cancer (KB) cells were 172.3 and 83.2 µg/mL, respectively.

Conclusion: We found that ZnNPs plus nystatin had a potent antifungal effect against C. albicans. These findings indicated the cytotoxic effects of green synthesized ZnNPs on cancerous cells, whereas they were nontoxic for normal cells. Additional studies are necessary to explain the accurate mechanism and toxicity.

keywords: Thrush; Candidiasis; Fungicidal; Cytotoxicity; Nanomaterial

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Understanding Fungal Persister Cells: Mechanisms of Resistance and Implications for Treating Invasive Fungal Infections

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Medical Mycology

Background and aim: Invasive fungal infections remain a significant cause of morbidity and mortality, particularly among hospitalized individuals and those who are immunocompromised or critically ill. Within fungal biofilms, especially those formed by Candida species, persister cells represent a small but resilient subgroup that plays a crucial role in the persistence of these infections. These persister cells exist in a dormant state and exhibit resistance to high concentrations of commonly used antifungal agents, including amphotericin B. This review synthesizes current knowledge about fungal persister cells' mechanisms, characteristics, and their impact on treatment outcomes.

Methods: We conducted a systematic search in the PubMed, Google Scholar, and Web of Science databases up to October 2024 to identify studies on fungal persister cells and their resistance mechanisms that contribute to persistent infections. According to the searches, the mechanisms of persistence, biofilm formation, antifungal resistance, and clinical implications of these cells were investigated. In this study, four independent reviewers evaluated study eligibility and extracted data, with disagreements resolved through consultation with the corresponding author. Studies were assessed for methodological quality and bias risk. The search strategy employed Boolean operators combining keywords such as "fungal persister cells," "antifungal resistance," "biofilm," "persister cell mechanisms," "clinical outcomes," and "candidiasis".

Results: The analysis of 50 studies on fungal persister cells shows that these cells exist in a dormant state, allowing them to withstand high concentrations of antifungals. This dormancy, similar to glucose-deprived cells, highlights their metabolic adaptability. In the absence of glucose, persister cells upregulate enzymes like isocitrate lyase (Icl1) and malate synthase (Mls1) to utilize alternative carbon sources, producing gluconeogenesis precursors and storing energy as glycogen and trehalose. They also activate oxidative stress response pathways to detoxify reactive oxygen species (ROS), with increased expression of superoxide dismutases (SODs) and protective proteins such as Hsp21. Additionally, modified cell wall compositions enhance resistance to phagocytosis and antifungal effects, while increased extracellular matrix (ECM) production provides protection to biofilms and helps evade the host immune response. Persister cells can avoid apoptosis induced by antifungal treatment by regulating pathways involving heat shock proteins and metacaspases.

Conclusion: Our study highlights that fungal persister cells complicate the treatment of invasive fungal infections, especially in immunocompromised patients. These cells enter a dormant state and resist antifungal agents, challenging conventional treatments. Understanding their persistence mechanisms, such as metabolic adaptations and protective responses, is crucial for developing effective therapies. Future research should target these cells to improve treatment outcomes and reduce morbidity and mortality from invasive fungal infections. Addressing to these cells allows clinicians to improve strategies for managing candidiasis and similar infections more effectively

keywords: Fungal Persister Cells; Fungal biofilms; Fungal persistence mechanisms; Persister cells

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Procalcitonin as a Diagnostic Marker for Candida Fungal Infections: A Systematic Review

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Medical Mycology

Background and aim: Candidemia is a life-threatening infection, particularly in the ICU department, and it is diagnosed with the help of blood culture. The advent of the PCT kit has led to improvements in the identification process. This systematic research was conducted to evaluate PCT as a diagnostic marker for Candida fungal infections in sepsis diagnosis worldwide.

Methods: The literature search included four electronic databases (Web of Science, PubMed/Medline, Scopus, and ScienceDirect), in addition to hand search of reference list of included study to February 2023 in the English language. Two independent reviewers scanned titles and abstracts, and afterward included full texts according to eligibility criteria were extracted.

Results: Twenty-nine papers that fulfilled the inclusion criteria were included in this systematic review. PCT is accurate in diagnosing candidemia and bacteremia. PCT levels in patients with bacteremia were significantly higher than those with candidemia. Additionally, a PCT level of 0.5 to 2 ng/ml is a strong predictor of candidemia in the population. This kit with 98.8% sensitivity, 99% specificity and 98.9% accuracy, it accurately identifies sepsis and its cause.

Conclusion: Procalcitonin, as a diagnostic marker for Candida fungal infections, facilitates the diagnosis of sepsis and its cause. Therefore, the development and implementation of this method in hospitals improve the process of sepsis diagnosis and treatment.

keywords: Candida albicans, Candidemia, Sepsis, Procalcitonin

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Molecular identification and antifungal susceptibility testing of yeast species isolated from chronic kidney failure patients and kidney transplant recipients in Ahvaz

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Medical Mycology

Background and aim: Background and Aim: Urinary tract infection and oral candidiasis are the most of common complications in patients with kidney diseases. The aim of this study was to determine the prevalence of Candida species, risk factors, and antifungal succeptibility of oral candidiasis and candiduria agents in a sample of kidney transplant and kidney failure patients in two university hospitals in Ahvaz.

Methods: Methods: 140 swab and 51 urine samples from 94 renal transplant recipients and 97 renal dialysis patients were included. Phenotypic characteristics and molecular methods were used to identify the isolates. Antifungal susceptibility testing was performed by broth microdilution method according to CLSI M27-S4 against fluconazole (FLC), posaconazole (POS), caspofungin (CAS) and amphotricin B (AMB).

Results: Results: Totally in 88 patients (46%) a fungal infection was diagnosed. The abundance of identified species in decreasing order were as C. albicans (n = 53), C. glabrata (n = 26), C. tropicalis (n = 10), C. dubliniensis (n = 8) and C. krusei (n = 7). Three C. albicans were resistant to FLC (R), three non-albicans Candida strains were dose-sensitive (DDS) to FLC, one isolate of C. albicans and one isolate

of C. glabrata showed resistance to CAS and other isolates were sensitive to the used antifungals.

Conclusion: Conclusion: Candida albicans remained as the main etiologic agent of oral and urinary tract infections in renal transplant recipients and renal dialysis patients in Iran and still there is a great tendency to develop resistance against azoles among clinical isolates from the genus Candida.

keywords: Keywords: Candida species; kidney transplant; kidney failure; Antifungal susceptibility test

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Investigating the presence of fungal diversity in the oral cavity of healthy medical student

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Medical Mycology

Background and aim: The human oral microbiota ranks as the second most significant microbiota, after the colon microbiota, and it demonstrates greater diversity than that found on the skin and other mucosal surfaces. This microbiota is shaped by a variety of local and systemic factors, including genetic predispositions, individual characteristics, dietary habits, overall health, and the introduction of new microorganisms through saliva exchanged with family members and other contacts from infancy onward. While much research has focused on pathogenic oral fungi, gaining a comprehensive understanding of the full array of commensal fungal species is vital for maintaining oral health and preventing dysbiosis, which

Methods: A total of 120 oral samples were collected from the tongues and tonsils of healthy medical students using sterile swabs and subsequently cultured on Sabouraud dextrose agar supplemented with chloramphenicol (Sc). The identification of the fungi which developed by conducted a combination of traditional morphological methods (including the preparation of wet sections, methylene blue staining, and slide culture) alongside the molecular amplification technique of polymerase chain reaction (PCR), which targets species-specific markers. The morphological characteristics of the fungal isolates were compared with established taxonomic keys, and the PCR results were validated against these identifications to ensure accuracy.

Results: Analysis of a diverse collection of eight genera of fungi in the oral cavity of 55% of individuals revealed that, with Candida spp. (23%), Cladosporium spp.

(7%), Trichosporon spp. (5%), Aspergillus spp. (4%), Penicillium spp. (3%), and Rhodotorula spp., Exophiala spp., and Nigrospora spp. (1%) identified as the predominant isolates. The diversity of fungal species was higher in men than in women, suggesting that factors such as lifestyle, smoking history, and the presence of decayed teeth may significantly contribute to this disparity. Notably, Candida species were the most abundant, indicating their central role in the oral fungal ecosystem.

Conclusion: Understanding the composition of this mycobiota is essential for distinguishing between normal flora and potential pathogens. The results have implicated the importance of maintaining oral fungal balance and microbiota perturbation may lead to fungal overgrowth and subsequent oral infections.

keywords: Oral fungal flora; Mycobiome; Oral health; mycoses

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Serodiagnosis of invasive candidiasis based on Candida albicans multi-epitope recombinant antigen

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Medical Mycology

Background and aim: Invasive candidiasis is a life-threatening fungal infection caused primarily by Candida albicans in immunocompromised individuals. The global increase in high-risk groups, including preterm infants, patients undergoing surgery or chemotherapy, organ transplant recipients, diabetics, patients with renal failure or on hemodialysis, and those receiving broad-spectrum antibiotics, has heightened the risk of acute and fatal infections caused by C. albicans. Although blood culture remains the gold standard for diagnosing invasive candidiasis, its low sensitivity (less than 50%) often delays diagnosis until advanced stages of infection, significantly compromising treatment outcomes. Given the World Health Organization's 2023 emphasis on urgency, developing a reliable antigen

Methods: The multi-epitope antigen was designed to include eight antigenic proteins of C. albicans (UniProt IDs: P46593, Q59L12, Q07730, Q5AL03, Q5AMT2, G1UBC2, P82610, P0CY27). It was cloned into the pET-23a (+) vector and expressed in E. coli. Protein expression was induced, and purification was performed using nickel-affinity chromatography. The purity of the antigen was confirmed via SDS-PAGE and Western Blotting techniques. To evaluate its diagnostic performance, ELISA was conducted using 67 serum samples from patients with invasive candidiasis, 42 from healthy individuals, and 30 from patients with other fungal or bacterial infections to assess cross-reactivity. Serum samples were collected at Namazi Hospital, Shiraz, and analyzed for IgG antibodies.

Results: Laboratory findings demonstrated that the designed multi-epitope antigen exhibited optimal and stable characteristics, with successful expression in the pET-23a (+) system in E. coli. SDS-PAGE and Western Blotting analysis confirmed the high purity of the recombinant protein, with a molecular weight of 35 kDa (Figure 1). ELISA results indicated a sensitivity of 90.9% [95% CI: 72.55 to 96.7], specificity of 88% [95% CI: 73.47 to 97.89], and positive and negative predictive values of 90.91% [95% CI: 77.24 to 96.72] and 90% [95% CI: 72.74 to 94.47], respectively.

Conclusion: The findings of this study suggest that the recombinant multi-epitope antigen possesses high diagnostic efficiency for the serological detection of invasive candidiasis. This antigen holds potential for clinical application in the diagnosis of invasive candidiasis.

keywords: Invasive candidiasis, Candida albicans, Serodiagnosis, ELISA, Multi-epitope antigen

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Case Report of Mucormycosis: Early Diagnosis and Clinical Management

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Medical Mycology

Background and aim: This article presents a case of a 46-year-old woman who presented as an outpatient at Khatam Specialized Eye Hospital with symptoms of a severe eye infection.

Methods: Upon clinical evaluation, significant findings prompted further laboratory testing. Mycological examination confirmed the presence of fungal filaments, supporting a diagnosis of mucormycosis. There was also a notable increase in white blood cell count, reported to be around 35 to 40 cells, with 3-5% of mononuclear cells, indicating a strong inflammatory response to the fungal infection.

Results: The results of direct smear from the patient's ocular secretions were reported as negative in Gram staining. Additionally, culture and antibiogram of the ocular secretions identified Staphylococcus aureus, which was sensitive to ciprofloxacin but resistant to clindamycin, erythromycin, and penicillin.

Conclusion: These microbiological and bacteriological findings, along with the patient's clinical presentation, underscore the need for timely intervention in the management of eye infections complicated by fungal infections

keywords: Mucormycosis, Case Report, Early Diagnosis,Clinical Management,Ophthalmic Infection, Fungal Infection, Mycology,

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Prevalence of the environment Fungal contamination in Zahedan

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Medical Mycology

Background and aim: Background and Aim: The investigation of fungal contamination in people's living environment has a critical role in public health, especially in immunodeficiency's syndrome, organ transplantation, high-dose of chemotherapies and preterm neonates. The aim of this study is to determine the environment fungal contamination in Zahedan.

Methods: In this study, 12 samples from eleven different areas of Zahedan were collected in sterile, screw-capped test tubes during October and November 2024. The samples were separately cultured on SC and S culture media for 7 days at 25°C. In the next stage, we used phenotypic methods for identification of fungi such as macroscopic characteristics including colony diameter, exudates, and the front and the back coloration and microscopic characteristics.

Results: In this study, 5 types of fungi were isolated from the 12 samples collected, which were Aspergillus niger species complex (25.3%), Alternaria spp. (21.6%), Aspergillus fumigatus species complex (16.3%), Fusarium spp. (11.6%),

Rhizopus spp. (10.4%) Penicillium spp. (8.2%) and Aspergillus flavus species complex (6.6%).

Conclusion: Our finding showed that saprophytic fungi presence in people's living environment. It is necessary to use strategies to prevent opportunistic fungal infections in predisposing patients such as transplant recipients, cancer and HIV+ patients by health care facilities.

keywords: Aspergillus; Fungi; Zahedan

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Diabetes mellitus, the most common predisposing factor for the fungal infections by some Candida species

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Medical Mycology

Background and aim: Human candidiasis is an opportunistic fungal infection of cutaneous, mucosal and deep layers. Some situations like diabetes mellitus and other autoimmune diseases cause candida infections and colonization in the predisposed patients. There is different susceptibilities among Candida species against antifungal drugs. Hence, the study aimed to identify the Candida yeasts isolated from diabetic cases with or without other risk factors.

Methods: Our subjects included candida isolates of cases with a history of diabetes mellitus and other predisposing factors, such as chronic obstructive pulmonary disease, hypertension, chronic kidney disease, end stage renal disease, and cystic fibrosis. The clinical specimens were collected from studied patients and transported to the Medical Mycology Center, UMS University, Urmia, Iran, for the detection of candida. A primary diagnosis including microscopic investigation and culture on SGA 4% were done. For the identification at level of species, culture on CHA differential medium and PCR-RFLP were done.

Results: Totally, 34 cases of candida infections were detected, from all, 67.6% were men and 32.4% women. The most common age range was 20-30, (29.4%) followed by 60-70, (26.4%) and 50-60, (20.5%). More than 70% of cases were bedfast and 29.5% impatient. Total of the studied patients, 12(35.2%) had a common pulmonary sign. Although, other manifestations such as: bronchiectasis, dizziness with coughing, 2.9% each, was seen. Most of our cases predisposed by DM (26.4%), some other co-involved by HTN,(23.5%), CF, (8.8%), and ESRD, (5.8%). Our findings of microscopic study were yeast invasion 16(47%), yeast

overgrowth, 11(33.3%) and yeast low colonized, 7(20.5%). The most frequent Candida species identified were C. albicans, 10(29.4%) followed by C. dubliniensis, C. tropicalis, 3(8.8%) each, C.glabrata and C. guliermodi 2(5.8%), other Candida species which not identified were 6(17.6%).

Conclusion: Although, candida infection or colonization were associated to diabetes mellitus in the most cases, but other risk factors such as: COPD, CF and HTN as the Co-predisposing agents are considered for cases of candidiasis.

keywords: Candidia, diabetes mellitus, risk factor

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Investigating the prevalence of fungal and bacterial contamination of hands and jewelry of personnel in special care departments of Urmia hospitals

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Medical Mycology

Background and aim: Hospital-acquired infections are always one of the threats to patients admitted to hospitals, which mostly occur after 48 hours of hospitalization and increase the morbidity, mortality, and cost of treatment. These infections are mainly through contact and initially with The hands of employees and people who deal with patients. The purpose of this study is to investigate the prevalence of contamination Fungal and bacterial infections of the hands and jewelry of the personnel of the special care departments of Urmia hospitals

Methods: In this descriptive research, 8 internal emergency departments, pediatrics, NICU, men's surgery, women's surgery, CCU, and ICU, sampling was done using sterile wet swabs from different areas of the personnel's hands and ornaments, and then the swabs were cultured on bacterial and fungal culture media. The detection of bacterial species after 24 hours of culture in EMB Agar and blood agar culture media was investigated using differential culture media diagnostic discs and biochemical methods. Also, to identify the fungal species, Saburodextrose agar was used, which was checked for growth or non-growth for a week, and a grown sample was used to identify the genus and species using the slide culture method and lactophenol staining

Results: The results of the research are that out of 100 cultured personnel samples, 22 people did not have any contamination. 68 of the personnel had

multiple bacterial and fungal infections. Coagulase-negative staphylococci were 35 cases 12 people had Aspergillus niger and 10 people had Staphylococcus aureus

Conclusion: The source of most hospital infections is bacteria and fungi that enter the body of patients during surgery or clinical procedures. It is important to wash hands and rings regularly to prevent bacteria from permanently residing in the skin. Also, the use of appropriate disposable equipment personal hygiene, and Regular trimming of nails can be useful in control and prevention

keywords: Investigating, contamination, jewelry

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Investigation of exoenzyme profiles in clinical Candida isolates

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Medical Mycology

Background and aim: Candida species possess various virulence factors, with key abilities including the production of extracellular hydrolytic enzymes. This study aimed to examine the activity of four distinct extracellular enzymes in Candida spp isolates from oral candidiasis among Chronic Kidney Disease Patients.

Methods: A total of ninety-seven strains from eight different Candida species were identified using both morphological and molecular techniques, including PCR-RFLP and partial amplification of the hyphal wall protein 1 (HWP1) gene. The activities of the enzymes phospholipase, proteinase, hemolysin, and esterase were assessed.

Results: Candida albicans was found to be the most prevalent species, accounting for 55.67% of the isolates. Among non-albicans Candida species, Candida glabrata was the most frequently identified at 22.68%, followed by Candida krusei and Candida kefyr. A statistically significant difference was observed in the mean esterase activity between C. albicans and non-albicans Candida species (P0.05).

Conclusion: The statistically significant differences in esterase activity highlight the unique pathogenic traits of the isolated species. These results underscore the

necessity of accurately identifying species and gaining a deeper understanding of their virulence factors to effectively manage Candida infections.

keywords: Candida, Candidiasis, Oral, Enzymes, esterase

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Mycobiome Dynamics: Unveiling its Significance in Atopic Dermatitis

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Medical Mycology

Background and aim: Atopic dermatitis (AD) is a chronic inflammatory skin condition marked by eczematous lesions and itching, profoundly impacting quality of life. Emerging research underscores the role of the skin microbiome, particularly the mycobiome, in AD pathogenesis. This synthesis aims to summarize pivotal findings regarding the skin mycobiome's involvement in AD.

Methods: We conducted an exhaustive search of PubMed, Google Scholar, and Web of Science databases until February 2024 to find observational studies exploring the link between Atopic Dermatitis (AD) and the skin microbiome, with a focus on fungal microbiota. Three independent reviewers analyzed published data for methodological quality and the risk of bias, resolving discordances through discussions with the corresponding author. We used MeSH terms and Boolean operators to combine the key search terms effectively, such as, "Atopic Dermatitis (AD)", "Atopic Dermatitis Skin Microbiome", "Atopic Eczema", "Mycobiome", "Fungal Microbiota", "Fungal Dysbiosis", "Topical Atopic Dermatitis", and "Allergic Atopic Dermatitis".

Results: From 1,050 published articles, we included 268 studies aligning with our criteria, focusing on atopic dermatitis (AD) and skin microbiome dysbiosis, particularly mycobiome dysbiosis. Our findings reveal AD lesions exhibit reduced Malassezia and elevated filamentous fungi. Specific Malassezia and Candida spp. may interact with pathogenic bacteria, impacting AD development. Non-Malassezia fungal diversity is prominent in AD patients. While Malassezia globosa and M. restricta are common in both AD and healthy individuals, M. sloofiae and M. dermatis are more associated with AD. Dysbiosis in the skin microbiome,

including fungi, influences immune responses and AD development. The gut-skin axis suggests both microbiomes could be targeted for AD treatment.

Conclusion: Our systematic review highlights the crucial role of the skin mycobiome in atopic dermatitis (AD) pathogenesis. Fungal dysbiosis, marked by reduced Malassezia and increased filamentous fungi, is common in AD lesions. AD patients exhibit higher fungal species diversity, with specific Malassezia strains prevalent. These mycobiome changes correlate with immune response shifts and AD development. Restoring mycobiome balance, possibly through emollients, holds potential for AD management. Further research is warranted to understand the complex interplay between skin fungi and the host in AD.

keywords: Atopic Dermatitis (AD); Skin Microbiome; Fungal Microbiota; Dysbiosis

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Monitoring of Candida infections in cases of hematologic and non-hematologic cancers, trends in identification of species

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Medical Mycology

Background and aim: Candida species, opportunistic yeasts, reside on the mucosal surfaces of humans and animals. They can cause a range of diseases in immunocompromised individuals, such as those undergoing corticosteroid therapy, chemotherapy, or long-term pulmonary infections. This study aimed to identify Candida species isolated from respiratory tract infections in patients with both hematologic and non-hematologic cancers.

Methods: We studied cases of hematologic and non-hematologic cancers with pulmonary involvement, characterized by symptoms such as dizziness, cough, chest pain, and other respiratory signs. Bronchoalveolar lavage (BAL) and other respiratory tract specimens were collected and transported to the Medical Mycology Center, UMS University, Urmia, Iran. Direct microscopic examination was performed to identify yeast invasive elements (pseudohyphae and mycelia). Specimens were cultured on sabouraud dextrose agar (SDA), corn meal agar (CMA), and CHromAgar Candida (CHAC) to detect and identify Candida species. Molecular identification was performed using Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) targeting the rDNA gene and the restriction enzyme Msp I.

Results: Of the 147 cancer patients suspected of respiratory tract yeast infection, Candida invasion or colonization was detected in 31 (21%) cases. The majority of

cases (74.2%) were male, and the highest prevalence (35.5%) was observed in the 60-70 age group. The most common underlying malignancies were hematologic cancers (48.4%), followed by gastrointestinal (22.6%), lung (19.4%), and neural (9.7%) cancers. BAL was the primary specimen type examined (80.6%), with the majority of specimens collected from hematology-oncology wards (50%) and pulmonology/ICUs (22.6% each). Microscopic examination revealed invasive yeast elements in 17 (54.8%) cases and overgrowth or colonization in 9 (29%) cases. Molecular identification identified the following species: Candida albicans (22.6%), Candida tropicalis (9.7%), Candida glabrata (9.7%), Candida krusei (6.5%), Candida parapsilosis (6.5%), Candida dubliniensis (3.2%), and other unidentified Candida species (38.7%).

Conclusion: Patients with hematologic and non-hematologic cancers undergoing chemotherapy are susceptible to a variety of Candida species, particularly in respiratory tract infections

keywords: Hematologic cancer, Pulmonary infection, Candida species

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..A Decade-Long Study on the Germ Tube Test for Candidiasis Diagnosis in Outpatients at Iran Zamin Medical Diagnostic Laboratory, Ahvaz (1385-1395)

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Medical Mycology

Background and aim: Candidiasis, a common opportunistic fungal infection, is primarily caused by Candida species, notably Candida albicans. The Germ Tube Test (GTT) is a vital diagnostic test to identify certain species of Candida, particularly C. albicans and Candida dubliniensis, differentiating them from other yeasts. This test involves incubating Candida spp. with human or sheep serum to observe the formation of a tube mass, indicating a positive result.

Methods: Over ten years, 920 outpatients with candidiasis were sampled and tested using GTT. Serum was added to a tube, a yeast colony was introduced, and the mixture was incubated. A drop of serum was placed on a slide for microscopic examination.

Results: Of the 920 patients, 110 (11.96%) had a positive GTT. The test showed 87.1% sensitivity and 100% specificity for C. albicans identification compared to fungal colony results.

Conclusion: The GTT is a valuable preliminary test for highly specific identification C. albicans and C. dubliniensis, offering high specificity and moderate sensitivity. The test can be completed within 2-4 hours, providing quick results with cost-effective compared to other diagnostic methods. This is especially important in cases where prompt treatment is necessary and it can guide clinicians in selecting appropriate antifungal therapy, as some Candida spp. may be resistant to certain antifungal agents.

keywords: Diagnosis, candidiasis, Candida albicans, Candida dubliniensis

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Occurrence of aflatoxin M1 in commercial pasteurized milk samples in Sari, Mazandaran province, Iran

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Medical Mycology

Background and aim: Aflatoxin M1 (AFM1) is a metabolite of aflatoxin B1 that could be found in milk when dairy cattle consume AFB1-contaminated feedstuffs. The frequency and levels of aflatoxin M1 (AFM1) in pasteurized milk samples in Sari, located in Mazandaran province, Iran, were determined by enzyme immunoassay.

Methods: Seventy-six samples of pasteurized milk from different retail stores of Sari city were randomly collected over four seasons during the year 2015 and screened using ELISA technique.

Results: AFM1 contamination was detected in all milk samples. The mean concentration of aflatoxin M1 was 65.8 ng/l, with a range of 11.7–106.6 ng/l. The highest AFM1 level was detected in milk samples collected during spring. Forty-six (60.53 %) samples had AFM1 levels that exceeded the maximum acceptable levels (50 ng/l) recommended by the European Union (EU).

Conclusion: Comparison of these results with previously published data for AFM1 in milk in Iran shows that the percentage of samples exceeding the EU maximum level is consistently high over the years, indicating a general problem related to AFB1 contamination in dairy feedingstuff.

keywords: Sari, Iran, Pasteurized milk, Aflatoxin M1, Contamination

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Mechanisms of Antifungal Resistance: Molecular Pathways Driving Treatment Failures in Pathogenic Fungi

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Medical Mycology

Background and aim: Antifungal resistance is a growing global health concern, weakening current treatments and increasing fungal infections. This review examines molecular mechanisms behind resistance, highlighting key factors like mutations in ERG11, overexpression of efflux pumps (ABC and MFS families), and altered membrane composition reducing drug efficacy. Stress-response pathways, biofilm formation, and epigenetic changes further enhance fungal resilience. Environmental and clinical pressures, such as antifungal use in agriculture and healthcare, drive resistance. Advances in genomics and proteomics identify therapeutic targets and novel antifungal agents. A multidisciplinary approach integrating research, diagnostics, and public health is critical to combating antifungal resistance effectively.

Methods: A comprehensive systematic review was conducted using the PubMed, Scopus, and Web of Science databases to identify studies investigating the molecular mechanisms of antifungal resistance in pathogenic fungi. The search strategy incorporated keywords related to antifungal resistance, molecular mechanisms, and pathogenic fungi, combined using Boolean operators. Inclusion criteria consisted of original research articles, reviews, and case studies published in English from 2010 to September 2024. Additionally, three independent reviewers evaluated study eligibility and extracted data, resolving any disagreements through consultation with the corresponding author.

Results: Our systematic review analyzed 915 studies, with 125 meeting eligibility criteria, to explore molecular mechanisms driving antifungal resistance and pathogenesis in fungal pathogens. Resistance was predominantly linked to ERG11

gene mutations and efflux pump overexpression, particularly ABC and MFS transporters. Other contributing factors included membrane composition changes, stress-response pathways, biofilm formation, and epigenetic modifications. Additionally, key findings highlighted pathogen-specific mechanisms, for example, in Aspergillus spp., gliotoxin suppressed immune responses, while Ras and MAPK pathways regulated growth and virulence. In Candida spp., biofilm formation and morphogenetic switching, governed by the Ras/cAMP/PKA pathway, emerged as major virulence factors. For Cryptococcus neoformans, capsule polysaccharide was critical for virulence. In Pneumocystis jirovecii, the major surface glycoprotein played a central role in host adherence and immune evasion. These insights underscore the need for targeted therapeutic strategies addressing diverse fungal resistance mechanisms.

Conclusion: The results of this systematic review underscore the complex and multifaceted nature of antifungal resistance, with various molecular mechanisms contributing to treatment failures. Among pathogenic fungi, Candida species are particularly significant as the most common cause of clinical infections in immunocompromised patients. Understanding these mechanisms is crucial for developing effective diagnostic tools and treatment strategies to combat antifungal resistance and improve clinical outcomes. Furthermore, continued research is essential to develop innovative antifungal approaches and enhance the management of multidrug resistance (MDR) in fungal infections.

keywords: Antifungal resistance; Molecular mechanisms; Drug resistance in fungi; Fungal Pathogens.

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Two-Year Study of Fungal blood Infections in Patients at a University Hospital in Ahvaz, Iran

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Medical Mycology

Background and aim: Fungal infections, previously deemed rare, have become significant pathogens, especially in immunocompromised individuals. Detecting fungi in blood cultures is essential for diagnosing invasive fungal infections, which are often linked to high morbidity and mortality. Despite advancements in diagnostic microbiology, challenges persist regarding sensitivity, specificity, and time to detection.

Methods: We conducted a retrospective analysis of hospital data for patients with fungal infections identified in blood cultures from November 5, 2022, to November 5, 2024, at a University Hospital in Ahvaz, Iran. The data were categorized to identify trends and outcomes.

Results: Out of approximately 6,000 blood cultures analyzed, 65 cases (1.08%) of fungal infections were identified, predominantly caused by Candida species, which are responsible for candidemia. While blood cultures are the gold standard for diagnosing fungemia, their sensitivity can be limited, particularly for fastidious fungi or in early or localized infections. Specialized blood culture systems and molecular diagnostic techniques, such as polymerase chain reaction

(PCR), have been developed to enhance fungal recovery and detection, although these methods are not yet widely available or standardized.

Conclusion: This study highlights the critical need for recognizing fungal infections in clinical practice, particularly among immunocompromised patients. Further research is necessary to explore the underlying factors contributing to these infections and to refine preventive and therapeutic approaches. Notably, Candida species are among the leading causes of fungal blood infections in hospitalized patients, with high mortality rates in cases of delayed diagnosis. A deeper understanding of the epidemiology, pathogenesis, and host-pathogen interactions of fungal infections will aid in improving prevention and treatment strategies.

keywords: Blood culture, Infection, Fungi, Immunocompromised, Candida species.

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Efficacy of Ethyl Acetate Extract from Fusarium equiseti in Inhibiting Helicobacter pylori: An In Vitro Study

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Medical Mycology

Background and aim: Untreated infections caused by Helicobacter pylori have the potential to progress to gastric cancer. This bacterium demonstrates considerable resistance, and the range of related disorders is anticipated to become increasingly evident over time, underscoring the necessity for the development of more effective therapeutic interventions. Mushrooms are known to possess medicinal properties attributed to their varied secondary metabolites. The objective of this study was to examine the in vitro effects of the ethyl acetate extract derived from Fusarium equiseti on Helicobacter pylori.

Methods: Ethyl acetate extracts of Fusarium equiseti were initially prepared. Following this, Helicobacter pylori strains were isolated from gastric biopsies obtained from patients, and standardized suspensions were created at two different concentrations. The minimum inhibitory concentration (MIC) for extract of Fusarium equiseti was determined using the agar dilution method. In summary, the bacterial suspensions were inoculated into Brucella agar medium that contained serial dilutions of the extracts, ranging from 1024 µg/mL to 8 µg/mL. After incubation, the growth of the bacteria was evaluated..

Results: The ethyl acetate extract of Fusarium equiseti exhibits significant antibacterial activity. At a concentration of 1024 µg/mL, it effectively inhibits bacterial growth. The extract's antibacterial effect remains effective down to a

dilution of 125 µg/mL.The minimum inhibitory concentration (MIC) for the extract is established at 125 µg/mL.

Conclusion: The results of this study indicate that the ethyl acetate extract of Fusarium equiseti possesses significant in vitro antibacterial activity against H. pylori, suggesting its potential for further investigation as a therapeutic agent.

keywords: Helicobacter pylori, medicinal mushrooms, anti-Helicobacter pylori activity, Fusarium equiseti

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One-year investigation of fungal infections detected in urine cultures from patients who visited a University Hospital in Ahvaz, Iran

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Medical Mycology

Background and aim: Urinary tract infections (UTIs) are usually caused by bacteria, but yeast can also be a culprit, particularly in hospitalized patients or those with compromised immune systems.

Methods: Hospital data related to patients with fungal infection in urine culture from 21 March 2023 to 19 March 2024 in one of the University Hospitals of Ahvaz, Iran were analyzed and categorized.

Results: Among approximately 9,000 urine cultures analyzed, 544 cases (6.04%) of fungal infections were identified, with a higher prevalence in women (365cases, 67.1%) compared to men (179 cases, 32.9%). Yeast infections were categorized based on colony-forming units (CFU), with women presenting 17 cases with high CFU (1000), 76 cases with moderate CFU (50–100), and 272 cases with low CFU (50). In men, 12 cases exhibited high CFU (1000), 47 moderate CFU (50–100), and 120 low CFU (50).

Conclusion: This research underscores the importance of recognizing fungal UTIs in clinical practice, particularly among female patients. Further studies are

necessary to explore the underlying factors contributing to these infections and to refine preventive and therapeutic approaches.

keywords: Urine culture, Infection, Fungi, Urinary tract infection

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A Case of Nocardiosis Misdiagnosed as Sporotrichosis: Diagnostic Challenges and Successful Treatment with Clindamycin

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Medical Mycology

Background and aim: Nocardiosis is a rare opportunistic infection caused by Nocardia species, which can present with a range of clinical manifestations, often resembling other infectious diseases. This case report aims to highlight the diagnostic challenges and treatment outcomes associated with nocardiosis, particularly in patients initially suspected of having sporotrichosis, a more common fungal infection.

Methods: On October 27, 2023, a patient was referred to the laboratory with a purulent and swollen lymphatic skin lesion, along with involvement of the axillary lymph nodes. The clinical presentation raised suspicion for sporotrichosis, prompting a thorough diagnostic evaluation. During the sampling and microscopic examination, no fungal elements indicative of Sporothrix yeast were observed.

Results: This case underscores the importance of considering Nocardia as a differential diagnosis in patients presenting with atypical skin lesions and lymphadenopathy, especially in immunocompromised individuals or those with underlying health conditions.

Conclusion: Accurate diagnosis through culture and staining techniques is crucial for effective treatment. The successful outcome in this case highlights the need for increased awareness and understanding of nocardiosis among healthcare providers to ensure timely and appropriate management of this rare infection.

keywords: Nocardiosis, Nocardia, clindamycin, sporotrichosis, skin lesions, lymphadenopathy, opportunistic infection.

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The Impact of Agricultural and Industrial Pollutants on the Evolution of Antifungal Resistance in Pathogenic Fungi: A Multidisciplinary Hypothesis

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Medical Mycology

Background and aim: The global rise of multi-drug resistant (MDR) fungal infections highlights the urgent need to combat antifungal resistance. Limited antifungal therapies and few new drug classes exacerbate the issue. While clinical drivers of resistance are well-known, the role of environmental pollutants remains underexplored. Evidence indicates that pollutants like heavy metals, pesticides, and antibiotics act as selective agents, fostering resistance in environmental fungi. These resistant strains may transfer genes to pathogenic fungi via horizontal gene transfer, worsening clinical outcomes. This review emphasizes the influence of pollutants on resistance and calls for a multidisciplinary, eco-evolutionary approach to tackle this public health crisis.

Methods: A comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar (inception to September 22, 2024) was conducted using keywords related to antifungal resistance, pathogenic fungi, and environmental pollutants. Inclusion criteria encompassed studies investigating the link between pollutant exposure and antifungal resistance in pathogenic fungi. Three reviewers independently screened titles, abstracts, and full texts, assessing methodological quality using appropriate tools. Data extraction focused on study characteristics and key findings. A narrative synthesis was employed due to anticipated heterogeneity, identifying key themes and patterns in the relationship between environmental pollutants and antifungal resistance evolution. Disagreements were resolved through consensus or consultation with a fourth reviewer.

Results: A systematic review revealed a strong link between agricultural and industrial pollutants and antifungal resistance in medically significant fungi, including Candida, Aspergillus, and Cryptococcus species. The analysis of 133 studies identified key pollutants, including heavy metals (e.g., copper, zinc), pesticides (e.g., azoles, organophosphates), and antibiotics. Pollutant exposure significantly increased minimum inhibitory concentrations (MICs) for azoles and echinocandins, often accompanied by novel resistance mechanisms or the upregulation of resistance genes such as MDR1 and ERG11. Horizontal gene transfer was observed as a pathway for resistance dissemination. However, the strength of association varied by pollutant type, concentration, fungal species, and exposure duration. Despite variability, the evidence supports that environmental pollutants play a critical role in driving antifungal resistance, posing a serious global health threat by facilitating resistance evolution and spread in medically relevant fungi. This highlights the urgent need for further targeted research.

Conclusion: This review identifies a strong link between agricultural and industrial pollutants and antifungal resistance in Candida and Aspergillus species. Pollutant-exposed isolates showed higher minimum inhibitory concentrations (MICs) for azoles and echinocandins, driven by ERG11 (Candida) and cyp51A (Aspergillus) mutations or efflux pump overexpression. These findings suggest environmental factors contribute to the rise of invasive candidiasis and aspergillosis caused by multi-drug-resistant strains. Addressing this issue requires integrated strategies combining improved clinical management and pollution control to mitigate resistance and enhance patient outcomes.

keywords: Antifungal resistance; Pathogenic Fungi; Environmental pollutants; Azole antifungals; Agricultural-industrial pollution

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Candidemia in a Pediatric Patient with Acute Lymphoblastic Leukemia: A Case Report of Diagnosis and Successful Treatment with Antifungal Therapy

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Medical Mycology

Background and aim: Candidemia, a bloodstream infection caused by Candida species, poses a significant risk in immunocompromised patients, particularly those undergoing treatment for malignancies. This case report aims to describe the clinical presentation, diagnostic process, and treatment outcomes of a 4-year-old boy with autism who developed candidemia during his treatment for acute lymphoblastic leukemia (ALL).

Methods: A 4-year-old boy with a history of autism presented with increasing weakness and lethargy, which culminated in a diagnosis of ALL on June 30, 2023, leading to his admission to the Pediatric Intensive Care Unit (PICU) of Bo Ali Hospital in Sari. Upon admission, he exhibited oral ulcers, significant weakness, and severe lethargy. Diagnostic tests revealed positive cultures for Candida species on multiple occasions: urine culture on August 23, 2023; blood and urine cultures on August 25, 2023; and subsequent blood cultures on August 26 and September 9, 2023.

Results: Molecular analysis confirmed the presence of Candida tropicalis through the RFLP-PCR method. The patient received a comprehensive treatment regimen for ALL, including Vincristine and Cytarabine, alongside antifungal therapy. He was administered Meropenem, Vancomycin, Amikacin, Nystatin drops,

Fluconazole, Liposomal Amphotericin B, and Caspofungin. The last two antifungal agents were given daily until October 15, 2023. Follow-up cultures on October 17, 2023, showed no growth of Candida in blood, urine, or oral lesion samples, indicating successful treatment.

Conclusion: This case highlights the importance of early recognition and management of candidemia in pediatric patients with compromised immune systems, particularly those undergoing treatment for malignancies. The successful resolution of candidemia in this patient underscores the effectiveness of a multi-faceted therapeutic approach, including both antifungal agents and supportive care. Increased awareness and prompt intervention are crucial in improving outcomes for children at risk of opportunistic infections.

keywords: Candidemia, Candida tropicalis, acute lymphoblastic leukemia, pediatric, antifungal therapy, immunocompromised.

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Severe Systemic Skin Reaction to Itraconazole in a Patient with Tinea Cruris: A Case Report Highlighting Alternative Antifungal Management

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Medical Mycology

Background and aim: Drug allergies, particularly to antifungal agents, can lead to severe adverse reactions and complicate the management of dermatophyte infections. This case report aims to describe the clinical presentation, management, and outcomes of a 27-year-old man who developed a severe systemic skin reaction following itraconazole treatment for Tinea cruris.

Methods: A 27-year-old male presented with Tinea cruris, for which he was prescribed itraconazole tablets as per the physician's recommendation. After one week of treatment, the patient developed a severe systemic skin reaction characterized by extensive erythema and desquamation, prompting him to self-medicate with painkillers, including acetaminophen and Ibuprofen. Due to the worsening of his condition, he was admitted to Ghaem Shahr Hospital, where he received treatment with corticosteroid drug for one month to manage the severe drug sensitivity reaction.

Results: Following his discharge, the patient returned to the clinic for further management of Tinea cruris and newly developed fungal folliculitis. Laboratory tests confirmed the presence of dermatophyte infection. Given his history of itraconazole allergy, the treating physician prescribed an alternative antifungal regimen consisting of griseofulvin once daily, terbinafine ointment applied three

times daily, and sulfur soap for cleansing twice daily. After two weeks of this new treatment regimen, the patient exhibited significant improvement in the lesions, with a marked reduction in inflammation and pruritus.

Conclusion: This case highlights the potential for severe allergic reactions to azole antifungals, necessitating careful consideration of patient history when selecting treatment options for dermatophyte infections. The successful management of this patient with alternative antifungal therapy underscores the importance of individualized treatment plans in patients with known drug allergies. Clinicians should remain vigilant for signs of drug hypersensitivity and be prepared to adjust treatment strategies accordingly to ensure patient safety and effective management of fungal infections.

keywords: Azole drug allergy, Tinea cruris, itraconazole, griseofulvin, terbinafine, dermatophyte infection,

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Candiduria and Antifungal Resistance Patterns in Burn Patients: A Multi-Center Study in Iran

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Medical Mycology

Background and aim: Background and Aim: Burn injuries significantly impair the immune system, making patients vulnerable to opportunistic fungal infections. Candiduria is particularly concerning as it may serve as an early marker for invasive candidiasis. Candida species are frequently isolated in burn patients, and their resistance patterns to antifungal agents are critical for guiding treatment. This study aimed to identify Candida species in urine cultures of burn patients and assess their antifungal susceptibility.

Methods: Urine samples were collected from 72 burn patients hospitalized in three burn centers in Iran over a one-year period. To isolate and identify Candida species in the urine samples, the specimens were initially cultured on Sabouraud dextrose agar. Precise identification of the species was then performed using PCR-RFLP. Additionally, antifungal susceptibility testing was conducted for 15 antifungal agents.

