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Exosomal MicroRNAs as a Novel Diagnostic Biomarker for Rapid Detection of *Mycobacterium tuberculosis* and Nontuberculosis Mycobacteria

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Background: Mycobacterium is able to use different immune mechanisms through the expression of different microRNAs (miRNAs) to survive within the host's cells. A significant difference, either in up- or downregulation of miRNAs' expression level, can present miRNA as a diagnostic biomarker in a disease. A significant difference in expression level of miRNAs from serum samples of patients infected with mycobacteria may also result in accelerating monocyte apoptosis. The current study aims to find any significant difference

in expression level of exosomal miRNAs derived from the serum samples and thus introduce it as a potential mycobacterial biomarker.

Methods: Exosomes were directly isolated from serum samples of 55 patients infected with *Mycobacterium tuberculosis* (MTB) and nontuberculosis mycobacteria and also 30 healthy subjects. The presence of exosomes was approved via transmission electron microscopy (TEM), dynamic light scattering, and flow cytometry. miRNAs were then extracted from the exosomes, and thus, the expression level of Hsa-miR-20a-5p, Hsa-miR-29a, Hsa-miR-let7e, and Hsa-miR-155 was monitored via quantitative polymerase chain reaction.

Results: A significant difference was determined in the expression level of miR-20a-5p, miR-29a, and miR-let7e ($P \leq 0.0001$); however, miR-155 expression level was significantly downregulated in TB cases. ROC curve showed diagnostic miRNAs with the AUC = 0.6933 for miR-20 ($P \leq 0.01$), AUC = 0.6011 for miR-29a ($P \leq 0.17$), AUC = 0.7322 for miR-let7e ($P \leq 0.002$), and AUC = 0.7456 for miR-155 ($P \leq 0.001$) for tuberculosis (TB). The expression level of miR-let7e, 20a, and 29a in *Mycobacterium avium* versus MTB was upregulated ($P \leq 0.01$, $P \leq 0.0001$, and $P \leq 0.0001$, respectively). Furthermore, the expression level of miRs let7e and 20a was upregulated in *Mycobacterium abscessus* versus MTB ($P \leq 0.0001$ and $P \leq 0.002$, respectively).

Conclusion: MicroRNAs released from exosomes, miR-20, miR-let7e, and miR-155 have revealed a diagnostic biomarker for TB. This study develops a deep understanding of the potential serum biomarkers for conclusive diagnosis of TB and non-TB mycobacteria.

Keywords: Exosomes, microRNAs, *Mycobacterium tuberculosis*, nontuberculosis mycobacteria

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Libyan Pharmacy Professionals' Knowledge, Attitudes, and Practices Regarding Generic Substitution for Prescribed Brand Medications

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Background: Generic substitution is considered a major cost-minimizing strategy to reduce pharmaceutical expenses without compromising health-care quality. However, general practitioners are most concerned about the safety and quality of generic products. This study aimed to explore the knowledge, attitude, and practice of pharmacy professionals regarding generic medicines in Tripoli, Libya.

Methods: A cross-sectional survey was conducted among community pharmacists working in community pharmacies in Tripoli, Libya, from February to March 2023. A self-administered eighteen-item questionnaire on knowledge, attitude, and practice of community pharmacists was utilized. The data were entered into Microsoft Excel 2016 and analyzed using frequencies and percentages.

Results: Out of 150 questionnaires distributed, only 119 of the participants gave their responses giving a response rate of 79.3%. Of the total eight knowledge items examined, about 93 (78.2%) respondents correctly replied to the statement “generic and brand medicines contain the same number of active ingredients,” 58 (48.7%) of participants stated that generic medicine has the same bioequivalence as a brand medicine, and 102 (85.7%) of participants agreed that brand-name drugs can be replaced with generic versions. While participants’ attitudes toward generic medicine were high, and majority of them 107 (89.9%) stated that the price difference between generic and brand-name drugs is a compelling reason to prescribe them. Most pharmacy professionals conveyed that they practiced the substitution of brand to generic and toward the generic medicine’s substitution and 114 (95.8%) of them encouraged prescribers to use generic medicines.

Conclusion: Pharmacy professionals working in community pharmacies in Tripoli had satisfied knowledge with a positive attitude toward generic substitution. Most of them had practiced and encouraged this practice. National Guidelines and Policies for Generic Medications are also necessary in Libya.