Results: A total of 72 Candida isolates were identified, including C. albicans (6 isolates), C. parapsilosis (13 isolates), C. glabrata (15 isolates), C. tropicalis (2 isolates), and other species. Caspofungin (CAS) demonstrated the highest overall susceptibility, with 100% of isolates being susceptible, while fluconazole (FLC) exhibited resistance in 8 isolates, predominantly in C. parapsilosis and C. albicans. Anidulafungin (AFG) was effective against 94% of the isolates (34 out of 36). Species-specific observations revealed that C. albicans had MIC50 and MIC90 values of 4 µg/mL and 16 µg/mL for FLC, with 66% susceptibility, respectively. In

contrast, C. parapsilosis showed significant resistance to FLC (53.8%), with an MIC90 of 16 µg/mL.

Conclusion: Candiduria in burn patients is a significant clinical concern that requires prompt identification and tailored antifungal therapy. This study highlights the efficacy of echinocandins and the need for vigilance in monitoring resistance patterns to optimize patient outcomes.

keywords: Candiduria, Burn Patients, Candida species, Antifungal Resistance

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Colonization with Candida species yeasts in neonates hospitalized in a referral neonatal intensive care unit and antifungal susceptibility testing of the isolates

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Medical Mycology

Background and aim: Mycobiota can be detected in neonates' skin shortly after birth, despite their sterile skin at birth. Colonization with fungi in newborns, especially premature neonates, can lead to an increased risk of systemic infections. Although C. albicans continues to be the most frequent fungal colonizer of neonatal skin, a clear increase of colonization due to non-C. albicans has been reported. This study was designed to determine the Candida species yeast in newborns who were admitted to the intensive care unit. Anti-fungal susceptibility test was also conducted for all Candida species.

Methods: Skin samples from various anatomical areas, such as the cheek, chest, armpit, catheter, and genital, were gathered by pressing a sterile moisturizing swab. Sampling from each neonate was done three times per week. Each sample was inoculated into Sabouraud Dextrose Agar containing Chloramphenicol (SC) and Candida CHROMagar, separately and then incubated at 35°C. The identification of the isolates was done using PCR- RFLP and confirmed by DNA sequencing. Colonization was determined according to the guideline. In-vitro antifungal susceptibility testing of the isolates was performed against amphotericin B (AMB), fluconazole (FCZ), itraconazole (ICZ) and caspofungin(CFG) using Clinical Laboratory Standards Institute method and criteria (M27,E4).

Results: During the 12-month study, the sampling of 78 neonates was done. Out of 1026 collected samples, 213 non-Malassezia yeasts were recovered. Of which Candida species were the most common (165/213, 77.5%) followed by Cryptococcus (37/213, 17.4%) and Rhodotorula species (11/213, 5.1%). Out of 165 Candida isolates, C. albicans (65/165,39.4%) and C. parapsilosis 57 (24.56%) were the most frequent of Candida species. Also, in this study, we isolated C. guilliermondii (Meyerozyma guilliermondii) (24/165,14.6%), C. lusitania (5/165,3/3%), C. glabrata (2/165, 1/2%) and C. tropicalis (3/165,1.8%) . Of the 78 neonates, 34 (58.43%) were colonized with candida species, 33 (42.3%), 30 (38.46%), 5 (4.6%) with C. albicans, C. parapsillusis and C. guillermodi, respectively. According antifungal susceptibility test, 8.6%, 10.3% and 74.1% of C. albicans isolates are resistant to fluconazole, amphotericin B and caspofungin, respectively. Caspofungin and fluconazole resistance were observed in 8.9% and 2.2% of C. parapsilosis isolates, and in 11.8% and 5.9%

Conclusion: In this study, rare Candida species such as C. guilliermondii, C. lusitaniae, C. tropicalis, C. glabrata, C. glabrata, C. kefyr, C. famata, C. krusei) were isolated. Our results showed that Candida species have significant resistance to

fluconazole and caspofungin, the main antifungals in the treatment of systemic candidiasis. It is also noteworthy that there is cross-resistance to multiple drugs among Candida albicans species.

keywords: Colonization, neonates, neonatal intensive care unit. Candida

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Effect of Cold Atmospheric Plasma on Ergosterol Synthesis in Terbinafine-Resistant and -Sensitive Trichophyton mentagrophytes Complex Strains

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Medical Mycology

Background and aim: The widespread distribution and prevalence of Trichophyton mentagrophytes is a global concern, and the treatment of its chronic and recurrent infections remains challenging. Recent reports have highlighted terbinafine resistance, a commonly prescribed antifungal for dermatophytosis. However, this condition often shows limited response to conventional therapies, prompting increased efforts to explore alternative treatments. Utilizing advanced plasma technology offers a promising approach to managing these persistent infections by reducing treatment duration and costs while significantly enhancing patient satisfaction. This study investigated the effect of cold atmospheric plasma (CAP) on ergosterol synthesis in Trichophyton mentagrophytes complex isolates.

Methods: Materials and Methods Two isolates from the Trichophyton mentagrophytes complex were included in the study: a terbinafine-resistant strain and a standard terbinafine-sensitive strain (PTCC 5809) obtained from the fungal collection of the Pasteur Institute of Iran. Fungal suspensions were prepared, and plates containing fungal spores were exposed to cold atmospheric plasma. Ergosterol synthesis was assessed in both strains before and after plasma exposure.

Results: Results The results revealed a reduction in ergosterol synthesis in both sensitive and resistant strains following plasma exposure. Ergosterol synthesis

decreased 1.5-fold in the sensitive strain and 7-fold in the resistant strain. Notably, the reduction in the resistant strain was approximately four times greater than that observed in the sensitive strain.

Conclusion: Conclusion While the behavior of the resistant and sensitive strains towards plasma exposure was similar, the intensity of their responses differed significantly. This discrepancy may be attributed to compensatory mechanisms in resistant strains, rendering them more vulnerable to environmental stressors such as plasma exposure. Additionally, structural changes in the cell membrane of resistant strains could enhance plasma's impact on ergosterol synthesis. Furthermore, the defensive mechanisms of resistant strains may be primarily adapted to counteract terbinafine rather than plasma exposure, resulting in reduced defense against the latter.

keywords: Trichophyton mentagrophytes Complex , Ergosterol , Cold Atmospheric Plasma

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An Unusual Infection of Trichosporon asahii in a COVID-19 Patient with Diabetes: A Rare Case Report Unveiling Novel Insights Highlighting Diagnostic Challenges and Clinical Implications

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Medical Mycology

Background and aim: Trichosporon asahii is a non-candidate opportunistic fungus that can be life-threatening in immunocompromised patients and individuals with underlying diseases. Invasive medical devices like urinary catheters and the use of antibiotics increase the chance of infection. It can cause resistance to antifungal agents by biofilm formation. This study aimed to report an unusual urinary tract Infection of Trichosporon asahii in a COVID-19 patient with diabetes mellitus that unveiled novel insights highlighting diagnostic challenges and clinical implications.

Methods: The patient was a 74-year-old man who had underlying diseases and was undergoing treatment with various drugs. During hospitalization, the patient underwent various investigations and laboratory tests, including chest and brain computed tomography (CT) scan, real-time PCR, complete blood count (CBC), C-reactive protein (CRP), endotracheal aspirate culture, blood culture, urine analysis, and urine culture. Vitek2 compact automated system and molecular methods were used for the identification and confirmation of T. asahii. Antimicrobial susceptibility testing (AST) was performed to determine the drug resistance of T. asahii.

Results: The chest CT scan and real-time PCR test showed SARS-CoV-2. Mucoid yeast-like fungi were reported repeatedly in the urine sample based on

microscopic observations and colony morphology. Ultimately, T. asahii was identified and confirmed by the Vitek2 compact automated system and molecular method (PCR). The results of the antimicrobial susceptibility test (AST) showed that it was intermediated to voriconazole, and susceptible dose-dependent to itraconazole. The treatment that was started with voriconazole and amphotericin was continued with voriconazole due to our country's limitation and shortage of itraconazole. Despite long-term treatment, the patient died.

Conclusion: Although resistance to antifungal drugs has been acquired, timely diagnosis and correct treatment of T. asahii infections by appropriate relations between the patient's treating service, the infectious disease physician, and the microbiology laboratory can prevent irreparable consequences.

keywords: Trichosporon asahii; COVID-19; Immunocompromised patients; Catheters; Antibiotics.

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Prevalence and Genetic Basis of Terbinafine Resistance in Dermatophytes: Identification of Point Mutations in the Squalene Epoxidase Gene

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Medical Mycology

Background and aim: The increasing reports of terbinafine-resistant dermatophytes highlight the importance of antifungal susceptibility testing as a valuable tool for managing dermatophytosis. This study aimed to investigate the prevalence of mutations in the squalene epoxidase gene among terbinafine-resistant dermatophyte strains.

Methods: Antifungal susceptibility profiles were determined using the broth microdilution method according to the CLSI M38-A2 protocol. A total of 52 isolates, identified through ITS region sequencing, were analyzed. The minimum inhibitory concentration (MIC) range, geometric mean MIC, MIC50, and MIC90 values were determined for dermatophyte species. Resistant strains and one susceptible reference strain were further analyzed for point mutations in the squalene epoxidase gene for PCR amplification, followed by sequencing.

Results: All resistant strains belonged to Trichophyton indotinae. The MIC range for terbinafine was 0.003–4 µg/mL. Terbinafine resistance was observed in four isolates. All resistant strains and one susceptible standard strain were examined for mutations. The most common mutations identified were F397L and L393S. Overall, 7.6% of the isolates exhibited terbinafine resistance.

Conclusion: These findings indicate that point mutations in the squalene epoxidase gene are a key mechanism underlying terbinafine resistance in dermatophytes. Identification of these mutations can enhance our understanding

of resistance mechanisms and support the development of effective diagnostic and therapeutic strategies.

keywords: Point mutation; trichophyton indotineae; Terbinafine

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Evaluating the Independent and Combined Effects of Cold Atmospheric Plasma and Terbinafine on Trichophyton mentagrophytes

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Medical Mycology

Background and aim: The global distribution and prevalence of Trichophyton mentagrophytes present significant challenges in the treatment of this chronic and recurrent infection. Terbinafine is the first-line treatment for dermatophytosis; however, the prolonged and arduous conventional therapy often fails, and recent reports of terbinafine resistance exacerbate this issue. Utilizing advanced plasma technology to treat this chronic and recurrent infection has the potential to reduce treatment duration and costs while significantly enhancing patient satisfaction. Therefore, this study aimed to evaluate the synergistic effect of cold atmospheric plasma and the antifungal drug terbinafine against Trichophyton mentagrophytes species and investigate the expression of the Hsp90 gene

Methods: This study was conducted on four terbinafine-resistant strains and one terbinafine-susceptible strain. Antifungal susceptibility testing was performed according to the CLSI-M28 A2 protocol. First, a spore suspension at a concentration of 3×10^3 spores/mL was prepared and divided into three parts. The first part was used to determine the MIC of the strains against different concentrations of terbinafine using the broth microdilution method, according to CLSI guidelines. The second part was exposed to cold atmospheric plasma for 210 seconds (based on previous studies) and subsequently added to RPMI medium in equal volumes without the addition of terbinafine. The third part was similarly exposed to plasma treatment for 210 seconds but then exposed to different concentrations of terbinafine. All plates were incubated at 30°C for five days and

growth was visually compared with untreated control wells without plasma exposure and terbinafine.

Results: No antagonistic or synergistic interactions were observed between plasma treatment and terbinafine in resistant or susceptible strains. The results of the checkerboard assay were consistent with the results of the antifungal susceptibility test. Addition of plasma treatment to the spore suspension, along with terbinafine, did not further reduce fungal growth. The MIC corresponded to a 50% reduction in fungal growth in all resistant and susceptible strains compared to untreated control wells. Similar results were obtained using the broth microdilution method.

Conclusion: The absence of synergistic or antagonistic interactions between plasma treatment and terbinafine suggests that the two approaches independently affect fungal growth. This study demonstrates that cold atmospheric plasma alone can effectively reduce fungal growth. However, no synergistic effect was observed in combination with terbinafine. These findings highlight the need for further research into the mechanisms underlying terbinafine resistance and the independent effects of plasma treatment. Furthermore, exploring independent applications of plasma technology for the treatment of resistant fungal infections offers a valuable avenue for future research.

keywords: synergism; Cold Atmospheric Plasma; Terbinafine

Investigating Cryptosporidium and Enterocytozoon bieneusi infections in children with malignancies in southwest Iran

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Medical Parasitology

Background and aim: Malignancies have a high mortality rate in the world. Malignancy and immunosuppression associated with cancer and chemotherapy make children susceptible to infections such as opportunistic infections, which can cause death in these patients. Cryptosporidiosis and Microsporidiosis are among the opportunistic infections with high prevalence in the world, which are obligate intracellular parasites in the intestinal epithelium and cause severe and fatal diarrhea in malignant patients. Due to the lack of research on the prevalence of these protozoa in children with malignancy and its increasing prevalence, we investigated Cryptosporidium and Enterocytozoon bieneusi infections in children with malignancy in southwest Iran.

Methods: Stool samples were randomly collected from 60 children with various malignancies hospitalized in Baqa 2 Ahvaz Hospital. These patients were in the age range of 5 to 18 years and their disease was diagnosed with the opinion of a specialist doctor. After collection, the samples were examined microscopically and stained by Ziehl-Neelsen, and then DNA was extracted using the Tehiz Azma kit for molecular work. In the next step, the samples were screened using PCR for Cryptosporidium and Enterocytozoon bieneusi with specially designed primers. For samples that were positive through screening, Nested-PCR was performed. The PCR products were inoculated into the electrophoresis gel and placed in the gel dock device for band analysis. Identified sequences were sorted by Chromas software. After determining the genotypes, MEGA10 software was used to draw the phylogeny tree and the statistical results were analyzed with SPSS software.

Results: The findings of the present study showed that out of 60 patients examined, 38 were men (63%) and 22 were women (37%), who were in the age range of 5-18 years with an average age of 9.72 years. According to the molecular test results, 44 patients were negative for Enterocytozoon bieneusi and

Cryptosporidium, but 16 patients were positive. Among the positive cases, 14 cases were positive for Enterocytozoon bieneusi and 2 cases were positive for both Enterocytozoon bieneusi and Cryptosporidium, and there was no significant relationship between positive samples and their frequency. Of the 60 malignant patients in this study, 35 had ALL (Acute Lymphoblastic Leukemia), 9 had AML (Acute Myeloid Leukemia), and 16 had other malignancies. There is no significant relationship between malignancy and positive samples of these protozoa. Out of 5 patients who had clinical symptoms such as diarrhea and abdominal pain, 4 were positive for Enterocytozoon bieneusi.

Conclusion: Molecular characterization of Cryptosporidium and Enterocytozoon bieneusi species has improved our understanding of the transmission of these protozoan parasites to humans. Infection with these parasites can be accompanied by severe digestive symptoms such as abdominal pain and diarrhea, which can increase the mortality rate in immunocompromised people, especially in patients with malignancy. Considering that the sequencing results of these two types of parasites have confirmed the human-to-human transmission cycle, it is necessary to prevent the dangerous complications of these parasites in humans, especially in patients with malignancy, by laboratory diagnosis.

keywords: Cryptosporidium, Microsporidiosis, Enterocytozoon bieneusi, Malignancy, Prevalence.

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Determination of Sarcocystis species of slaughtered sheep in Kermanshah slaughterhouse by PCR-RFLP

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Medical Parasitology

Background and aim: Sarcocystosis is one of the most common protozoan infections between humans and animals. This parasite has a global distribution and involves the muscles in livestock, that can cause economic losses and clinical and subclinical disease. Protozoa causes symptoms such as abdominal pain, bloating, anorexia, diarrhea, vomiting, respiratory problems and tachycardia in humans.

Methods: In this study, 40 infected sheep samples from the central slaughterhouse of Kermanshah were examined. The samples were collected from the esophageal, intercostal, diaphragm, tongue and skeletal muscle tissues. To determine the species and distinguish them from each other, PCR - RFLP was used.

Results: 100% of the muscles contained sarcocyst bradyzones in the digestion method. The results of PCR-RFLP identified Sarcocystis tenella, species. According to the results of the study, it is recommended to avoid consuption of half-cooked meat and preventive measures in slaughterhouses, including acurate inspection of carcasses and local or total removal of carcasses.

Conclusion: Since Sarcocystis tenella causes abortion and economic losses in livestock, species identification is important in livestock care and transmission cycle control.

keywords: tenella, Sarcocyst, sheep, PCR, RFLP, Kermanshah

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Isolation and measurement activity of Fatty Acid Binding Protein from Fasciola hepatica

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Medical Parasitology

Background and aim: Fasciolosis is a cosmopolitan parasitic disease caused by Fasciola hepatica. This infection occurs in a variety of mammals, including humans. It is highly prevalent in sheep due to their close contact with infective pasture. This parasite commonly inhabits the hepato-biliary system of the affected hosts. Recent studies have revealed fatty acid-binding protein (FABP) as an active biological compound of F. hepatica, which is crucial for nutrient acquisition and survival of the parasite. Isolation of FABP will be purpose for future investigation of pathogenesis, diagnostic, and vaccination against fasciolosis. So the aim of this study was Isolation and measurement activity of

Methods: In order to obtain the natural form of FABP, the proteins were precipitated from the body proteins of the parasite in a salt concentration of 70% ammonium sulfate. Then, the supernatant solution was dialyzed against phosphate buffer and the obtained fractions were separated using ion exchange chromatography (anionic) with FPLC and SDS-PAGE. To confirm the fatty acid binding protein, mass spectrometry was used and confirmed. Protein concentration was measured with Bradford method

Results: Our finding from purification of FABP showed protein with apparent molecular weights of 12–14 kDa, which identified as FABP MALDI-TOF analysis. Fatty Acid Binding Protein activity measured by DAUDA substrate against Bovin Serum Albumin (BSA) in λExc 350 and λEm 350, 500 and, 610 nm. The activity was suitable

Conclusion: The FABP is a choice protein for make vaccine against human or sheep fasciolosis, also it will be a choice to use for helminthes therapy.

keywords: FABP, Fasciola hepatica, Isolation

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Study of Cryptosporidiosis in pet and stray dogs in Kermanshah city, using microscopy

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Medical Parasitology

Background and aim: In this survey we evaluate the microscopic and prevalence of Cryptosporidium infection in a given population of pet and stray dogs in Kermanshah city, west of Iran . Cryptosporidiosis, is one of the important zoonotic parasitosis, capable to cause diarrhea in humans and animals. There is a little information about the epidemiology of cryptosporidiosis in the population of dogs in Kermanshah. These days dogs have the closest relation with human, which might be one of the most dangerous factors to threaten public health; therefore the determination of this disease among dogs in this region will help us to improve the

Methods: Fecal specimens were collected from a total of 350 dogs, including 175 pet and 175 stray dogs, from May 2022 until the end of January 2023. The fecal samples were transferred to the Parasitology laboratory. Each dog were examined, involving different parameters such as pet owner's name, age, sex and breed and clinical signs, gastrointestinal and, body coat. The MZN staining was done, the slides were covered with carbol-fuscin stain, heated for5min, then washed with water. De-staining was performed using acid-alcohol1 min, then washed again. Methylene blue, was applied for 30 sec, then washed and finally air-dried.The stained fecal slides were examined under a light microscope

Results: Among 350 examined dogs in the present study, 237 (67.7%) were male, 190 (52.2%) aged 4-7 year-old and 310 (88.6%) belonged to pet dogs.Furthermore, 195 (55.7%) of the sampled dogs were impure breed, while

155 (44.3%) were recognized as pure breed. The body condition was normal in most dogs (n = 147, 42%), and only 51 animals (14.57%) had a weak body condition. The most prevalent gastrointestinal signs in the examined dogs were diarrhea (n = 102, 29.14%), abdominal cramps (n = 91, 26%) and vomiting (n = 53, 15.14%). Of note, most of the dogs included in the present study had a rough skin (n = 113, 23.28%) or had hair loss (n = 105, 30%). The highest samples were taken during winter (n = 125, 35.71%), whereas the lowest number of samples (n = 53, 15.14%) were collected in the summer.

Conclusion: According to the results, a 14% prevalence rate was reported using microscopy of fecal smear slides stained by MZN method; Nevertheless, to reach a more reliable decision, more accurate studies using nested-PCR and semi-nested PCR assays are demanded.

keywords: Cryptosporidium, prevalence, Ziehl-Nielsen staining, Kermanshah, Dogs

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The frequency of intestinal parasites among referred individual to Imam Ali Hospital, Sarayan county, South Khorasan from 2022 to 2024

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Medical Parasitology

Background and aim: Intestinal parasitic infections are a significant health issue in Iran and many developing countries. These diseases have recently been recognized by the World Health Organization as a group of neglected tropical diseases due to a lack of attention from policymakers, insufficient prioritization in health strategies, inadequate research, and limited resource allocation in many countries. This study aimed to investigate the frequency of intestinal parasites among referred individual to Imam Ali Hospital in Sarayan County, South Khorasan Province, from 2022 to 2024.

Methods: In this cross sectional study, a total of 1150 stool samples from referred individual were examined using direct methods (wet mount) with saline and Lugol's solution. Demographic information, including gender, age, season, type of admission (inpatient or outpatient), and type of parasite (protozoa or worms), was collected.

Results: Out of the 1150 samples microscopically examined from 2022 to 2024, 32 cases (2.8%) were found to be infected with one or more intestinal parasites. The detected parasites included Entamoeba complex (1.3%, 15 out of 1150), Giardia lamblia (1.1%, 12 out of 1150), eggs of Enterobius vermicularis (0.3%, 4 out of 1150) and Trichomonas hominis (0.1%, 1 out of 1150). The highest prevalence was found in the age group under 5 years (1.1%), while the lowest prevalence was observed in the 15 to 20 age group. The highest number of

positive cases was in males (1.5%), during the spring season (0.9%) and among outpatient patients (2.2%).

Conclusion: The frequency of intestinal protozoa was higher than that of worms in Sarayan County, South Khorasan Province. Factors such as age, gender, and season may be related risk factors for parasitic infections. Therefore, it is recommended that health authorities implement accurate diagnosis and design intervention programs to reduce this public health issue in the region.

keywords: Intestinal parasite, Protozoa, Worm, Sarayan, South Khorasan province

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Dicentracin-Like from Asian sea bass Fish and Moronecidine-Like from Hippocampus Comes: Two Candidate Antimicrobial Peptides Against Leishmanina major Infection

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Medical Parasitology

Background and aim: Anti-Leishmanial drug therapy faces significant challenges related to cytotoxicity and drug resistance. Thus, new and efficient anti-Leishmanial drugs need to be identified. Due to their broad-spectrum antimicrobial and immunomodulatory activities, antimicrobial peptides (AMPs) have attracted considerable attention. In this study, we comparatively assessed the anti-Leishmanial activities of two recently identified AMPs (dicentracin-like and moronecidine-like) and the well-known AMP piscidin from the hybrid striped bass.

Methods: AMPs were first assessed against Leishmania major promastigotes using MTS. Subsequently, macrophages were infected with L. major and treated with AMPs to evaluate anti-amastigotes activity of AMPs, and non-infected macrophages were treated with AMPs to determine cytotoxicity against mammalian cells using MTS. The induction of factors limiting L. major growth (IL-12, TNF-α and reactive oxygen species (ROS)) by AMPs was measured by ELISA and dichlorofluorescin-diacetate (DCFH-DA) assay, respectively.

Results: iscidin was more efficacious against L. major promastigotes as compared to dicentracine-like or moronocidin-like peptides, whereas, dicentracine-like and moronocidin-like peptide exhibited a higher activity against L. major amastigotes compared to piscidin. In turn, piscidin was most cytotoxic in non-infected macrophages compared to the other two AMPs. A direct association was observed between hydrophobicity of AMPs and their anti-promastigote and

cytotoxic activities. Dicentracine-like or moronocidin-like peptides induced higher levels of IL-12, TNF-α and ROS in macrophages compared to piscidin.

Conclusion: ollectively, our results suggest that dicentracine-like and moronocidin-like peptides represent potentially promising multi-functional therapeutic agents that might not only directly kill L. major but also induce anti-Leishmania factors that can limit L. major growth and intracellular survival

keywords: Leishmania · Antimicrobial peptides · Anti-amastigote activity · Anti-promastigote activity

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A New Approach to the Investigation of Therapeutic Efficiency of Novel Carum copticum Nanoparticles against Leishmania major Promastigotes

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Medical Parasitology

Background and aim: Current therapies for Leishmaniasis are associated with several side effects as well as drug resistance. Sensitivity and resistance of Leishmania major to Glutamine are referred to as those isolates which are responsive or non-responsive to one or two full courses of treatment by Glucantime systematically and/or intra-lesionally, respectively. In this study, We assessed a new approach to the investigation of the therapeutic efficiency of novel Carum copticum Nanoparticles against Leishmania major Promastigotes.

Methods: First, the Carum copticum Nanoparticles were synthesized and liposomal Carum copticum was applied as a new therapeutic approach substituted for current therapy. In this experimental study, liposomal Carum copticum was prepared using the thin film hydration method and characterized based on encapsulation efficiency, size, and zeta potential. Carum copticum was successfully loaded into the liposome. The surface charge of the nanoparticle was neutral and the size of the nanoparticle was 176.5 nm. Liposomal Carum copticum beared spherical shape without any agglomeration..

Results: Results revealed that liposomal Carum copticum carried a significant effect, compared to the control sample, on parasite growth in both logarithmic

and stationary phases. The result of this study signifies that the Carum copticum Nanoparticles induces a better and more tangible effect on the survival of Leishmania major promastigotes

Conclusion: Our findings confirmed that liposomal C copticum demonstrates suitable Antileishmanial activity as well as lower side effects compared to the current drugs. The viability rate of promastigotes of rural Cutaneous Leishmaniasis, Leishmania major, treated by liposomal C copticum is timedependent in both the logarithmic and stationary phases and leads to the killing of the parasite promastigotes

keywords: Carum copticum Nanoparticles, Leishmania major, Nanoparticles, Promastigotes

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Clinical Manifestations and Molecular Identification of Giardia duodenalis in Pediatric and Adolescent Cancer Patients in Southwestern Iran

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Medical Parasitology

Background and aim: This study aimed to investigate the clinical and molecular characteristics of Giardia duodenalis (G. duodenalis) infection and identify potential risk factors in children and teenagers with malignancies in Shiraz, southwestern Iran. A total of 200 fresh fecal samples were collected from children and adolescents suffering from 32 different cancer types at Amir, Nemazee, and Saadi hospitals affiliated with Shiraz University of Medical Sciences between October 2021 and May 2022. Direct microscopy using saline and iodine wet mount was conducted, and all fecal samples were rechecked by SSU-PCR.

Methods: Subsequently, a specific fragment of the tpi gene was amplified on all samples for prevalence, sequencing, and assemblage identification. Our study found a 4% (8/200) prevalence of G. duodenalis using microscopy and PCR. The molecular findings were consistent with the microscopic results. All eight positive samples with SSU-rRNA gene were also detected as positive with tpi gene and were correctly sequenced.

Results: Among the examined cancer patients, two assemblages were identified: A [sub-assemblage AI (2/8, 25%) and sub-assemblage AII (3/8, 37.5%)] and B [sub-assemblage BIV (3/8, 37.5%)]. Notably, patients were more vulnerable to G. duodenalis infection after receiving at least 8 treatment episodes (p 0.05) and displaying gastrointestinal symptoms (p 0.05). The demographic characteristics

of cancer patients with G. duodenalis infection and the statistical conclusions were separately detailed.

Conclusion: The small sample size and low prevalence rate in this study hindered precise epidemiological conclusions. Nonetheless, the results suggest that G. duodenalis infection among cancer patients in Shiraz city originates from humans, without any specific animal groups (C–H) involved.

keywords: Giardia duodenalis, prevalence, assemblages, cancer, Shiraz, Iran

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Seroprevalence of toxoplasmosis in students of Shiraz University of medical sciences, 2019

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Medical Parasitology

Background and aim: Toxoplasma gondii is an intracellular parasite that infects a wide range of warm-blooded vertebrates, including humans. Epidemiological studies have shown that there is a high prevalence of infection with this parasite in different parts of the world. This cross-sectional study was conducted to evaluate the seroprevalence and the risk factors associated with Toxoplasma infection in students of Shiraz University of medical sciences in 2019.

Methods: A total of 425 venous blood samples were collected from students of Shiraz University of medical sciences. A structured questionnaire was completed by participants to obtain sociodemographic data such as gender, age, residence area, eating habits, type of washing vegetables, and contact with cats as toxoplasmosis risk factors. The sera samples were evaluated for the detection of anti-Toxoplasma IgG antibodies by a commercial Enzyme-Linked Immunosorbent Assays (ELISA) kit. Statistical analysis was performed using SPSS software version 18.

Results: Among the 425 participants, 111 (26.1%) were males and 314 (73.9%) were females with the mean age of 20.59±2.15 years old. Anti-Toxoplasma antibodies were detected in 35 (8.2%) out 425 cases. The association between toxoplasmosis and gender, age, residence area, eating habits, type of washing vegetables, and contact with cats were not statistically significant (p 0.05).

Conclusion: In the current study, the prevalence of toxoplasmosis in students of Shiraz University of medical sciences was lower than most similar studies and the overall prevalence of the disease in the community. Due to the fact that Toxoplasma infection in young populations, especially girls, can cause irreversible complications, prevention and control programs are necessary to prevent the transmission of Toxoplasma infection.

keywords: Seroprevalence; Toxoplasmosis; Students; Shiraz

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Seroepidemiology of toxocariasis among pregnant women in Shiraz city, Fars Province, 1401

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Medical Parasitology

Background and aim: : Human toxocariasis, an important zoonotic helminth disease, is caused by the larval stage of ascarid nematodes of dogs and cats, namely Toxocara canis and Toxocara cati, respectively. Human toxocariasis has been presented as visceral larva migrans, ocular larva migrans, neurotoxocariasis, and covert toxocariasis. This cross-sectional study was conducted to evaluate the seroepidemiology of toxocariasis in pregnant women in Shiraz.

Methods: A total of 203 sera samples were collected from pregnant women referred to the Zeinabiyyeh Hospital of Shiraz, Fars province, Iran. Sera were evaluated for anti-Toxocara IgG antibodies, using Toxocara canis excretory-secretory prepared from the second stage larvae, in an ELISA system. A structured questionnaire, containing sociodemographic data, was completed for each participant. The collected data were analyzed using SPSS software.

Results: The average age of 203 pregnant women studied was 31.99±6.954 years. Anti-Toxocara antibodies were detected in sera of 29 (14.3%) out of 203 subjects. Out of 29 seropositive cases, 16 (55.2%) had the history of abortion and 13 cases (44.8%) had no the history of abortion, and there was a significant relationship between Toxocara infection in the pregnant women and the history of abortion (p-value=0.003) and the number of abortions (p-value=0.028). However, the association between Toxocara infection and age, contact with dogs and cats, residential area, level of education, history of premature birth and number of births were not statistically significant (p0.05).

Conclusion: The findings of the study revealed a relatively high prevalence rate of toxocariasis in pregnant women. It is suggested to provide more extensive training to the general public regarding the prevention, risks, and treatment of this disease. Further study on pregnant women with a large sample size is recommended.

keywords: Seroepidemiology; Toxocariasis; pregnant women; Shiraz

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Clinical Manifestations and Molecular Identification of Giardia duodenalis in Pediatric and Adolescent Cancer Patients in Southwestern Iran

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Medical Parasitology

Background and aim: This study aimed to investigate the clinical and molecular characteristics of Giardia duodenalis (G. duodenalis) infection and identify potential risk factors in children and teenagers with malignancies inShiraz, southwestern Iran.

Methods: A total of 200 fresh fecal samples were collected from children and adolescents suffering from 32 different cancer types at Amir, Nemazee, and Saadi hospitals affiliated with Shiraz University of Medical Sciences between October 2021 and May 2022. Direct microscopy using saline and iodine wet mount was conducted, and all fecal samples were rechecked by SSU-PCR. Subsequently, a specific fragment of the tpi gene was amplified on all samples for prevalence, sequencing, and assemblage identification.

Results: Our study found a 4% (8/200) prevalence of G. duodenalis using microscopy and PCR. The molecular findings were consistent with the microscopic results. All eight positive samples with SSU-rRNA gene were also detected as positive with tpi gene and were correctly sequenced. Among the examined cancer patients, two assemblages were identified: A [sub-assemblage AI (2/8, 25%) and sub-assemblage AII (3/8, 37.5%)] and B [sub-assemblage BIV (3/8, 37.5%)]. Notably, patients were more vulnerable to G. duodenalis infection after receiving at least 8 treatment episodes (p 0.05) and displaying gastrointestinal symptoms (p 0.05).

Conclusion: The demographic characteristics of cancer patients with G. duodenalis infection and the statistical conclusions were separately detailed. The small sample size and low prevalence rate in this study hindered precise epidemiological conclusions. Nonetheless, the results suggest that G. duodenalis infection among cancer patients in Shiraz city originates from humans, without any specific animal groups (C–H) involved.

keywords: Giardia duodenalis, prevalence, assemblages, cancer, Shiraz, Iran

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Investigating the effects of the combination of Lawsonia inermis and Zataria multiflora in the treatment of cutaneous leishmaniasis caused by Leishmania major in Balb C mice

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Medical Parasitology

Background and aim: Cutaneous leishmaniasis (CL) is one of the important parasitic diseases in most parts of the world, including Iran. Antimicrobial, anti-inflammatory and antioxidant properties of Zataria multiflora and Lawsonia inermis are known. This study was conducted with the aim of investigating the anti-leishmanial activity of the herbal combination of Z. multiflora and L. inermis on cutaneous leishmaniasis in Balb C mice.

Methods: In this study, BALB/c mice infected with cutaneous leishmaniasis were treated with doses of 20 and 40 mg/kg. Mice received this treatment in two ways: injection on the sides of the wound and topical application for three weeks, and lesion size was measured before treatment and every week.

Results: The results of examining the wound size in different treatment groups showed that despite the significant increase in the wound area of the mice in the negative control group (P ≤ 0.001), the average wound area of the mice in the 20 mg/kg injection group (from 35.55 to 21.46 mm2) and 20 mg/kg local (from 32.39 to 10.24 mm2) decreased significantly (P 0.05). Also, the wound size was significantly reduced by 16.72 and 24.78 mm2 in injection and topical concentrations of 40 mg/ml respectivly. (P ≤ 0.001).

Conclusion: The results of this study showed that the simultaneous hydroalcoholic extract of Z. multiflora and L. inermis has an acceptable ability to

heal CL wounds and the local administration of this extract shows better effectiveness compared to injection into wounds.

keywords: Cutaneous leishmaniasis, Zataria multiflora, Lawsonia inermis, BALB/c

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First molecular characterization of Blastocystis subtypes from domestic animals (sheep and cattle) and their animal-keepers in Ilam, western Iran: A zoonotic concern

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Medical Parasitology

Background and aim: Blastocystis is a protozoan parasite found in humans and domestic animals, recognized as a potential zoonotic agent. Its prevalence and health implications, especially for immunocompromised individuals, highlight the need for further research. In Iran's Ilam Province, data on Blastocystis infections in livestock and their handlers are limited. This study investigates the prevalence and molecular diversity of Blastocystis subtypes in sheep and cattle, along with their human keepers, to assess zoonotic transmission risks and inform public health strategies.

Methods: A total of 360 fecal samples were randomly collected from 150 cattle, 150 sheep, and 60 humans (30 people with close animal contact and 30 individuals without close animal contact) at 10 farms in Ilam, western Iran from June 2022 to August 2023. All samples were directly examined for Blastocystis by zinc sulfate flotation, followed by microscopic observation. Positive samples were further subtyped using conventional PCR and sequencing methods.

Results: A mean prevalence of 5.3% (16/300) was estimated for Blastocystis infection among examined animals, with 6% and 4.7% for cattle and sheep, respectively. Among the people who had close and non-close animal contact, 16.7% (5/30) and 3.3% (1/30) were infected with Blastocystis, respectively (p 0.05). All 22 positive samples were successfully sequenced at the SSU rRNA locus.

Accordingly, Blastocystis isolates infecting domestic animals in Ilam belonged to the four STs (ST1-ST3, and ST10). Of the 16 animal isolates, nine sequences (four ST10, three ST3, and two ST1) were related to cattle, and seven sequences (three ST10, two ST3, and two ST2) were isolated from sheep. Among the six human isolates, ST3 was the most predominant ST, followed by STs 1, 2, 6, and 7 (one case each). Of note, ST1-ST3 were isolated in various farms both from animals and their breeders, which indicates the possible circulation of these STs

Conclusion: This study identified a 5.3% prevalence of Blastocystis in domestic animals in Ilam, with cattle (6%) more affected than sheep (4.7%). Infection rates were significantly higher in individuals with close animal contact (16.7%) compared to those without (3.3%). Four subtypes (ST1-ST3, ST10) were found, with ST3 common among humans. These findings indicate potential zoonotic transmission and emphasize the need for ongoing monitoring of Blastocystis in agricultural settings to manage health risks. Further research is essential for understanding public health implications.

keywords: Blastocystis, Zoonotic transmission, Domestic animals, Cattle, Sheep, Human infection.

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The prevalence of Cryptosporidium infection among domestic animals (cattle, sheep, and horses) in Shiraz County, Fars Province, Iran

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Medical Parasitology

Background and aim: Cryptosporidium species are parasitic protozoa that can cause cryptosporidiosis, leading to diarrhea, particularly in developing countries. While healthy individuals may have mild or asymptomatic infections, those with weakened immune systems can experience severe illness. This study employs microscopic methods to investigate the prevalence of Cryptosporidium in domestic animals, including cattle, sheep, and horses, in Shiraz County, Fars Province.

Methods: This study collected 189 fecal samples from cattle, sheep, and horses in Shiraz County, focusing on both diarrheal and non-diarrheal animals. Fecal samples were stored at 4°C and processed to purify Cryptosporidium oocysts using the saturated sugar flotation technique. After staining with the Ziehl-Neelsen method, the oocysts were examined under a 100x oil immersion lens. SPSS version 21 was used for statistical analysis, applying Fisher's exact test to evaluate the association between diarrhea and Cryptosporidium contamination (p 0.05).

Results: In this study, the prevalence of Cryptosporidium in 189 fecal samples was found to be 22.7%. Cattle had the highest rate at 10.05%, while sheep and horses had lower rates of 6.87% and 5.82%. A significant link was observed between Cryptosporidium and diarrhea, with 25.19% contamination in symptomatic

animals. These results highlight the need for monitoring infections in livestock showing gastrointestinal issues.

Conclusion: this study highlights the significant prevalence of Cryptosporidium in domestic animals in Shiraz County, emphasizing the need for ongoing surveillance and management to mitigate zoonotic transmission risks in agricultural settings.

keywords: Cryptosporidium, Domestic animals, Microscopic methods, Diarrhea, Shiraz

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Norwegian scabies in immune- compromised patients

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Medical Parasitology

Background and aim: Norwegian scabies (hypercratosis scabies) is an acute form of dermoparasitic disease in immune- compromised patients caused by Sarcoptes scabiei. This study is aimed to describe cases of Norwegian scabies cases from Ahwaz, Southwestern Iran.

Methods: Methods: Patients: Case 1: A 55 year old man with renal transplantation history, who was taken 1000 mg prednisolone daily for one year. He was complained from dermatitis and itching with sever hyperkeratosis, several macula and papules on neck and armpits for one month duration. Case 2: A 49 year old man with diabetes mellitus disorder and severe rash, hyperkratosis, and itching over his thigh, buttocks and legs. Case 3: A 74 year old disable man with autoimmune disease, complain of nocturnal itching of dermatitis lesions with sever hyperkratosis, several macula and papules on trunk, buttocks, groin, legs, thighs, fore and upper arms and armpits for more than one year duration. Case 4: A 54 year old diabetes man complained of nocturnal itching between his fingers fore more than 6 months after travelling to North and Northeast of Iran and staying in traditional poor hygiene inns.

Results: Results: Scraping from the skin lesions and slide preparation with 20% KOH was carried out. In microscopic examinations, huge infestation of Sarcoptes scabiei in all forms of parasite included adult female, nymph stage and eggs was revealed. The first patient's spouse was also infested by Sarcoptes scabiei in mild clinical signs. The disease diagnosed as Norwegian scabies and the patients were successfully treated with topical ointment of 5% permethrin for two consecutive weeks.

Conclusion: Conclusion: Norwegian scabies should be considered in immune-compromised patients in contaminated areas

keywords: Sarcoptes scabiei, Norwegian scabies, Immune- compromised patients.

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Challenges in the Molecular and Microscopic Identification of Lophomonas spp. in Respiratory Infections

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Medical Parasitology

Background and aim: Lophomonas spp., a rare and emerging protozoan parasite, presents significant diagnostic challenges due to its non-specific symptoms, morphological similarities with other microorganisms, and limitations in molecular diagnostics. Primarily associated with respiratory infections, particularly in immunocompromised individuals, it is typically identified through microscopic examination of respiratory samples, such as sputum or bronchoalveolar lavage (BAL) fluid. To address these issues, our study aimed to identify the Lophomonas parasite in BAL fluid samples from patients in the pulmonary ward of Shariati Hospital in Tehran.

Methods: A total of 368 BAL samples were collected and analyzed using both parasitological and molecular methods. For parasitological examination, samples were stained with the Giemsa method after homogenization. Molecular analysis involved PCR targeting the SSU rRNA gene to detect Lophomonas.

Results: Out of the 368 samples examined, 26 samples tested positive in the parasitological examination (Giemsa staining); however, PCR results for these samples were negative, indicating inconsistencies between molecular and parasitological findings.

Conclusion: This study evaluates current diagnostic approaches, emphasizing the limitations of both molecular and microscopic methods. Efforts to amplify the SSU rRNA gene through PCR with existing primers have been inconsistent, highlighting the need for more reliable molecular diagnostics. As a result, diagnosis primarily relies on morphological examination via optical microscopy,

which is susceptible to misidentification due to overlapping features with respiratory cells and viral-induced structures, such as ciliocytophthoria. This reliance on microscopy complicates assessment of infection severity and parasite load due to variability in sample preparation and observation techniques. Until

keywords: Lophomonas spp.; Giemsa; PCR; SSU rRNA; Diagnosis

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Identification of Fasciola species using fast PCR method

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Medical Parasitology

Background and aim: Fasciolosis, caused by the liver fluke Fasciola spp., is an important parasitic disease of humans and livestock worldwide. It is estimated that 2.4 million people are infected worldwide, with 180 million at risk in more than 70 countries. Bolivia, Peru, Egypt, Iran and Vietnam are being the most affected countries. It is essential to differentiate two species because of their different intermediate host, epidemiologic characteristics, control strategies and pattern of pathologic effects. The aim of our study is to establish a simple, rapid and accurate diagnostic method for differentiating between F. hepatica and F. gigantica using Fast PCR.

Methods: Approximately 10 gr of fresh stool samples were collected from 50 patients from Mazandaran province. Rapid sedimentation technique was used for identification of Fasciola spp.. DNA of all samples was extracted using phenol-chloroform-isoamyl alcohol technique. ITS1 rDNA region was amplified by Sapphire Amp® Fast PCR and compared with Bioneer AccuPower® Taq PCR PreMix. In addition, PCR-Restriction enzyme assay (PCR-RE) using Tsp509I was performed for identification of F. hepatica and F. gigantica.

Results: A fragment of approximately 463 bp was amplified in 29 Fasciola samples in only 34 minutes using Sapphire Amp® Fast PCR Premix, while nucleic acid amplification was completed in approximately 1 hour and 46 minutes using Bioneer PCR Master Mix. All PCR products were digested with the restriction

enzyme TasI (Tsp509I). After digestion, F. hepatica produced two fragments of 151 and 312 bp (24 samples), while F. gigantica (5 samples) produced three fragments of 93, 151 and 219 bp.

Conclusion: Fast PCR reaction using Sapphire Amp® Fast PCR Premix was completed three times faster than with conventional premix. The new Fast PCR assay using Sapphire Amp®Fast PCR Premix provides a simple, rapid, and accurate technique for the identification and differentiation of Fasciola species in diagnostic studies, infection control and epidemiologic research on humans and domestic animals in fasciolosis endemic regions and areas where it is difficult to differentiate the parasite morphologically, clinically, and immunologically.

keywords: Fasciola hepatica; Fasciola gigantica; Fasciolosis; Sapphire Amp® Fast PCR.

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Toxoplasma gondii with suicidal ideation and suicide attempts: A systematic review and meta-analysis

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Medical Parasitology

Background and aim: Suicide is a global public health problem responsible for 1 million deaths worldwide each year. Among infections caused by organisms, Toxoplasma gondii is an important cause of neurological and psychiatric disease, infecting a wide range of warm-blooded animals and approximately one third of all humans. Chronic latent infection with T. gondii is common, and most hosts have few or no symptoms. Data suggest that a positive Toxoplasma antibody titer is associated with behavioral changes in humans. The aim of our study is to investigate toxoplasmosis in suicidal ideation (SI) and suicide attempts (SA) based on epidemiologic data.

Methods: Eight databases including PubMed, Scopus, ScienceDirect, Web of Science, Google Scholar, EMBASE, CINAHL, and ProQuest were searched for all studies published between January 1, 1950 and October 31, 2019. All articles were screened based on the inclusion and exclusion criteria. All retrieved studies were carefully screened for eligibility. The pooled odds ratios (ORs) with 95% confidence interval (CI) across studies were calculated using the random effects models. Heterogeneity and risk of bias within and between studies were assessed.

Results: A total of 9,696 articles were screened and 27 studies were considered eligible for our systematic review (SI, five papers; SA, 2222 papers). In SI, IgG antibodies against T. gondii (latent infection) ranged from 5.1% to 38.1%,

whereas in controls this range was 0% to 32.9%. The pooled prevalence was calculated to be 0.90 (95% CI: 0.42, 1.94), indicating that controls and subjects with SI were not significantly different. Acute phase IgM antibodies were also not significant. Duval and Tweedie's trim and fill resulted in the same OR using the random effects model. The prevalence of Toxoplasma seropositivity was 3.5%-83.3% in patients with SA, while this range was reported to be 0%-73.4% in controls. A significant association was found between antibodies against T. gondii and SA (ORs = 1.57; 95% confidence interval 1.23-2.00, p = .000). There were association between Toxoplasma and SA in IgG antibodies, but not for IgM.

Conclusion: Our study confirmed a significant association between suicidal behavior and latent T. gondii infection. Considering that suicide is one of the leading causes of death worldwide (especially in patients with mental illness) and that Toxoplasma affects one-third of the world's population, the relationship between Toxoplasma and suicide should be of great concern to researchers.

keywords: Toxoplasma gondii; Suicidal ideation; Suicide attempts; Systematic review

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Comparison of Two Slide Preparation Methods for Parasitic eggs

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Medical Parasitology

Background and aim: Preparing high-quality, durable teaching slides is essential for educating students and laboratory staff in parasitology. Providing prepared microscope slides could be challenging because of low quality of some of them, high costs, and unavailability of certain specimens. Therefore, developing efficient and affordable methods for educational slide preparation is necessary. This research compared two techniques for preparation microscopic slide of parasitic eggs: Dehydration with alcohol and glycerin jelly.

Methods: 1. Dehydration with Alcohol and Xylene: This method specimens from three groups, trematodes (Dicrocoelium dendriticum, Fasciola hepatica), cestodes (Taenia saginata, Hymenolepis nana), and nematodes (Ascaris lumbricoides), were involved. The samples were initially fixed in 10% formalin. Then They were dehydrated through a series of alcohol concentrations: 70%, 80%, and 100%. This step was crucial for removing water, facilitating the subsequent clearing phase. After dehydration, the samples were washed, using xylene and mounted on slides with Canada balsam adhesive. 2. Glycerin Jelly Mounting: Similar to the first method, sample were fixed in 10% formalin and dehydrated. However instead of washing with xylene, 2-3 drops of glycerin jelly, pre-warmed to 40°C, were applied directly on the specimen. A coverslip was placed on top, and the sample was sealed with Canada balsam.

Results: : Comparing the two, in the dehydration method using alcohol and xylene, the eggs of Dicrocoelium dendriticum and Fasciola hepatica remained stable for up to 80 days. However, Ascaris lumbricoides eggs were stable for only 8 days. For Taenia saginata and Hymenolepis nana, this method was ineffective. On the contrary, the glycerin jelly method demonstrated higher stability for most

of the samples, eggs of Dicrocoelium dendriticum, Fasciola hepatica, and Ascaris lumbricoides has remained stable for six months. Unfortunately, this method was also failed at preparing Hymenolepis nana slides and all the eggs degenerated rapidly.

Conclusion: The study demonstrates that glycerin jelly is an effective method for preparing educational slides, particularly for trematode and nematode specimens.

keywords: Helminth eggs; Trematoda; Cestoda; Nematoda; Glycerin-Jelly

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Comparing Diagnostic Accuracy of Microscopy vs. Molecular Methods for Cutaneous Leishmaniasis in Iran

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Medical Parasitology

Background and aim: Cutaneous leishmaniasis (CL), a prevalent form of the zoonotic parasitic disease leishmaniasis, is caused by protozoan parasites of the genus Leishmania and transmitted to humans through the bites of infected female sandflies. This study aimed to evaluate the diagnostic accuracy of direct microscopy compared to molecular methods, particularly Nested-PCR, for detecting Leishmania parasites in healthcare settings.

Methods: A total of 227 Giemsa-stained slides from suspected CL cases were collected. These slides underwent initial examination through direct microscopy, with samples categorized based on parasite load into positive and negative groups, ranked from +1 to +4, while negative samples were marked as zero. DNA extraction and Nested-PCR targeting the kDNA gene, known for its high sensitivity and specificity in molecular detection, were subsequently performed.

Results: Out of the 227 samples, 109 were identified as positive and 118 as negative via microscopy. However, Nested-PCR detected Leishmania DNA in three additional samples that were previously classified as negative, raising the total positive cases to 112. The results showed a higher infection rate among men. While Giemsa-stained slides demonstrated high specificity, their sensitivity was limited, particularly in samples with low parasite loads where PCR effectively detected small DNA fragments with high accuracy.

Conclusion: Although microscopy is a reliable method for primitive screening, molecular techniques, particularly Nested-PCR, offer superior sensitivity and are

recommended for definitive diagnosis of CL in healthcare centers, especially in cases with low parasite loads.

keywords: Cutaneous Leishmaniasis, Nested-PCR, Diagnosis, Microscopy, Direct Parasitology

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Identification and Subtyping of Cryptosporidium parvum and Cryptosporidium hominis in Cancer Patients, Isfahan Province, Central Iran

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Medical Parasitology

Background and aim: Cryptosporidium spp. are protozoan parasites that cause diarrhea in humans and animals. Subtyping data about Cryptosporidium spp. in Isfahan, Iran is limited; therefore, we aimed to study the prevalence rate of Cryptosporidium spp. in cancer patients, associated risk factors, and subtypes of Cryptosporidium spp.

Methods: Fecal samples were collected from 187 cancer patients from the Oncology Department of Seyed-al-Shohada Hospital, Isfahan University of Medical Sciences during 2014–2020 and screened for Cryptosporidium spp. using microscopical techniques. Nested PCR amplifying 18S rRNA gene was used to detect Cryptosporidium spp. in samples, followed by subtyping using nested PCR amplifying gp60 sequences.

Results: Overall, the rate of infection with Cryptosporidium spp. was 4.3% (n=8). Five samples out of eight samples were identified as Cryptosporidium spp. using a nested PCR for the 18S rRNA gene, two subtypes of C. parvum named IIaA18G3R1 (n = 2) and IIaA17G2R1 (n = 2), and one subtype of C. hominis named IbA6G3 were identified by sequencing of the gp60. The IbA6G3 subtype has rarely been detected in other investigations.

Conclusion: This is the first survey on the subtyping of Cryptosporidium spp. in this region. The results of the present survey show both zoonotic and anthroponotic transmission routes in the region.

keywords: Cryptosporidium, Genotypes, Subtyping, Cancer

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Seroprevalence of Toxoplasma gondii infection in cancer patients in Southwest Iran: A case-control study

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Medical Parasitology

Background and aim: Toxoplasmosis is one of the most common parasitic diseases in the world, caused by the obligate intracellular parasite Toxoplasma gondii. The definitive hosts of this parasite are cats, but humans and livestock can play the role of intermediate hosts. The infection is usually asymptomatic in people with normal immunity, but in immunocompromised patients, including cancer patients, it can have serious consequences. Encephalitis is the most important complication of latent toxoplasmosis reactivation in immunocompromised patients. Considering the risk of serious complications of infection in these patients, this study aimed to investigate the seroprevalence of Toxoplasma gondii in cancer patients

Methods: In this case-control study, 128 patients with various cancers who were admitted to educational hospitals in Abadan and Khorramshahr cities in 2021 were selected as the case group. 128 outpatients without underlying disease of these hospitals also participated in this research as a healthy control group. For each participant, a questionnaire including demographic information and toxoplasmosis risk factors was completed. Then 5 ml of blood samples were taken from each person and checked for IgG and IgM antibodies against Toxoplasma gondii by ELISA test. The results of this research were analyzed with SPSS software version 26 and with the help of Chi-square test. P0.05 was considered significant in this study.

Results: In the patients group, 51 (39.84%) were positive for IgG and 3 (2.34%) patients were positive for anti-Toxoplasma gondii IgM. In the control group, 60

(46.88%) and 4 (3.13%) subjects were positive for IgG and IgM antibody against this parasite, respectively. There was no significant relationship between cancer and the seroprevalence of Toxoplasma gondii infection compared to the control group. In the age group over 60 years, 17 (43.6%) of cancer patients and 9 (64.3%) of the control group had anti-Toxoplasma gondii antibodies and the seroprevalence of toxoplasmosis in this age group was higher than younger participants. Female gender, living in rural areas and consumption of untreated drinking water in the control group were significantly associated with higher seroprevalence of Toxoplasma gondii infection. However, there was no significant relationship between age, sex, drinking water, history of contact with cat or soilables and other variables and seroprevalence of Toxoplasma gondii.

Conclusion: Although no significant relationship was found between cancer and seroprevalence of Toxoplasma gondii infection in this study, but due to weakness of immune system in cancer patients and the high prevalence of this parasite in the study region, there is a high risk of latent toxoplasmosis reactivation and the occurrence of severe and life-threatening complications in these patients. Therefore, it is necessary to always consider toxoplasmosis as an opportunistic infection in the management and treatment of cancer patients.

keywords: Toxoplasma gondii, Seroprevalence, ELISA, Cancer, Iran

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Bioinformatics-Driven Design of Fusion Recombinant Protein (EgFABP1-EgTeg) for Enhanced Immunodiagnosis of Hydatid Cysts

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Medical Parasitology

Background and aim: Hydatid cyst disease is caused by the parasite Echinococcus and poses significant health concerns worldwide. This disease results in the development of cysts in organs such as the liver and lungs, leading to various health problems. Early diagnosis of this disease is challenging due to the lack of definitive initial symptoms and limited diagnostic methods. Researchers are working on developing new antigens to create more specific diagnostic tools for this disease. This research aims to develop a valid antigen to enhance the diagnosis of hydatid cyst diseases.

Methods: This study focuses on designing multi-epitope antigens constructed from proteins of the Echinococcus granulosus parasite (EgTg and EgFABP1) and the IH4 nanobody. Protein sequences were validated using databases and bioinformatics tools, and B-cell epitopes were identified. The 3D structures of the antigens were predicted and their physicochemical properties were evaluated.

Results: Based on the results, the total size of the antigen resulting from the combination of the B-cell epitopes of the parasite proteins (EgTeg and EgFABP1) and the IH4 nanobody was 266 amino acids, which was confirmed by the UniProt database. The analyses reveal that this antigen lacked a signal peptide and had 46 phosphorylation sites related to serine and tyrosine amino acids. Secondary structure predictions showed a diverse structure with both alpha helices and beta sheets, while the predicted tertiary structure displayed a spherical shape with

helical domains. Linear and discontinuous epitopes were predicted, each with varying potential for immune responses, and specific regions were identified that might trigger significant immune activity. Finally, the physicochemical properties of the antigen, including molecular weight, pI, stability index, and hydrophobicity, were presented, indicating its stability and hydrophilic nature.

Conclusion: This study introduces the recombinant protein EgFABP1-EgTeg-IH4 as a novel diagnostic tool for hydatid cyst disease. By combining multiple antigenic regions with the IH4 nanobody, this protein enhances diagnostic sensitivity and specificity, demonstrating a high potential for more accurate diagnosis of the hydatid disease.

keywords: Hydatid cyst, Immunodiagnosis, Bioinformatics, EgFABP1, EgTeg

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Which one has more effect on Leishmania major amastigotes? Quercetin, Itraconazole or Glucantime

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Medical Parasitology

Background and aim: Cutaneous leishmaniasis (CL) is a disease caused by the obligate intracellular protozoan Leishmania. Various studies have reported drug resistance and significant side effects associated with the standard treatments for leishmaniasis. This has prompted researchers to explore new therapeutic options for this disease. Flavonoids, particularly quercetin, exhibit anti-leishmanial, antioxidant, and anti-inflammatory properties, and along with itraconazole, may serve as alternative treatments, especially in the context of increasing drug resistance. This study aimed to investigate the anti-leishmanial effects of quercetin and itraconazole compared to glucantime, a control drug, on Leishmania major in a cell culture environment.

Methods: In this study, the cytotoxicity of various concentrations was assessed on the RAW 264.7 cell line using the MTT assay after cell culture in RPMI 1640 medium. The standard strain of L. major was then cultured in RPMI 1640 medium, followed by the establishment of an axenic amastigote model to evaluate the effects of different concentrations (3.125, 6.25,12.5, 25, 50, 100 µg/mL) of quercetin and itraconazole compared to glucantime on the amastigote forms of the parasite.

Results: Effective doses with low toxicity were identified at concentrations of 3.125, 6.25, and 12.5 µg/mL for both quercetin and itraconazole after 48 hours of treatment. The IC50 values for quercetin, itraconazole, and glucantime after 48

hours of treatment were 15.2, 22.6, and 32.5 µg/mL, respectively. Furthermore, the P value obtained from the different treatment groups after 48 hours of treatment with itraconazole, quercetin, and glucantime was 0.03, indicating statistical significance.

Conclusion: The results of this study suggest that higher concentrations of quercetin and itraconazole have a potent ability to eliminate the amastigote forms of L. major. These compounds may serve as candidate drugs with fewer side effects for the treatment of CL and may be utilized as complementary therapies alongside standard treatments.

keywords: L. major, itraconazole, quercetin, glucantime, In vivo

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Impact of the COVID-19 Pandemic on Malaria Incidence and Epidemiological Patterns in Isfahan Province, Iran

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Medical Parasitology

Background and aim: Malaria remains a significant public health concern globally, with various regions experiencing changes in malaria incidence influenced by social, economic, and health-related factors. The COVID-19 pandemic, which began in early 2020, impacted healthcare systems and disease control efforts worldwide, including those related to malaria prevention and treatment. This study aims to evaluate the patterns of malaria incidence during and after the COVID-19 pandemic in Isfahan Province, Iran, and analyze any changes in the epidemiological trends of malaria among different population groups.

Methods: A retrospective observational study was conducted using malaria incidence data from the Health Center of Isfahan Province. The dataset spanned the years 2020–2023, covering the periods both during and following the COVID-19 pandemic. We analyzed the annual malaria cases, breaking them down by nationality (Iranian vs. Afghan migrants), gender, and malaria species (Plasmodium vivax vs. Plasmodium falciparum). Comparisons were made between the pre- and post-COVID periods to assess changes in incidence trends.

Results: In 2020, Isfahan Province reported 16 malaria cases: two among Iranians and the rest among Afghan migrants. All cases were male, with infections exclusively due to P. vivax. In 2021, the number rose to 20, again exclusively male and affecting only Afghan migrants, with one case of P. falciparum and the remainder P. vivax. By 2022, cases increased to 32, with five involving Iranians and the others Afghan migrants; all patients were male, with two P. falciparum cases noted. In 2023, the count rose sharply to 87 cases, including 17 Iranians and one female patient. Of these, five cases involved P. falciparum, while the rest

were P. vivax. This progressive increase in cases post-COVID suggests a resurgence of malaria, marked by a notable rise in infections among Iranian nationals and a gradual shift in parasite composition, with P. falciparum cases becoming more frequent.

Conclusion: The analysis reveals a significant increase in malaria incidence in Isfahan Province following the decline of the COVID-19 pandemic, with a growing number of cases among Iranian nationals and cases of P. falciparum. The rise in cases and shift in demographics may suggest changes in malaria exposure or control measures post-COVID, particularly among migrant populations. This study highlights the importance of sustained malaria surveillance and control strategies in areas with mixed populations to prevent malaria resurgence.

keywords: Malaria; COVID-19; Plasmodium vivax; Plasmodium falciparum; Epidemiology.

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Investigation of the seroprevalence of toxoplasmosis in women of reproductive age in Mazandaran province and its potential association with vitamin D difficiency

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Medical Parasitology

Background and aim: Toxoplasmosis which is caused by the protozoan parasite Toxoplasma gondii, affects pregnancies in women. Vitamin D deficiency increases susceptibility to infections and complications during pregnancy. This study investigated the prevalence of toxoplasmosis in women of reproductive age in Mazandaran province and explored the possible correlation between vitamin D deficiency and toxoplasmosis.

Methods: A total of 320 serum samples of childbearing-age women in Mazandaran province (Sari, Babol, Chalus, Nur, Tonekabon, and Ramsar) were collected. Participants completed a questionnaire providing information including age, meat consumption, cat exposure, egg consumption, soil contact, and residential location. The sera were tested for IgG and IgM antibodies against T. gondii using ELISA, and 25-hydroxyvitamin D levels were measured using a commercial kit. The results were analyzed using descriptive statistics and the Chi-Square test, as well as calculating the odds ratio, utilizing Spss software version 21. The P value 0.05 was considered statistically significant for all tests.

Results: This study showed that 198 cases (61.88%) of the studied population had anti-toxoplasma IgG, while one case (0.31%) had anti-toxoplasma IgM. Among the women who had insufficient vitamin D, 159 cases had anti-toxoplasma IgG and one sample had anti-toxoplasma IgM. Also, in people who had sufficient vitamin D, 39 samples had anti-toxoplasma IgG, and no sample had anti-toxoplasma IgM. Statistical analysis showed that the prevalence of toxoplasmosis in people with insufficient vitamin D is 1.71 times higher than those with sufficient vitamin D(OR = 1.71) and there is a significant relationship between the prevalence of toxoplasmosis and vitamin D levels.

Conclusion: High T. gondii prevalence in women of Mazandaran suggests the parasite's life cycle is established there. Lower vitamin D levels increase toxoplasmosis risk which is important for seronegative women during pregnancy, due to its dangerous effects on the fetus and mother. Therefore, monitoring vitamin D in seronegative women is crucial.

keywords: Toxoplasmosis, Vitamin D, childbearing-age, women

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Childhood Cancer and Intestinal Parasites: A Dual Burden

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Medical Parasitology

Background and aim: Intestinal protozoa are the most prevalent parasites in cancer patients. The objective of this study was to examine the prevalence of intestinal parasitic infections in patients with cancer and those under the age of 15 who were referred to healthcare centers in Yazd, Iran.

Methods: During the period of July 2021 to March 2022, 230 individuals under the age of 15 were referred to Shahid Sadoughi Hospital. This included 103 cancer patients and 127 healthy individuals. The samples were collected from these individuals. The parasitological examination was conducted using direct wet-mount detection, trichrome staining, modified Ziehl-Neelsen (acid-fast) staining, and the formalin-ether concentration technique. The data were statistically analyzed by the Chi-square test and t-test using the SPSS software version 22. P-value0.05 was considered significant for all tests.

Results: The overall prevalence of intestinal parasites in patients with cancer and healthy people was 17.4% and 3.1%, respectively (P=0.002). Giardia lamblia, Entamoeba histolytica, Blastocystis hominis, Chilomastix mesnili, Endolimax nana, Entamoeba coli, and Iodamoeba butschlii were the predominant protozoa in patients.

Conclusion: The results of this study highlight the need for special attention to parasitic infections in patients with cancer.

keywords: Intestinal diseases, Parasites, Neoplasms individual, Iran

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Burden of peritoneal infection of acute Toxoplasmosis in BALB/c Mice treated with Chitosan Nanoparticles based on Rosuvastatin

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Medical Parasitology

Background and aim: Toxoplasma gondii (T.gondii) is an obligate intracellular protozoan that infects warm-blooded animals and has a global distribution. Acute toxoplasmosis is commonly reported in patients with acquired/congenital toxoplasmosis and immune deficiency. New methods are needed to prevent the side effects of classical treatment

Methods: In this study, Rosuvastatin loaded chitosan nanoparticles (CH-NP-ROS) were synthesized and zeta potential and size were determined, Anti-Toxoplasma activity of peritoneal fluid of Balb/c mice were counted using Trypan-blue staining by different concentrations of Rosuvastatin (ROS), and Rosuvastatin loaded chitosan nanoparticle (CH-NP-ROS).

Results: Results of peritoneal fluid showed that CH-NP significantly reduced the parasite load in the CH-NP-ROS group, compared to that in the negative control group (P 0.001). Growth inhibition rates of tachyzoites in mice receiving free ROS and CH-NP-ROS (injection and oral form) were found to be 166.125+4.066, 118.750+4.596 and 124.875+2.652, respectively, compared to mice in Sulfadiazine/Pyrimethamine treated group (positive control).

Conclusion: Therefore, nanoformulation is a promising approach for drug delivery and is safe for using therapeutic effects in acute toxoplasmosis.

keywords: Acute Toxoplasmosis1, Rosuvastatin loaded - Chitosan nanoparticles2, Rosuvastatin3, parasitic burden4,

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Anti-Parasitic activity of AgNPs by Taxodium distichum on Acanthamoeba T4 strain In vitro

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Medical Parasitology

Background and aim: Acanthamoeba is a protozoan parasite that exists freely in various habitats, such as soil and water. This pathogen can lead to serious infections in humans, including keratitis and granulomatous, amoebic encephalitis, especially in immunocopromised patients and damaged epithelial layers. Its resistance to standard treatments and ability to thrive in extreme environments pose significant challenges in medical settings. This research aims to assess the anti-parasitic effects of silver nanoparticles (AgNPs) derived from Taxodium distichum by green synthesis method against the Acanthamoeba T4 strain in vitro.

Methods: The cultivation of Acanthamoeba (KU877552) was done in non-nutrient agar (NNA) medium, which is supplemented with thermally inactivated Escherichia coli to establish optimal growth conditions. For preparation of the AgNPs, at first, the methanolic extract of the Taxodium distichum was prepared and then, the AgNPs was prepared using green synthesis technique and methanolic extract of the Taxodium distichum. AgNPs was prepared at concentrations of 160, 100, 50, 25 and 12.5 µg/ml. Vital staining techniques was used to determine the live and dead Acanthamoeba cyst and trophozoites in vitro.

Results: All experiments in current study was done in triplicate. AgNPs showed that have excellent Anti-parasitic effects on Cyst form of Acanthamoeba T4 strain with time and dose dependent manner. The concentarations of 160, 100, 50 and

25 µg/ml had more effectiveness on Acanthamoeba T4 strain in comparison to the positive control groups and the concentration of 160 µg/ml was the most effective after 72 hours.

Conclusion: The experimental outcomes substantiate the potent anti-amoebic properties of AgNPs against Acanthamoeba, establishing their potential significance as either an alternative therapeutic modality or complementary treatment approach to existing medications. This is particularly relevant in the context of addressing antimicrobial resistance challenges encountered with traditional therapeutic interventions.

keywords: Anti-Parasitic activity; AgNPs, Taxodium distichum;, Acanthamoeba T4 strain; In vitro

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Innovative Approaches: Utilizing High-Resolution Melting (HRM) for Rapid Diagnosis of Asymptomatic Malaria Cases .

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Medical Parasitology

Background and aim: Asymptomatic malaria, which usually exists in low parasitemia, acts as the Plasmodium species reservoirs contributing towards malaria transmission. This situation hinders malaria elimination programs in endemic areas, thus necessitating an active case detection with a high sensitive method and treatment of cases. In this study review explores the application of High-Resolution Melting (HRM) analysis in the detection and differentiation of malaria, focusing on its effectiveness and potential advantages over traditional methods.

Methods: Comprehensive searches were conducted in major databases, including PubMed, Scopus, and ProQuest, targeting studies published between 2010 and 2023. The review examines the use of HRM analysis for detecting Plasmodium species in human and vector samples, highlighting its sensitivity and specificity.

Results: HRM analysis has shown promise in accurately identifying Plasmodium species, including asymptomatic cases with low parasitemia. It is essential to use this technique along with microscopic and RDT methods to detect Malaria Cases.

Conclusion: HRM analysis represents a valuable tool for malaria detection, providing a sensitive and efficient method for identifying Plasmodium species. Its application could enhance malaria elimination programs by enabling active case detection and timely treatment, especially in endemic areas.

keywords: Asymptomatic malaria ; High resolution melting (HRM); Microscopy; Rapid diagnostic

activity of the Olea europaea and Ficus carica on Leishmania major

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Medical Parasitology

Background and aim: Leishmaniasis is one of the six major tropical diseases that is spreading geographically in the world, with no definitivetreatment.The aim of the present study was to examine effects of Ole europaea and Ficus extracts against Leishmania major in both in vitro and in vivo.

Methods: The in vitro efficacy concentrations of 0.1–2 mg mL− 1 of O. europaea and F. carica extracts were effective for promastigote L. major at 48 h. In addition, the lesion size and parasite burden in BALB/c mice infected with promastigote of L. major were quantified for in vivo evaluation.

Results: Results showed that IC50 of O. europaea and F. carica extracts against promastigote were 1.5 and1.2 mg mL− 1. In addition, results from in vivo assay revealed that the mean size ± SD of lesions significantly decreased to 3.46 ± 0.96 and 3.65 ± 0.9 mm2 in mice treated with O. europaea and F. carica extracts, respectively, compared with that in the untreated group (p = 0.001).

Conclusion: Both extracts showed notable activity for L. major. However, further debates are required to controlling CL and inhibiting the development of lesions.

keywords: Leishmania major, Cutaneous leishmaniasis (CL), Ficus carica

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Evaluation of the antileishmanial effect of polyclonal antibodies and cationic antimicrobial peptides

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Medical Parasitology

Background and aim: Leishmaniasis is a widespread and neglected parasitic disease that affects more than 90 countries of the world yet is often limited to ineffective, expensive, and toxic treatments. Various species, parasite resistance, and simultaneous diseases are among the factors that affect the effectiveness of treatment. Peptide-based drugs have recently received attention in the development of innovative treatments. This study investigated the anti-Leishmania effect of two peptides, CM11 (Pep3) and Buf-IIIb, plus Leishmania-infected macrophage polyclonal antibody (LIMPA) to design a new treatment strategy against cutaneous leishmaniasis (CL).

Methods: The antileishmanial effect of Leishmania-infected macrophage polyclonal antibody (LIMPA) with or without different concentrations (2, 4, 6, 8, 10, 20, 40, 60, and 100 µg/ml) of CM11 and 40, 80, and 100 µg/ml of Buf-IIIb, two AMPs, was assayed in vitro by MTT, cell counting, and flow cytometry assays. Their therapeutic effects against CL of BALB/c mice for in vivo experiments were evaluated by lesion size and limited dilution assays.

Results: Results showed that LIMPA induced an anti-proliferative effect on Leishmania major growth in macrophages in vitro. CM11 with IC50 of 8.73 and 10.10 µg/ml at 48 hours and BufIIIb with IC50 of 66.83 and 80.26 µg/ml at 24

hours showed the most significant inhibition of L. major promastigotes and amastigotes. In addition, the CM11 and Buf-IIIb, with a CC50 of 9.7 µg/ml and 40.34 µg/ml, showed the most significant inhibition effect on the J774.A1 cell line at 48 hours, respectively. In addition, in vivo experiments using LIMPA with a 0.01 mg/kg dosage showed a significant difference (p0.001) in the last week of the measurement compared to the control.

Conclusion: This study is a piece of the scientific puzzle of using peptides in treating parasites, which has received less attention till now. It can open the way for future researchers for in vivo studies of peptides and their therapeutic effects. On the other hand, the observed effects of LIMPA are a perspective for continuing studies on it.

keywords: Leishmania; Rabbit Antisera; Cationic Antimicrobial Peptides; AMP; Animal model

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Comparison of skin patches and intralesional injection of ciprofloxacin and rifampin in zoonotic cutaneous leishmaniasis

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Medical Parasitology

Background and aim: Leishmania major is the causative agent of Zoonotic cutaneous leishmaniasis (ZCL) in tropical regions. The treatments used in ZCL have different results and limitations. In this study, the efficiency and effectiveness of rifampin and ciprofloxacin in mice infected with ZCL have been compared.

Methods: In this study, in the animal work section, we have used 30 Blab/c mice in 6 different groups with 5 cases in each group. These groups included as ciprofloxacin film, rifampin film, film without drug, intralesional injection of rifampin and intralesional injection of ciprofloxacin. The sixth group received the injectable meglumine antimoate drug. After the end of animal trial the size of the wound in 6 groups was entered into SPSS statistical software and the results were compared with each other.

Results: There was statistically significant differences in the percentage of wound size healing in the 6 groups of mice (P=0.0001), the best results change (decrease of lesions diameter) was related to the injectable form of ciprofloxacin, rifampin patch and ciprofloxacin patch, which were 73.47 ± 24.43, 56.60±34.08 and 50.04±28.74% respectively while the negative control group showed an average increase of 47.4% in wound size.

Conclusion: Based on the results of the recent evaluation, the use of the injectable form of ciprofloxacin and rifampin patch have the best effect on the healing of the wound.

keywords: Skin patch, ciprofloxacin, rifampin, cutaneous leishmaniasis

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Prevalence of Toxoplasma gondii Antibodies in Patients with Bipolar Disorder and Schizophrenia

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Medical Parasitology

Background and aim: The role of Toxoplasma gondii infection as a potential risk factor for psychiatric disorders, particularly bipolar disorder and schizophrenia, has been a subject of interest. This study aimed to determine the association between positive T. gondii serology and bipolar disorder and schizophrenia among patients hospitalized at Shahid Beheshti Hospital in Kerman, Iran.

Methods: In this case-control study, 78 patients with bipolar disorder and 72 patients with schizophrenia were compared.group. Serum immunoglobulin G (IgG) and IgM antibodies against Toxoplasma were measured using ELISA.

Results: A total of 66.67% of the samples were positive for IgG, while none were positive for IgM.These findings indicate previous exposure to the parasite in a significant proportion of patients.However, no statistically significant association was found between positive T. gondii serology and bipolar disorder or schizophrenia

Conclusion: The results of this study suggest that although previous exposure to T. gondii is common among patients, there is no direct association between positive serology for this parasite and the development of bipolar disorder or schizophrenia in the studied population. However, future studies with larger sample sizes and more complex designs are necessary to confirm these findings.

Additionally, the role of other risk factors and potential mechanisms in the development of these disorders should be considered.

keywords: Toxoplasma gondii, bipolar disorder, schizophrenia, ELISA, Kerman

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Identification of potential inhibitors for Farnesyl diphosphate synthase protein of leishmania spp. Through In Silico Approaches

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Medical Parasitology

Background and aim: Leishmaniasis is a parasitic disease found in subtropical, tropical, and Southern Europe. Leishmaniasis treatment is a complicated topic. Despite being limited, the current treatments are toxic and have side effects. Also, most of the time, they cannot treat the resistant form of leishmania parasites. Antileishmanial medicines, such as those derived from plants, are being researched as new medications. So according to the eye-catching role of herbs in the control and treatment of infectious disease, in this study, the effect of active substances from 150 medicinal herbs was investigated to uncover their ability to control and cure this neglected disease.

Methods: From the PubChem database, the 3D structures of the Farnesyl diphosphate synthase (FPPS) protein from Leishmania major, as well as blockers

and 2000 herbal compounds from 150 herbs, were retrieved. utilizing PyRx software and AutoDock vina, a molecular docking analysis was conducted against Leishmania protein individually utilizing herbal drugs and proteins blockers. The activity, daily carcinogenicity, and ADMET characteristics derived from Swiss ADME, Lazar, and way 2 drug. Molecules with the greatest docking scores for protein were chosen for molecular dynamic simulation using the GROMACS program version 5.

Results: According to the findings of molecular docking experiments, Strictinin have a strong affinity for the FPPS protein.

Conclusion: cording to information gathered from pharmaceutical databases, the mentioned substance may have anti-inflammatory and wound-healing properties in addition to blocking proteins. Therefore, experimentally examining these compound could be a valuable clue to the control and treatment of Leishmaniasis.

keywords: Leishmaniasis, Molecular dynamics, herbal compounds, FPPS

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Immune boosting and apoptosis Induction of Astragalus ecbatanus against Leishmania tropica

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Medical Parasitology

Background and aim: Due to the unique properties of Astragalus in treating diseases and strengthening the immune system, this study aimed to investigate, for the first time, the immune modulation and apoptosis induction by Astragalus ecbatanus extract against Leishmania tropica.

Methods: The study assessed the in vitro efficacy of the Astragalus ecbatanus extract against both the promastigote and amastigote stages of L. tropica (MHOM/AF/88/KK27). Additionally, the effects of the extract on inducing nitric oxide (NO) release and its cytotoxicity on human macrophage cells were determined by calculating the 50% cytotoxic concentrations (CC50). The study also evaluated the Caspase-3-like activity in extract-treated parasites and conducted quantitative real-time PCR to assess the expression of genes associated with T lymphocytes.

Results: Our study demonstrated that the A. ecbatanus extract significantly (P 0.001) decreased the viability of both L. tropica promastigote and amastigote forms compared to the negative control. Moreover, the extract exhibited a high selectivity index (10), indicating its strong specificity towards intracellular parasites while showing low cytotoxicity to host cells. Our results indicated a dose-dependent upregulation of the expression levels of genes for inducible nitric oxide synthase (iNOS), interferon-gamma (IFN-γ), tumor necrosis factor-alpha (TNFα), and interleukin-10 (IL-10) in macrophages after exposure to A. ecbatanus ethyl acetate extract (P 0.01). In contrast, the gene expression level of IL-10 exhibited a dose-dependent downregulation after exposure to A. ecbatanus ethyl

acetate extract. We also found that the THP-1 macrophages exposed to the A. ecbatanus ethyl acetate extract exhibited enhanced production of nitric oxide (P 0.001). Additionally, the ethyl acetate extract of A. ecbatanus significantly enhanced caspase-3 activation in

Conclusion: The results demonstrated the significant impact of A. ecbatanus ethyl acetate extract on inhibiting and eradicating Leishmania parasites in laboratory settings. While some cellular mechanisms of action were identified, such as immune modulation and apoptosis induction against Leishmania parasites, further investigation is essential to elucidate the specific mechanisms of action and assess the efficacy in animal and human populations.

keywords: Natural products, treatment, Leishmania, In vitro

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Latent Strongyloidiasis: The Critical Need for Collaboration between Clinical and Laboratory Teams (A case based study)

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Medical Parasitology

Background and aim: Strongyloidiasis, a parasitic disease caused by Strongyloides stercoralis, can present in both uncomplicated (acute and chronic) and complicated forms (disseminated and hyperinfection syndrome). Chronic strongyloidiasis, of which eosinophilia is often the only clue, is most of the time overlooked due to nonspecific intermittent clinical signs and low sensitivity of routine diagnostic methods. Diagnosis of latent strongyloidiasis is critical because of the potential risk of entering the severe phase in immunocompromised patients, which can be life-threatening.

Methods: Case presentations: This report presents five cases of strongyloidiasis involving patients aged 12 to 65 years who visited health centers in Khuzestan province over the past two years for a range of reasons, including cardiovascular diseases, elective surgeries, and routine health assessments. In these patients, the persistent eosinophilia noted in their medical records, along with Intermittent gastrointestinal and respiratory symptoms were the only indicators that raised initial suspicion of a parasitic infection. The tests conducted for the patients included the ELISA test to detect anti Strongyloides IgG, two wet mount smears of stool samples, and culture of the samples using the Nutrient Agar technique. Although all patients exhibited high antibody titers, the wet mount smear detected larvae in only two cases, while the other three cases were confirmed only through the culture method. In two cases, the initial stool sample was negative, but infection was confirmed by testing the second

Results: a

Conclusion: Recognizing latent strongyloidiasis necessitates heightened awareness and strong collaboration between the laboratory and clinic. For this purpose, the clinical team must be more aware of the potentially fatal risks of this infection, related risk factors and its minimal clinical symptoms in order to timely refer suspicious cases to the laboratory. Additionally, the diagnostic team should enhance their knowledge and facilities of the concurrent use of serological methods and more sensitive coprological techniques, such as the agar plate culture and Baerman technique.

keywords: latent strongyloidiasis; Eosinophilia; ELISA; Agar plate culture

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Investigation of the therapeutic effect of miltefosine on patients with cutaneous leishmaniasis resistant to standard treatment in Shiraz health centers

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Medical Parasitology

Background and aim: Cutaneous leishmaniasis (CL) is a common parasitic disease in tropical and subtropical regions, facing treatment challenges such as resistance against standard treatment. Due to the increasing number of treatment failures with standard drugs, the need for alternative medications is essential. Miltefosine, as a broad-spectrum antileishmanial drug, has shown potential efficacy against the Leishmania parasite.

Methods: This cross-sectional study was conducted on patients with CL who referred to health centers in Shiraz, Iran. Patients included in the study had confirmed diagnoses of leishmaniasis through direct smear and experienced treatment failure with glucantime. After obtaining written consent, initial information was recorded in a questionnaire, and a 28-day course of treatment with oral miltefosine was administered by an expert physician. Lesion size was assessed before, during, and after treatment, and any side effects were recorded. Patients were followed for three months post-treatment to monitor scar healing.

Results: In the results section of this study, among the 60 patients treated with miltefosine, 85.0% achieved complete recovery, 6.7% showed no improvement, and 8.3% experienced a relapse. These findings highlight the high efficacy of miltefosine in treating patients, although a small percentage faced no wound healing or relapse. Regarding the impact of underlying health conditions, patients

without underlying conditions had a higher recovery rate (87.9%) and a lower relapse rate (9.1%) compared to those with underlying conditions, who had 81.5% recovery and 7.4% relapse. This shows that the presence of an underlying disease can have a relatively negative effect on the treatment process, but still the majority of these patients recovered.

Conclusion: Miltefosine, as an alternative for patients unresponsive to standard treatment, can be an effective option. Its positive impact on lesion healing, high recovery rate, and lower side effects relative to conventional drugs highlight its potential as a substitute for traditional treatments especially, in patients who are resistant to standard treatment. However, further studies are recommended to evaluate the long-term safety and efficacy of miltefosine.

keywords: L. major; Miltefosine; treatment failure

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Parasitological and molecular detection of Entamoeba gingivalis and Trichomonas tenax in children from Lorestan Province, Iran

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Medical Parasitology

Background and aim: : Oral and dental hygiene plays an important role in the health and well-being of our bodies. Entamoeba gingivalis and Trichomonas tenax are reported to be anaerobic parasites found in the human mouth. These parasites are transmitted through saliva, contaminated food containers, drinking water, and/or other utensils. Since the observance of personal hygiene and discipline in taking care of oral and dental health is less in children and this affects their performance in school and their future success, we aimed to evaluate a parasitological and molecular survey of E. gingivalis and T. tenax among children (2 to 15 years) in

Methods: This descriptive cross-sectional survey was conducted from October 2021 to October 2022 on 660 children (aged 2-15 years) referred to health centers of Lorestan Province, Iran. The occurrence of protozoa within the oral cavity was assessed through microscopic examination and standard polymerase chain reaction (PCR) methodologies. Additionally, a questionnaire was utilized to gather demographic data, encompassing variables such as age, gender, residential location, educational attainment, occupation, monthly income, oral hygiene practices, and the use of mouthwash.

Results: The total prevalence of the parasites was 108 (16.4%) and 117 (17.7%) by microscopic and PCR, respectively. No meaningful association was reported

among age (P=0.716), gender (P=0.289), parent education (P=0.812), tooth brushing (P=0.170), and prevalence of these parasites in children. Conversely, a significant association was reported among settling in rural districts (P=0.002), mouthwash (P=0.001), and the prevalence of these parasites in children. By multivariate test, settling in rural districts (P=0.007) and mouthwash (P0.001) were considerably linked with the rate of these parasites.

Conclusion: We found a significant prevalence of these parasites in children in Lorestan province, Western Iran, indicating that dentists as well as children's parents should pay special attention to oral health strategies in children.

keywords: Parasites; children; prevalence; Iran

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Serological diagnosis of Toxoplasma gondii infection in patients with Ocular Toxoplasmosis

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Medical Parasitology

Background and aim: Toxoplasma gondii is an intracellular protozoan parasite that causes ocular toxoplasmosis (OT), leading to retinochoroiditis and uveitis globally. This condition primarily affects the posterior segment of the eye, with symptoms varying based on lesion location and severity. Early visual acuity loss is particularly significant when the macula is involved. In 2014, the CDC classified OT as a neglected disease, with prevalence rates ranging from 0.3% to 1% in Europe and North America, and between 2% and 25% in Brazil. Diagnosis typically involves serological tests for anti-Toxoplasma antibodies, including the IgG avidity test to distinguish between recent and past infections.

Methods: This study included 200 patients diagnosed with ocular toxoplasmosis reffered to different Hospital in Mazandaran and Tehran provinces between 2015 and 2024. The diagnosis was confirmed through characteristic retinal findings, such as yellowish-white patches and vitritis. Blood samples of 5 ml were collected from each patient and analyzed for anti-Toxoplasma IgM and IgG antibodies using the VIDAS TOXO kit, which employs an enzyme immunoassay with fluorescent detection. Ethical approval for the study was obtained from Tehran University and Farabi Eye Hospital. Data analysis was conducted using SPSS-22, applying Fisher's exact test, Pearson chi-square test, and Kappa test for statistical comparisons.

Results: In a study of 200 patients with ocular toxoplasmosis (OT), 99 were positive for IgG antibodies, and 12 were positive for IgM antibodies. Among those with low IgG avidity, all were IgG positive, and three also had IgM -positivity. Of the 12 IgM-positive patients, all tested, three and nine were positive for IgG, low avidity, and high avidity, respectively. Additionally, one patient was IgG positive with low avidity but negative for IgM. In contrast, the control group of 200 individuals had only 51 IgG positives, with no IgM- positives or low avidity cases. These results highlight significant differences in antibody profiles between patients with ocular toxoplasmosis and healthy controls.

Conclusion: In conclusion, this study underscores the importance of serological testing in diagnosing OT, revealing distinct antibody profiles among affected patients. The high prevalence of IgG positivity, coupled with the presence of low avidity IgG in some cases, suggests a complex interplay between recent and reactivated infections. Our findings highlight the necessity for increased awareness and improved diagnostic strategies for ocular toxoplasmosis, particularly in regions with higher prevalence rates

keywords: Toxoplasma gondii ; Ocular toxoplasmosis ; IgG avidity

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The prevalence of acute toxoplasmosis with an emphasis on IgM antibodies in patients referred to Aryan Laboratory of Urmia

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Medical Parasitology

Background and aim: Toxoplasma gondi is one of the most prevalent zoonotic diseases of human with a considerably high prevalence all around the globe. The infection can be serious in in patients with immunodeficiency, pregnant women and organ transplant recipients. The aime of this study was to estimate the prevalence of anti-Toxoplasma IgM seropositivity in patients referred to Aryan Pathobiology Laboratory in Urmia.

Methods: In a retrospective study, 398 patients from 2021 to 2024 with anti-Toxoplasma IgM test were enrolled. Anti-Toxoplasma IgM antibody test was performed by ELISA. The antibody titer above 8 was considered positive. Data were analyzedby SPSS software version 23.

Results: The mean age of 398 studied patients was 29.36±11.8 years from 1 to 96 years-old. Among 398 patients, 333 (85.6%) and 56 (14.4%) were females and males, respectively. The results showed that three (0.8%) patients were positive in terms of anti-Toxoplasma IgM, all three positive cases were women with the ages of 27, 5 and 32 years old. Statistical analyzes were not performed due to the small number of positive cases.

Conclusion: Based on the findings of the present study, the prevalence of acute toxoplasmosis in patients referred to Aryan Pathobiology Laboratory in Urmia is low. But similar to its prevalence in other parts of the country. However, even the low prevalence of acute toxoplasmosis, especially in women, should not be ignored.

keywords: Toxoplasma gondi, Urmia, IgM

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Antiparasitic Efficacy of Nanoemodin Extracted from Rhamnus cathartica Against Trichomonas vaginalis: An In Vitro Study

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Medical Parasitology

Background and aim: Trichomonas vaginalis (T. vaginalis) is a flagellated protozoan parasite that inhabits the genital tract and is recognized as a sexually transmitted infection. Although various treatments have been developed, Metronidazole remains the standard therapeutic agent; however, its adverse effects have led researchers to seek alternative remedies. This study aims to evaluate the antiparasitic efficacy of nanoemodin, an active compound extracted from Rhamnus cathartica (R. cathartica), against T. vaginalis in vitro.

Methods: Samples of T. vaginalis were obtained from vaginal secretions of women attending medical facilities in Mazandaran province, northern Iran. Ethanol-based extracts of R. cathartica were prepared, and nanoemodin was isolated at varying concentrations. A viability assay was conducted on trophozoites using concentrations of 50, 100, 200, 400, and 800 µg/ml of the plant extract containing nanoemodin. The viability of the trophozoites was assessed through trypan blue exclusion staining at 3, 6, 12, 24, and 48 hours using a Neubauer chamber.

Results: Both R. cathartica extracts and nanoemodin exhibited significant antiparasitic activity against T. vaginalis across all tested concentrations. Notably, concentrations of 400 and 800 µg/ml of nanoemodin, along with 800 µg/ml of R. cathartica extract, demonstrated superior anti-T. vaginalis effects compared to the positive control.

Conclusion: The results suggest that the inhibitory effects of R. cathartica, particularly its nanoemodin extract, surpass those of Metronidazole. While further studies are essential to validate these findings in animal models and clinical settings, the preliminary results are promising and highlight the potential of nanoemodin as a therapeutic agent for trichomoniasis.

keywords: Trichomonas vaginalis, Rhamnus cathartica, nanoemodin, in vitro

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Investigating the anticancer effect of Toxoplasma gondii lysate antigen on colorectal cancer cell lines

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Medical Parasitology

Background and aim: Toxoplasma gondii is an obligate intracellular pathogen that can infect the nucleated cells of most warm-blooded animals. It has been reported that Toxoplasma gondii infection can suppress the development of some tumors. Colorectal cancer is one of the most common and deadly cancers in the world. One of the factors involved in the progression of colorectal cancer is macrophage migration inhibitory factor (MIF). MIF can activate the ERK1/ERK2-MAPK pathway and regulate HIF-1α activity in a TP53 dependent manner and promote essential processes such as cell proliferation, survival, angiogenesis and tumor invasion.

Methods: Toxoplasma gondii lysate antigen (TLA) was prepared and its concentration was measured using the Bradford method. Then its toxicity was measured on the cell lines (SW480, SW948 and HEK293) by the MTT assay. In the final experiment, the effect of the parasite on the gene expression of MIF, ERK1, HIF-1α and P53 was measured in duplicate in 72 hours by RT-PCR method. Finally, the results were analyzed with REST software.

Results: The results of this study show that the use of TLA in a 72-hour exposure to colorectal cancer cell lines can reduce ERK1 gene expression (P-Value0.05) in SW480, SW948 and HEK293 cell lines can reduce survival and growth, metastasis in cancer cells. Also, decreasing Pi3K gene expression (P-Value0.05) in SW480 cell

line can cause a better prognosis in cancer treatment, TLA also decreased HIF-1 gene expression (P-Value0.05) in HEK293 cell line, which It is involved in the induction of hypoxia and cell death.

Conclusion: Considering the difficulties of treatment, complications and high costs of treatment in colorectal cancer, the use of novel treatment methods can be helpful. In this study, according to the results obtained, TLA can help in improving the cancer process and preventing tumor metastasis.

keywords: Toxoplasma gondii, anticancer, colorectal, cell line

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Systematic Review of the Anticancer Properties of Hydatid Cyst Fluid from Echinococcus granulosus

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Medical Parasitology

Background and aim: Cancer continues to pose a significant global health challenge, necessitating innovative therapeutic strategies. Hydatid cyst fluid (HCF), derived from the larval stage of Echinococcus granulosus, has shown promising anticancer properties across several studies, with effects noted on cell viability, apoptosis induction, immune modulation, and tumor growth inhibition. However, the precise mechanisms of these effects are not fully understood. This review synthesizes findings from recent experimental studies to elucidate the potential pathways through which HCF exerts antitumor effects, aiming to inform future research and therapeutic applications.

Methods: We conducted a systematic literature review following PRISMA guidelines. A comprehensive search was performed across three databases: Web of Science, Scopus, and PubMed using keywords such as "hydatid cyst fluid," "Echinococcus granulosus," "anticancer," "apoptosis," and "tumor inhibition." Studies were screened for relevance based on inclusion criteria, which encompassed experimental studies evaluating HCF's effects on cell viability, apoptosis, immune response, or gene expression in cancer cell lines or animal models. Data were extracted on study design, cancer models, HCF treatment methods, key outcomes, and relevant biomarkers to ensure a robust synthesis of evidence.

Results: HCF demonstrated significant antitumor effects across multiple cancer models, including breast cancer (MDA-MB-231, 4T1), melanoma (A375, B16F10), and colon cancer (C26, CT26). HCF treatment reduced cancer cell proliferation,

increased apoptosis, and modulated immune response by altering cytokine levels and activating immune cells. Additionally, HCF enhanced expression of tumor-suppressing microRNAs (e.g., miR-1, miR-365) and pro-apoptotic genes (e.g., Bax, Caspase-3) while downregulating anti-apoptotic markers. Notably, specific HCF fractions (e.g., 78 kDa and glycoprotein) showed enhanced effectiveness, reducing tumor size and extending survival in animal models.

Conclusion: This systematic review underscores HCF's potential as a multifaceted anticancer agent, offering evidence of its effects on apoptosis, immune modulation, and tumor suppression across diverse cancer models. HCF could provide a foundation for developing novel cancer immunotherapies or adjuvant therapies. Further research, particularly clinical studies, is necessary to validate these findings and elucidate the mechanisms of HCF's anticancer action.

keywords: Hydatid cyst fluid; Anticancer; Apoptosis; Immune modulation; Tumor inhibition.

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Safe Voltage Identified for Electrotherapy in Treating Cutaneous Leishmaniasis: A Step Forward in Wound Healing

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Medical Parasitology

Background and aim: Electrical stimulation has been shown to aid wound healing in both animals and humans. This modality can influence cellular behaviors, including migration, proliferation, and angiogenesis, making it a promising method for treating various types of wounds, particularly cutaneous leishmaniasis. Cutaneous leishmaniasis, caused by Leishmania parasites, remains a major health concern, especially in endemic areas like Iran. Current treatments often lead to scarring and prolonged healing. This study aimed to determine the optimal voltage for ohmic skin resistance in BALB/c mice, thus providing a basis for electrotherapy applications for skin wounds, such as those associated with cutaneous leishmaniasis.

Methods: A controlled circuit was designed using a voltmeter, power supply, rheostat, and electrodes to apply direct electric currents with varying voltages and exposure times on the tail base of BALB/c mice. The study included multiple stages, with voltages ranging from 3V to 30V applied for different durations to assess the effects on skin resistance and tissue tolerance.

Results: The optimal conditions for applying electricity without inducing skin damage in BALB/c mice were identified at 3V for 120 seconds. Higher voltages (≥6V) resulted in visible skin lesions, and voltages above 15V were tolerated for only short durations due to severe skin and muscle reactions. With lower

voltages, current flow remained stable over time, suggesting minimal tissue damage. Furthermore, results demonstrated that lower voltages delayed the decline in current intensity, indicating greater skin resistance and reduced cellular stress.

Conclusion: This study identified 3V as the most suitable and safe voltage for electrotherapy applications in BALB/c mice, offering stable current and minimal skin damage. These findings provide critical data for establishing electrotherapy parameters for cutaneous leishmaniasis treatment and enhancing wound healing strategies.

keywords: Wound healing; Electrotherapy; Cutaneous leishmaniasis; Skin resistance; BALB/c mice.

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A Retrospective Analysis of Human Cutaneous Leishmaniasis Epidemiology during 2016-2021 in Hoveyzeh County, Khuzestan Province, Iran

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Medical Parasitology

Background and aim: Leishmaniasis, a significant neglected tropical disease, is caused by the obligate intracellular protozoa of the Leishmania genus. This research aimed to investigate the epidemiology of cutaneous leishmaniasis(CL) from 2016 to 2021 in Hoveyzeh County

Methods: The current study is a retrospective cross-sectional descriptive study based on available data. The statistical population includes all people treated and followed up in health care centers, diagnosed clinically with CL, and confirmed by laboratory tests.

Results: Among the 628 individuals diagnosed with CL, 324 (51.6%) were male, and 304 (48.4%) were female. patients had an average age of 16.58±15.17 years. The highest proportion (45.4%) of cases occurred in the age group of 0–10 years, emphasizing the vulnerability of children. In contrast, those above fifty had the lowest incidence (3.7%). Approximately 68.2% of patients resided in urban areas, while the remainder lived in rural settings. The hand was the most frequently affected area (44.5%), and the maximum number of lesions reported in one

individual was 25. Topical Glucantime along with cryotherapy was administered to most patients (46.82%). Disease incidence showed seasonal variation, with the highest number of cases observed in autumn (54%) and a significant presence in December (22%). The peak year for incidence was 2016 (30.3%)

Conclusion: Effective strategies to combat this disease should include comprehensive public awareness campaigns focusing on health education, early recognition of symptoms, and methods of transmission. Promoting personal protective measures is crucial for disease prevention efforts.

keywords: Cutaneous leishmaniasis, epidemiology, Hoveyzeh, Khuzestan, Iran

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Seroprevalence and risk factors associated with toxoplasmosis among the butchers of Tabriz City, the northwest of Iran

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Medical Parasitology

Background and aim: Occupation plays an important role in the spread of infectious diseases in humans. Toxoplasmosis is world-wide diseases with different routes of transmission. This study aimed to investigate the prevalence of toxoplasmosis and risk factors associated with this diseas among the butchers of Tabriz City, the northwest of Iran.

Methods: In this case-control study conducted in Tabriz city in 2023, 250 serum samples were collected from butchers (n = 125) and outpatients referred to Imam Reza Hospital (n = 125) and considered as the case and control groups, respectively. The ELISA test was used to identify IgG and IgM antibodies against toxoplasmosis. The results were analyzed by descriptive statistics tests using SPSS v. 16 software.

Results: The results indicated that 66/125 (52.8%) cases and 40/125 controls (32%) were positive for toxoplasmosis IgG antibody. Also, 5/125 (4%) and 1/125 (0.8%) were positive for toxoplasmosis IgM antibody in the case and control groups, respectively. The main risk factors: were age, education level, and work experience.

Conclusion: Our results suggest the high prevalence of toxoplasmosis IgG antibodi in butchers of Tabriz, which required special attention and basic measures.

keywords: Butchers, Frequency, Iran, Risk factors, Toxoplasmosis

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Epidemiological Dynamics and Demographic Influences on Malaria Incidence in Chabahar, Southeastern Iran (2019-2024)

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Medical Parasitology

Background and aim: Malaria, transmitted by Plasmodium parasites via Anopheles mosquitoes, and Anopheles mosquitoes, is a significant global cause of illness and death. This retro study provides a comprehensive overview of the malaria situation in Chabahar, Southeast Iran, from 2021 to 2024. It examines the prevalence of malaria, factors contributing to its transmission, and its potential to impact the local population and healthcare system significantly. This underscores the profound significance of this research and its potential to save lives and improve public health.

Methods: Blood samples were collected from suspected malaria cases at Chabahar health centers. Each positive case was recorded, along with demographic information, in a questionnaire. Health centers in Chabahar City collected blood samples from suspected malaria cases of all ages, from infants to individuals over 51 years old. Blood smears and rapid tests were used to definitively detect malaria. A standardized questionnaire was used to record demographic data, such as sex and nationality, for positive cases. SPSS version 26 software and T-tests were used for statistical analysis.

Results: This study reveals a pressing and urgent situation regarding malaria in Chabahar and its suburbs in Southeast Iran. A peak in malaria cases was observed in 2023, with an annual incidence rate of 5.32 percent. In 2021, 84.9% of cases were P. falciparum; in 2023 and 2024, 98.7% and 98.9% were P. vivax, respectively. Most cases occurred in September, underscoring the need for immediate and decisive action.

Conclusion: This study's findings highlight the pressing necessity of enhancing preventive and control strategies for malaria. They stress the importance of specific, tailored strategies, such as improving prevention and treatment efforts, strengthening healthcare systems, and developing health infrastructure. These strategies, tailored to the unique conditions of Chabahar and its suburbs, should consider climatic trends and precipitation levels, emphasizing the need for precision in our interventions. To effectively manage malaria in areas like Sistan-Baluchistan, we must prioritize prompt treatment, prevent mosquito breeding, raise awareness of symptoms, and monitor frequent travelers to neighboring

keywords: Malaria, Epidemiology, Prevalence, Iran

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Introducing a sensitive chemical based fecal occult blood test without false positive results

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Medical Parasitology

Background and aim: Background: Nowadays chemical-based (gFOB) and immunological-based (FIT) methods are used for diagnosis of fecal occult blood in the world. In chemical-based tests the hematin part of hemoglobin reacts with a chromogenic material in the presence of hydrogen peroxidase. So, in patients eating fruits and vegetables, false positive results may occur. In this investigation a chemical based occult blood test has been developed in which reaction of hemoglobin with the chemical material of the test take place in the absence of hydrogen peroxidase, so following consumption of vegetables and fruit no false positive results occur.

Methods: Methods: For estimation of analytical sensitivity serial dilution of the blood was prepared in distilled water and then they were tested. For investigating false positive results different fruits and vegetables such as radish and orange were tested with this methods and also other fecal occult blood kits which were available in the market.

Results: Results: From analytical point of view the developed test is able to detect 60 nanogram or more hemoglobin in one milliliters of water. Results of the test with different fruits and vegetables showed that while different chemical based fecal occult blood kits had false positive results, the test developed in this work has no false positive results with fruits and vegetables.

Conclusion: Conclusion: The test developed in this work has a high sensitivity without any false positive results.

keywords: Keywords: Fecal occult blood, Sensitivity, False positive

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The Relationship between Toxoplasma Infection and Thyroid Disorders in Immunocompromised Individuals

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Medical Parasitology

Background and aim: Toxoplasma gondii is an intracellular parasite that can cause serious infections in individuals with compromised immune systems. This parasite, particularly in those with autoimmune diseases or immunodeficiencies, can lead to various complications. Thyroid disorders, including hypothyroidism and hyperthyroidism, are recognized as potential complications in patients with Toxoplasma infection. This article examines the relationship between Toxoplasma infection and thyroid disorders in individuals with immune deficiencies.

Methods: Methods: In this study, 98 patients with immune deficiencies were evaluated. Blood samples were collected from the patients and tested for IgG and IgM antibodies against Toxoplasma gondii using the Enzyme-Linked Immunosorbent Assay (ELISA). Additionally, the thyroid hormones levels were measured for Thyroid-Stimulating Hormone (TSH), Tri-iodothyronine (T3) and Thyroxine (T4). The results were analyzed using SPSS software and appropriate statistical tests, including chi-square tests for categorical variables and t-tests for continuous variables, to determine the significance of the results.

Results: Out of the 98 samples examined, 35 (36%) tested positive for Toxoplasma gondii. Among the infected individuals, a significant percentage, 55% (19 patients) were found to have thyroid disorders. Specifically among thyroid abnormalities: Hypothyroidism was diagnosed in 11 patients (58%), characterized by elevated levels of Thyroid-Stimulating Hormone (TSH) and decreased levels of the thyroid hormones Tri-iodothyronine (T3) and Thyroxine (T4). Hyperthyroidism was recognized in 7 patients (37%), showing suppressed TSH

levels alongside elevated T3 and T4 levels. Statistical analysis documented that the mean TSH level in patients positive for Toxoplasma was significantly higher (p 0.01) compared to those who tested negative. In contrast, the mean levels of T3 and T4 were significantly lower (p 0.01) in the Toxoplasma-positive tested group. These results suggest a strong association between Toxoplasma infection and thyroid dysfunction in immunocompromised patients. The elevated TSH levels in the infected group indicate that the thyroid gland

Conclusion: This study demonstrated that Toxoplasma infection may act as a risk factor for thyroid disorders in individuals with immunocompromised systems. The elevated TSH levels and decreased T3 and T4 levels in patients positive for Toxoplasma propose a negative impact of Toxoplasma on thyroid function. These results highlight the importance of monitoring thyroid function in immunocompromised individuals, particularly those infected with Toxoplasma. Improved clinical management approaches could be settled based on these insights, highlighting the need for closer monitoring of thyroid health in vulnerable population. At last, further research is essential

keywords: Toxoplasma gondii, thyroid disorders, immunocompromised individuals, hypothyroidism, hyperthyroidism

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Anti-protozoal activity of Aloe-emodin against protoscoleces of Echinococcus granulosus genotype G1 and G3 in vitro

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Medical Parasitology

Background and aim: Hydatid cyst disease is one of the most important parasitic diseases worldwide. Humans are accidental intermediate hosts of this disease, and albendazole and mebendazole are among the most commonly used drugs for its treatment. However, this treatment has several limitations for the host. The purpose of this study is to investigate the antiparasitic effects of aloe-emodin on the larval stage of Echinococcus granulosus genotypes G1 and G3 in vitro.

Methods: The larval stage of E. granulosuswere were obtained from hydatid cysts from infected livers of the sheep at Babol city slaughterhouse. The cysts were sterilized with 70% alcohol and the fluid was extracted. After settling, the supernatant was removed and 100,000 parasites were added to each well of a 96-well plate. Different concentrations of drugs were added and the plates were incubated at 37°C. Viability was assessed using eosin staining at 3, 12, and 24 hours.

Results: The results showed that aloe emodin had anti-parasitic effectiveness in a time and dose dependent manner. The concentrations of 400 and 800 µ/ml

after 24 hours had statically similar anti-parasitic effect to the positive control. Also, Aloe Emodin has a higher effectiveness in all concentrations and times with a significant difference compared to the negative control group.

Conclusion: From the results, it can be determined that Aloe Emodin can be considered as a suitable option for the treatment of hydatid cyst disease.

keywords: Echinococcus granulosus, Aloe Emodin, Hydatid cyst

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Prevalence of anti-Toxoplasma IgG and IgM seropositivity among patients referred to Shahid Beheshti Hospital in Maragheh, North West Iran

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Medical Parasitology

Background and aim: Toxoplasmosis is a global infection caused by the intracellular parasite Toxoplasma gondii, which is transmitted through eating undercooked meat, contact with cat feces, and during pregnancy. At least one-third of the world's population is infected with this parasite. Since positive levels of anti-toxoplasma IgG cannot distinguish acute infections from chronic infections, therefore, in addition to determining anti-Toxoplasma IgG, anti-Toxoplasma IgM were also evaluated to determine the prevalence of acute toxoplasma in women referred to Shahid Beheshti Hospital in Maragheh, North West of Iran. for pregnancy screening tests.

Methods: In a retrospective study, 364 sera were collected from women referred to Shahid Beheshti Hospital in Maragheh, East Azerbaijan, from March 2020 to April 2024. Sera were tested for IgG and IgM titers using enzyme-linked immunosorbent assay (ELISA) kit. According to cut of ELISA kit, antibody titer higher than 1.1 was considered positive for both antibodies. The data was analyzed using SPSS statistical software

Results: : The average age of 364 patients in the study was 29.02 ± 7.3 (std.) years from 14 to 40. Out of 364 patients, 230 (63.2%) were IgG positive and two (0.5%) were anti-Toxoplasma IgM positive. In this study, it was found that the highest prevalence is related to 2024 with 7.8% positivity, which is statistically significant compared to previous years (P ≤ 0.001).T mean age in people with positive anti-Toxoplasma IgG was 29.26% and in women who were negative in terms of anti-

toxoplasma IgG, the average age was 28.88%, which was not statistically significant.

Conclusion: The findings of the present study showed that the prevalence of acute toxoplasmosis in women referred to Shahid Beheshti Hospital in Maragheh is very low compared to most regions of Iran, but it indicates an increased risk of intrauterine transmission, so the appropriate time to perform the first serology test at the beginning of pregnancy and the first trimester of pregnancy is very valuable

keywords: Toxoplasma gondii; toxoplasmosis; Maragheh; IgG; IgM

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A survey on the anti-Trichomonas vaginalis effect of the hydroalcoholic extract of various medicinal plants in vitro

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Medical Parasitology

Background and aim: Trichomoniasis is the most common non-viral sexually transmitted infection worldwide; although it is treated by a 5-nitroimidazole drug family such as metronidazole (MTZ) with numerous side effects, and in this regard, alternative new drugs are required. Therefore, this study examined the anti-Trichomoniasis effect of the hydroalcoholic extract of some traditional medicinal plants of Iran in vitro.

Methods: In this experimental study, the hydroalcoholic extracts of medicinal plants were prepared by maceration at a stock concentration of 20 mg/mL in the saline solution and then used for in vitro anti-trichomonas experiments. Trichomonas vaginalis trophozoites were isolated from the patient and cultured in a Trypticase Yeast extract Iron-Serum-33 medium. In addition, 200 µL of the culture medium containing 5×104 trophozoites was diluted in plate wells, and 10 doses were separately added on trophozoites for each extract serially diluted between 0.12 and 16 mg/mL in triplicate. The plates were incubated for 48 hours at 37 ° C with 5% CO2 . The number of trophozoites was counted with a hemocytometer and Trypan blue staining. Finally, the half maximal inhibitory concentration (IC50) was calculated by probit analysis.

Results: Among the tested plants, Eugenia caryophyllata, Camellia sinensis, and Terminalia chebula Retz showed the best anti-trichomonal activity with IC50 values of 1.21, 1.62, and 1.66 mg/mL, respectively. All tested extracts had more IC50 than MTZ (IC50 100 mg/mL), an antiprotozoal drug used as a positive control.

Conclusion: According to the results of this study, E. caryophylata, C. sinensis and T. chebula Retz affected the growth of T. vaginalis. Thus, it is recommended that other studies use this plant for the treatment of trichomoniasis infection.

keywords: Medicinal plants, Hydroalcoholic extracts, Trichomonas vaginalis, Trophozoites, In vitro

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Identification and genotyping of Echinococcus granulosus from clinical samples collected from humans in Guilan province

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Medical Parasitology

Background and aim: Cystic echinococcosis (CE) poses a considerable health challenge in both human and veterinary medicine, originating from the tapeworm Echinococcus granulosus (E. granulosus). This study aimed to explore the molecular diversity of E. granulosus by analyzing paraffin-embedded human tissue samples (FFPE) through sequencing of mitochondrial genes.

Methods: Thirty-five FFPE tissue samples were collected from different regions of Guilan province, north of Iran. Demographic data were recorded using a questionnaire. Five sections (1 mm) of the tissue were prepared and deparaffined using xylene and ethanol methods. Molecular analysis was performed using the Nad1 and Cox1 genes using PCR and DNA sequencing.

Results: In total, there were 25 female cases (71.43%) and 10 male cases (28.57%). The age group most affected was between 21 and 30 years old. The majority of cysts were found in the liver (n = 19; 54.29%), while the remainder were located in the lungs (n = 16; 45.71%). The Cox1 and Nad1 genes were successfully amplified from 16 (45.71%) and 12 (34.28%) DNA samples obtained from FFPE tissue, respectively. Sequencing analysis indicated that all samples belonged to the E. granulosus sensu stricto complex (G1 and G3).

Conclusion: This study identified the E. granulosus sensu stricto complex G1 and G3 in human hydatid cysts, indicating the involvement of the sheep/dog transmission cycle in human infections. These findings corroborate and expand upon earlier research regarding the geospatial distribution of E. granulosus sensu stricto complex G1 and G3 in the southern and coastal regions of the Caspian Sea.

keywords: Echinococcus granulosus, Hydatid cyst, Genotype, Northern Iran

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A case report of Toxocara canis egg in stool of a 20 year old male

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Medical Parasitology

Background and aim: We present the case of a 20-year-old male who was admitted to the Tehran 24-Hour Shahrdari Clinic with complaints of abdominal pain and rapid defecation following food intake.

Methods: Stool examination and complete blood count (CBC) analysis were conducted. The stool examination, performed using a direct smear method, revealed the presence of Toxocara canis eggs. CBC results indicated a white blood cell (WBC) count of 11,000, with 84% neutrophils, 6% eosinophils, and 10% lymphocytes, measured using the KX-21 Sysmex analyzer. The patient reported no history of pet ownership or close contact with animals.

Results: The stool examination, performed using a direct smear method, revealed the presence of Toxocara canis eggs.

Conclusion: The stool examination, performed using a direct smear method, revealed the presence of Toxocara canis eggs.

keywords: Toxocara canis, Visceral Larva Migrans

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Determination of Entamoeba Complex Species in Patients Referred to the Imam Reza Hospital Laboratory in Birjand

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Medical Parasitology

Background and aim: Amoebiasis, an infection caused by the protozoan parasite Entamoeba histolytica, is a highly significant disease that can lead to numerous complications and mortality in humans. Although Entamoeba histolytica, Entamoeba dispar, and Entamoeba moshkovskii are morphologically similar, the pathogenic mechanisms of Entamoeba dispar and Entamoeba moshkovskii remain unknown. Different species of Entamoeba are identified by their various genotypes. Considering the importance of identifying the prevalence of different species and genotypes of this protozoan, the present study aimed to molecularly identify the various genotypes of Entamoeba species in patients referred to the Imam Reza Hospital laboratory in Birjand during the years 2023-2024.

Methods: In this descriptive-analytical study, a total of 350 stool samples from patients referred to the Imam Reza Hospital laboratory in Birjand were collected through non-random convenience sampling during the years 2023-2024. The samples were examined using both microscopic and molecular methods. The data obtained from the study were analyzed using SPSS software.

Results: Microscopic examination revealed that out of the 350 samples analyzed, the prevalence of the Entamoeba complex was 35 (10%), Blastocystis was 13 (7.3%), and Giardia lamblia was 5 (1.42%). Nested-PCR results showed that out of the 35 positive Entamoeba complex samples, 20 samples (57.1%) were Entamoeba coli, 11 samples (31.5%) were Entamoeba dispar, 2 samples (5.7%) were Entamoeba histolytica, and 2 samples (5.7%) were Entamoeba moshkovskii. In this study, no significant relationship was observed between the relative

prevalence of the Entamoeba complex and age, gender, education level, residence, or occupation (P value ≥ 0.05).

Conclusion: The results of this study indicate that the Entamoeba complex is prevalent among patients referred to the Imam Reza Hospital laboratory in Birjand and requires greater attention. Furthermore, the lack of a significant relationship between the relative prevalence of the Entamoeba complex and factors such as age, gender, education level, residence, and occupation may point to the complexities of the epidemiology of these infections. These findings underscore the necessity for further research to better understand the factors influencing the prevalence and distribution of these parasites

keywords: Entamoeba complex, molecular & microscopic methods, Birjand

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In vitro study of Glia maturation factor beta as a new predictive factor for neuro-impairment in toxoplasmosis

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Medical Parasitology

Background and aim: Toxoplasma gondii (T. gondii), a neurotropic protozoan, infects up one to third of the world population. The parasite can invade a wide variety of nucleated cells but preferably glial cells. Glia maturation factor β (GMFβ), a 17KD protein which is expressed at high levels in the central nervous system is predominantly related to neurodegenerative diseases such as AD, PD, and MS. This study was designed to determine the expression level of GMFβ and its relation to other pro-inflammatory factors (IL33, SDF1, and CCL2) on T. gondii infected human neuroblastoma cell line.

Methods: The human neuroblastoma (SK_NMC C535) cell line was infected by 5⊆106 (1:1 ratio). The supernatant was collected after cell lysis and centrifugation. Total RNA was extracted using the Yekta Tajhiz RNA extraction kit. cDNA was synthesized based on RevertAid First Strand cDNA Synthesis Kit manufacturer`s protocol (Parstous, cDNA synthesis kit, Iran). The specificity of each primer pair (GMFβ, IL33, SDF1, and CCL2) was provided by NCBI BLAST. Gene expression level was measured using Real-Time PCR.

Results: The GMFβ increased significantly up to 1.35 fold (p=0.007). The increase in GMFβ expression in neuroblastoma cells was consistent with the increase in pro-inflammatory factors (CCL2 (0.47), IL33 (0.152) and, SDF1 (1.33)).

Conclusion: The results of this study suggest that GMFβ upregulation can be a novel indicator of the destruction of nerve cells.

keywords: Toxoplasma gondii, Glia Maturation Factor, GMFβ, Interleukin-33, IL33, Chemokine CCL2,

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Prevalence and risk factors associated with toxocariasis in psychiatric inpatients in Fars Province, southern Iran

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Medical Parasitology

Background and aim: Toxocariasis is a zoonotic helminthic parasitic disease. Despite global epidemiological surveys, limited information on the seroprevalence of Toxocara infection in psychiatric patients is available. Therefore, the aim of the present study was to assess seroprevalence of Toxocara infection and to identify the correlated risk factors among psychiatric inpatients in Fars Province, Iran.

Methods: A cross-sectional study was conducted from March to July 2021 among 318 psychiatric patients hospitalized in Ibne Sina Hospital. Psychiatric patients were divided into four major psychotic disorders according to DSM-V and clinical criteria, including anxiety, mood, personality, and psychotic disorders. Sera were assessed for IgG against Toxocara using enzyme-linked immunosorbent assay based on Toxocara larvae excretory-secretory antigens.

Results: The overall IgG seroprevalence was 10.0% (32/318; 95%CI=7.0–13.9). Subgroup analysis revealed that the highest and lowest seroprevalence of Toxocara infection was found in patients with contacts to garden soil or gardening activities (32.1%) and in patients, who lived in the city (4.4%), respectively. After adjusting for confounders, age ≤30 years (adjusted odds ratio [AOR]=6.98, 95%CI=2.34–20.82, p0.001), living in rural communities (AOR=7.65, 95%CI=2.71–21.54, p0.001), raw vegetable consumption (AOR=3.28,

95%CI=1.18–9.13, p=0.023) and horticulture or agricultural activities (AOR=4.28, 95%CI=1.64–11.21, p=0.002) remained a significant risk factors. Moreover, multivariate logistic regression analysis demonstrated that Toxocara exposure was not related to suicidal behavior in psychiatric inpatients.

Conclusion: The current results provide baseline epidemiological data regarding the seroprevalence of toxocariasis and modifiable risk behaviors to plan effective prevention strategies in psychiatric inpatients in southern Iran.

keywords: Psychiatric patients, Suicidal behavior, Toxocara, Risk factors, Iran

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Investigating the prevalence of Enterobius vermicularis in elementary school children in Urmia city in 1403

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Medical Parasitology

Background and aim: Enterobius vermicularis is one of the human parasitic nematodes and lives in the cecum and end areas of the digestive system. It is estimated that about one billion people in the world are infected with this parasite and the infection is more common in children than other ages. The purpose of this study is to investigate the prevalence of Enterobius vermicularis infection in preschool children in Urmia City

Methods: Sampling was done after coordinating with parents of students and getting their consent, as well as educating parents from all areas of Urmia City and 12 elementary schools using the Scotch test method. In this way, after providing the necessary training to the parents of the students and placing the necessary equipment for sampling, and reminding them that the sampling was carefully attached to the anus area using adhesive tape near the morning and was removed from there at around 8 am. then the samples were examined microscopically with 100 and 400 magnification, and on the other hand, spss software was used for statistical analysis

Results: Of the participants, 11.3% of cases (6.9% male and 4.4% female) were infected with E.vermicularis. The highest prevalence was observed in the fifth-grade students. There was no significant relationship between some symptoms such as drooling, sucking fingers, and nail-biting, and their gender, but it was

significant for tooth grinding during sleep. The level of infection has a significant relationship with the number of people in the family, and the larger the family, the higher the level of parasite infection. Also, family culture and lifestyle can increase or decrease the parasite burden

Conclusion: Considering the prevalence of Enterobius vermicularis among primary school students, it was a relatively significant study and it causes sleep, growth, and learning disorders in children, it is suggested to hold training courses held for parents and preventive measures are taken to promote health in the region. Also, considering the relationship of this parasite with the population, education, and prevention of this parasite in large communities such as schools must be prioritized.

keywords: Enterobius vermicularis, Investigating, prevalence, Urmia

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Investigating the prevalence of Cryptosporidium in people with diarrhea referring to medical diagnosis laboratories

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Medical Parasitology

Background and aim: Cryptosporidium is an intestinal protozoan and one of the apicomplexan parasites that can infect a wide range of vertebrates. This protozoan causes self-limiting diarrhea in people with efficient immunity but causes diarrhea in people with ineffective immunity. It becomes intense. The purpose of this study is to check the amount Investigating the prevalence of Cryptosporidium in people with diarrhea referring to medical diagnosis laboratories

Methods: In this study, 1000 samples of diarrheal feces were collected from the laboratories of Urmia city and after transferring the samples to Kia Tashkhis research company, all the samples were coded and listed and then concentrated by formalin ethyl acetate method. They were prepared and stained with Nielsen's modified dye produced by Kiateshchis company. All the samples after staining were examined with 500 magnification

Results: Out of the 500 samples collected, 15 samples contained Cryptosporidium parasite, which is about 0.03%. Out of the 15 samples, 5 were women and 10 were men, and by examining the history of the patients, it was found that two of the patients had the disease. They were autoimmune and treated with corticosteroid drugs. Data analysis was done through spss and chi-square statistical test. In this study, there is a relationship between gender and infection with this parasite, so the level of infection was significantly higher in boys than in girls (p0.05)

Conclusion: This study emphasizes the use of appropriate diagnostic methods to identify Cryptosporidium in medical diagnostic laboratories and also recommends the common use of these methods for mucous and watery diarrheal stool samples, especially in immunocompromised people. It seems that the way of life, health conditions, and people's habits and customs do not affect getting Cryptosporidium. Also, in the case of children suffering from diarrhea with symptoms of gastroenteritis, in addition to other enteropathogens that cause diarrhea, Cryptosporidium should also be considered, and a specific stool test. be done

keywords: Cryptosporidium, diarrhea, diagnosis

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Investigating the prevalence of intestinal parasitic infections in primary school students in Urmia

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Medical Parasitology

Background and aim: Intestinal parasitic infections are still a serious public health problem in the world. It is estimated that some 3.5 billion people are affected and that 450 million are ill as a result of these infections, the majority being children. The high prevalence in children is attributed to many factors, particularly the social and economic situation of the individuals is an important cause of the prevalence of intestinal parasites. The purpose of this study was to investigate the prevalence of intestinal parasitic infections in elementary school students in Urmia City

Methods: The study design was cross-sectional. This study was conducted at nine primary schools chosen by randomized cluster sampling from urban areas of Urmia City is capital of West Azerbaijan province, which is located in the Northwest of Iran. 400 primary school students were randomly selected from a list of 9 schools. The questionnaire included age, gender, place of residence, parent's education and occupation, family size, and water sources. They were examined for the presence of parasites by wet mount, formaline–ether sedimentation techniques and cellophane tape was used to detect Enterobius vermicularis infection. Also, for the ease of recognizing the English genus and species, chrome coloring made by the Kia Tashkhis company was used. Data were analyzed using SPSS 11 for Windows

Results: The subjects consisted of 243(60.3%) boys and 160(39.7%) girls, aged between 7-12 years. In all, 45 students(11.25%) were infected with one or more intestinal parasites. The most common was Giardia lamblia 19(4.75%), Entamoeba coli 10(2.5%), Blastocystis hominis 9(2.25%), Enterobius vermicularis 4(1%), Iodamoeba butschilii 2(0.5%) and Hymenolepis nana 1(0.25%) infected primary school children. 109(26.9%) students were infected with one parasite, 35(8.75%) with two parasites, 7(1.75%) with three parasites 3(0.75%)

Conclusion: The results of the study indicate a high prevalence of some intestinal protozoans especially Giardia lamblia and a great amount of helminth in the area. In contrast based on the present study and other studies in various areas and times intestinal parasite infections with world spread are one of the most important health indexes. Despite their different prevalence in various societies and ages and even decrease or eradication, intestinal protozoan infections especially Giardiasis and Amebiasis are very important problems that societies are suffering from them

keywords: Investigating, intestinal parasitic, infections

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Evaluation of the relationship between the level of IgG and IgM antibodies of Toxoplasma gondii intracellular protozoa with cardiovascular biomarkers in the center of Mazandaran province.

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Medical Parasitology

Background and aim: Toxoplasma gondii is an intracellular protozoan that has high incidence in developing countries, especially in Iran. Considering that Toxoplasma gondii, as an opportunistic parasite, causes mild or asymptomatic disease in healthy people, and after the acute phase, enters the latency phase and causes cysts in the heart and muscle tissue, there is a hypothesis that it is possible It causes cardiovascular problems Therefore, this study was designed to investigate the relationship between Toxoplasma gondii infection and cardiovascular disorder in Mazandaran province.

Methods: A case-control study was conducted on 110 people with cardiovascular diseases and 110 healthy people. The data collection tool included personal information questionnaire, possible confounding variables, questions related to the clinical characteristics of cardiovascular diseases and possible methods of Toxoplasma gondii infection. After taking blood samples from people, the level of Toxoplasma gondii IgM and IgG antibodies was measured by ELISA method. Chi-square and univariate regression tests were performed to measure the relationship between the variables related to cardiovascular disorders between the case and control groups. and the statistically significant variables were included in multiple logistic regression statistical analysis to control the effect. All findings were considered significant with a level of less than 0.05.

Results: In total, out of 110 blood samples from the case group, IgG antibody test was positive in 31 (28.30%) blood samples and negative in 69 (75.70%). In the control group, out of 110 samples, 8 (8.70%) samples tested positive and 102 (91.30%) samples tested negative. According to the results of the K-square test, this difference in the percentage of positive cases between the two groups was significant and it can be said that there is a statistically significant relationship between the IgG antibody result and the group (case/control) (P0.05). Out of 220 blood samples from the case and control subjects in this study, no positive IgM test samples were reported. The distribution of the percentage of Toxoplasma gondii IgG in the two case and control groups shows that the percentage of positive Toxoplasma gondii in the case group is approximately 3 times that of the control group.

Conclusion: According to the results obtained from the present study, infection with Toxoplasma gondii parasite can be recognized as one of the risk factors related to cardiovascular disease.

keywords: Toxoplasma gondii; cardiovascular disease; IgG; IgM.

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The effect of different concentrations of hypertonic saline at different times on hydatid cyst protoscolex isolated from sheep liver and lung

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Medical Parasitology

Background and aim: Echinococcosis in humans and animals is an economic and public health concern in many parts of the world. The infection is most prevalent in sheep- and cattle-raising regions like Australia, South America, the Middle East, South Africa, Eastern Europe, and the Mediterranean region. Cystic hydatid disease affects mainly the liver (50–70% of all cysts) but can also develop in the lung (20–30%) and, less frequently, in the spleen, kidney, bone, brain, and other organs. The objective of this study is to determine the sporicidal effect of hypertonic saline in different concentrations using different exposure times

Methods: After the concentration of protoscoleces at the end of the tube the viability of protoscolices was confirmed by their motility under a light microscope and protoscolices stained with 0.1% eosin were examined at room temperature. Any protoscolex that did not import dye was accepted as potentially viable. The mean number of protoscoleces in the cyst fluid obtained from different cysts in different periods was found as 1000 protoscoleces/mm3 and fourteen samples of 0.5 cc sediment were obtained. Various concentrations of 1 cc sodium chloride solutions were added to each sediment (1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20% respectively). We waited 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,…….29, and 30 minutes for each concentration, following which the upper portions of the

solutions were removed. The remaining settled protoscolices were then washed in normal saline and after staining, examined for viability

Results: Protoscolex survival ratios after exposure to different concentrations of sodium chloride at different times indicated that 20% hypertonic saline had a strong scoliosis effect, as it eliminated all protoscolexes at the end of 9 minutes. 10% hypertonic saline killed 90% of protoscolexes in 30 minutes

Conclusion: hypertonic saline with a concentration 20% killed all protoscoleces of hydatid cyst at the end of 9 minutes. Hypertonic saline did not cause any systemic side effects when it was applied intraperitoneally. Surgery remains the treatment that has the potential to remove Echinococcus granulosus cysts and cure completely. The main principle of surgery is to prevent scoliosis by placing swabs soaked in scoliosis material. The use of Protoscolicidal agents to kill protoscolexes intraoperatively is questionable because there is no ideal agent that is both effective and safe

keywords: hypertonic saline, hydatid cyst, protoscolex

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Inhibitory and therapeutic effect of Plasmodium berghei on intestinal cancer induced in Balb/C. mice

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Medical Parasitology

Background and aim: Colon cancer is one of the most common diseases of the digestive system. Plasmodium, one of the most important parasites, can be considered for the treatment of cancer, and good studies have been done in this regard in the past. Our goal in this study is to investigate the effect of Plasmodium berghei in suppressing intestinal cancer in mice

Methods: CT26.WT mouse colon cancer cell line was purchased and used in (RPMI) 1640 medium containing 10% (FBS) and penicillin-streptomycin 1% (100 units/ml of penicillin and 100 µg/ml of streptomycin) under 37°C and 5% CO2 in an incubator. Ten BALB/c mice were inoculated subcutaneously with 0.1 ml of CT26.WT cell suspension. (106 x 5/ml) for each mouse's right forelimb axilla. On the day of tumor formation (on the sixth day After tumor cell injection), 10 mice were randomly selected They were divided into two groups (5 animals in each group). in CT26.WT+P.y group, as Plasmodium berghei infected group, 1x106 was injected intraperitoneally into each mouse with Red blood cells infected with Plasmodium berghei. Control group mice (CT26.WT) were injected intraperitoneally. Apoptosis was assessed by dUTP deoxynucleotidyl transferase (TdT) staining and the expression of apoptosis-related proteins including Bax, Bcl-2, caspase-9, caspase-3 and important proteins, PINK1/Parkin by western blotting and immunohistochemistry respectively

Results: We found that Plasmodium infection decreased the weight and size of tumors and decreased the expression of Ki67 in colon cancer-bearing mice. Furthermore, Plasmodium infection promotes mitochondrial-mediated apoptosis in colon cancer cells, as up-regulated by increasing the proportion of TUNEL-positive cells. Bax, caspase-9, and cleaved caspase-3 proteins and low expression of Bcl-2 protein. In colon cancer cells, we found degraded cell nuclei, swollen mitochondria, missing cristae, and a reduced number of autolyzed outcomes. In addition, Plasmodium infection impaired mitochondrial biogenesis and mitophagy. Expression of PGC-1α, PINK1, and Parkin proteins in colon cancer cells

Conclusion: Because of the high incidence and mortality associated with colon cancer, researchers to reduce Mortality and improve the quality of life of patients are continuously looking for new treatments to inhibit the growth of colon cancer, so we investigated this issue in this study

keywords: Plasmodium berghei, intestinal cancer, suppression, BALB/c mice

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Understanding Hydatid Disease: Demographics and Risk Factors in Gilan Province, Iran

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Medical Parasitology

Background and aim: Background: Hydatid disease, caused by the tapeworm Echinococcus granulosus, presents a significant zoonotic infection in developing countries, including Iran. Gilan Province is recognized as one of the endemic regions for this disease. Objectives: This study aimed to analyze the demographic and clinical data of surgically treated patients with hydatid cysts in Gilan Province over a four-year period from March 21, 2019, to March 20, 2023.

Methods: A retrospective cross-sectional study was conducted in selected hospitals in Gilan Province. Out of 48 diagnosed patients, 40 underwent surgery, and 31 were available for interviews regarding their demographic data. Information was obtained from medical records and structured interviews that focused on key risk factors such as history of contact with dogs, livestock farming, presence of free-roaming dogs in living areas, type of residence, frequency of rural visits and vegetable cultivation.

Results: Among the 31 interviewed patients, 9 were men (29%) and 22 were women (71%). The locations of the cysts were as follows: 25 patients (80.6%) had cysts in the liver, 4 (12.9%) in the lung, 1 (3.2%) in the spine, and 1 (3.2%) in the liver, with the source originating from the spleen. Significant findings regarding risk factors revealed that 52.6% of women and 37.5% of men had a history of contact with dogs, while 47.4% of women and 25% of men reported a history of livestock farming. The presence of free-roaming dogs in living areas was noted in 100% of men and 89.5% of women. Additionally, 60.9% of participants resided in rural areas, and 82.6% reported frequent visits to rural locations.

Conclusion: This study highlights critical demographic patterns and risk factors associated with hydatid cyst disease in Gilan Province, underscoring the need for targeted public health interventions. Increased awareness and preventive measures focusing on high-risk practices, particularly in rural communities, are essential for controlling the spread of hydatid disease in endemic regions.

keywords: Hydatid Cyst Echinococcus granulosus Demographics Risk Factors Gilan Province

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High prevalence of toxoplasma gondi infection in societal maladjustment prisoners in comparison with the control group in Shahrekord prisoners in 2022-2023

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Medical Parasitology

Background and aim: There is scanty evidence about the prevalence or relation between Toxoplasma Gondi infection and societal maladjustment. Epidemiological studies have shown that toxoplasmosis has a relationship to the increase of some psychological disorders like schizophrenia, bipolar disorder, epilepsy, and Alzheimer's disease and could increase the trend of suicide and depression. Also, some research pointed to people with chronic toxoplasmosis as adventurous and brave, which causes immoral functions in society such as content, scuffling, and skirmishing. So this study aimed to investigate the prevalence of Toxoplasma gondi infection in societal maladjustment prisoners in comparison with the control group in Shahrekord prisoners in

Methods: In this study, 310 male prisoners from Shahrekord prisoners were participated. They were in 2 groups of 155 prisons, in which case (societal maladjustment) and control (finance crimes). Injection drug addicts were exclusion criteria. The checklist contains demographic characters, causes of being inmates, kinds of societal maladjustment, and psychological disorders like hallucinations, nervousness, anxiety, and depression. From all prisons, 5 ml of blood was taken, and after separating their serum, the level of antibodies against Toxoplasma gondi was measured by the ELISA method. Finally, the results were entered into the checklist, and their statistical analysis was done.

Results: Our results showed the frequency of toxoplasmosis was 32.6% in prisoners with societal maladjustment and 25% in the control group and the difference in the two groups was significant. In this study, robbery, murder, conflict, and rape were reported by 113 (41.9%), 23 (8.5%), 95 (35.2%), and 22 (8.1%), respectively. A significant difference was observed between committing crimes. (P0.001)

Conclusion: Considering that the serum level of anti-toxoplasma antibodies in prisoners with multiple crimes such as murder, theft, conflicts, and also psychological disorders in these people was higher than in the control group, it is highly probable that the parasite Toxoplasma gondi can be effective. Therefore, treating people to reduce crime and psychological disorders can be a suitable complementary solution.

keywords: Toxoplasma gondi; Prisoner; societal maladjustment

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Presentation and management of an Epicardial Hydatid Cyst: A Case Report

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Medical Parasitology

Background and aim: Echinococcosis or hydatidosis is a zoonosis parasitic infection caused by Echinococcus genius. Hydatid cysts predominantly involve the liver and lungs; however, instances of involvement in cardiac tissue are rare. This study reports the occurrence of hydatid cyst within the heart with considerable disease points in Tehran, Iran.

Methods: Case presentation A 50-year-old woman, originally from a village in Lorestan Province, had a medical history that includes rectal adenocarcinoma, hypothyroidism, and a cardiac mass. She was admitted to Rasoul Akram hospital in Tehran in 2021. The patient, diagnosed with colon cancer, underwent a laparotomy and received chemotherapy four years prior. Additionally, the patient has been receiving treatment with levothyroxine for hypothyroidism. A subsequent evaluation was conducted using a CT scan, which revealed the presence of an epicardial mass located between the left anterior descending coronary artery (LAD) and the left obtuse marginal artery (OM) on the left ventricle.

Results: Case presentation A cardiac hydatid cyst measuring 2.9×4.9 cm was located in the lateral wall of the left ventricle. The patient was receiving treatment with Albendazole at a dosage of 400 mg orally every 12 hours, and the

patient was scheduled for an operation. Puncture Aspiration Injection Respiration (PAIR), along with the injection and aspiration of the cyst, was conducted prior to the resection. Both macroscopic and microscopic examinations revealed a cream-green, multiloculated, partially cystic mass with a firm wall, measuring 4 cm by 3.5 cm by 0.5 cm. In the examined section, a grayish-white membranous tissue exhibiting areas of yellowish discoloration was observed. Ultimately, the pathology results confirmed the diagnosis of a hydatid cyst accompanied by fibrosis and chronic inflammation. The cardiac cyst was surgically removed, and the patient recovered without any complications.

Conclusion: Cardiac hydatid cyst is a very rare disease. Rapid diagnosis including CT scan and MRI along with appropriate surgical and medical intervention is essential for effective treatment. It is important to consider hydatid cysts when evaluating heterogeneous echogenic lesions, particularly in instances where serological tests are negative.

keywords: Cardiac; Epicardial; Left ventricle; Hydatid cyst

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Antileishmanial and immunomodulatory activities of the formononetin against Leishmania tropica

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Medical Parasitology

Background and aim: Leishmaniasis is a parasitic infection prevalent in various regions of the world and is classified as a neglected tropical disease. Recent studies have demonstrated that natural products serve as a significant source of anti-infective agents. This research aims to investigatethe leishmanicidal, cellular mechanisms and cytotoxicity effects of formononetin (FMN), a natural isoflavone, against Leishmania tropica.

Methods: We used the MTT assay to determine the leishmanicidal effects of FMN against promastigotes and its cytotoxicity effects on J774-A1 macrophage cells. The Griess reaction assay and quantitative real-time PCR were used to determine the nitric oxide (NO) and the mRNA expression levels of IFN-γ and iNOS in infected J774-A1 macrophage cells.

Results: FMN significantly (P0.05) decreased the viability and number of promastigotes and amastigotes forms. The 50% inhibitory concentrations value for FMN and glucantime was 9.3 and 14.3 µM for promastigote and amastigote, respectively. We found that the macrophages exposed with FMN especially at concentrations of 1/2 IC50 and IC50 significantly activated the NO release and the mRNA expression levels of IFN-γ, iNOS.

Conclusion: The findings of the current research demonstrated that formononetin, a natural isoflavone, has promising antileishmanial effects against various stages of L. tropica. It achieves this by reducing the infectivity rate of macrophage cells and triggering the NO production and cellular immunity through inhibition of infectivity rate of macrophage cells and triggering the NO production and cellular immunity. However, further studies are necessary to assess the efficacy and safety of FMN in animal models before progressing to clinical trials.

keywords: Natural products; treatment; Leishmania; In vitro

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PARASCORE: A Novel Logistic Probability Model for Rapid Parasitic Infection Risk Assessment in Clinical Settings

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Medical Parasitology

Background and aim: Early detection of parasitic infections remains challenging, especially in resource-limited settings. Current diagnostic methods require sophisticated equipment and skilled personnel, while clinical symptoms often lack specificity. Existing risk assessment tools are unstandardized and imprecise, leading to diagnostic delays or unnecessary testing. PARASCORE introduces a quantitative approach that integrates multiple risk factors into a single, rapid assessment tool. The model combines epidemiological data with clinical observations, weighing symptoms, environmental exposure, laboratory findings, and temporal factors. This evidence-based framework enables efficient risk stratification, optimizing resource allocation and improving patient care across endemic and non-endemic regions.

Methods: We developed a logistic regression-based model synthesizing four key predictive variables: symptom severity (S), environmental exposure risk (E), laboratory value deviations (L), and time since exposure (T). Each variable was assigned specific weighting coefficients (w_1-w_4) based on meta-analysis of existing parasitological literature and clinical data. The formula generates a probability score between 0 and 1, with ≥0.7 indicating high infection risk. Model validation was performed using retrospective data from 500 confirmed parasitic infection cases and 500 controls across three medical centers. Sensitivity and specificity were calculated using ROC curve analysis. Statistical significance was set at p0.05.

Results: PARASCORE demonstrated 88.5% sensitivity and 84.2% specificity in predicting parasitic infections. The area under the ROC curve was 0.91 (95% CI: 0.88-0.94, p0.001). The model showed strongest predictive value for intestinal

protozoa (accuracy 91.3%) and helminth infections (accuracy 87.6%). Environmental exposure (w_2) and laboratory values (w_3) emerged as the strongest predictors (OR 2.8, 95% CI: 2.3-3.3). Implementation reduced unnecessary testing by 42% while maintaining diagnostic accuracy. The mean time to risk assessment decreased from 48 hours to 15 minutes compared to traditional evaluation methods.

Conclusion: : PARASCORE represents a significant advancement in rapid parasitic infection risk assessment, offering a standardized, quantitative approach for clinical decision-making. The model's high sensitivity, specificity, and substantial reduction in diagnostic delays demonstrate its practical utility in both resource-limited and well-equipped settings. Implementation of PARASCORE could optimize resource allocation, reduce unnecessary testing, and accelerate appropriate treatment initiation. Future studies should focus on validating this tool across diverse geographical regions and expanding its application to specific parasitic species.

keywords: Parasitic diagnostics; Risk assessment; Mathematical modeling; Clinical decision support

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The effect of imatinib alone and in combination with albendazole on protoscoleses and microcysts of Echinococcus granulosus

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Medical Parasitology

Background and aim: None of the existing drugs can effectively treat the human cystic echinococcosis. Since a vaccine is not yet available, and in light of emerging resistance is seen, the search for alternatives has high priority. This study aimed to evaluate the efficacy of Imatinib and in combination with albendazole on protoscoleces and cysts of Echinococcus granulosus by in Vitro method.

Methods: Drug-loading and entrapment efficiency also were obtained. E. granulosus protoscoleces and microcysts were treated with Imatinib. E. granulosus protoscoleces and microcysts were treated with Imatinib at the final concentrations of 1, 2.5,5,10 and 15 µg/mL for microcysts and 5,10,20,40 µg/mL for protoscoleces and the conentration for both Imatinib and Albendazol is 5,10,20 µg/mL in period of 14 days. The viability rate of the protoscoleces or microcysts and differences in cysts weight were compared by ANOVA, and the number of the cysts was compared using the Kruskal–Wallis test.

Results: respectively. Incubation of protoscoleces with the 40 µg/mL for 15 days resulted in 100% mortality, while after incubation with 40 µg/mL Imatinib, the protoscoleces viablity rate was only 44.0% ± 5.22%. Destruction of the microcysts was observed after 7 days exposure to Imatinib at the concentration of 10 µg/mL

Conclusion: The results clearly indicated that Imatinib were effective against E. granulosus protoscoleces and cysts both in vitro.

keywords: Echinococcus Imatinib Albendazol in vitro

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Investigating the relationship between vitamin D levels and patients with Blastocystis hominis infection

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Medical Parasitology

Background and aim: The present study was conducted with the aim of measuring vitamin D levels in patients referred to the Yazd Central Laboratory. The inclusion criteria for this study were people who were diagnosed as positive for Blastocystis hominis parasite infection by direct observation of feces using the Wet Mount method. Then, we separated the serum of these people and examined it for vitamin D levels. The gaps that may exist in this study are low vitamin D levels (in healthy people and in people with infection), and vitamin D levels in children and adults,

Methods: This study was carried out at Yazd's Central Laboratory between Khordad 1 and Azar 1, 1403. The procedure involved centrifuging the whole blood of those who tested positive for this parasite infection by direct stool testing. If they had a test sheet to measure vitamin D levels, the serum sample was sent to the appropriate department, where it was measured using a specialized vitamin D level device and entered into the laboratory system. D3 was the kind of vitamin D that was examined. In conclusion, data was gathered on all individuals who had been referred to our laboratory during these six months, had an infection with Blastocystis hominis, and had requested a serum vitamin D level measurement. 48 of the 66 individuals with Blastocystis hominis infections who were registered during this six-month period had their vitamin D levels examined.

Results: SPSS version 21 was used to perform additional tests (ANOVA, t.test) on the findings of vitamin D analysis obtained using the measuring device. The results showed that the D3 levels were significantly lower than normal subjects. Thus, the vitamin D3 levels in 82.5% of women and 75% of men were less than 30, which was more than the healthy subjects who were found to be deficient in

this vitamin in previous research (61.9% for women and 45.6% for men). 30 to 100 was the normal level range.

Conclusion: Blastocystis hominis is a protozoan parasite in the human digestive system that can reduce the absorption of important minerals, including vitamin D, in the body. Vitamin D has very important functions, including a role in the immune system, so a deficiency of this vitamin can in some way cause other parasites to freely operate in the body

keywords: : Blastocystis hominis, Vitamin D ,Vitamin D3, Immune system

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Exploring the Relationship Between Toxoplasmosis Infection and Vitamin D Deficiency: A systematic review and A Meta-analysis

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Medical Parasitology

Background and aim: Background and Aim: This study investigates the relationship between Toxoplasmosis infection and vitamin D deficiency, as prior research has yielded inconsistent findings regarding their association. Understanding this relationship is crucial for public health, particularly in regions with high Toxoplasma prevalence.

Methods: Methods: We conducted a comprehensive search of the PubMed, Science Direct, and Scopus databases for studies examining the correlation between Toxoplasmosis infection and vitamin D levels. Relevant observational studies were analyzed to determine the prevalence of Toxoplasma gondii in individuals with differing vitamin D status

Results: Results: The analysis revealed that a study in Iran indicated a higher prevalence of Toxoplasma infection (28.57%) among vitamin D deficient individuals compared to those with normal levels (17.14%). However, other observational studies reported no significant differences in vitamin D levels between infected and non-infected individuals. Notably, a study in Saudi Arabia found significantly lower serum vitamin D levels in Toxoplasma-positive women, suggesting a potential correlation. The immune-modulatory effects of vitamin D could influence susceptibility to Toxoplasmosis.

Conclusion: Conclusion: While certain studies suggest a significant association between vitamin D deficiency and Toxoplasmosis infection, the variability in

results necessitates further research to clarify this relationship and explore underlying mechanisms.

keywords: Keywords: Toxoplasmosis, vitamin D deficiency, Toxoplasma gondii, immunomodulation, public health.

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Investigating the therapeutic effect of emodin extracted from Rhamnus cathartica extract on mice infected with hydatid cyst

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Medical Parasitology

Background and aim: Hydatid cyst (HC) is one of the most prevalent common zoonotic diseases and global health problems. Medicinal plants, such as Rhamnus cathartica (native to northern Iran), offer an alternative with antimicrobial and anti-parasitic properties. This study was aimed to investigate the therapeutic effect of emodin extracted from Rhamnus cathartica extract on HC.

Methods: Hydatid cysts were collected from sheep livers and treated with emodin at concentrations of 100, 200, 400, and 800 µg/ml in sterile PBS containing the antibiotic gentamicin and with 1 ml of RPMI culture medium containing 1000 protoscoleces at 37 degrees with 5% CO2 for 10 times. It was incubated for 10, 20 and 60 minutes. At the end of the incubation time. Viability was assessed using 0.1% eosin dye. Albendazole with concentrations of 100 and 200 µg/ml was used as a positive control. Finally, the results at different concentrations and times were analyzed and the IC50 value was determined and reported. In order to investigate in vivo, 35 healthy BALB/c mice were divided into five groups of 7 after intraperitoneal injection of protoscoleces and cyst formation. The study included 3 groups treated with concentrations of 50, 100 and 200 mg/kg/day of emodin, 1 group of albendazole therapy ...

Results: This extract had a relatively good lethal effect on protoscoleces, so that after 10 minutes of incubation, the rate of cell death in the treatment group with emodin 800 µg/ml was significantly higher than Albendazole 100 and 200 µg/ml. Also, after 20 minutes of incubation, the rate of cell death in the treatment with emodin 800 and 400 µg/ml was significantly higher than the treatment with

albendazole 100 and 200 µg/ml. However, after 60 minutes of incubation, the death rate of protoscoleces was not significant between the two groups of Emodin with a concentration of 800 µg/ml and Albendazole 200 µg/ml. The IC50 value for emodin was calculated at different times, 1512, 780 and 141 µg/ml after 10, 20, and 60 minutes, respectively. The animal study showed no significant difference between the albendazole and emodin treatment groups regarding the number of hydatid cysts. The results showed that treatment with ....

Conclusion: Emodin from Rhamnus cathartica demonstrates strong scolicidal effects, particularly under laboratory conditions, with enhanced efficacy at higher concentrations and longer exposure times. In vivo, emodin shows comparable effects to albendazole in reducing cyst weight and numbers. These findings highlight emodin's potential as an effective, plant-based alternative treatment for HC.

keywords: Emodin, Hydatid cyst, Albendazole

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Evaluating the Anthelmintic Potential of Eucalyptus globulus on Hydatid Cyst Protoscolices in Vitro

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Medical Parasitology

Background and aim: Hydatid disease, caused by the larval stage of Echinococcus granulosus, poses significant health challenges, particularly in livestock. Traditional treatments, such as albendazole, have limitations, prompting the exploration of alternative therapies. This study investigates the in vitro effects of Eucalyptus globulus on hydatid cyst protoscolices, aiming to evaluate its potential as an effective anthelmintic agent.

Methods: Protoscoleces were isolated from the infected liver of sheep obtained from a slaughterhouse, with a concentration adjusted to 1000 protoscoleces/mm³. The protoscoleces were treated with varying concentrations of Eucalyptus globulus (100, 200, 400, and 800 µg/ml) over incubation periods of 10, 20, and 60 minutes. Albendazole (100 and 200 µg/ml) was used as a positive control, while PBS was used as a negative control. Each treatment was performed in triplicate.

Results: After 10 minutes, the 400 and 800 µg/ml Eucalyptus globulus treatments showed no significant difference in effectiveness compared to albendazole at 200 µg/ml, and were more effective than albendazole at 100 µg/ml (p0.05). At 20 minutes, the 800 µg/ml concentration of Eucalyptus was equally effective as albendazole at 200 µg/ml, with significant differences observed against albendazole at 100 µg/ml (p0.05). After 60 minutes, the cell death rates in the 800 µg/ml Eucalyptus group were not significantly different from those in both albendazole groups (p0.05). The calculated IC50 values for Eucalyptus globulus extract were 1036, 923, and 286 µg/ml at 10, 20, and 60 minutes, respectively.

Conclusion: Eucalyptus globulus demonstrates significant in vitro efficacy against hydatid cyst protoscolices, comparable to standard treatments like albendazole, particularly at higher concentrations and shorter incubation times. These findings suggest that Eucalyptus globulus may serve as a promising alternative or adjunctive therapy for hydatid disease, warranting further in vivo studies to confirm its therapeutic potential

keywords: Hydatid cyst, Eucalyptus, Protoscoleces, Albendazole

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Evaluation of the anti-leishmanial effects of Eucalyptus microtheca on Leishmania major in vitro

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Medical Parasitology

Background and aim: Cutaneous leishmaniasis is an endemic disease in Iran and worldwide. Current treatments are associated with significant disadvantages, including high toxicity and numerous side effects, therefore, the identification of new treatment methods is essential. Pharmacological studies have shown that Eucalyptus exhibits a wide range of effects, including gastrointestinal, anti-inflammatory, analgesic, antidiabetic, antioxidant, antimicrobial, antiparasitic, insecticidal, oral and dental health benefits, dermatological, nasal, and numerous other properties. This study aims to investigate the cell cytotoxicity and anti-leishmanial effects of Eucalyptus microtheca against Leishmania major in vitro.

Methods: : The RAW 264.7 cell line and promastigotes of Leishmania major were cultured in RPMI-1640 medium supplemented with FBS and antibiotics. The IC50 and CC50 values of Eucalyptus microtheca against promastigotes, RAW 264.7 cells, and amastigotes of L. major were evaluated in vitro.The MTT assay was performed to determine IC50 and CC50 values using Eucalyptus microtheca concentrations of 1 mg/mL, 0.5 mg/mL, 0.25 mg/mL, and 0.125 mg/mL on promastigotes and cell line.

Results: : Eucalyptus microtheca inhibited the growth of Leishmania major promastigotes and amastigotes in vitro. The IC50 values of Eucalyptus microtheca were 0.1 and 0.04 mg/ml in 24 and 48 hours, respectively. The MTT assay reveals that it is non-toxic in a 48-hour test.

Conclusion: Eucalyptus microtheca is a potential antileishmanial agent

keywords: Eucalyptus microtheca; IC50; CC50; antileishmanial, Leishmania major

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Comparison of Humoral and Cellular Immune Response of Different Types of COVID -19 Vaccines

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Medical Virology

Background and aim: The importance of vaccines as an effective solution in controlling infectious diseases and during epidemics has always been considered. SARS-CoV-2 virus, with its ability to infect several host species and due to its high prevalence and wide circulation, genetic diversity and frequent recombination of its genome, and frequent interactions between humans and animals, has faced scientists with great challenges in the process of producing vaccines and medicine. The aim of this review is to evaluate humoral and cellular immune responses induced by different vaccines from several studies conducted worldwide.

Methods: After the introduction of a wide range of vaccines, there have been many concerns and discussions about their quality and efficiency, the type of triggered/induced immune response, their ability to provide prolonged protection, and their effectiveness against variants of concern. Therefore, in this review, with the aim of comparing the humoral and cellular immune responses caused by different SARS-CoV-2 vaccines, we reviewed and summarized about 40 articles published around the world.

Results: The most effective vaccine against different strains of Covid-19 is the mRNA vaccine, followed by subunit, viral vector, and inactive vaccines.Among mRNA vaccines, Moderna induces more immunity because the amount of injection in each dose of Pfizer is 100 µg/ml and Moderna dose is 100 µg/0.5 ml. Among the viral vector vaccines, the Sputnik V elicited a stronger immune response than the AstraZeneca vaccine, because the AstraZeneca uses a chimpanzee adenovirus and the Sputnik V vaccine uses a human adenovirus type 5. Among the inactivated vaccines, Sinovac elicited a stronger immune response compared to Sinopharm. The Sinopharm induced Treg, Ts and Breg cells, while

the Sinovac induced higher levels of activated NK and Th cells. AstraZeneca induced higher levels of memory B-cells, CD8+ T-cells, CD4+ T central memory cells, and regulatory T-cells, while Pfizer and Moderna induced higher levels of plasma blasts, CD4+ T-cell effectors, and memory B-cells.

Conclusion: Several factors can affect the effectiveness of vaccines, such as the type of vaccine used, the way it is stored and transported, the strains of SARS-CoV-2, the age and immune status of the person receiving the vaccine, the infection history, and the intervals between doses. In the end, regardless of the type of vaccine, it should be mentioned the general effect of all vaccines in reducing the mortality and severity of the disease and finally ending the epidemic.

keywords: COVID-19 Vaccines, Cellular and Humoral Immunity, Vaccine Effectiveness

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Human papillomavirus (HPV) prevalence in HIV positive women

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Medical Virology

Background and aim: Human papillomavirus (HPV) is a sexually transmitted virus and persistent infection with high-risk HPV types leads to cervical cancer. Human immunodeficiency virus (HIV) plays an important role in HPV infection. HIV-positive women have a higher risk of HPV infection and cervical cancer due to a decrease in the level of CD4 lymphocytes. In Iran, few studies have been done in this field, therefore the aim of this study is to investigate the prevalence of HPV in HIV positive women.

Methods: In the current study, 50 cervical swab samples from HIV-positive women aged 23-66 years who had referred to Iranian Research Center for HIV/AIDS located in Imam Khomeini Hospital in Tehran, were investigated after completing the consent form. Universal primers MY 09/11 and GP 5+/6+ were used in the nested polymerase chain reaction to identify HPV in the received samples.

Results: The prevalence of HPV was 78% (n= 39/50) and the average age of women with HIV in this study was 43.26 years old. In total, 40% (n= 20/50) of women with HIV were 40 years old, of which 80% (n= 16/20) were HPV positive. In this study 47/50 HIV positive women had a sexual partner, of which 37/47 (78.72%) were HPV positive. Also, 60% (n= 30/50) of women were married and 73% (n= 22/30) of them were HPV positive. In terms of education level, they were classified into three groups: high school 36% (n= 18/50), high school 60% (n= 30/50) and high school 4% (n= 2/50). In these three groups, 66.67% (n= 12/18),

83.33% (n= 25/30) and 100% (n= 2/2) were HPV positive respectively. All the women in this study 50/50 are urban. 18/50 (36%) women with CD4 500 cell/mm3, of which 13/18 (72.22%) were HPV positive.

Conclusion: Considering the high prevalence of HPV and the high incidence of cervical cancer in HIV-positive women, especially in developing countries such as Iran, in order to detect precancerous lesions and cervical cancer in time, there is a need for organized programs for screening and the use of preventive vaccines in sexually active women.

keywords: Human papillomavirus; Persistent infection; Human immunodeficiency virus; Cervical cancer

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Dengue virus in Middle East and North Africa

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Medical Virology

Background and aim: Dengue virus (DENV) with single-stranded RNA genome belongs to Flaviviridae family, and it has 4 serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and is responsible for Dengue Fever (DF). Aedes aegypti and Aedes albopictus are vector mosquitos that can transmit DENV to humans. There is little focus on the prevalence of DENV in Middle East and North Africa, therefore in this study, we summarize the recent studies related to the rate of DENV in four countries including: Sudan, Iran, Saudi Arabia, and Pakistan to highlight the importance of DENV prevalence in these areas.

Methods: The rate of DENV increased by 30-folds, with affecting over 100 countries. DENV impacts on more than 100 million people worldwide each year. It has been predicted that about 60% of the people will be infected to DF worldwide. In Central and South America, Southeast Asia, the Western Pacific region, Africa, and Australia the DENV is endemic.

Results: Dengue virus in Sudan In Sudan, different studies between1976 to 2024 showed that the prevalence of DENV ranged between 0.7% - 90%). Dengue virus in Iran In Iran, several studies between1970 to 2024 showed that the DENV prevalence ranged between (0% - 7.6%). Dengue virus in Saudi Arabia In Saudi Arabia, several studies between1994 to 2024 showed that the DENV prevalence was between (0.1% - 100%). Dengue virus in Pakistan In Pakistan, different studies between1983 to 2024 showed that the DENV prevalence varied between (6.8% - 72%).

Conclusion: Various studies show that Sudan in North Africa, and Pakistan and Saudi Arabia in the Middle East have the highest prevalence of DENV. Southeast of Iran like Sistan and Baluchestan is at risk of DENV prevalence due to its

neighbor with Pakistan and Southeastern countries and travelers who coming from these areas. The high prevalence of the DENV in Saudi Arabia, especially the city of Makkah, is due to the arrival of pilgrims who come from different countries and may be carriers of this virus.

keywords: Dengue virus (DENV), Dengue Fever (DF), vectors, prevalent

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Evaluating the effect of Adenovector on the expression of CyclinA in cell cycle and repair system of HUVEC cells.

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Medical Virology

Background and aim: The role of Adenovirus vector on the cell cycle remains to be completely elucidated. Herein, the extent of adenovirus-expressing GFP (Ad-GFP) effect on the Cyclin A expression has been examined. Any alterations in Cyclin A expression can disrupt cell cycle processes and maintain genomic stability.

Methods: In this study, human umbilical vein endothelial cells (HUVECs) were transduced with Ad-GFP, in a non-cytopathic concentration, based on viability assay. Then the RNA of transduced cells were extracted and real-time PCR was used to measure Cyclin A expression at 6, 12, and 24 hours post-transduction.

Results: The results showed no significant change in Cyclin A expression at the 6-hour. However, by 12 hours, a significant decrease was evident, becoming even more at 24 hours. This downward trend suggests that Ad-GFP transduction may interfere with the cell cycle progression and delay DNA repair processes over time, potentially affecting the efficiency of the repair pathway.

Conclusion: In conclusion, the study highlights a significant decline of cycline A after vector transduction in HUVECs. Further investigation is needed to understand the long-term effects of Cyclin A modulation in gene therapy.

keywords: Adenovector; Cell cycle; Endothelial cell; Genome stability; DNA repair

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Unraveling the enigma: The emerging significance of pulmonary surfactant proteins in predicting, diagnosing, and managing COVID-19

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Medical Virology

Background and aim: Severe cases of COVID-19 often lead to the development of acute respiratory syndrome, a critical condition believed to be caused by the harmful effects of SARS-CoV-2 on type II alveolar cells. These cells play a crucial role in producing pulmonary surfactants, which are essential for proper lung function. Specifically focusing on surfactant proteins, including Surfactant protein A (SP-A), Surfactant protein B, Surfactant protein C, and Surfactant protein D (SP-D), changes in the levels of pulmonary surfactants may be a significant factor in the pathological changes seen in COVID-19 infection.

Methods: This study aims to gain insights into surfactants, particularly their impacts and changes during COVID-19 infection, through a comprehensive review of current literature. The study focuses on the function of surfactants as prognostic markers, diagnostic factors, and essential components in the management and treatment of COVID-19.

Results: In general, pulmonary surfactants serve to reduce the surface tension at the gas–liquid interface, thereby significantly contributing to the regulation of respiratory mechanics. Additionally, these surfactants play a crucial role in the innate immune system within the pulmonary microenvironment. Within the spectrum of COVID-19 infections, a compelling association is observed, characterized by elevated levels of SP-D and SP-A across a range of manifestations from mild to severe pneumonia. The sudden decline in respiratory function observed in COVID-19 patients may be attributed to the decreased synthesis of surfactants by type II alveolar cells.

Conclusion: Collectin proteins such as SP-A and SP-D show promise as biomarkers, offering potential avenues for predicting and monitoring pulmonary alveolar injury in the context of COVID-19. This clarification enhances our understanding of the molecular complexities contributing to respiratory complications in severe COVID-19 cases, providing a foundation for targeted therapeutic approaches using surfactants and refined clinical management strategies.

keywords: COVID-19, pulmonary surfactant protein, SARS-COV2, SP, surfactant proteins

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Updated diagnostic approaches for CCHFV: from laboratory research to clinical application

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Medical Virology

Background and aim: Crimean-Congo Hemorrhagic Fever Virus (CCHFV) is a tick-borne virus causing severe hemorrhagic fever with high mortality rates. Rapid and accurate diagnosis is essential for proper patient management and controlling outbreaks. Over the years, a variety of diagnostic methods have been developed, ranging from laboratory-based molecular techniques to point-of-care tests for bedside application.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords CCHFV; ELISA; RT-PCR; Diagnosis, 43 articles related to inclusion criteria were extracted and then analyzed.

Results: Molecular techniques like RT-PCR remain the gold standard for early-stage diagnosis due to their high sensitivity and specificity. Serological methods, such as ELISA, are valuable for detecting antibodies in later stages of infection. However, these tests may fail to detect early infections. Rapid diagnostic tests, though less accurate than molecular methods, are useful in resource-limited settings and at the point of care.

Conclusion: The evolution of diagnostic techniques from laboratory-based assays to portable, user-friendly devices marks a significant advancement in CCHFV management. While molecular diagnostics offer superior accuracy, their requirement for specialized equipment limits their widespread use. Future

diagnostic tools should focus on improving sensitivity and portability, especially in low-resource areas where CCHFV is endemic. Overall, integrating advanced diagnostics with bedside tools could enhance early detection and improve clinical outcomes for CCHFV patients.

keywords: CCHFV; ELISA; RT-PCR; Diagnosis.

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mRNA Vaccines: Revolutionizing Diagnosis and Treatment in Viral Diseases

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Medical Virology

Background and aim: mRNA vaccines have emerged as a groundbreaking advancement in immunology, significantly impacting the management and prevention of viral diseases, particularly during the COVID-19 pandemic. This systematic review aims to evaluate the efficacy, safety, and diagnostic potential of mRNA vaccines, focusing on their applications in diagnosing and treating viral infections.

Methods: A comprehensive search was conducted across multiple databases, including PubMed, Scopus, and Web of Science, to identify studies published between 2019 and 2024. Keywords such as "mRNA vaccines," "diagnosis," "treatment," and "viral infections" were utilized. Inclusion criteria encompassed peer-reviewed articles discussing mRNA vaccines' diagnostic or therapeutic applications. Data extraction and quality assessment were performed independently by two reviewers. Data from the selected studies were synthesized using qualitative and quantitative methods.

Results: Out of 50 studies, findings were categorized into three sections: efficacy, safety, and diagnostic applications. Efficacy: mRNA vaccines, such as Pfizer-BioNTech and Moderna, showed high efficacy in preventing COVID-19, significantly reducing symptomatic cases and severe outcomes with two-dose vaccinations. Safety: The safety profile was favorable, with common mild adverse events like injection site reactions, fatigue, and headache. Serious adverse events were rare (less than 0.05%), even in large-scale studies. Diagnostic Applications: Emerging research indicates mRNA vaccines' potential in diagnosing viral infections by measuring immune responses, allowing rapid and accurate detection of diseases like SARS-CoV-2.

Conclusion: mRNA vaccines exhibit remarkable efficacy and safety in preventing viral infections, with significant diagnostic potential. Their rapid development and deployment during the COVID-19 pandemic underscore their versatility and importance. Continued research is essential to fully harness the potential of mRNA technology in both diagnostic and therapeutic domains.

keywords: mRNA vaccines, diagnosis, treatment, viral infections, COVID-19.

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Expression Pattern of Cholesterol 25-Hydroxylase and Serum Level of 25-Hydroxycholesterol and Relevant Inflammatory Cytokines in Patients with Varying Disease Severity of COVID-19

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Medical Virology

Background and aim: Fifty intensive care unit (ICU) patients and outpatients with SARS-CoV-2 and 25 healthy controls were studied. Gene expression of CH25H and relevant inflammatory cytokines was quantified in peripheral blood mononuclear cells by real-time polymerase chain reaction.

Methods: Fifty intensive care unit (ICU) patients and outpatients with SARS-CoV-2 and 25 healthy controls were studied. Gene expression of CH25H and relevant inflammatory cytokines was quantified in peripheral blood mononuclear cells by real-time polymerase chain reaction.

Results: The expression of CH25H and serum levels of 25HC were significantly higher in ICU patients with SARS-CoV-2. Notably, IFN-α levels increased in healthy controls. However, compared to healthy controls, IFN-β was considerably higher in outpatients. Finally, statistical analysis shows that no correlation was found between CH25H and IFN-α expression; nevertheless, a lower correlation was found with IFN-β.

Conclusion: The data revealed that CH25H and 25HC levels increase after SARS-CoV-2 infection. In the other word, decreased levels of those factors in severe patients compared with mild patients may indicate the importance of their function in controlling the progression of the disease.

keywords: 25HC; CH25H; COVID-19; IFN-α; IFN-β

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Frequency of genotypes 31, 33, 35, 39 and 45 of human papillomavirus in cervical samples

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Medical Virology

Background and aim: Uterine cervix cancer is the third most common cancer among women and the second leading cause of death due to malignancy in women. HPV is involved in approximately 99.7% of squamous cell carcinoma of the cervix worldwide. In 2012, the International Agency for Research on Cancer declared that there is sufficient epidemiological, experimental and mechanistic evidence regarding the carcinogenicity of genotypes 31, 33, 35, 39, 45 of HPV in causing uterine cervix cancer. The aim of study was to assess the frequency of these HPV genotypes in cervical samples of patients attending the gynecology clinic in Zanjan Mousavi Hospital.

Methods: This study was conducted as a cross-sectional and descriptive study. The study population included all women attending the women's clinic at Ayatollah Mousavi Hospital in Zanjan in the year 1399 (2020-2021), from whom HPV tests were obtained from Pap smear samples. The sampling method was a complete enumeration. A total of 210 samples were examined. Initially, HPV cases were identified, and then genotypes 31, 33, 35, 39, and 45 of HPV in these samples were investigated using PCR and agarose gel electrophoresis. The association between HPV genotypes and the recorded demographic and clinical information of the individuals was also analyzed and examined.

Results: The prevalence of genotypes 31, 33, 35, 39, and 45 in 14 HPV-positive Pap smear samples was examined, revealing that one individual was infected with genotype 31. The estimated prevalence of this genotype was 7.1%. Among

these samples, none of the patients were found to be infected with genotypes 33, 35, 39, or 45.

Conclusion: Considering the relatively low prevalence of HPV in the population of women attending the women's clinic at Ayatollah Mousavi Hospital, the prevalence of genotypes 31, 33, 35, 39, and 45 is also expected to be relatively lower than other studies. Therefore, it is recommended that, due to economic, social, and cultural limitations in Zanjan, similar studies with larger sample sizes be conducted in communities with fewer limitations to investigate other low-risk and high-risk genotypes.

keywords: Specific Genotypes; Human papilloma virus; Cervix

Abstract Book - 16th International Congress of Medical Lab. and Clinic
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Lineage and Sublineage Analysis of Human Papillomavirus Type 58 in Iranian Women

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Medical Virology

Background and aim: Variant analysis of distinct HPV types is important from different aspects including epidemiology, pathogenicity, and evolution.

Methods: For this reason,the full sequence of the E6 and E7 genes of HPV 58 was examined in 130 HPV 58-infected cervical samples using PCR and sequencing.

Results: Our results revealed that three lineages A, B, and D were found in this study; among which the B lineage was more common (91.50%). About sublineages, all samples of the B lineage belonged to the B1 sublineage, and samples that were classified as the A and D lineages were found to belong to the A1 (0.77%), A2 (5.38%), A3 (1.50%), and D2 (0.77%) sublineages. No statistically significant differences were found between lineages and stages of disease or amino acid changes (P0.05).

Conclusion: Our results showed that lineage B, sublineage B1, was dominant in Iran. However, more studies with larger sample sizes from different parts of Iran are essential for assessing the pathogenicity risk of HPV 58 lineages in Iranian women with cervical cancer.

keywords: Human papillomavirus, HPV 58, lineage, sublineage, cervical cancer

Abstract Book - 16th International Congress of Medical Lab. and Clinic
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Prevalence of hepatitis D virus among HBsAg-positive individuals in Khorramabad city, 2019

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Medical Virology

Background and aim: Co-infection of HBV and HDV leads to more severe hepatitis, with a higher risk of acute liver failure and hepatocellular carcinoma (HCC). This study aimed to assess the prevalence of HDV in HBsAg-positive patients in Khorramabad, which has not been previously evaluated.

Methods: A total of 200 patients who tested positive for HBsAg were included in this study. Venous blood samples were collected in EDTA-free tubes. An ELISA test was performed to detect antibodies against HDV, and positive samples were further confirmed using RT-PCR. Population data were analyzed using SPSS software, and a P value ≤0.05 was considered statistically significant for all tests.

Results: Out of the total participants, there were 119(59.5%) men and 81(40.5%) women. The age of the patients varied from 5 to 89 years, with an average age of 49.66 years. The HDV ELISA test was performed on HBsAg-positive individuals, yielding positive results for 37(18.5%) patients. Additionally, 10(5%) patients showed borderline infection. The HDV RT-PCR results indicated that 42(21%) individuals tested positive. The prevalence of HDV showed a statistically significant difference between urban and rural areas with respect to molecular RT-PCR testing (P=0.032). Additionally, women, married individuals, and drug addicts were found to be at a higher risk of HDV infection.

Conclusion: There is a high prevalence of HDV infection among patients who test positive for HBsAg in Khorramabad. Therefore, assessing the prevalence of HDV

in HBsAg positive patients can aid in ensuring timely diagnosis and appropriate treatment for these individuals.

keywords: HBV, HDV, HBsAg, Prevalence, Co-infection.

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Leveraging the Power of Myxoma Virus in Cancer Therapy: A Systematic Review and Meta-Analysis

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Medical Virology

Background and aim: Cancer remains a leading cause of morbidity and mortality worldwide, necessitating the development of innovative therapeutic strategies. Oncolytic virotherapy using Myxoma Virus (MYXV) has shown promising potential across various cancer models. This meta-analysis and systematic review aim to consolidate and analyze existing data on the efficacy, immune modulation, and synergistic effects of MYXV in treating cancer.

Methods: A comprehensive search was conducted using PubMed, Google Scholar, and other databases to identify relevant studies published up to 2023. Keywords included "Myxoma Virus," "Oncolytic Virotherapy," "Cancer Treatment," "Immune Modulation," "Melanoma," "Ovarian Cancer," and "Cisplatin." Inclusion criteria encompassed studies that investigated MYXV's effects on cancer cells or animal models. Data extraction focused on study design, sample size, methods, results, and conclusions. Statistical analysis was performed to assess the overall efficacy and safety of MYXV.

Results: Five key studies were included in the analysis: Impact on T Lymphocytes: MYXV effectively reduces the proliferation of activated T lymphocytes, facilitating the transfer of the virus to cancer cells without substantial immune system interference. Immune System Modulation: Engineered MYXV strains expressing IFN-γ and CD47 demonstrated enhanced lymphocyte infiltration and improved tumor suppression in melanoma models, indicating robust immune response and improved survival rates. Synergy with Cisplatin: MYXV enhances the efficacy of cisplatin in ovarian cancer models by modulating the tumor microenvironment and reducing immunosuppressive cytokines, leading to better therapeutic outcomes. Preclinical Efficacy: MYXV showed significant oncolytic

activity across various cancer models, reducing tumor size, inducing apoptosis, and activating antitumor immune responses.

Conclusion: This meta-analysis and systematic review underscore MYXV's therapeutic potential in cancer treatment. The virus's ability to modulate the immune response, synergize with chemotherapy agents like cisplatin, and effectively target cancer cells highlights its promise as a novel oncological therapeutic. Further clinical trials are necessary to validate these findings and translate them into clinical practice.

keywords: Myxoma Virus, Oncolytic Virotherapy, Cancer Treatment, Immune Modulation, Melanoma

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In vitro anti-HSV1 activity of aqueous extract of Teucrium stocksianum

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Medical Virology

Background and aim: Background and Aim: Herpes simplex virus type 1 (HSV-1) causes oral herpes, which is a highly contagious infection that is spread around the world and is transmitted through infected saliva. Different species of Teucrium have antimicrobial properties, especially against Staphylococcus aureus. In Iran, there is a species of this plant called Teucrium stocksianum.

Methods: Methods: In this study, Teucrium stocksianum extract was used to investigate its antiviral effects against HSV-1. The toxicity and antiviral effects of its extract was directly studied at different concentrations and times using the MTT assay. Also, the effects of the extract on reducing the expression of the UL46, US6(gD)viral gene was investigated using real-time PCR method.

Results: Results: Aqueous extract of Teucrium stocksianum significantly reduced virus replication at the concentrations of 25 to 100 µg/ml at 2 h before virus infection, at the same time and 4 h after virus infection. The study showed that the concentrations of 25 to 100 µg/ml of the aqueous extract were not toxic to cells. In real-time PCR results, especially at 2 h before infection with the virus, Teucrium stocksianum aqueous extract was the most effective agent against the HSV-1 virus.

Conclusion: Conclusion: Therefore, Teucrium stocksianum aqueous extract can be considered as an effective new treatment for HSV-1 infections.

keywords: Keywords: Teucrium stocksianum, HSV-1, Aqueous extract, UL46, US6(gD)

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Design of a multi-epitope-based vaccine consisted of immunodominant epitopes of structural proteins of SARS-CoV-2 using immunoinformatics approach

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Medical Virology

Background and aim: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has shown rapid global spread and has resulted in a significant death toll worldwide. In this study, we aimed to design a multi-epitope vaccine against SARS-CoV-2 based on structural proteins S, M, N, and E.

Methods: We identified B- and T-cell epitopes and then the antigenicity, toxicity, allergenicity, and similarity of predicted epitopes were analyzed. T-cell epitopes were docked with corresponding HLA alleles. Consequently, the selected T- and B-cell epitopes were included in the final construct. All selected epitopes were connected with different linkers and flagellin and panHLA DR binding epitopes (PADRE) as an adjuvant were used in the vaccine construct. Furthermore, molecular docking was used to evaluate the complex between the final vaccine construct and two alleles, HLA-A*02:01 and HLADRB1*01:01. Finally, codons were optimized for in silico cloning into pET28a (+) vector using SnapGene.

Results: The final vaccine construct comprised 11 CTL, HTL, and B-cell epitopes corresponding to 394 amino acid residues. In silico evaluation showed that the designed vaccine might potentially promote an immune response.

Conclusion: According to our findings, the designed vaccine is a good candidate for the development of a vaccine against severe acute respiratory syndrome coronavirus-2. Further in vivo preclinical and clinical testing is required to determine the safety and efficacy of the designed vaccine.

keywords: Syndrome Coronavirus- 2 (SARS-CoV-2), Multi-epitope Vaccine, Structural Proteins

Abstract Book - 16th International Congress of Medical Lab. and Clinic
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Setup and Optimization of a Semi-Nested PCR Test for the Detection of HTLV-1 Virus

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Medical Virology

Background and aim: Human T-cell Leukemia Virus Type 1 (HTLV-1) is an oncovirus affecting around 25 million people globally, with northeastern Iran as an endemic region. Approximately 7% of infected individuals develop adult T-cell malignancies or neurological conditions like TSP/HAM. There is no definitive treatment, making early detection critical to managing spread. HTLV-1 is transmitted via breastfeeding, sexual contact, and blood transfusions. Traditional serological tests lack sensitivity in early infection stages, whereas PCR-based methods, especially semi-nested PCR, offer greater accuracy. This study optimized a semi-nested PCR targeting the HBZ gene, assessing its sensitivity, specificity, and reproducibility in clinical samples.

Methods: Fifty blood donor samples were collected from Khorasan Razavi Province. The HTLV-1 positivity of these samples was confirmed using standard serological tests. Two sets of primers for the semi-nested PCR test were designed specifically for the HBZ gene sequence. The volumes, component concentrations, and temperatures for each step in the PCR reaction were carefully adjusted to ensure optimal performance. This optimization was critical for achieving high sensitivity and specificity in detecting the viral gene. In the next step, two-step semi-nested PCR reaction was performed under optimal conditions. The PCR products were visualized using 1.5% agarose gel electrophoresis. To determine the LOD for the HBZ gene copies in HTLV-1 using the semi-nested PCR, a positive sample with a concentration of 1.2 × 10^5 copies/µL of the HBZ gene was serially diluted and tested by PCR.

Results: The HBZ gene was successfully amplified in all 50 HTLV-positive samples, showing a band of 106 base pairs in the second stage. No amplification was observed in negative samples or in samples with other common human viruses, such as HCV, HBV, HIV, and HSV, confirming the high specificity of this test. The LOD of this assay was determined to be 1.2 × 10^1 copies/µL, indicating the high sensitivity of this method.

Conclusion: The semi-nested PCR test designed and optimized in this study serves as an effective and sensitive method for identifying HTLV virus infections. This method is advantageous due to its simplicity and high accuracy in detecting the viral genome.

keywords: HTLV-1; Semi-Nested PCR; HBZ; TSP/HAM; ALT.

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Establishment of a Real-Time PCR Method for Determining the Proviral Load of HTLV-1 Virus Using the HBZ Gene

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Medical Virology

Background and aim: The Human T-cell lymphotropic virus (HTLV) is the first known oncogenic retrovirus in humans. Types 1 and 2 of this virus are associated with two major diseases in humans; Adult T-cell Leukemia/Lymphoma (ATLL) and Tropical Spastic Paraparesis/HTLV-1-associated Myelopathy (HAM/TSP). The HBZ gene is one of the key genes of this virus, encoded on the antisense strand, and enhances the proliferation of infected cells independently of the tax gene. Serological methods bring limitations in diagnosing the virus during its latent phase. Due to the risk of virus transmission through blood products, this study aimed to design a real-time PCR test based.

Methods: Primers and probes were designed using bioinformatics tools for a 106 bp region of the HBZ gene. Then genomic DNA was extracted from peripheral blood mononuclear cells (PBMCs). Next the PCR product of HBZ gene was insert into TOPO TA cloning vector (PCR 2.1 TOPO), which was subsequently used as a standard for setting up the real-time PCR assay. Through serial dilutions, a standard curve was established, and the real-time PCR assay was optimized using the TaqMan probe method to determine viral load.

Results: The PCR product for the HBZ gene was sequenced, and the result was confirmed in the NCBI database through a BLAST search. The PCR product used as a standard for the real-time PCR assay. The standard curve displayed a linear slope of: -3.2 and R^2 :0.97, indicating the assay's linearity and efficiency. Repeatability of the assay was evaluated at both intra-assay and inter-assay levels, showing that the limit of detection (LOD) was 12× 102 copies/µL, indicating high sensitivity of this method.

Conclusion: The designed qPCR method could efficiently detect the viral load with high sensitivity. The functionality of this method can be evaluated using positite samples in further studies. This method can also provide a rapid, accessible, and cost-benefit technique for the prognosis of HTLV-related diseases.

keywords: Viral load, Real-Time PCR, HBZ , HTLV-1

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Adenovirus is a hope for cancer treatment

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Medical Virology

Background and aim: Adenovirus is a double edge knife which not only can suffer your body, but also could be used in cancer treatment. The practical side of this virus come from a vital ability in putting its own gene in host nucleus. So, the virus gene will be transcriptted by factors that are present in host cells. This feature is so unique while we can replace virus gene with healthy ones.

Methods: A comprehensive literature review was conducted, examining studies clinical outcome of using Adenovirus for cancer treatment.

Results: Cancer is one of the most prevalent in the world. Duo to the fact that Adenovirus has specific life cycle there is hope for using it in cancer treatment by omitting the draw back sides of this virus. This therapy has a long way to pass but, it could change the treatment of almost all cancer.

Conclusion: Summery, there is hope for cancer therapy by using Adenovirus but, it is still a virus and threaten our health. This virus can cause disease or change receptors of the cells and interleukin were secreted by the body as a reaction of virus present. All of this prosses could help body to come over the damage cells.

keywords: Adenovirus, Cancer, Breast Cancer, Lung Cancer, Leukemia, Colon Cancer, Bladder

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Measures and Challenges in Increasing the Capacity of Medical Diagnostic Laboratories during the COVID-19 Pandemic: A Systematic Review"

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Medical Virology

Background and aim: Surge capability refers to a healthcare facility's ability to expand its resources and skills during emergencies or crises, including increasing staff, equipment, space, and management policies to maintain high-quality patient care. Medical laboratories must also enhance their diagnostic testing capabilities in emergencies, such as pandemics. The COVID-19 pandemic disrupted laboratory operations, highlighting the need for planning surge capacity, especially in clinical laboratories, to ensure quality health services and improve diagnostic abilities during crises. This study examined the procedures, policies, and experiences of health systems in various countries in enhancing the capacity and functionality of medical diagnostic laboratories during the pandemic.

Methods: This study refers to a scientific assessment that includes all published research, except for review studies in peer-reviewed journals from October 23, 2021, to April 19, 2024. Seven digital databases, including PubMed, Scopus, MEDLINE, CINAHL, Embase, PsycINFO, and Ovid, were searched using various keywords such as "surge capability," "laboratory," "COVID-19 pandemic," "emergency capability," "capacity building," "clinical laboratories," "COVID-19 health laboratories," "corona pandemic," and "SARS-CoV-2" to collect relevant

information. The extracted data were organized based on the PICO framework (Population, Intervention, Comparison, and Outcomes) and included participant characteristics, exposure to disasters or emergencies, primary and secondary outcomes, general information, study characteristics, missing data, and quality assessments.

Results: From the preliminary search, 32 qualifying papers were reviewed, identifying four key areas: 1-Strengthening Laboratory Capacity: Fifteen articles highlighted the COVID-19 pandemic's role in prioritizing laboratory capacity enhancement. Strategies like automated RNA extraction, sample pooling, and establishing cell laboratories improved testing efficiency and accuracy, while rapid diagnostic tests (RDTs) increased capacity. 2-Challenges and Innovations in Testing: Eight articles discussed the urgent need for increased testing capacity and infrastructure, with the diagnostics industry contributing innovations such as pooled testing and specific reporting systems while adapting to changing demands. 3-Proactive Approaches to Pandemic Preparedness: Five articles emphasized collaboration between organizations like the CDC and FDA to expand testing capacity and invest in preparedness. 4-Investment in Public Health Laboratories: Four articles underscored the importance of investing in public health laboratories to enhance responses to disease outbreaks and support global health systems.

Conclusion: Surge laboratory capacity and investing in public health laboratories are essential for improving responses to epidemics. It is recommended to enhance collaboration between organizations and develop innovative technologies to increase testing capacity and preparedness for future outbreaks.

keywords: COVID-19; Surge capacity; laboratories; Public Health

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The impact of HPV in immunodeficient women

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Medical Virology

Background and aim: Immunocompromised patients such as HIV positive patients, organ transplant recipients and patients with autoimmune diseases do not have the ability to deal with various infections, as a result, this group of patients has a higher risk of contracting various infections and cancers compared to immunocompetent populations. Women with HIV have a higher risk of HPV infection and progression to various malignancies due to a decrease in the level of CD4 lymphocytes. Therefore the aim of this narrative review is to investigate the impact of HPV in immunodeficient women.

Methods: In this narrative review, Google Scholar, PubMed and Elsevier databases have been used and information related to these databases has been collected.

Results: Women with HIV have a higher risk of HPV infection and progression to various malignancies due to a decrease in the level of CD4 lymphocytes. Also, due to immunodeficiency in this group of women, HPV clearance decreases, and conversely, high-risk HPV types and co-infection with multiple high-risk HPV types increase.

Conclusion: Developed countries have implemented extensive programs for timely screenings and the use of preventive vaccines to control HPV infection in the general population and high-risk groups such as HIV-positive women. Unfortunately, developing countries lack regular and specific programs to control HPV infection. For this reason, to control HPV infection and reduce HPV-related

cancers, we need special programs to control HPV infections and HPV-related cancers in these countries.

keywords: Cervical cancer; Human papillomavirus; Immunocompromised patients; Human immunodeficiency virus

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Correlation between arterial oxygen saturation and lung involvement in the CT scan of hospitalized COVID-19

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Medical Virology

Background and aim: Currently, COVID-19 is considered a global threat to society. The symptoms of COVID-19 in patients are nonspecific and cannot be used for accurate diagnosis. However, some patients suddenly develop ARDS (acute respiratory distress syndrome). The aim of this study is to determine the correlation between arterial oxygen saturation in hospitalized patients with COVID-19 at Valiasr Hospital in Zanjan and the findings of CT scan images.

Methods: The present study was a cross-sectional study. The medical records of patients with COVID-19 at Valiasr Hospital were examined. The intended time period was from Farvardin to Shahrivar 1400 (March to September 2021), but due to the prolonged approval process of the proposal, the records of the year 1401 were reviewed to have more up-to-date information. Demographic information, clinical symptoms, radiological and laboratory evidence, and arterial oxygen saturation percentage were extracted from the records and recorded in the relevant checklist. The results of lung scans were documented according to the radiologist's report. Finally, the extracted data were entered into SPSS software version 26 for analysis. The Kruskal-Wallis test was used to examine the correlation between saturation percentage and the severity of involvement, and the ordinal logistic regression model was used to assess this correlation in the presence of demographic variables, underlying diseases, clinical symptoms, and laboratory evaluations.

Results: 56% were male. Their age was 69.06±17.05 years. 81.2% had underlying disease, with high blood pressure in 46.9%. 80.2% had a history of drug use, high

blood pressure drug was the most commonly used drug with 47.7%. The most common symptom was cough (71.6%). 40.1% had moderate severity of symptoms. respiratory complications were seen in 49.4%. The SPO2 of the patients was 86.24 ± 9.99. 38.6% had mild lung involvement and the most common CT scan complication was alveolar complication (82.2%). 87.3% of patients improved and 12.5% died. It was significant inverse relationship between the percentage of oxygen saturation and the severity of the conflict (P0.001).The logistic regression showed significant relationship between severity of CT scan findings with age, clinical symptoms, laboratory findings, and in each of these variables, with a one percent increase in oxygen level, the chance of severe lung involvement is between 5 and 17 percent. decreases.

Conclusion: The results of the present study indicate a significant inverse correlation between arterial oxygen saturation level and the severity of lung involvement. Therefore, it is recommended to prospectively and longitudinally investigate the association between arterial oxygen saturation and CT scan changes in patients with COVID-19.

keywords: Blood oxygen saturation, lung CT scan, Covid-19

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Lineage and sub lineage analysis of human papilloma virus type 51 and 59 in Iranian women

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Medical Virology

Background and aim: HPV is the most common sexually transmitted infection globally, causing various cancers, particularly cervical cancer. Among over 400 HPV types, 14 are considered high-risk (HR), including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. These can lead to persistent infections and cancer development. In line with these, this study carried out a nucleotide sequence analysis to fnd the circulating HPV 51 and HPV 59 lineages and sublineages in Iran.

Methods: A study conducted from 2018 to 2020 aimed to characterize the lineages and sublineages of HPV 51 and HPV 59 in Iran. The study population included 142 formalin-fixed paraffin-embedded (FFPE) samples from Imam-Khomeini Hospital in Tehran, consisting of 98 invasive cervical cancer and 44 cervical intraepithelial neoplasia (CIN) samples. Additionally, 135 ThinPrep Pap Test samples positive for 12 high-risk HPV types were analyzed, along with 44 HPV 51-positive and 22 HPV 59-positive samples previously genotyped. DNA was extracted from the samples, and HPV genomes were detected using nested-PCR and sequenced. The sequences were analyzed using Bioedit software and compared to reference sequences for HPV 51 and HPV 59. A phylogenetic tree was constructed using the maximum likelihood method, and statistical analysis was performed using Fisher's exact test, with significance set at P 0.05.

Results: Among 142 FFPE specimens, HPV 51 and 59 were detected in 1 (0.7%) and 4 (2.8%) of samples, respectively. Also, among 135 ThinPrep Pap Test specimens that were screened for these two types, HPV 51 and 59 were found in

6 (4.4%) and 8 (5.9%) samples, respectively. To determine the line- ages and sublineages, in total, 51 HPV 51-infected speci- mens [CIN 2–3 (HSIL)/ICC=9, CIN 1 (LSIL)=8, and nor- mal=34 samples] and 34 HPV 59-positive samples [CIN 2–3 (HSIL)/ICC=7 CIN 1 (LSIL)=4, and normal=23 samples] were included in this study. Lineage analysis of HPV 51 showed that both the A and B lineages were found in our samples. The A lineage was detected in 41 out of 51 HPV 51-infected samples (80.4%) and the remaining samples were infected with the B line- age (19.6%). Among samples that were infected with the A lineage, all four diferent sublineages were detected as

Conclusion: Our results showed that the A lineage, sublineages of A1 and A4, of HPV 51 are more prevalent and distributed in Iran. Concerning HPV 59, both lineages A and B were detected in our samples. However, further studies with larger sample sizes are mandatory to estimate the pathogenicity risk of HPV 51 and 59 variants in Iran. The integration status of these types into the host genome can be examined in the future. It is highly recommended that the characterization of HLA molecules in diferent HPV 51 and 59 variants

keywords: Human papillomavirus · Type 51 · Type 59 · Lineage

prevalence of cardiac arrhythmias in hospitalized COVID-19 patients

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Medical Virology

Background and aim: For years, COVID-19 has become a global problem. This virus affects multiple organs in the body and can cause patients to experience various complications, one of which is cardiovascular complications. Multiple evidence suggests an increased occurrence of arrhythmias in COVID-19 patients. Therefore, the aim of our study was to investigate the prevalence of arrhythmias in COVID-19 patients and identify the predisposing factors for arrhythmia development in COVID-19 patients hospitalized at Valiasr Hospital in Zanjan in the year 2021.

Methods: The study population included all adult patients with positive PCR-COVID or suspected symptoms of COVID-19 who were referred to Valiasr Hospital in Zanjan from 1st Farvardin to the end of Esfand in the year 1400. These patients were admitted to the COVID emergency department, COVID patient wards, COVID ICU, or other hospital departments for specific reasons. The necessary information was extracted from their medical records. The data were entered into the SPSS software, and the frequency of different arrhythmias during hospitalization was determined based on variables. The relationship between complications and variables was analyzed using this software.

Results: 56% were 65 years.70% had at least one underlying disease. 44% had mild covid. 18.6% at least one arrhythmia.6.8% sinus tachycardia,3.8% RBBB,2.8% AF,2.6% LBBB, 2% sinus bradycardia,1.6% F.PAC, 1.4% f.PVC, 0.8% First Degree AV Block, 0.6% V.Tac. 0.4% had PSVT. Arrhythmia were 24.5% in men and 11% in women. 11.6% between 18-35 years old, 6.4% between 35-50 years,20% between 50- 65 years , 21.7 65 years had at least one arrhythmia.Arrhythmia occurred in

21% with and 12.7% without underlying disease.People with mild, moderate, severe and critical covid had arrhythmia,10.4%,21.0%,35.7% and 33.3%, respectively. with mild, moderate, severe pulmonary involvement, arrhythmia was seen in 13.9%, 23.1% ,34.7% respectively. 14.7% and 34.6% who were hospitalized in covid ward and ICU had arrhythmia.Arrhythmia occurred in 19.6% with electrolyte disorder and 17.9% without it. partial recovery in 57% who had arrhythmia; 15% of these patients had complications, 7.5% were hospitalized in ICU, 20.5% died.

Conclusion: The results of this study showed that 18.6% of patients had arrhythmia during hospitalization. In patients with covid-19, the prevalence of arrhythmia is directly related to male gender, older age, underlying disease, more severe covid-19 involvement, more severe pulmonary involvement, lower ejection fraction and hospitalization in ICU, and with having or not having electrolyte disorders or none One of the electrolyte disorders (separately) is unrelated. Therefore, it is better to consider heart problems, including arrhythmias, in dealing with patients with Covid-19.

keywords: Prevalence, cardiac arrhythmias, Covid -19

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Cervix microbiomes and Human Papilloma Virus infection associated with cervical cancer development; A systematic review

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Medical Virology

Background and aim: The human microbiome maintains mucosal homeostasis across various anatomical sites, including the female reproductive system. The cervicovaginal microbiome is a complex ecosystem that influences host immune responses and creates conditions that facilitate viral infections and progression to cervical intraepithelial neoplasia. This study aims to bridge the gap in understanding how alterations in normal vaginal flora influence susceptibility to Human Papillomavirus (HPV) infections and the progression to cervical cancer. The objective is to elucidate the relationship between the vaginal microbiome and HPV virulence, with the ultimate goal of informing preventive and therapeutic strategies.

Methods: The research involved a comprehensive investigation of studies examining the effect of normal flora on the development and progression of cervix cancer in HPV-positive individuals.". 32 articles identified through searching PubMed database, results were conducted from 2011 to 2024 duplicates were eliminated. All potentially relevant publications were retrieved in full, and then the eligibility criteria were applied to the full texts of these studies. finally12 studies included. using keywords such as "normal flora," "bacterial normal flora," "fungal normal flora," "cervical cancer," "tumor

suppress factor," "tumor marker," and "cervical cancer and squamous cell carcinoma

Results: In healthy women of reproductive age, the cervix and vagina are predominantly colonized by one or a few species of Lactobacillus, which produce lactic acid, maintaining a low vaginal pH (typically below 4.5) and other antimicrobial substances. While high-risk HPV infections are recognized as significant risk factors for cervical cancer, they alone do not fully explain the development of severe precancerous cervical dysplasia or subsequent cancer progression. This suggests that additional factors within the cervicovaginal microenvironment contribute to cervical carcinogenesis. Episodes of dysbiosis, marked by a depletion of Lactobacillus species replaced by diverse anaerobic bacteria, lead to an increase in vaginal PH. Vaginal dysbiosis has been linked to cervical cancer development through mechanisms like disrupted immune regulation, enhanced HPV infection, and increased inflammation. Disruptions in microbial community homeostasis can initiate and promote cancer through various complex mechanisms.

Conclusion: The microbiome plays a crucial role in cancer development associated with HPV, influencing the tumor microenvironment and offering potential therapeutic avenues. Elevated serum levels of miR-18a and PD-L1 in affected individuals may serve as valuable biomarkers. Moreover, manipulating the microbiota through probiotics or vaginal microbiota transplantation may provide effective strategies for clearing HPV infections, reversing cervical intraepithelial neoplasia, and preventing the progression of cervical cancer.

keywords: Cervical Cancer, HPV, Normal flora

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A study on the relationship between anemia and human parvovirus B19 viremia in dialysis patients

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Medical Virology

Background and aim: Parvovirus B19 is recognized as a possible cause of chronic anemia in patients with end- stage renal disease (ESRD) undergoing hemodialysis. This can result from reduced erythropoietin secretion, red blood cell lifespan or immune suppression. Patients with chronic anemia or pancytopenia are required to be evaluated for parvovirus B19 viremia as part of their workup. In this study, we assessed parvovirus B19 viremia and its relationship with anemia in ESRD patients undergoing hemodialysis.

Methods: A total of 127 ESRD patients undergoing hemodialysis were enrolled for this study. The complete blood count was obtained from all participants. Parvovirus B19 viremia was detected through nested PCR targeting the NS1 gene.

Results: Of the studied individuals, 86 (67.7%) were anemic and parvovirus B19 viremia was detected in 21 (16.5%) patients. No significant differences were found between anemic and non-anemic patients regarding age, sex, duration of dialysis, and parvovirus B19 viremia.

Conclusion: In our study, parvovirus B19 viremia was not associated with anemia in ESRD patients undergoing hemodialysis. Further large-scale studies are required to better clarify the role of parvovirus B19 in ESRD patients with anemia.

keywords: B19 Viremia, Anemia, Hemodialysis, PCR

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Hepatitis B and hepatitis C infections in the city of Semnan between 2021 and 2022: A Seroepidemiological Research

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Medical Virology

Background and aim: Hepatitis B and C viruses are the major public health concerns of the globe. Viral hepatitis is primarily associated with severe health complications, such as liver cirrhosis, hepatocellular carcinoma, hepatic fibrosis, and steatosis, and these viruses remain a significant problem worldwide, particularly among developing countries like Iran. The prevalence of hepatitis B is 296 million and hepatitis C is 58 million people in the world, and the prevalence of hepatitis B is 0.12 to 1.1% and hepatitis C is 0.3% in Iran. This study was conducted to investigate the seroepidemiology of hepatitis B and C in Semnan, Iran.

Methods: This cross-sectional study included 1847 people who visited the Semnan health reference laboratory from September 2021 to September 2022. Participants´ demographic data were collected and their blood samples were taken and tested for hepatitis B Surface Antigen (HBsAg), and hepatitis C virus Antibody (HCV Ab). The collected data was analyzed using SPSS 26.0 statistical software.

Results: The Persons of mean age was 31.6±12.02, and from the samples tested, 1% were positive for HBsAg, and 0.5% were positive for anti-HCV. Among the referred people, 32.8% were pregnant, of which 5 (0.8%) persons were HBS-Ag positive. Results indicated that gender was not significantly associated with HBS-Ag (p 0.05) and HCV-Ab (p 0.05). on the other hand, Examining the relationship between age and HBS-Ag showed that there is a negative correlation between age and HBS-Ag (p 0.01, r = -0.062). However, there was no correlation between age and HCV-Ab (p 0.05). Also, co-infection with HBV and HCV was not observed in the province of Semnan.

Conclusion: According to the study's findings, Semnan province had a lower frequency of HBV and HCV than other Iranian regions where earlier research had been done. In addition, the normal immunization regimen for those aged 20 to 60 should incorporate the hepatitis vaccination, and high-risk groups should continue to receive vaccinations.

keywords: Hepatitis B; Hepatitis C; Seroepidemiological.

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The prevalence and clinical features of co-infection with SARS-CoV-2 and influenza virus during the COVID-19 pandemic in Semnan, Iran

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Medical Virology

Background and aim: COVID-19 and influenza are both contagious respiratory diseases. Influenza virus can increase the severity of COVID-19 infection in the cold months of the year through damage to respiratory ciliated cells which may cause an increase in hospitalization, disease symptoms and mortality rate. Therefore, the purpose of this study was to ascertain the frequency of co-infection with the influenza virus and SARS-CoV-2, as well as the impact of co-infection on clinical outcomes in hospitalized patients suffering from respiratory problems within Semnan City, Iran.

Methods: In this cross-sectional descriptive study, we investigated 1267 hospitalized patients with respiratory problems between September 2021 and March 2022. Two nasopharyngeal and oropharyngeal throat swab samples were collected from each patient and tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A, and influenza B viruses using real-time reverse-transcriptase– polymerase-chain-reaction (RT-PCR). The collected data were analyzed with χ^2 test, ANOVA, paired Student's t-test and Pearson's

correlation coefficient test in different groups. Analyzes were done with SPSS 26.0 software.

Results: In total, 29.6% (n=375) of patients had confirmed positive results for SARS-CoV-2, and their median age was 55.4 ± 24.63 years. It was found that 1.9% (n=7) and 0.5% (n=2) of COVID-19 patients had co-infections with influenza viruses A and B, respectively. In 2.4% of the cases, co-infection with COVID-19 and influenza was found. 8 out of 9 patients (88.8%) recovered, while one patient (11.1%) died. Co-infection did not significantly correlate with cancer (p=0.588), diabetes (p=0.202), hypertension (p=0.530), or any other illness. Also, Associations of death and co-infection with diabetes, cardiovascular disease, or CKD, it showed that a statistically significant correlation was present only between diabetes and death. Based on ANOVA test to look at associations of death and co-infection with diabetes, cardiovascular disease, or CKD, it showed that there was no significant association of co-infection with diabetes (p=0.202), hypertension (p=0.530), cancer (p=0.588), and other diseases.

Conclusion: Although a low proportion of COVID-19 patients have influenza co-infection, the importance of such co-infection, especially in high-risk individuals and the elderly, cannot be ignored. Given the prevalence of influenza co-infection, increased coverage of flu vaccination is encouraged to mitigate the transmission of the influenza virus during the ongoing COVID-19 pandemic and reduce the risk of severe outcomes and mortality.

keywords: COVID-19; influenza A and B; co-infection.

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Investigating the relationship between cycle threshold of SARS-CoV-2 RT-PCR, clinical features and laboratory data in patients with neurological and autoimmune disorders

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Medical Virology

Background and aim: Coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has profoundly impacted global health and economy. Notably, the virus can persist in various organs post-infection, potentially triggering chronic inflammation and long-term health issues, including neurological and autoimmune disorders. This study investigates the association between cycle threshold (Ct) values of SARS-CoV-2 RT-PCR, clinical manifestations, and laboratory findings in hospitalized COVID-19 patients with neurological and autoimmune diseases.

Methods: This cross-sectional study included 86 COVID-19 patients hospitalized in Kowsar and Amir-Al-Momenin hospitals, affiliated with Semnan University of Medical Sciences, from September 2022 to March 2023. Nasopharyngeal and oropharyngeal swab samples were collected and analyzed using RT-PCR. Clinical data, including demographic information, clinical manifestations, and laboratory parameters, were statistically analyzed using SPSS software (version 26). Variables with p-values ≤ 0.05 were considered significant.

Results: The study cohort comprised 38 males (44.2%) and 48 females (55.8%), with a median age of 61 years. Neurological diseases were present in 12 patients

(14.0%), and autoimmune diseases in 6 patients (7.0%). The mean age of patients with neurological diseases was significantly higher compared to those without (74.75 vs. 66.24 years, p = 0.045). No significant differences were found in clinical parameters such as fasting blood glucose (FBG), white blood cell (WBC) count, and liver function tests (AST, ALT) between patients with and without neurological or autoimmune diseases. Survival analysis indicated a marginally significant association between neurological diseases and survival rates (p = 0.05), with no significant association for autoimmune diseases.

Conclusion: This study did not find significant associations between Ct values of SARS-CoV-2 RT-PCR and the presence of neurological or autoimmune diseases in COVID-19 patients. While Ct values reflect viral load, other factors such as pre-existing conditions, genetic predisposition, and immune responses might play more critical roles in the development of these conditions. Further large-scale, prospective studies are necessary to elucidate these complex relationships and improve patient management strategies.

keywords: COVID-19; SARS-CoV-2; neurological diseases; autoimmune diseases; viral load.

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The TGFβ signaling pathway could be effective in the pathogenesis of human lymphotropic virus type 1 evidence from a systems biology study;

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Medical Virology

Background and aim: HTLV1 is responsible for two critical diseases in humans: ATLL and HAM/TSP. Due to very long latent period, lack of vaccine, resistance of virus to chemotherapy and different methods of virus transmission, we will witness its spread in the next few years not only in Iran but also in the whole world. ATLL is a rare progressive disease with poor prognosis. Considering the importance of ATLL, in this study, we demand by using and integrating high-throughput microarray data, to identify the most important microRNAs involved in the induction of ATLL disease, based on the presentation of a messaging network model

Methods: After purposeful search in informations sites and qualitative review of obtained data, the data were processed using R software and miRNAs with different expression (DEMs) were detected based on the value of log fold change. The gene targets of miRNAs were obtained using miRDB online tool .The protein-protein interaction network of gene targets was drawn and analyzed with STRING database. The sub-network was extracted using cytoscape. Pathway analysis was done, and proteins participating in the enriched pathways were selected to

propose the implicated signaling network using the information available on the website ENRICHR and KEGG message transduction. An intracellular control gene, RPLP0, and three other key genes were selected and were evaluated in 10 healthy participants, 10 ACs and 10 ATLL patients using real-time PCR.

Results: From the data set (GSE 31629), mir-20a-5p, was identified as an important microRNA with different expression in the patient group in comparison with the healthy and asymptomatic carrier group. It was found that TGF-β signaling pathway is related to 1HTLV pathogenesis. TGF-β1, TGFBR1 and TGFBR2, which have a key role in regulating the mentioned pathway, were selected. Real-time PCR results showed that the expression level of TGF-β1 and TGFBR2 are decreased in ATLL compared to healthy subjects. The expression level of TGFBR1 was increased significantly in ATLL patients compared to healthy donors and asymptomatic carriers

Conclusion: In this study, by collecting different data, using high-throughput data integration and bioinformatics techniques, some miRNAs and genes involved in the immunopathogenesis of ATLL were identified. The expression level of these genes between patients and healthy groups' were significantly different. So by drawing a model of the messaging network involved and the possible role of genes in pathogenesis, the pathways involved in carcinogenesis as well as in the treatment of these patients can be identified.

keywords: Human T-cell lymphotrophic virus type 1, HTLV1, Adult T-cell leukemia/lymphoma,

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The Role of Antioxidants in Reducing Oxidative Stress and Increasing Longevity in AIDS Patients

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Medical Virology

Background and aim: The HIV virus, which causes AIDS, can induce oxidative stress in the body, leading to cell damage and a weakened immune response that may hinder treatment success over time. To counteract these effects, individuals can enhance their antioxidant defenses by incorporating vitamins like C and E into their diet, as well as minerals such as selenium and zinc. Additionally, consuming tea and vegetables rich in plant compounds like flavonoids and carotenoids can help rebalance oxidant and antioxidant levels in the body, potentially extending the lifespan of individuals with AIDS.

Methods: To investigate the relationship between oxidative stress, HIV/AIDS, and antioxidants, we conducted a study focusing on relevant journals. We used keywords such as "HIV and oxidative stress," "AIDS treatment and antioxidants," and "vitamins in HIV patients" to guide our searches in databases like PubMed, Google Scholar, and Scopus. Our inclusion criteria centered on studies that specifically addressed the role of antioxidants in reducing oxidative stress and increasing longevity in patients with AIDS, while excluding unrelated articles.

Results: Excessive production of free radicals and reactive oxygen species (ROS) can lead to significant damage to cellular structures, including proteins, lipids, and DNA. This damage disrupts essential cellular functions such as intercellular communication, metabolism, and transport systems. In AIDS patients, such

oxidative damage can further weaken the immune system, making them more vulnerable to opportunistic infections and other health complications. Additionally, HIV infection inherently induces oxidative stress due to the virus's direct effects. Infected cells produce ROS as part of their nature, and the disease also triggers oxidative stress through heightened inflammatory pathways in immune cells. The complex interplay of these factors underscores the challenges faced by individuals living with HIV/AIDS and highlights the importance of understanding and managing oxidative stress in these patients

Conclusion: Therefore, people with HIV/AIDS should maintain a healthy diet rich in antioxidants to help combat oxidative stress and its dangerous consequences in the body. Additionally, antioxidant supplements can be taken in some cases to help combat the oxidative consequences of HIV.

keywords: Antioxidants; Oxidative Stress; HIV/AIDS; Increasing Longevity

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Molecular mechanisms of HPV persistence and progression: Highlighting the role of psychosocial stress and immune responses

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Medical Virology

Background and aim: Human papillomavirus (HPV) is a double-stranded DNA virus from the Papillomaviridae family. This virus is primarily transmitted through sexual contact and direct skin-to-skin contact. HPV represents a large family of viruses and is the most common sexually transmitted infection. According to statistics from the World Health Organization, cervical cancer is one of the leading causes of death in women of reproductive age in developing countries and is considered the fourth most common malignancy among women globally, following breast, colorectal, and lung cancers. The present study aims to provide a comprehensive review of HPV and examine the impact of psychological stress

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including Human papillomavirus, psychological stress, inflammation, immunity and cervical carcinoma were investigated and combined using Boolean operators (e.g., AND, OR).

Results: The importance of the article is how stress affects the response of the immune system related to HPV infection. However, during psychosocial stress, a decrease in the Th1 type of immune response is seen, and there is a shift towards a Th2 response. HPV-induced early-stage local Th2 inflammatory response, characterized by the presence of antibody-producing cells, creates an immunosuppressive microenvironment that promotes tumor growth. Concerning the course of HPV manifestations, it has been observed that a higher number of life stressors in at least the previous 6 months, the absence of social support and

the types of personal coping mechanisms employed, all influence HPV progression. In women with cervical dysplasia, a connection between greater stress experiences and dysregulation of specific immune responses has been observed. Once HPV enters a cell via the α6 integrin there are three possible sequences: latent infection, subclinical infection, and clinically manifest disease. HPV proliferation in

Conclusion: Present findings suggest that stress is an important risk factor for HPV manifestation development and carcinogenesis. Understanding the key factors and processes clears the way for effective prevention and therapeutic intervention and also gives researchers a better picture of how stress influences HPV infections and how to improve disease management and outcomes. Even though psychological factors have not been considered in many past epidemiological studies, they are now understood to be important in the setting of frequent and sometimes very serious illnesses such as HPV

keywords: Human papillomavirus, psychological stress, inflammation, immunity, cervical carcinoma

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Innovative Application of NBS Superfood as an Adjuvant Therapy to Address Therapeutic Challenges in Infectious Diseases: Clinical Trial Findings in Patients with COVID-19-Related ARDS

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Medical Virology

Background and aim: Addressing the challenges in treating infectious diseases, including pathogen resistance, drug inefficacy, and the emergence of new infectious agents, to develop more effective therapeutic strategies as adjunctive therapy.

Methods: The study randomly assigned 400 patients with Covid-19-related ARDS into two groups: intervention (n=200) and control (n=200). The intervention group received NBS powder (1.5 grams/day) for two weeks in addition to standard antiviral therapy, while the control group received a placebo with the same antiviral therapy. Blood samples were collected from all participants, and various laboratory parameters indicating inflammatory response and immune cell status were assessed.

Results: The intervention group displayed a statistically significant decrease in mean serum levels of inflammatory markers, including CRP (15.39 vs. 48.49, p0.001), ESR (14.28 vs. 34.03, p0.001), D-Dimer (485.18 vs. 1009.13, p=0.001), and CPK (68.93 vs. 131.48, p0.001), highlighting the anti-inflammatory potential of

NBS (Figure1). Additionally, a significant increase in mean lymphocyte count was observed in the intervention group (1537.06 vs. 1152.60, p0.001) (Figure2). More patients in the intervention group normalized CRP, ESR, D-Dimer, and CPK levels compared to the control group (p0.001). Additionally, the intervention group had a significantly lower mortality rate (8.5%) than the control group (31%, p=0.001), highlighting the potential life-saving impact of NBS supplementation alongside standard antiviral treatment.

Conclusion: NBS Superfood significantly reduced mortality rates in patients by modulating inflammatory responses and enhancing lymphocytic function. NBS Superfood has the potential to minimize the challenges of target-specific therapies and provide effective therapeutic assistance to patients regardless of the type of pathogens.

keywords: adjunctive therapy - Covid-19 - Infectious disease

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Aqueous extract of Areca catechu L. anti-viral efficacy against in-vitro anti-HSV1

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Medical Virology

Background and aim: Background and Objectives: HSV-1 is known as a very contagious virus and the main cause of cold sores or fever blisters. Herein, the aqueous extract of Areca catechu L. was evaluated for its anti-HSV-1 activity, compared to the standard control (acyclovir). Also, the effect of extract on the expression of UL46 and US6 genes that accumulate late in viral infection, was studied.

Methods: Materials and Methods: The aqueous extract was obtained by the maceration of powdered plant in boiling water. Its anti1viral activity was evaluated on Vero cells infected with HSV-1 at different times: 2 h pre-infection, simultaneous infection, and 4 h post-infection, using MTT assay. The effect of extract on the expression of genes was investigated with quantitative real-time PCR

Results: Results: The aqueous extract of A. catechu induced the inhibition of infection with the IC value of 110.52 ± 1.36 µg/ml. Also, it reduced the expression of UL46 when it was added 2 h pre-infection at 100 µg/ml. Moreover, reduction of expression of US6 was observed at the same concentration when the extract was used simultaneously with the occurrence of infection and 4 h post-infection.

Conclusion: Conclusion: A. catechu can be considered an essential element of natural-based anti-HSV-1 agents.

keywords: Areca catechu; Gene expression; Herpes simplex virus type 1

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Common rotaviruses circulating in Iran,2023-2024

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Medical Virology

Background and aim: Background and Aim: Rotaviruses are the dominant cause of severe acute gastroenteritis in children under 5 years of age, which is responsible for causing an estimated 128,500-215,000 deaths in children, and mostly occur in the lower-income countries of Asia and Africa. In the pre-vaccine era of countries such as Iran, since rotavirus remains the most predominant viral agent of acute gastroenteritis (range, 15.3%–67.6%), identify the different combinations of G and P genotypes of Iranian RVA strains at the population level, which might influence susceptibility to rotavirus gastroenteritis.

Methods: 300 stool specimens were screened by PCR for detection RAV and Nested RCR for genotyping during 2023 to 2024 from the children's hospital in Tehran.

Results: Out of a total of 300 stool samples, 100 samples (33%) were positive for rotavirus and after G and P genotyping, the combination of G3P [8] RVA strain (50%) predominant.

Conclusion: In Iran genotype combination G1P [8] accounted for over 50% of all RVA infections, although G3P [8], G4P [8], G9P [4] and G9P [8] were occasionally documented as the most common combination. The data presented in this study indicate a change in the pattern of rotavirus genotypes in the Iranian population. Therefore, continuous monitoring and identification of circulating RVA strains before RVA vaccination can provide a better understanding of the genetic structure of Iranian RVA strains and help to choose the appropriate vaccine before starting the national vaccination program.

keywords: Rotavirus Group A

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Possible relationship between HPV and Trichomonas vaginalis in the development of cervical cancer

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Medical Virology

Background and aim: Cervical cancer is one of the most common malignancies in women all over the world, and one of the important causes of its occurrence is infection with the human papillomavirus (HPV), which causes more than 70% of cervical cancer. On the other hand, studies show that the infection and inflammation caused by the Trichomonas vaginalis parasite along with HPV infection can increase the carcinogenic effect of this virus with cytotoxicity and destruction of the basement membrane of cells.

Methods: In the review, the keywords HPV, cervical cancer, sexually transmitted disease, T. vaginalis, and heat shock proteins (HSP) were searched. Databases such as Google Scholar and PubMed were used from 2017 to 2024. Finally, 14 articles were selected and comprehensively studied.

Results: HPV virus especially serotypes 16 and 18, is one of the most important causes of cervical cancer. Many factors contribute to persistent HPV infection and advanced cervical lesions including biological, behavioral, and environmental factors, age, number of sexual partners, use of contraceptives and T. vaginalis. T. vaginalis is a flagellated protozoan pathogen of the human reproductive system and has played a very important role in the continuation of HPV by inducing inflammatory responses and releasing lytic enzymes, destroying the mucous

layers of the cervix. parasite reducing vaginal fluids, disrupting the mucosal barrier with IgA immunoglobulin lysis. Also, the reduction of vaginal lactic acid bacteria facilitates the entry of HPV into the layers of the epithelium and causes the integration of viral DNA with the host DNA, and by overexpressing viral oncogenes and promoting the adhesion and invasion of the virus, activates the carcinogenesis mechanism.

Conclusion: About the prevention of cervical cancer, annual pap smear tests, protected intercourse, avoiding oral sex and injecting Gardasil vaccine. On the other hand, it is necessary to conduct more studies related to the effect of T. vaginalis and the effect of HPS proteins in the development of cervical cancer.

keywords: HPV, cervical cancer, Trichomonas vaginalis, Sexually transmitted diseases (STD).

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Setup and Optimization of RT-PCR for the Detection of Hepatitis B Virus Pregenomic RNA

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Medical Virology

Background and aim: Hepatitis B is a major public health issue, causing approximately 1 million deaths in 2022 due to cirrhosis and liver cancer. A key challenge in diagnosis and treatment is the persistence of covalently closed circular DNA (cccDNA) in infected cells, which sustains viral replication. Pregenomic RNA (pgRNA), transcribed from cccDNA, mediates replication and is reverse-transcribed into new viral genomes. Unlike HBsAg, which may indicate non-replicating virus, HBV pgRNA reflects active viral replication. This study aims to develop a RT-PCR test to detect hepatitis B via pgRNA, providing a reliable marker of ongoing infection.

Methods: Positive samples were collected from the serum of HBV-infected donors who tested positive for HBsAg. Due to its high sensitivity, the Trizol method was used to extract viral RNA, followed by cDNA synthesis. RT-PCR was performed using a primer pair targeting the viral core gene. The concentrations of the reaction components were then adjusted to ensure maximum specificity. The optimal cycling temperatures were determined using a temperature gradient. Finally, the band corresponding to the target gene was visualized by 1.5% agarose gel electrophoresis.

Results: In positive samples, the HBV core gene was amplified, and the resulting band was observed on electrophoresis, indicating the presence of HBV pgRNA in the serum of the hepatitis B donor.

Conclusion: When HBV DNA levels are low or in cases of intermittent viremia, this test can detect active viral infection in individuals with hepatitis B.

keywords: Hepatitis B Virus; pgRNA, Pregenomic RNA; RT-PCR;

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A New Frontier in Breast Cancer Treatment: The Role of Oncolytic Viruses in Tumor Immunomodulation-A systematic review

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Medical Virology

Background and aim: Breast cancer is a major contributor to cancer-related deaths, especially in its metastatic form, where resistance to conventional treatments often limits effectiveness. These treatments typically lack the ability to specifically target tumor cells, leading to significant side effects. Oncolytic virotherapy, which uses viruses engineered to selectively attack cancer cells while activating the immune system, presents a novel and promising alternative. This study aims to examine the potential of oncolytic virotherapy for breast cancer, focusing on its underlying mechanisms, current limitations, and how it might be integrated with existing therapies.

Methods: A systematic literature review was conducted using Google Scholar and PubMed, with search terms such as “breast cancer,” “oncolytic virus,” and “immunotherapy.” Research from 2017 to 2024 was reviewed, with particular attention to studies addressing the effectiveness of viral therapy, immune activation, and targeted tumor destruction. The review focused on aspects of immune modulation, tumor cell lysis, and challenges in delivery.

Results: Finally 6 articles were included in the study. The findings indicate that oncolytic viruses can promote immune cell infiltration in breast tumors, effectively transforming them from "cold" (immunologically inactive) to "hot" (responsive to immune-based therapies). In preclinical models, viruses like

adenovirus and herpes simplex virus have shown potential for reducing tumor size, especially when used in combination with chemotherapy or immune checkpoint inhibitors. However, challenges remain, such as viral neutralization by the immune system and the difficulty of targeting tumors through systemic delivery, suggesting a need for improved methods.

Conclusion: Oncolytic virotherapy shows considerable promise as a targeted strategy for breast cancer, with the potential to boost immune responses and reduce tumor growth. Moving forward, further research to enhance delivery and develop combination approaches will be essential for its successful integration into breast cancer treatment.

keywords: Breast Cancer; Oncolytic Virus; Virotherapy; Immunotherapy; Tumor Microenvironment.

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Prevalence and Implications of Human Papillomavirus Infection Among Women Aged 18-60 in Iran: A Meta-Analysis of 2,000 Cases

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Medical Virology

Background and aim: Human papillomavirus (HPV) infection is one of the main causes of cervical cancer worldwide, affecting millions of women annually. In Iran, HPV epidemiology poses an important public health challenge. This study systematically analyzed the prevalence of HPV infection among women aged 18–60 years in Iran and identified the most common types of HPV associated with these infections.

Methods: Data were collected from studies published between 2010 and 2023 focusing on women aged 18–60 years who underwent HPV testing. Inclusion criteria were to provide clear HPV prevalence rates and identify genotypes. The meta-analysis included 2000 women from urban and rural health centers. Prevalence rates were extracted and statistical analyses were performed to assess the overall infection rates and the most frequently detected viral types.

Results: The overall HPV prevalence among the investigated women was 20.4%. High-risk HPV types are frequently identified, emphasizing public health implications. The most common genotypes were HPV-16 (45%), HPV-18 (30%), HPV-31 (12%) and HPV-33 (8%). Demographic analysis showed that the rate of infection was significantly higher in women aged 25-35 compared than in the older groups, indicating a critical intervention window.

Conclusion: The high prevalence of HPV, especially high-risk genotypes, indicates an urgent need to increase awareness and develop prevention strategies in Iran.

The association between HPV and cervical cancer warrants comprehensive public health initiatives including vaccination programs for young women. Education campaigns should address HPV stigma and promote regular screening for early detection and management of cervical precancerous lesions. This meta-analysis shows the prevalence of HPV infection among Iranian women, emphasizing the need for public health measures to increase vaccination and screening rates. Addressing the gaps in awareness and access to

keywords: HPV (Human Papillomavirus), Prevalence, Cervical Cancer, Public Health, HPV Vaccination

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Prevalence of West Nile anti-virus antibodies in industrial slaughterhouse staff and comparison with control group

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Medical Virology

Background and aim: West Nile virus is an encephalitis-causing virus. It is an arbovirus belonging to the Flaviviridae family. The virus has spread to different geographical areas. The environment can be a contributing factor to this infection. This virus is also circulating in Iran. One of the World Health Organization's slogans is occupational health, which is very important. According to extensive studies, occupations such as slaughter are among the most high-risk occupations in the field of this disease

Methods: Sampling was not imposed on the participants in the study, and the disposable surplus of the approved sample of 940483 was used. ELISA assessment was performed in two groups of industrial slaughterhouse staff and a control group using an ELISA assessment kit. For the control group, the discarded surplus of serum samples referred to the laboratory of Ghaem Special Clinic (in the same age and sex group as the slaughterhouse staff) was used randomly to obtain consent and observe ethical codes, including confidentiality of the individual's name.

Results: Ninety participants with eligibility criteria were divided into two groups and included in the study. The mean age (standard deviation ± Mean) was 45.06 10.70. With a minimum of 18 and a maximum of 65 years. Quantitative values of the ELISA test were 0.13±0.37 in the target group (standard deviation ± Mean) and 0.10 ± 0.27 in the control group (standard deviation ± Mean) (P-Value = 0.038). The results, based on the age range of sick and healthy individuals studied,

indicate (standard deviation ± Mean) 37.23 ± 10.38 years among patients and (standard deviation ± Mean) 48.98±8.55 years among individuals Was healthy (P-Value = 0.000).

Conclusion: This study's results provide evidence of the risk of people being exposed to emerging viruses in the workplace. Therefore, the need for more extensive and complementary studies to gain the necessary insight into the circulation of viruses in more expansive geographical areas and different scenarios of high-risk and involved jobs is strongly felt. Also, good physical health and young age are not protective parameters against the disease, as the average age of people with positive titers of antibodies against West Nile virus was significantly lower than that of healthy people.

keywords: West Nile virus; ELISA; antibody; slaughterhouse

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Role of Respiratory Syncytial Virus (RSV) and Influenza in Patients with Otitis Media with Effusion (OME)

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Medical Virology

Background and aim: Otitis media is a group of inflammatory and infectious diseases that is a leading cause of referral for systemic therapy worldwide, often resulting in serious complications, particularly in developing countries. Otitis media with effusion is characterized by the accumulation of high viscosity fluid behind the healthy tympanic membrane in the middle ear, with an unclear etiology. The aim of this study is to explore the roles of respiratory syncytial virus and influenza in otitis media with effusion in affected patients.

Methods: This study utilized an analytical epidemiological approach on 53 patients with otitis media with effusion who underwent myringotomy and VT implantation due to surgical necessity. Middle ear fluid samples were collected during the operation and analyzed using PCR with specific primers for respiratory syncytial virus (RSV) and influenza.

Results: A total of 53 patients, comprising 30 men (56.6%) and 23 women (43.4%) with an average age of 3.98 ± 1.70 years, were included in the study. RSV was detected in samples from 44 patients (83.0%), while it was not found in samples from 9 patients (17.0%), showing a statistically significant difference (P=0.000). Influenza virus was present in samples from 4 patients (7.5%) and absent in samples from 49 patients (92.5%), also demonstrating a statistically significant difference (P=0.000).

Conclusion: The findings of this study suggest that RSV likely plays a significant role in the pathogenesis of otitis media with effusion, while influenza virus may not be a major contributor and may not warrant further investigation in future studies.

keywords: otitis media with effusion, respiratory syncytial virus, influenza virus

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Defenders in the Shadows: TRIM21 and TRIM22 as Key Modulators in Infectious Disease Immunity

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Medical Virology

Background and aim: TRIM21 and TRIM22 are increasingly recognized as central modulators in the immune response to infectious diseases, playing crucial roles in identifying and counteracting pathogens. These proteins belong to the tripartite motif (TRIM) family and contribute to host immunity by engaging with viral components and regulating immune signaling pathways.

Methods: Studies incorporating in vitro and in vivo analyses reveal their mechanisms, focusing on immune responses, protein interactions, and transcriptional regulation. This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords TRIM21, TRIM22, Infectious disease, 83 articles related to inclusion criteria were extracted and then analyzed.

Results: TRIM21 is highlighted for its ability to bind antibody-coated viral proteins in the cytoplasm, effectively marking them for proteasomal degradation, while TRIM22 suppresses viral replication by modulating transcriptional activity.

Conclusion: Together, TRIM21 and TRIM22 provide a dynamic layer of immune defense, suggesting potential therapeutic applications. Targeting these pathways could enhance immune responses to viral infections, offering promising strategies for managing infectious and inflammatory diseases.

keywords: TRIM21, TRIM22, Infectious disease.

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Application of Biosensors in Diagnosis of Human Parvoviruses

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Medical Virology

Background and aim: Human parvovirus B19 is a viral pathogen that causes acute and usually self-limiting disease. Because the B19 virus predicates erythroid progenitor cells, it can cause a transient aplastic crisis in immunocompromised individuals. This infection has been associated with nonimmunologic fetal hydrops during pregnancy; also, B19 can persist for months in immunocompromised individuals. In B19 infection, viremia with a high titer is observed for approximately one week. After that, a specific immune response is critical to control the infection. Although molecular and serologic tests commonly diagnose the B19 virus, laboratory diagnostic tests have limitations.

Methods: The development of a B19 virus biosensor platform can be divided into three phases; 1) detection of various bioreceptors such as B19 DNA or proteins, human immunoglobulins, and human microRNA (miRNA); 2) hybridization detection methods such as electrochemical, piezoelectric, colourimetric, fluorescent, magnetic, and acoustic technologies, and 3) use of an immobilized bioreceptor such as a DNA probe, ligand, enzyme, antibody/antigen.

Results: A biosensor is a portable analytical device detecting at least one biological or chemical substance. Biosensors allow the detection of viral diseases in a sensitive, rapid, simple, and inexpensive manner. Biosensors are distinguished according to the type of biological detection element or the type of physicochemical conversion. Depending on the type of transducer, biosensors are divided into optical, piezoelectric, electrochemical, and thermal biosensors.

Conclusion: Biosensing technologies have been used as novel diagnostic tools for diagnosing viral pathogens. As susceptible instruments, biosensors provide results in a fraction of the time required by conventional methods. Because B19 diagnosis plays an essential role in infection control and public health interventions, developing a biosensor may be a crucial tool in detecting B19 infection. For the detection of human parvovirus B19, an inexpensive, effective, and rapid biosensor may be considered as an alternative.

keywords: : Human Parvovirus B19; Biosensor; Molecular and Serological Diagnosis

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Graphene Oxide Nanosheet as a Promising Antiviral Nano-Warrior: In Vitro Efficacy against Herpes Simplex Virus Type 1

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Medical Virology

Background and aim: Viruses are nanoscale entities and could be regarded as natural nanomaterials. Since viruses and nanoparticles operate at the same length scale, nanotechnology provides novel strategies to battle viruses through diagnostic, preventive, and therapeutic interventions. Among various nanomaterials, graphene oxide (GO) nanosheets have revolutionized clinical medicine in the past ten years, thanks to its unique and inspiring physicochemical characteristics, such as chemical stability, good biocompatibility, significant bioactivity, easy functionalization, low-cost mass production, and so forth. In this context, we aimed to explore the virucidal potential of GO nanosheets. Herpes simplex virus type 1 (HSV-1) was used as enveloped virus model.

Methods: FTIR spectroscopy, Raman spectroscopy, EDX analysis, DLS/ZP measurements, and TEM were performed to characterize and confirm the formation of GO nanosheets. The MTT assay was used to assess the cytotoxicity of GO nanosheets on Vero cells (African green monkey kidney cell line). To evaluate the antiviral potential of GO nanosheets, a virucidal assay was conducted by incubating HSV-1 with sub-toxic concentrations of GO nanosheets at 37°C for 1 hour, followed by infection of Vero cells at 37°C. The antiherpetic potency was determined using the 50% tissue culture infectious dose (TCID50) and real-time PCR (qPCR) assays. TCID50 and qPCR were employed to evaluate

the effect of GO nanosheets on the production of viable viruses and the copy number of viral genomic DNA, respectively.

Results: The MTT results showed that the viability of Vero cells remained above 90% up to a concentration of 100 µg/mL. Incubation of HSV-1 with 100 µg/mL of GO nanosheets could result in 1.9 log10 TCID50/mL reduction in virus titers, with an inhibition rate of approximately 49% in the copy number of viral genomic DNA (P value 0.05).

Conclusion: The findings from this research highlight the potential of GO nanosheets as an effective virucidal agent. The best-known mechanisms responsible for the antiviral effects of GO nanosheets include two primary actions: (i) the physical disruption of viral envelopes caused by the sharp edges of the GO nanosheets and (ii) the interaction between the inherent negative charge of GO nanosheets and various viral components, which interfere with viral integrity. While the prophylactic potential of this nanodrug is promising, its effectiveness and safety must be verified through in vivo animal trials.

keywords: HSV-1; Graphene oxide; Nanotechnology; Nanodrug; Virucidal

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Graphene Oxide Nanosheet for Combating Influenza Virus H1N1: An In Vitro Study

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Medical Virology

Background and aim: Various methods have been explored to eliminate viruses, including ultraviolet (UV) light, chemical disinfectants, and metallic materials. However, the overuse of these approaches may contribute to viral mutations. As a result, nanomaterials with inherent antiviral properties offer a promising solution for preventing the transmission of viral infections. Graphene oxide (GO) nanosheets, a rising star among carbon-based materials, hold significant potential for next-generation antiviral therapies due to their environmental safety and cost-effective production. This research aimed to assess the ability of GO nanosheets to destroy viruses. Influenza virus A/Puerto Rico/8/1934 H1N1 (PR8) was used as enveloped virus model.

Methods: FTIR spectroscopy, Raman spectroscopy, EDX analysis, DLS/ZP measurements, and TEM were performed to characterize and confirm the formation of GO nanosheets. The MTT assay was used to assess the cytotoxicity of GO nanosheets on MDCK cells. To evaluate the antiviral potential of GO nanosheets, a virucidal assay was conducted by incubating PR8 with sub-toxic concentrations of GO nanosheets at 37°C for 1 hour, followed by infection of MDCK cells at 37°C. The anti-flu potency was determined using the 50% tissue culture infectious dose (TCID50) and real-time PCR (qPCR) assays. TCID50 and qPCR were employed to evaluate the effect of GO nanosheets on the production of viable viruses and the copy number of viral genomic RNA, respectively.

Results: The MTT results showed that the viability of MDCK cells remained above 90% up to a concentration of 125 µg/mL. Incubation of PR8 with 125 µg/mL of GO nanosheets could result in 1.7 log10 TCID50/mL reduction in virus titers, with an inhibition rate of approximately 41% in the copy number of viral genomic RNA (P value 0.05).

Conclusion: This research will demonstrate the potential of integrating GO nanosheets into various technologies, such as sludge treatment systems, water filters, face masks, air purifiers, antiviral surfaces, wearable sensors, and biosensors. The interaction between GO nanosheets and the virus will disrupt the viral lipid bilayer and significantly prevent the viral particles from infecting cells. This wet lab/in vitro study opens new avenues for developing a much-needed nanoweapon to prevent flu infections.

keywords: Influenza virus H1N1 (PR8); GO nanosheets; Nanomedicine; Nanodrug; Air purifier

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Trigger mechanisms of viral infections in Diabetes

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Medical Virology

Background and aim: Diabetes is a chronic, complex, and multifactorial disease. Many aspects of this condition remain unknown, although some studies have shown an association between viral infections and the progression of diabetes. This study aims to investigate the relationship between viruses and the development of type 1, type 2, and gestational diabetes

Methods: This investigation identified relevant literature by searching in the Scopus, PubMed, Google Scholar, and Web of Science databases. The keywords used were "viral infections," "Diabetes," and "Gestational Diabetes," focusing on publications from 2020 to 2024. Selection criteria included original research articles, clinical trials, and case reports, with only English-language articles considered.

Results: Viral infections can destroy pancreatic beta cells "Crime scene" through three main mechanisms: direct invasion (molecular mimicry), hit-and-run scenario, and induced oxidative stress. Chronic infection can induce endoplasmic reticulum stress, the generation of neoantigens and autoantibodies, apoptosis, and subsequent β-cell destruction. Antiviral medications have shown promise in preserving beta cell function after diabetes onset. The impact of antiviral therapies in maintaining residual insulin production in newly diagnosed patients reinforces the hypothesis that viral infections may act as triggers for the onset of diabetes in individuals with a genetic predisposition. Studies have linked several viruses, such as Coxsackievirus B, Herpesviruses, Hepatitis C, SARS-CoV-2, and

others, to the development of diabetes. A temporal relationship has been observed between the emergence of initial autoantibodies and signs of enterovirus infection, both in siblings of children with diabetes and in those with an increased genetic risk for the condition due to their HLA genotype.

Conclusion: Diabetes remains a considerable challenge for patients, affecting them physically, emotionally, and in terms of their treatment. Several research studies have indicated that viruses may play a role in the onset of diabetes. Understanding the role of viruses in the development of various forms of diabetes will enhance our knowledge of the disease and improve management strategies. Utilizing in silico techniques, machine learning, and Boolean network analysis, along with laboratory and clinical studies, can help identify key pathways involved in disease progression. This approach may ultimately facilitate the discovery of

keywords: Diabetes mellitus; viral infection; immune system

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The prevalence of human bocavirus (HBoV) among patients with gastroenteritis in Tehran

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Medical Virology

Background and aim: Human bocavirus (HBoV) is an emerging viral infection affecting the respiratory and gastrointestinal tracts. This study aimed to assess the epidemiology and genotype distribution of HBoV in patients experiencing acute gastroenteritis (AGE).

Methods: A total of 150 stool samples from patients exhibiting clinical symptoms of AGE were obtained from hospitals across different regions of Tehran, Iran. Samples were collected and evaluated for the presence of HBoV using real-time polymerase chain reaction (PCR). For sequencing, the nested-PCR method was employed, targeting the viral protein-1/2 (VP-1/2) region.

Results: HBoV was detected in 7 out of the 150 (4.6%) fecal samples analyzed. The detection rates were nearly identical across genders. Main clinical manifestations in HBoV-positive patients included diarrhea (100%), malaise (100%), fever (90.9%), fatigue and weakness (72.7%), vomiting (63.6%), and cramps and abdominal pain (63.6%). Sequencing of the VP1 region confirmed the presence of only HBoV-2 and HBoV-3 genotypes in this study.

Conclusion: : This study delineates the distribution of HBoV genotypes among AGE patients in Tehran, Iran, suggesting a potentially significant role for HBoV as an etiological agent of AGE cases in the region. Further studies across various parts of Iran are recommended to elucidate the role of HBoV as AGE pathogens. In addition, the findings reveal HBoV-2 as the predominant genotype in Iranian AGE patients.

keywords: Human bocavirus, acute gastroenteritis, genotypes, diarrhea

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The overview of biosensors and Human Respiratory syncytial virus (hRSV): A systematic review

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Medical Virology

Background and aim: Respiratory syncytial virus (RSV) causes more than 30 million cases of lower respiratory tract infections (LRTIs) and approximately 3 million hospitalizations globally each year. Although RSV is particularly dangerous for young children, but also older adults, and those with underlying health conditions or suppressed immune systems are in danger. Therefore, the rapid diagnosis of this virus infection is crucial for ensuring patients receive timely and effective treatment, as well as for preventing the spread of the disease. Many conventional techniques were used against RSV. However, some of the techniques are time-consuming, expensive, or labor-intensive. Recently, the Biosensors has gained attention

Methods: This review involved gathering original articles published in English from various databases, including PubMed, Scopus, Web of Science, and Embase, spanning the period from August to November 2023. Additionally, the reference lists of the articles were examined for further relevant sources in google scholar. Among 253 electronically searched citations, 28 articles met the inclusion criteria.

Results: Genosensors, particularly those employing surface-enhanced Raman scattering (SERS) and optical detection exhibited the greatest potential and extensive application for diagnosing RSV. The application of biosensors is growing for RSV detection, offering high sensitivity and accuracy, with the rapidity of these sensing methods being equally important.

Conclusion: The findings indicate that the most prevalent techniques for detecting RSV are immunofluorescence (IF), ELISA, cell culture, and RT-PCR (Real-time PCR). While molecular methods are both quick and sensitive, they necessitate advanced laboratory equipment and trained personnel capable of interpreting the results. In contrast, biosensors provide a speedy, reliable, and cost-effective diagnostic approach, making their enhancement crucial, especially in resource-limited environments.

keywords: Human Respiratory syncytial virus (hRSV); biosensors; Genosensors

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The Role of Surfactant Protein-D Gene Polymorphism in COVID-19 Susceptibility and Clinical Outcomes

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Medical Virology

Background and aim: COVID-19, caused by SARS-CoV-2, presents a wide range of clinical manifestations, from asymptomatic cases to severe illness. Pulmonary surfactant protein D (SP-D) plays a crucial role in lung immune defense and is affected by genetic variations, such as the rs721917 polymorphism, which has been linked to respiratory diseases. Emerging evidence suggests its potential role in COVID-19 outcomes; yet, its impact remains understudied. This study aimed to investigate the association between the rs721917 polymorphism of the SP-D gene and COVID-19 susceptibility and severity in an Iranian population, providing insights into the genetic factors influencing disease outcomes.

Methods: This retrospective case-control study, approved by the Ethics Committee of Jundishapur University (IR.AJUMS.REC.1401.503), involved 135 participants. From February to May 2022, 111 COVID-19-positive patients were admitted to Razi Hospital in Ahvaz, Iran, confirmed by clinical symptoms and qualitative PCR. The control group consisted of 24 asymptomatic individuals with negative PCR results. COVID-19 severity was classified into five stages based on clinical and laboratory assessments. Genomic DNA was extracted from peripheral blood using the Sinacolon Kit, and Tetra-ARMS-PCR was employed to amplify the rs721917 SNP. The PCR products were visualized by gel electrophoresis and sequenced. Statistical analyses were performed using SPSS 22.0, with χ^2, ANOVA, and t-tests, and a significance level set at p 0.05 for genotype comparisons and Hardy-Weinberg equilibrium.

Results: This study analyzed 135 participants, including 111 COVID-19 patients (15 mild, 42 moderate, 37 severe, 17 critical) and 24 asymptomatic individuals. The mean age was 56.6 ± 17.4 years, with 57% female and 43% male participants.

Disease severity increased with age (p 0.05). Severe cases had higher leukocyte counts, D-dimer levels, and inflammatory markers (p 0.05). SFTPD rs721917 genotyping showed significant associations with disease severity. The TT genotype was most frequent in severe cases, associated with a 3.8-fold higher ICU/CCU hospitalization risk (p 0.05). The CT genotype appeared more in moderate cases, while the CC genotype was less frequent in severe cases. The T allele was linked to higher severity stages (p 0.05). Genotype frequency varied by gender but not by age, and no significant correlation with mortality was observed (p 0.05).

Conclusion: This study highlights the significant association between the SFTPD rs721917 TC polymorphism and COVID-19 severity. The TT genotype was linked to increased disease severity and ICU/CCU hospitalization risk, underscoring the role of surfactant protein D in immune defense. These findings emphasize the importance of genetic profiling in identifying individuals at higher risk for severe outcomes. Future research should explore SP-D serum levels, other SARS-CoV-2 variants, and diverse populations to better understand the genetic factors influencing COVID-19.

keywords: COVID-19; SARS-CoV-2; Pulmonary Surfactant-Associated Protein D; Polymorphism; Single Nucleotide

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Identification of Potential Biomarkers for COVID-19 and Influenza Viruses Using a Network-Based Approach

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Medical Virology

Background and aim: COVID-19, caused by SARS-CoV-2, and influenza virus are major respiratory diseases with global health impacts. While they share similarities in transmission, symptoms, and immune responses, they differ in terms of severity, mortality rates, and systemic effects. Despite extensive research, the genetic mechanisms driving host responses remain unclear. This study uses microarray technology to analyze differential gene expression, aiming to identify key hub genes and enriched pathways common to both diseases. By uncovering these molecular mechanisms, the study aims to enhance understanding of their pathogenesis and contribute to the development of more effective therapeutic strategies.

Methods: Gene expression data for COVID-19 (GSE157103) and influenza virus (H1N1) (GSE21802) were retrieved from the Gene Expression Omnibus (GEO) database (https://www.ncbi.nlm.nih.gov/geo). The dataset comprised 94 COVID-19 patient samples, 23 non-COVID-19 samples, 36 critical H1N1 patients, and 4 healthy controls. Differentially expressed genes (DEGs) were identified using GEO2R, with criteria of p-value 0.05 and log fold change (logFC) 1 or -1. Common up-regulated DEGs between COVID-19 and influenza were identified using the Venny tool (https://bioinfogp.cnb.csic.es/tools/venny/). Gene ontology (GO) and KEGG pathway enrichment analyses were performed using Enrichr (https://maayanlab.cloud/Enrichr). Protein-protein interaction (PPI) networks were constructed with STRING (https://string-db.org/) and visualized using Cytoscape 3.9.0. Top hub genes were selected using degree centrality and clusters from the CytoHubba and MCODE plugins. Potential drugs targeting common up-regulated DEGs between the COVID-19 and influenza virus datasets were

identified via the Enrichr and DSigDB databases, applying an adjusted p-value threshold of 0.05.

Results: A total of 1,637 DEGs were identified in COVID-19, including 1,045 up-regulated, and 1,160 DEGs in influenza, with 566 up-regulated. Venny analysis revealed 106 shared up-regulated DEGs between the two diseases. Functional enrichment analysis highlighted their involvement in GO biological processes such as "defense response to bacterium, symbiont, and virus." GO cellular components included "specific granules," "granule lumen," and "secretory granule lumen," and GO molecular functions involved "double-stranded RNA binding," "adenylyltransferase activity," and "protein heterodimerization." KEGG pathway analysis indicated roles in the "cell cycle," "progesterone-mediated oocyte maturation," and "oocyte meiosis." The PPI network constructed included 85 nodes and 759 edges. Based on degree centrality, hub genes identified in cluster 1 were TYMS, CDK1, CCNB2, CDC25A, DTL, and HMMR. Therapeutic compounds such as piroxicam, LUCANTHONE, leptomycin B, and calcitriol were identified via Enrichr and DSigDB, with significant P-values (0.05), suggesting their potential to regulate these hub genes and related pathways.

Conclusion: This study provides valuable insights into shared molecular targets, biological pathways, and potential therapeutic compounds for COVID-19 and influenza. The identified hub genes offer promising diagnostic and therapeutic prospects for these diseases. Additionally, these findings can guide future research on pathogen-specific interventions to improve treatment strategies for COVID-19 and influenza.

keywords: COVID-19; influenza; protein-protein interaction; Network-based; hub genes.

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Systems Biology and Bioinformatics Analysis of COVID-19 Co-Infection in Lung Cancer Patients: Pathways and Therapeutic Targets

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Medical Virology

Background and aim: COVID-19, caused by SARS-CoV-2, and lung cancer are major global health concerns. While COVID-19 became a pandemic in 2019, lung cancer is the leading cause of cancer-related deaths. Patients with pre-existing conditions, particularly those with lung cancer, face a higher risk of severe COVID-19 outcomes, especially those undergoing chemotherapy. Non-small-cell lung cancer (NSCLC) patients are particularly vulnerable, highlighting the need for effective treatments for COVID-19 and NSCLC co-infection. This study analyzes gene expression data from both diseases to identify differentially expressed genes (DEGs) using microarray technology. It aims to identify hub genes and enriched pathways for potential therapeutic strategies.

Methods: Gene expression data for COVID-19 (GSE157103) and lung cancer (GSE33532) were retrieved from the Gene Expression Omnibus (GEO) database (https://www.ncbi.nlm.nih.gov/geo). The dataset included 94 COVID-19 patient samples, 23 non-COVID-19 samples, 80 lung cancer tumor samples, and 20 matched normal lung samples. Differentially expressed genes (DEGs) were identified using GEO2R with a p-value 0.05 and log fold change (logFC) 1 or -1. Common up-regulated DEGs between COVID-19 and lung cancer were determined using the Venny tool (https://bioinfogp.cnb.csic.es/tools/venny/). Enrichment analysis for gene ontology (GO) and KEGG pathways was performed using Enrichr (https://maayanlab.cloud/Enrichr). Protein-protein interaction (PPI) networks were constructed with STRING (https://string-db.org/) and visualized using the Cytoscape 3.9.0. The most significant hub genes were

identified based on degree centrality and clusters using CytoHubba and MCODE plugins. Potential drug candidates targeting the shared up-regulated DEGs were identified through the Enrichr and DSigDB databases, applying an adjusted p-value threshold of 0.05.

Results: A comparative genomic analysis identified 1,637 DEGs in COVID-19, with 1,045 up-regulated, and 2,948 DEGs in lung cancer, including 1,263 up-regulated. Overlap analysis using Venny revealed 151 shared up-regulated DEGs between the two conditions. Functional enrichment analysis highlighted these genes' involvement in GO biological processes like "mitotic sister chromatid segregation" and "mitotic spindle organization." Their related GO cellular components included the "spindle microtubule cytoskeleton" and "mitotic spindle," while GO molecular functions involved "microtubule binding" and "single-stranded DNA helicase activity." KEGG pathway analysis emphasized their roles in the "cell cycle" and "oocyte meiosis." The PPI network, constructed via STRING, consisted of 130 nodes and 4,769 edges. Key hub genes identified in cluster 1 based on degree were CDK1, TOP2A, TTK, KIF11, KIF2C, BUB1, DLGAP5, and KIF23. Potential therapeutic compounds, including LUCANTHONE, methotrexate, ciclopirox, and resveratrol, were identified through Enrichr and DSigDB, showing significant activity (P 0.05) in targeting these pathways.

Conclusion: This study identifies key hub genes and biological pathways shared between COVID-19 and lung cancer, offering promising targets for therapeutic strategies. The results suggest potential biomarkers for diagnosis and treatment, with identified drug candidates that may modulate disease-related pathways. These findings provide valuable insights for future research on co-infection therapies for COVID-19 and lung cancer.

keywords: COVID-19; Lung Neoplasms; hub genes; protein-protein interaction; Systems Biology

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Advances in Nanotherapeutic Strategies for HPV-Related Cancers: Delivery Systems, Gene Editing, and Preclinical Models

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Medical Virology

Background and aim: Human papillomavirus (HPV) is a major cause of various cancers, including cervical and oropharyngeal cancers, accounting for 4.5% of global cancer cases. Despite the availability of vaccines, treatment options for HPV-related cancers, especially in advanced stages, remain limited. Current therapies, such as surgery, radiotherapy, and chemotherapy, are non-specific, often leading to resistance, recurrence, and severe side effects. Nanotherapy, utilizing nanoparticles for targeted drug delivery, gene editing, and immune activation, offers a promising alternative. However, most nanotherapies are still in preclinical stages due to challenges in scalability and model limitations. This review examines recent advances in nanotherapeutic strategies for HPV-associated cancers.

Methods: A systematic review of studies published between 2019 and 2024 was conducted using databases such as PubMed, Scopus, and Web of Science. Keywords like "HPV nanotherapy," "nanoparticles for HPV," and "gene-targeted therapies for HPV cancers" were employed to identify relevant research. Selected articles emphasized advancements in small molecule delivery, gene-editing technologies, nanovaccines, and the evaluation of preclinical models. The focus was on innovative methodologies, improved delivery mechanisms, and efficacy in preclinical settings.

Results: Nanoparticles have shown substantial promise in improving the efficacy, selectivity, and safety of treatments for HPV-related cancers. They enhance the delivery of small molecules, such as imiquimod, curcumin, and cisplatin prodrugs,

offering better selectivity for cancer cells while reducing side effects. Gene-targeted therapies, including RNA interference (RNAi) and CRISPR/Cas9, effectively silence HPV oncogenes E6 and E7, restoring tumor-suppressor pathways such as p53 and pRb. CRISPR-based approaches have demonstrated stable gene editing and tumor inhibition in preclinical models. Furthermore, nanovaccines targeting E7 peptides or mRNA triggered strong cytotoxic T-cell responses, extending tumor-free survival in mouse models. Despite these advances, clinical translation remains limited, with only nab-paclitaxel progressing to Phase 2 trials. Preclinical studies have revealed limitations in traditional models (e.g., 2D cultures and xenografts), leading to the adoption of more advanced models, including organoids and transgenic mice, to better simulate human tumor environments.

Conclusion: Nanotherapy offers a promising, transformative approach for treating HPV-associated cancers by enabling precise drug delivery, reducing toxicity, and improving therapeutic efficacy. Advances in small molecule delivery, gene editing, and cancer vaccines hold great potential for enhancing patient outcomes. However, challenges such as scalable production, regulatory obstacles, and the limitations of preclinical models need to be addressed to facilitate clinical implementation. The integration of advanced preclinical models and multimodal therapeutic strategies could expedite the clinical translation of nanotherapy, providing more effective and targeted treatments for HPV-related cancers.

keywords: HPV-related cancers; Nanoparticles; Gene-targeted therapy; Cancer nanovaccines; Nanomedicine.

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Nanopore Sequencing Technology to Detection of viruses

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Medical Virology

Background and aim: Nanopore sequencing is an innovative method for analyzing DNA and RNA sequences that utilizes the physical properties of nanopores (tiny holes embedded in membranes) to read genetic information. As biological molecules such as DNA or RNA pass through these nanopores, they cause unique changes in electrical current, enabling the determination of nucleotide sequences. Unlike traditional sequencing methods such as Sanger sequencing, nanopore offers several advantages, including the ability to generate long reads, simplified sample preparation, and rapid sequencing. This study aims to explore the principles, advantages, and applications of nanopore sequencing, focusing specifically on its role in viral diagnostics.

Methods: PubMed and Web of Science were searched (2020-2024). The keywords were " Nanopore" and "infectious disease diagnostics" and "Viral Diagnostics". Articles were extracted by two reviewers independently.

Results: The nanopore sequencing thecnology was used for detection of DNA and RNA viruses in different clinical samples clinical samples such as SARS-CoV-2 and influenza virus. Also, assembly new viral references genome has been conducted by the technology. In nanopore thechnology RNA viruses can be detected directly and also the results call real time. In this method also single viral genome are sequenced as a result recombination events between RNA viruses can be detected easily. In some cases, sensitivity of nanopore technology to detection of universal Faviviruses was comparable with PCR based methods.

Conclusion: Nanopore sequencing is a groundbreaking technology that is transforming the field of genetic analysis. Its ability to provide long reads, rapid sequencing, complete genome analysis, and mutation detection makes it a

versatile tool for genomic research and diagnostics. It addresses challenges that traditional methods cannot overcome. Nanopore sequencing is not merely a technological advancement but also a crucial tool for understanding genetics and combating diseases. Its applications in infectious disease diagnostics, viral genome studies, and microbiome monitoring establish it as a cornerstone of modern life sciences.

keywords: Nanopore, Infectious Disease Diagnostics, Viral Diagnostics

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Detection of SARS-CoV-2 using loop-mediated isothermal amplification method: A Review

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Medical Virology

Background and aim: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) pandemic, which caused an immense burden on human health and the global economy. As a result, the demand for fast, cost-effective, accurate, and technically convenient diagnostics has increased. One of the proposed methods is reverse transcription loop-mediated isothermal amplification (RT-LAMP) and LAMP tests, which are currently being investigated for the clinical diagnosis of coronavirus disease. Therefore, we have reviewed and summarized related articles on this matter.

Methods: Multiple databases, including PubMed, Google Scholar, Scopus, and Web of Science were investigated using the terms "LAMP", "coronavirus", and "diagnosis". The search was limited to original and clinical studies assessing the sensitivity and specificity of RT-LAMP or LAMP, published in 2023. Duplicate and irrelevant articles were excluded.

Results: A total of 10 studies were collected, and the reported sensitivity was in the range of 89.5-100% and a specificity of 100% has been observed in several of them. Detection of LAMP products were based on colorimetry, fluorescence, and cyclic voltammetry. All studies used PCR-based methods as the reference. Five studies used the Nucleocapsid (N) gene for detecting SARS-CoV-2 in 688 clinical samples of saliva, nasopharyngeal swabs, buccal, and nasal exudate, with high sensitivity and specificity ranging from 89.5-100% and 97.2-100%. The N and ORF1a target genes were used in one study with 129 saliva and nasal samples, reporting a sensitivity and specificity of 97.7% and 97.60%. Furthermore, in this review, some effective suggestions were mentioned for improving the LAMP

tests, such as using trypsin buffer and heating to avoid the RNA extraction step, using five LAMP primers instead of six, and the electrochemical test for detection.

Conclusion: In recent years, significant progress has been made in detecting coronavirus via LAMP and RT-LAMP assays, which are considered excellent options for rapid, efficient, and sensitive diagnostic methods. Also, there have been some complementary techniques based on the mentioned studies that resulted in the high performance of the LAMP test. Nonetheless, further research and evidence are needed to confirm that LAMP and RT-LAMP are capable of fully replacing other methods in the clinical diagnosis of coronavirus.

keywords: SARS-CoV-2; loop-mediated isothermal amplification (LAMP); diagnosis.

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Development of Human Viral Diagnostic Kits Based on Phage Display Method

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Medical Virology

Background and aim: he rapid and accurate diagnosis of viral infections is crucial for effective treatment and epidemic management. Traditional diagnostic methods, such as serological assays and PCR, have limitations in sensitivity and specificity. Phage display technology, which involves the expression of peptide or antibody libraries on the surface of bacteriophages, presents a promising alternative for the development of diagnostic kits. This systematic review examines the advancements and efficacy of phage display-derived diagnostic kits for human viral pathogens, emphasizing their potential in clinical applications.

Methods: A comprehensive literature search was conducted in databases such as PubMed, Scopus, and Web of Science, focusing on studies published between 2010 and 2023. Keywords included "phage display," "viral diagnostics," "antibody development," and "human viruses." Inclusion criteria were studies that reported the development or assessment of diagnostic kits using phage display technology for human viral pathogens. Data extraction included authors, year of publication, study design, types of viruses, diagnostic performance, and clinical applicability. A total of 25 studies met the inclusion criteria and were subjected to qualitative analysis.

Results: The review indicates a growing trend in utilizing phage display for the development of viral diagnostic kits. Notable advancements include the successful identification of specific peptide ligands for hepatitis B virus (HBV), human immunodeficiency virus (HIV), and SARS-CoV-2. The sensitivity and specificity of phage display-derived antibodies often exceed those of conventional methods. Moreover, the modularity of phage display allows for

rapid optimization and customization of diagnostic assays. However, challenges remain, such as the need for extensive validation in diverse clinical settings and the scaling-up of production for commercial use. Furthermore, potential cross-reactivity and the immunogenicity of phage-derived antigens require careful consideration in kit design.

Conclusion: Phage display technology shows immense potential in the development of human viral diagnostic kits, providing innovative platforms for the rapid, sensitive, and specific detection of viral pathogens. Continued research and development, along with rigorous clinical validation, will be essential to translate these promising laboratory findings into effective diagnostic solutions. Future studies should focus on integrating phage display with microfluidics and multiplexing techniques to enhance diagnostic capabilities further. The ongoing advancements in this field may significantly impact public health strategies against viral outbreaks.

keywords: Phage display, Diagnostic kits, HumanViral Diseases

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Frequency of anelloviruses in patients with COVID-19 infection and healthy control group in the Tabriz: Northwest of Iran

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Medical Virology

Background and aim: The relationship between human anelloviruses (AVs) and the host's immune status has gained increasing attention in recent years. AVs, particularly torque teno viruses (TTV), are non-pathogenic viruses commonly present in human blood and body fluids, and their replication levels are believed to reflect immune system activity. Infection with other pathogenic viruses, such as SARS-CoV-2, has been hypothesized to impact the frequency and replication dynamics of AVs. However, the specific role of AV replication and the presence of AV-associated microRNAs (miRNAs) during COVID-19 remains uncertain. Understanding whether these changes correlate with immune suppression and disease progression could help elucidate the interplay.

Methods: In this case-control study, 210 individuals were recruited and categorized into two main groups: COVID-19 patients and healthy controls. The COVID-19 group was further stratified into severe and mild subgroups based on disease severity. Plasma and respiratory samples were collected from each participant, and the presence of TTV DNA was analyzed using quantitative PCR. In plasma samples that tested positive for TTV DNA, miRNA profiles associated with TTV were subsequently analyzed to assess their potential contribution to disease severity. The analysis aimed to compare viral DNA and miRNA levels

between severe and mild COVID-19 cases and the healthy control group to identify any statistically significant associations.

Results: The study found a significantly higher prevalence of TTV DNA in the plasma of severe COVID-19 patients (27.1%) compared to healthy individuals (11.4%), with a p-value of 0.048. This suggests a potential link between increased TTV viral load and the severity of COVID-19. However, no statistically significant differences were observed in the levels of other anelloviruses, such as TTMV and TTMDV, or in the presence of TTV-associated miRNAs, in either plasma or respiratory samples. These findings indicate that while TTV DNA levels may be associated with disease severity, other markers of AV activity, including miRNAs, may not have a direct impact on the progression of COVID-19.

Conclusion: The results of this study suggest that TTV viral load in plasma could serve as a potential biomarker for monitoring immune status in COVID-19 patients. This observation highlights the broader hypothesis that non-pathogenic viruses such as TTV might play an indirect role in modulating immune responses and influencing clinical outcomes during severe viral infections. Although TTV miRNAs did not show significant correlations with disease severity in this study, their potential as diagnostic or prognostic markers warrants further investigation. These findings underscore the need for additional research to validate TTV DNA.

keywords: Torque Teno Viruses, Anelloviruses, COVID-19, SARS-CoV-2, Co-infection

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Investigation of cross-reactivity of SARS-CoV-2 neutralizing antibody with autoimmune antibodies in patients with COVID-19

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Medical Virology

Background and aim: COVID-19 disease is caused by the SARS-COV-2 virus. Against infectious diseases, the humoral and cellular immune systems are activated to deactivate the virus. After infected with COVID-19, antibodies of different classes are formed. The IgG class antibody with long persistence in the body will be able to provide long-term protection. But this antibody can react with self-antigens in the body and cause autoimmune diseases. These antibodies outside the body and in serology detection methods can give false positives. The aim of this study is to investigate the cross-reaction between IgG antibody against COVID-19 with HCV, HIV, CCP, RF, ANA antibodies

Methods: This project is a cross-sectional study that was conducted on patients with COVID-19. Serum sampling from patients with COVID-19 was 20 days from the time of diagnosis to complete the opportunity to produce antibodies of the IgG class. After sampling the serum of the control group and the patient, the cross-reactivity to the target antigens of the following antibodies was investigated using the ELISA method (HCV, HIV, CCP, RF, ANA). The statistical analysis was reported on the comparison of the two groups as mean and standard deviation. And independent t-test was used to compare between two groups

Results: : In the control group, no cross reaction was observed for any of the antibodies. But in the case of RF, the amount of RF was higher in 2 women. In the group of patients, there was no cross-reaction and false positive related to antibody with infectious antigens. But in connection with Anti-ccp, it was higher in the group of patients. But no significant difference was observed between the two groups

Conclusion: This study aims to investigate the cross-reaction between natural antibodies created after contracting corona with rheumatoid factor antigens, citrullinated peptide antigens (CCP), nuclear antigens (ANA) and viral antigens such as HIV. HCV was also investigated. No cross reactions or false positives were observed in both groups. To check the cross-reactivity, more sampling was needed and also the use of different kits available in the market

keywords: COVID-19, Rheumatoid factor, Anti-CCP

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Assessment of BK and JC Viruses in Semen of Infertile Males and Their Impact on Sperm Health

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Medical Virology

Background and aim: Due to the high prevalence of human polyomaviruses BK and JC infections in the urinary tract and male genital tract, the effect of this virus on male fertility is possible. The aim of this study was to determine the prevalence of BK virus and JC virus in the semen of infertile and fertile men and its relationship with sperm health factors.

Methods: In this cross-sectional case-control study, which was conducted in 2023 semen samples from 50 fertile men and 50 infertile men were collected from men referred to the Yazd Research and Clinical Center for Infertility. DNA was extracted using Amplisens kit, as well as the presence of BK virus and JC virus was investigated by real time PCR method using GeneProof kit. The results were entered into the SPSS V. 20 software and analyzed by Chi-square and T-tests.

Results: The incidence of BK viral infection showed that the frequency of viral BK infection was zero among the fertile and infertile men. Out of the 50 people in the infertile group, 9 ones were infected with the JC virus, and among the fertile people, 15 were infected with JC virus. Statistical analysis showed that the prevalence of the JC virus the fertile and infertile men was not significant (p=0.160).

Conclusion: The results showed that in infertile group, the values of the factors related to semen quality in infected patients were lower than those without infection, these results could indicate the effect of the JC viral infection on sperm quality, although no significant differences were observed compared to the non-infected patients.

keywords: Male Infertile, Polyomaviruses, JC Virus, BK Virus, Sperm

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Development and validation of a Multiplex RT-qPCR method for the simultaneous detection of influenza type A, B and SARS-COV-2 viruses

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Medical Virology

Background and aim: The study aimed to evaluate diagnosis and differentiation between SARS-COV-2 and influenza viruses using Multiplex qPCR molecular method, highlighting the importance of these methods in disease management.

Methods: This study designed primers and probes for a specific virus, focusing on the hemagglutinin region (HA) of influenza A, the M region of influenza B virus, and the RdRp region of SARS-COV-2. Optimization was performed using qPCR methods, and the method's analytical sensitivity was calculated. Bioinformatic analysis was conducted, and the method was compared to a commercial kit, Generi-Biotech Company (GB SARS-CoV-2 Influenza A/B).

Results: The optimal binding temperature and RdRp primer were chosen for optimization. The analytical kit's sensitivity was measured using 500 copies of SARS-COV-2, 250 copies for influenza A, and 500 copies for influenza B.

Conclusion: The present current kit has the ability to identify influenza A, B, and Covid-19 viruses in a single sample, and with only a series of materials and equipment, a series of tests can be performed simultaneously and leading to providing useful information for patients suffering from respiratory diseases with common symptoms. According to the results obtained from this study, the

accuracy and sensitivity of this kit are very high and it reduces the false negative and positive results caused by other methods and enables the diagnosis of the disease in

keywords: Multiplex qPCR method, Influenza A and B viruses, SARS-COV-2.

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Epstein–Barr virus Viral Load in Upper Respiratory Tract Samples of Hospitalized Patients with COVID-19

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Medical Virology

Background and aim: The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has resulted in a global health crisis, with varying disease severity and outcomes. Co-infections and the reactivation of latent viruses, such as Epstein-Barr Virus (EBV), may influence the progression and severity of COVID-19. EBV is a ubiquitous virus that typically remains dormant in the host, but it can reactivate under conditions such as immunosuppression or concurrent infections. The current study investigates the potential role of EBV reactivation in the severity and outcomes of COVID-19 by analyzing EBV viral load and lytic gene expression in upper respiratory tract samples from hospitalized patients.

Methods: This retrospective cross-sectional study included 87 hospitalized COVID-19 patients, categorized into two groups based on clinical outcomes: 47 with poor outcomes (e.g., ICU admission, intubation, or death) and 40 with good outcomes (discharged in stable condition). Upper respiratory tract swabs were collected and analyzed for EBV viral load using TaqMan real-time PCR to quantify the BALF-5 gene and for EBV reactivation using quantitative RT-PCR to measure the expression of the BZLF-1 gene. Clinical data, including demographic, laboratory, and treatment information, were also recorded and analyzed.

Results: Of the 87 patients, 76 (87.4%) tested positive for EBV. The case group (poor outcomes) had significantly higher EBV BALF-5 copy numbers and BZLF-1 gene expression compared to the control group (p 0.001). EBV-positive patients

had a higher incidence of ICU admission and intubation (100%) compared to EBV-negative patients. Additionally, EBV reactivation was significantly associated with poorer clinical outcomes, including death ($p = 0.015$). Laboratory markers such as CRP, WBC, and D-dimer were elevated in EBV-positive patients, particularly in those with adverse outcomes. Correlation analysis revealed significant positive relationships between EBV viral load and markers of inflammation and organ dysfunction, including CRP, WBC, D-dimer, and creatinine. However, EBV reactivation did not correlate with patient age or gender.

Conclusion: The study suggests that EBV reactivation in the upper respiratory tract may contribute to the severity of COVID-19, potentially exacerbating inflammation and organ dysfunction. High EBV viral load and lytic gene expression, particularly the BZLF-1 gene, were associated with poorer clinical outcomes in COVID-19 patients. These findings highlight the importance of considering co-infections and latent virus reactivation in the management of COVID-19, especially in patients with severe disease. Further research is needed to explore the mechanisms by which EBV reactivation influences COVID-19 pathogenesis and patient outcomes.

keywords: Reactivation; SARS-CoV-2; COVID-19; Epstein-Barr virus; Co-infection

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Association of Human Papillomavirus Infection in Tissue samples with Stage and Grade parameters in Patients with Head and neck squamous cell carcinoma

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Medical Virology

Background and aim: The relationship between human papillomavirus (HPV) and head and neck squamous cell carcinoma (HNSCC) has been documented in previous studies. However, the associations between demographic factors, clinicopathological features, and histological characteristics of HNSCC patients with the molecular detection of HPV require further investigation.

Methods: This cross-sectional study enrolled 71 patients diagnosed with HNSCC between April 2017 and June 2023. HPV detection was performed using the MY09 and MY11 primer sets. A significance level was set at p 0.05.

Results: Among the cohort, 39 patients (54.9%) were identified with advanced-stage cancer. The majority of patients (61.9%) were classified as Grade I. HPV was detected in 12 patients (16.90%) within tumor tissues and in 5 patients (7.04%) at adjacent healthy tissue margins (P = 0.01). A significant correlation was observed between histological grade and HPV infection among HNSCC patients (P = 0.01). Additionally, there was a notable increase in HPV infection rates in the advanced-stage group compared to the early-stage group (P 0.05).

Conclusion: The findings of this study demonstrate a significant association between HPV infection and demographic, clinical, and histological factors in HNSCC patients, including age, cancer stage, and histological grade. Overall, the results from real-time PCR analysis suggest a substantial role for HPV infection in the pathogenesis of HNSCC malignancies, warranting further research into its implications for patient management and treatment strategies.

keywords: Head and neck squamous cell carcinoma, human papillomavirus, stage, Grade

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The prevalence of HBV, HCV, and HIV among hemodialysis patients of a hospital in Mashhad

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Medical Virology

Background and aim: Hepatitis and acquired immunodeficiency are major health concerns in high-risk patients with renal failure undergoing hemodialysis. This might be due to the number of blood transfusions, age, and dialysis duration. We aimed to investigate the prevalence of HBV, HCV, and HIV in hemodialysis patients to determine the effectiveness of preventive measures already in place and the possible correlation between various risk factors and viral infection in the Hemodialysis Center in Mashhad, Iran.

Methods: Sixty-five patients were included in a retrospective cross-sectional study. The demographic information was collected. Hepatitis B surface antigens, anti-HCV, and anti-HIV antibodies were screened using ELISA.

Results: Out of 65 patients, 34 (52.3%) were male, and 31 (47.7%) were female. Mean duration of dialysis was 30.68 ± 26.39 months, and the mean age was 64.95 ± 14.09 years. We found 9 (13.8%) patients that were HBV positive (HbsAg-positive), and 3 (4.6%) patients were HCV positive. Sex and the number of blood transfusions were found to be risk factors for HBV infection and had statistical significance (p = 0.02 and p = 0.01, respectively). No statistical significance was found between HBV- and HCV- positivity and the mean age of patients (p = 0.84 and p = 0.76, respectively). All patients were HIV-negative.

Conclusion: Prevalence of HBV was high and significant. More preventive measures need to be developed, and further studies should be conducted to examine the effectiveness of these measures. Moreover, evaluating the prevalence rates of HBV, HCV, and HIV in other hospitals and dialysis centers in Mashhad is recommended to minimize viral infections. Initial HBV vaccination for patients that require hemodialysis is crucial.

keywords: HIV; HBV; HCV; hemodialysis; prevalence

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Comparison of Electrochemiluminescence Assay with PCR for the Detection of HBS, HCV, HIV: A Cross-sectional Study

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Medical Virology

Background and aim: Virus infections continue to pose a significant public health challenge worldwide, highlighting the need for accurate and timely diagnostic methods. Electro chemiluminescence Assay (ECLIAs) are widely utilized for the detection of HBS, HIV and HCV due to their rapidity and cost-effectiveness. However, it is essential to evaluate their diagnostic performance to ensure reliability. The aim of this study is to detect the presence of Hepatitis B, C, and HIV surface antigens in selected samples using ECLIA and to compare these results with the detection of HBS, HCV, and HIV Deoxyribonucleic Acid (DNA) using a molecular assay.

Methods: A cross-sectional study was conducted using serum samples collected from blood donors at the Blood Transfusion Center in Bushehr Province of four months, with prior ethical clearance obtained. The results of ECLIA, and the viral loads of HBV, HCV and HIV were determined using PCR and were cross-tabulated to assess differences in diagnostic sensitivity. The positivity rates and correlation between ECLIA and PCR results were estimated. All statistical analyses were performed using Stata software version 17.0.

Results: Out of 9,007 samples, 7 tested positive for Hepatitis B surface antigen (HBsAg), 2 tested positive for HIV using the ECLIA method, and 2 tested positive for HBsAg using the PCR method. McNemar's test indicated that the sensitivity of ECLIA differed significantly from that of HBS, HCV, and HIV DNA PCR. A significant

positive correlation was observed between ECLIA and HBS, HCV, and HIV DNA PCR.

Conclusion: The findings indicate that in environments where accurate diagnosis is essential—especially for screening and monitoring treatment efficacy—molecular assays continue to be the preferred option, despite their higher cost and complexity. However, in resource-limited settings, ECLIAs can still serve a valuable role in viral marker screening programs.

keywords: ECL, PCR, HIV, HBS, HCV

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Correlation between Elevated Bradykinin Concentrations and Death by COVID-19

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Medical Virology

Background and aim: To investigate BK pathway dysregulation among and between COVID-19 survivors and the deceased.

Methods: This case-control study was performed between 2020 and 2022 in Imam Hasan Hospital, Bojnurd, Iran. SARS-CoV-2 infected patients, comprising 40 deceased and 15 surviving patients, were recruited according to specific inclusion and exclusion criteria. A blood sample was taken from subjects during the disease. Blood BK levels in subjects (the groups of patients (55) and control (15)) were measured by the ELISA technique. All patients were selected from individuals over 18 years old with real-time PCR-proven SARS-CoV-2 infection. Also, the studied patients did not have metabolic syndrome (blood pressure, abdominal obesity, diabetes, cardiovascular disease). SPSS version 26 was used to compare the means.

Results: The blood serum BK level was significantly related to the outcome of COVID-19 disease (P=0.006) using a multiple logistic regression test. A week before death, a significant increase in the blood BK levels among deceased patients compared to survivors was seen (p=0.0001). The probability of death in patients with SARS-CoV-2 infection linearly increased by 4% (OR = 1.04) for each pg/ml increase in the BK level.

Conclusion: There is a close relationship between the rise in BK concentration during a COVID-19 infection and the disease outcome.

keywords: Bradykinin, COVID-19, SARS-CoV-2, inflammatory protein

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In vitro effect of some nucleoside reverse transcriptase inhibitors against HSV-1 replication

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Medical Virology

Background and aim: Herpes simplex virus type 1 (HSV-1) is one of the most prevalent, incurable virus infections worldwide, belonging to the Herpesviridae family. Alongside this, the current study was aimed to evaluate the effect of some NRTIs against HSV-1 replication in Vero cell line.

Methods: Initially, the SwissTargetPrediction server was used to predict the interactions between HSV-1 thymidine kinase and acyclovir, stavudine, zidovudine, didanosine, and entecavir. The effect of each component on Vero cell viability was assessed by the MTT assay. After treatment, the cell supernatants were collected, and HSV-1 replication was analyzed by quantitative real-time PCR.

Results: The qPCR results revealed that viral titers were reduced 41, 40, 19, 44, and 31-fold in the presence of acyclovir, zidovudine, stavudine, didanosine, and entecavir, respectively.

Conclusion: The results showed that some NRTIs, especially didanosine, have surprisingly remarkable effects against HSV-1 in cell culture; therefore, it is recommended to investigate their activity against acyclovir-resistant isolates.

keywords: Herpes Simplex Virus, NRTIs, Acyclovir, Zidovudine, Didanosine

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Unraveling Dermatological manifestations after COVID-19: Insights from Skin Pigmentation and Hair Loss Patterns

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Medical Virology

Background and aim: In addition to respiratory symptoms, COVID-19 has been linked to many clinical manifestations, such as changes in skin pigmentation and hair loss. The objective of this research was to examine these manifestations.

Methods: Cross-sectional research was performed at Afzalipour Hospital in Kerman, Iran, between June and August 2021. COVID-19-recovered patients were included in the study, and data was obtained via medical records, verbal interviews, and self-administered questionnaires. Statistical investigations evaluated the relationships between manifestations, demographic factors, and clinical indications.

Results: Among the 190-study population, 76.3% encountered alopecia, while 15.3% indicated changes in skin pigmentation. The prevalence of hair loss was considerably higher among females (P=0.002). The hair loss patterns exhibited characteristics similar to telogen effluvium (TE), with a higher occurrence in the frontal region of the head. There was a relationship between hair loss and the level of arterial oxygen saturation.

Conclusion: This research emphasizes a significant prevalence of alopecia after the recovery from COVID-19, especially among females. It is crucial to provide proactive care and support to people who have recovered from COVID-19, including customized therapies that specifically target post-COVID-19 problems.

keywords: COVID-19; Female alopecia; Hair loss; Post inflammatory hyperpigmentation, Telogen Effluvium.

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The prevalence of EBV infection in renal transplant receipts in population of Adults Iranian: A systematic review and Meta-analysis

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Medical Virology

Background and aim: EBV is of human herpesvirus 4 family and one of the most common viruses in human that associated with enormous infections and cancers such as PTLD. Also, in renal transplant recipients due to receive immunosuppression drugs are more susceptible. Actually with inhibiting immune system in these patients; EBV virus is activated. So that causes allograft rejection. Therefore, the prevalence of EBV infection in renal transplant recipients is important and this study has been checked population of adults Iranian.

Methods: A systematic review and meta-analysis study was conducted to investigate the prevalence of EBV infection in renal transplant in population. The study included articles published in both English and Persian languages and utilized various databases such as Medline, Google Scholar, PubMed, Web of Science, Magiran, and thesis database of medicine universities up to May 2024. The pooled prevalence of the condition was calculated using random effects models for pooled analysis. All statistical analyses were conducted using STATA version 17.

Results: Out 21 of studies initially identified, 10 met the inclusion criteria, involving a total of 2073 renal transplant recipients. Among of these 1029 person had EBV IgM or Acute Infection positive 32% (95% CI = 24 -41%) And 1673 person were EBV IgG positive or chronic Infection 65% (95%CI=54-78 %) after transplantation.

Conclusion: Although the majority of primary EBV infections are asymptom but The results of reviewed studies showed that EBV activation was a secondary form of a previously existing infection and demonstrated a very high level of EBV seropositivity in transplant patient. Therefore, to manage EBV infection in renal transplant recipients is necessary.

keywords: Epstein-Barr-Virus; renal transplant; Prevalence ; Systematic review Meta _analyses .

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MicroRNA-enhanced coxsackievirus B3: A targeted strategy for oncolytic virotherapy

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Medical Virology

Background and aim: Oncolytic virotherapy is a cutting-edge treatment using natural or genetically engineered viruses to target and destroy diseased cells. Current cancer treatments, such as surgery or chemotherapy, often have irreversible impacts on patients' quality of life, highlighting the need for innovative approaches like oncolytic virotherapy. These viruses are designed to remain inactive in healthy cells while selectively replicating and killing target cells, such as cancer cells. Coxsackievirus B3 (CVB3), an RNA virus from the Picornaviridae family, has shown strong tumor-destroying capabilities against various cancers.

Methods: This study aimed to explore the role of Coxsackieviruses in oncolytic virotherapy for cancer treatment. A systematic review was conducted using the PubMed and ScienceDirect databases, focusing on scientific articles published between 2020 and 2024. Keywords such as "virotherapy", "Coxsackievirus", "miRNA" and "cancer treatment" along with their combinations, were used to identify relevant studies. The screening process began with an assessment of titles and abstracts for relevance, followed by a detailed analysis of full-text articles that met the inclusion criteria. Eligible studies specifically addressed the use of Coxsackieviruses in cancer treatment, while irrelevant or low-quality studies were excluded. Data from the selected articles were systematically extracted and analyzed to assess the efficacy and mechanisms of action of Coxsackieviruses in virotherapy. The findings were synthesized to highlight the potential of this approach as a complementary method in cancer therapy.

Results: This study demonstrates that through genetic engineering, the CVB3 virus can be modified to achieve higher selectivity in targeting cancer cells while reducing its toxicity to vital tissues such as the heart and pancreas. The modified versions of miR-CVB3, with tissue-specific microRNA target sequences (e.g., miR-1, miR-133, miR-216, and miR-375) integrated into their genomes, have not only shown enhanced safety profiles in animal models but also effectively destroyed various types of cancer cells. Additionally, these viruses, with the incorporation of tumor-suppressor microRNA sequences (miR-145/143), exhibit greater genetic stability and have successfully lysed breast cancer cells, lung adenocarcinoma cells, and small cell lung cancer cells (SCLS), while significantly reducing their toxicity to cardiomyocytes. The modified CVB3 virus not only destroys cancer cells but also shifts immune profiles and boosts immune activation. These findings pave the way for the development of genetically engineered viruses for cancer virotherapy with improved safety and efficacy.

Conclusion: The findings of this study underscore the transformative potential of Coxsackievirus B3 (CVB3) in oncolytic virotherapy, demonstrating its promise in effectively targeting cancer cells while minimizing harm to vital tissues. The incorporation of tumor-suppressor microRNA sequences and tissue-specific adaptations enhances its safety, efficacy, and genetic stability. These advancements position virotherapy as a promising, less invasive alternative or complement to traditional cancer treatments. However, further research and clinical trials are essential to translate these findings into practical applications, paving the way for safer and more personalized approaches in cancer therapy.

keywords: virotherapy; Coxsackievirus; cancer treatment; miRNA.

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Effectiveness of Urine Samples for Detecting HPV in Women and Cervical Cancer Screening

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Medical Virology

Background and aim: Cervical cancer remains a significant global health issue, with low participation in screening programs hindering early detection and prevention efforts. Urine-sample human papillomavirus (HPV) testing is a non-invasive alternative that could improve accessibility and patient compliance. This study aims to evaluate the effectiveness of urine-sample HPV testing for cervical cancer screening and assess its acceptability among patients.

Methods: A systematic review of secondary studies was conducted, adhering to Cochrane guidelines. Searches in Medline, Embase, and the Cochrane Library identified five studies meeting inclusion criteria. The analysis focused on the sensitivity, specificity, and acceptability of urine-sample HPV testing, including meta-analyses and observational studies. Key endpoints included diagnostic accuracy, patient comfort, and screening participation rates.

Results: Urine-based HPV tests demonstrated high diagnostic accuracy, with sensitivity and specificity values of 87% and 89%, respectively, for detecting any HPV. Tests targeting high-risk HPV strains, such as types 16 and 18, showed sensitivity of 77% and specificity of 98%. Participants reported high comfort levels with urine self-collection, with studies indicating it as a favorable alternative to traditional methods. However, challenges such as the lack of standardized detection protocols and regulatory approvals persist.

Conclusion: Urine-sample HPV testing is a promising non-invasive and cost-effective method that could enhance participation in cervical cancer screening programs, addressing low turnout rates. Its high diagnostic accuracy and patient acceptability suggest significant potential to improve global cervical cancer

prevention efforts. Further research is needed to refine methodologies and achieve regulatory validation.

keywords: cervical cancer, HPV testing, urine samples, non-invasive screening, prevention programs

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Oncolytic viruses inducing pyroptosis as a novel approach to tumor immunotherapy: A Systematic Review

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Medical Virology

Background and aim: Oncolytic viruses (OVs) are viewed as a promising approach for treating cancer due to their ability to specifically target and eliminate tumor cells. Investigating the oncolytic mechanisms mediated by OVs is crucial for their clinical use. Pyroptosis is a recently identified type of programmed cell death that shows potential as an antitumor strategy. This process is characterized by the release of pro-inflammatory cytokines and immunogenic factors when the cell membrane ruptures. In this study we define pyroptosis as those types of cell death that is immunogenic and describe the synergistic combination of OVs and pyroptosis to reach potent tumor immunotherapy.

Methods: A comprehensive collection of information was achieved from medical databases including PubMed, Scopus, and Web of Science. In order to identify related articles, keywords related to this topic including oncolytic viruses, virotherapy, pyroptosis and immunotherapy were investigated and combined using Boolean operators (e.g., AND, OR). The screening process began with an assessment of titles and abstracts for relevance, followed by a detailed analysis of full-text articles that met the inclusion criteria. Data from the selected articles were systematically extracted to assess the efficacy of oncolytic viruses- induced pyroptosis to tumor immunotherapy.

Results: Recent studies have highlighted the mechanisms and benefits of OVs in triggering pyroptosis, particularly through the activation of Gasdermin E (GSDME). It has been reported that the depletion of GSDME resulted in decreased cytotoxic T lymphocyte (CTL) recruitment and reduced effectiveness of OVs virotherapy, indicating the critical role of pyroptosis in eliciting an immune response against tumor. In addition, pyroptosis is characterized by the release of intracellular contents that stimulate a potent inflammatory response in the tumor microenvironment. Thus, treatment by OVs inducing pyroptosis, through induction of pro-inflammatory genes expression and enhancing the recruitment of immune cells, can lead to a cascade of specific anti-tumor immune responses and reprogramming of the immunosuppressive tumor microenvironment, resulting in excellent tumor inhibition efficacy. Morover, the induction of pyroptosis leads to the release of immune stimulants like High Mobility Group Box 1 (HMGB1), which further supports an inflammatory environment conducive to anti-tumor immunity.

Conclusion: This knowledge offers valuable guidance for selecting and developing effective virus-based immunotherapies by OVs-induced pyroptosis. Investigating how different tumor types respond to OVs-induced pyroptosis will also be crucial for tailoring therapies to individual patient needs.

keywords: oncolytic viruses; virotherapy; pyroptosis; immunotherapy.

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Comparative Effectiveness of Phage Therapy and Conventional Antibiotics in Treating Antibiotic-Resistant Infections: A Molecular Perspective

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Medical Virology

Background and aim: The rise of antibiotic-resistant infections poses a critical challenge to modern medicine. As traditional antibiotics lose their effectiveness, alternative therapies such as phage therapy are garnering attention. This article delves into the molecular mechanisms underpinning the efficacy of phage therapy compared to conventional antibiotics in combating antibiotic-resistant infections. Antibiotic resistance typically arises through several molecular mechanisms. These include the production of enzymes like beta-lactamases that degrade antibiotics, modifications of target sites that reduce drug binding, increased efflux of antibiotics from bacterial cells, and alterations in metabolic pathways to bypass the effects of antibiotics.

Methods: Bacteria can acquire resistance genes via horizontal gene transfer, further exacerbating the problem. Conventional antibiotics combat bacterial infections through various mechanisms. Beta-lactams, such as penicillin, inhibit cell wall synthesis by targeting penicillin-binding proteins. Aminoglycosides, like gentamicin, disrupt protein synthesis by binding to the bacterial ribosome. Fluoroquinolones, such as ciprofloxacin, interfere with DNA replication by inhibiting DNA gyrase and topoisomerase IV. While these mechanisms are effective against susceptible bacteria, they become ineffective when resistance mechanisms are present. Phage therapy employs bacteriophages, viruses that specifically infect and lyse bacteria. Bacteriophages recognize and attach to specific receptors on the bacterial surface, inject their genetic material, and hijack the bacterial machinery to produce progeny phages. The bacterial cell eventually lyses, releasing new phages to infect other bacterial cells. This process, known as

the lytic cycle, is highly specific to the target bacteria and does not affect human cells or beneficial microbiota.

Results: Comparative studies have shown that phage therapy can be as effective, if not more so, than conventional antibiotics in treating antibiotic-resistant infections. For instance, phage therapy has demonstrated success in treating chronic infections such as those caused by Pseudomonas aeruginosa, a pathogen known for its resistance to multiple antibiotics.

Conclusion: Clinical trials and compassionate use cases have reported promising outcomes, including the resolution of infections unresponsive to antibiotics. However, challenges remain, such as the need for personalized phage preparations, regulatory hurdles, and the potential for phage resistance.

keywords: Clinical trials, Antibiotics, Phage therapy

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Oxidative stress severity's as a hallmark in the COVID-19 patients

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Medical Virology

Background and aim: The outbreak of COVID-19 needs to understand the mechanisms and identify effective treatments. Thus, the aim of this study was to evaluate the antioxidant status and oxidative stress parameters as a possible key mechanism in asymptomatic, non-severe, and severe COVID-19 patients.

Methods: This study is a case-control study that was performed on patients referred to the Persian Gulf Martyrs Hospital of Bushehr University of Medical Sciences, Bushehr, Iran, from May 2021 to September 2021. A total of 600 COVID-19 patients (non-severe and severe group) and 150 healthy volunteers of the same age and sex were selected during the same period. On the first day of hospitalization, 10 ml of venous blood was taken from subjects. Then, hematological, biochemical, serological, antioxidant and oxidative stress parameters were determined.

Results: Our results indicated that ESR, CRP, AST, ALT, and LDH significantly augmented in severe group as compared to non-severe and normal groups (P≤0.05). It observed that the levels of FRAP, G6PD activity, as well as SOD activity significantly reduced in non-severe patients in comparison to severe and normal group (P≤0.05). We found that MDA content and NO metabolite markedly increased in non-severe patients as compared to the severe group. Furthermore, The negative correlations were observed between the death and LYM count (r=-0.27, P-value0.0001), SOD activity (r=-0.24, P-value0.0001), as well as the saturation of oxygen (r=-0.32, P-value0.0001). However, the positive correlation

was observed between the death and CRP (r=0.27, P-value0.0001), AST (r=0.26, P-value0.0001), LDH (r=0.32, P-value0.0001), and MDA level (r=0.32, P-value0.0001).

Conclusion: Taken together, it seems that the balance between antioxidant and oxidant was disturbed in Covid 19 patients in favor of oxidant markers. Also, this situation was more aggravation in severe patients as compared to non-severe group.

keywords: oxidative stress, antioxidant, MDA, SOD

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Prevalence and genotype distribution of high-risk and low-risk human papillomavirus (HPV) in a cross-sectional study population

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Medical Virology

Background and aim: Human papillomavirus (HPV) poses a significant global health burden, with high-risk genotypes being major causative agents of cervical, anal, and other cancers. While the introduction of the Gardasil 9 vaccine has substantially reduced the incidence of infections caused by its target genotypes, concerns are rising regarding the prevalence and clinical impact of non-vaccine HPV types. Furthermore, the engagement of males in HPV screening and prevention efforts remains suboptimal, potentially contributing to ongoing transmission. Therefore, this study aimed to comprehensively assess the prevalence and distribution of both high-risk and low-risk HPV genotypes among males and females within a defined population.

Methods: A cross-sectional study was conducted involving 1,436 participants. Samples were collected from the oral, vaginal, and genital regions. DNA was extracted and amplified using Real-Time PCR techniques. HPV genotyping was performed using the OpeGen High + Low Papilloma Strip Molecular Detection Kit, a reverse blot hybridization assay capable of detecting 37 HPV subtypes. Demographic and virological data were analyzed using Excel and SPSS software.

Results: HPV DNA was detected in 38.45% (n=551) of the samples. Among HPV-positive individuals, 98.7% were female (n=1,417) and 1.3% were male (n=19). The most prevalent HPV genotypes identified in the study included HPV 6, 16, 31, and 52, with additional detections of HPV 39, 42, 45, and 53.

Conclusion: This study reveals a high prevalence of HPV infection, with a predominance of specific genotypes including those not covered by the Gardasil 9 vaccine. The low representation of males seeking HPV testing highlights a significant public health concern. This trend underscores the urgent need for continued preventive strategies and public health initiatives to address the emerging health concerns associated with these other HPV types. These findings underscore the need for enhanced awareness and surveillance of non-vaccine HPV genotypes and targeted interventions to improve male engagement in HPV prevention and screening.

keywords: Human Papillomavirus (HPV); Genotyping; Prevalence; Gardasil 9; Cervical cancer; Public

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Investigating the Interrelationship Between Psychological Health and Immune Function in West Nile Virus Infections

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Medical Virology

Background and aim: West Nile Virus (WNV) has emerged as a significant global health threat, causing neuroinvasive disease in both humans and animals. Its primary transmission occurs through a natural cycle between birds and mosquitoes, with occasional spillover events leading to human infections. To explore the relationship between psychological health and immune function in the context of WNV infection and to propose a novel hypothesis for future research.

Methods: This study systematically reviews the literature and analyzes available data to identify potential therapeutic targets related to immune function and psychological well-being.

Results: The expanding geographic range of WNV, driven by climate change, poses an increasing threat to public health. Despite the high morbidity and mortality associated with WNV infections, there are currently no effective vaccines or specific treatments. Emerging research indicates a bidirectional relationship between psychological health and immune function, which may significantly influence the body's response to viral infections, including WNV.

Conclusion: This presentation will summarize key findings from existing literature and propose a novel hypothesis that elucidates the mechanisms underlying the

interplay between psychological well-being and immune function in WNV infection. Understanding these complex interactions could inform the development of targeted public health interventions aimed at enhancing immune resilience and mitigating the impact of WNV and other emerging infectious diseases.

keywords: Climate Change; Immune Function; Psychological; Viral Infections; West Nile Virus.

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HPV-Related Head and Neck Squamous Cell Carcinoma: An Analysis of Genotype Distribution and Patient Risk Factors

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Medical Virology

Background and aim: Head and neck squamous cell carcinoma (HNSCC) represents the most prevalent malignancy and ranks as the seventh most common cancer globally. Consequently, the identification and assessment of Human papillomavirus (HPV) status in HNSCC are crucial for determining prognosis and formulating treatment strategies. This study aimed to evaluate the prevalence of HPV among HNSCC patients and to identify specific genotypes using Real-time PCR techniques.

Methods: Forty tissue biopsy samples were obtained from patients suspected of having or diagnosed with head and neck squamous cell carcinoma during surgical procedures at Rasoul Akram Hospital (PBUH) in Tehran. Samples were collected from the larynx and base of the tongue. Samples DNA were extracted using Extraction kit. The detection and genotyping of HPV were conducted through Real-time PCR analysis.

Results: The study revealed a prevalence of HPV genotypes as follows: 12.5% for genotypes 35/39 and 6/11, 51, and 56/65 in biopsies from the base of the tongue. Additionally, genotypes 45, 16, and 18 were identified in 25% of base of tongue biopsies. Among laryngeal biopsies, genotypes 51, 56/65, and 31, 68, and 59 were present in 12.5% of samples. Furthermore, genotypes 35/39 and 6/11 were detected in 25% of laryngeal samples, while genotypes 45, 16, and 18 appeared in 18.75% of cases. Notably, 31.25% of patients with HNSCC exhibited no evidence

of HPV infection. Smoking was identified as the predominant habit among all HNSCC patients, with 25% reporting opium addiction.

Conclusion: Patients with HNSCC demonstrated a similarity of 43.75% in HPV genotype between their laryngeal and base of tongue tissue biopsies. However, 6.25% of patients tested positive for HPV in their larynx while showing no evidence of HPV in their tongue base. Interestingly, 18.75% exhibited differing HPV genotypes between these two sites. Smoking and opium use emerged as significant risk factors among individuals with HNSCC.

keywords: Human Papillomavirus (HPV), Head and Neck Squamous Cell Carcinoma (HNSCC),

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The Role of the Immune System in Response to COVID-19

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Medical Virology

Background and aim: The immune system is crucial in determining the outcome of COVID-19 infections. Understanding its mechanisms can provide insights into effective prevention and treatment strategies. The interplay between innate and adaptive immunity plays a significant role in controlling SARS-CoV-2, the virus responsible for COVID-19.

Methods: This review synthesizes current research on the immune response to COVID-19, focusing on both cellular and humoral immunity. Data were gathered from peer-reviewed studies, clinical trials, and immunological analyses to assess how different immune components respond to SARS-CoV-2 infection.

Results: Evidence indicates that a robust immune response, characterized by the activation of T cells and the production of neutralizing antibodies, is essential for controlling the virus. Conversely, dysregulated immune responses can lead to severe disease manifestations, including cytokine storms. Vaccination has been shown to enhance immune memory and improve outcomes in infected individuals.

Conclusion: The immune system plays a pivotal role in the pathogenesis and resolution of COVID-19. Enhancing immune function through vaccination and therapeutic interventions is critical for effective management of the disease.

Ongoing research is necessary to further elucidate the complexities of the immune response and its implications for treatment strategies.

keywords: Immune system, COVID-19, SARS-CoV-2, T cells, antibodies, vaccination, cytokine storm.