Keywords: Brand drug, generic medicine, pharmacy professional, substitution

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Investigation Abutment Stress Shielding Distribution on Titanium Alloy Biomaterial under Bruxism Chewing Cycles: Three-dimensional Finite Element Chewing Simulation

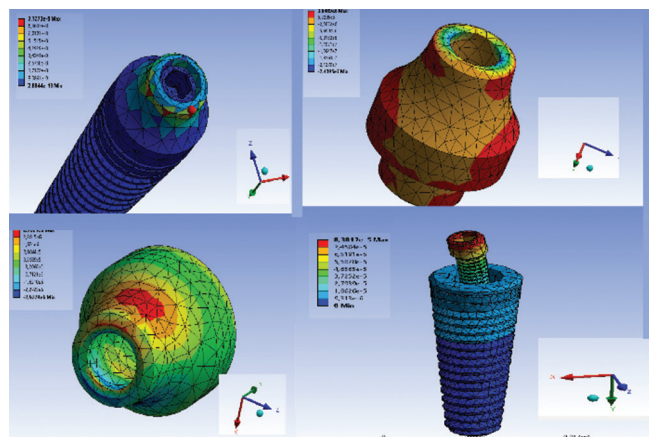
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GRAPHICAL ABSTRACT



Background: Biomaterials have three main classes: metals, polymers, and ceramics which are used to repair living tissues and organs or to interact with physiological systems. Titanium material is preferred as a biomaterial due to its superior mechanical and chemical behavior in living tissue. In addition, a more optimum material selection can be made by obtaining new material behaviors with titanium alloys. As the elderly population increases in various countries, the demand for artificial implants also increases. Approximately 80% of commercial implant devices are made of metallic biomaterials to correct deformities in the skeletal system.^[1] **Methods:** To expand the clinical applications of metal-based dental implants, it is envisaged to develop new alloys that are strong enough, offer a low elastic modulus, and are stable in the physiological environment. As mentioned in

the literature, Ti-Zr and Ti-Nb-Zr alloys appear to be promising candidates for dental implant applications.^[2] Bruxism can be defined as the force exerted by voluntary or involuntary jaw movement on teeth and dental materials. The continuity and complex structure of this mechanism may expose implant materials placed in the human mouth to various damage mechanisms. These damage mechanisms can significantly change the effective lifespan of the biomaterial placed in the mouth. For this reason, simulating *in vivo*, *in vitro*, and finite element analysis of the environment to which biomaterials placed in the human body are exposed using test methods has been of great importance to material behavior. This study aims to analyze the damage mechanisms that the Ti-5Zr implant material placed in the human mouth may be exposed to in the bruxism chewing mechanism using the finite element analysis method. In many studies in the literature, chewing movement has been simulated in laboratory environments.^[3-6] The ability of chewing simulators to generate damage mechanisms has a great impact on the accuracy of test results. This study aims to analyze the bruxism wear mechanism using the finite element method. **Results:** Thanks to this method, it was possible to model the experimental results with mathematical modeling, and thus the experimental results were evaluated more comprehensively after the Bruxism chewing test process. In addition, the ability to control the laboratory test environment in real-time in a computer-controlled system environment allowed the experimental process to be simulated as live tissue modeling. The data obtained as a result of this study show that there are various stress accumulations in the abutment area that form the implant. Stress accumulation makes the integration of the implant with the body difficult and may affect its mechanical behavior. **Conclusions:** To minimize stress accumulation, it is necessary to choose a material that is close to the elastic modulus of the jaw bone. Thus, a more homogeneous load distribution will be achieved during the bruxism chewing cycle process.

Keywords: Biomaterials, bruxism wear mechanism, finite element analysis

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REFERENCES

1. Bordbar-Khiabani A, Gasik M. Electrochemical and biological characterization of Ti-Nb-Zr-Si alloy for orthopedic applications. *Sci Rep* 2023;13:2312.
2. Cordeiro JM, Beline T, Ribeiro AL, Rangel EC, da Cruz NC, Landers R, et al. Development of binary and ternary titanium alloys for dental implants. *Dent Mater* 2017;33:1244-57.
3. Yilmaz EC, Polat M. Design and manufacture of computer-controlled wear device for biomedical material: A different ambient pH experimental application. *Biomed Biotechnol Res J* 2023;7:558-62.
4. Yilmaz EÇ. Influence of lubricating conditions on the two-body wear behavior and hardness of titanium alloys for biomedical applications. *Comput Methods Biomech Biomed Engin* 2020;23:1377-86.
5. Schmeiser F, Arbogast F, Ruppel H, Mayinger F, Reymus M, Stawarczyk B. Methodology investigation: Impact of crown geometry, crown, abutment and antagonist material and thermal loading on the two-body wear of dental materials. *Dent Mater* 2022;38:266-80.
6. Yilmaz EC, Sadeler R. Effects of contact-stress on wear behavior of zirconia-reinforced lithium silicate glass-ceramic. *Biomed Biotechnol Res J* 2020;4:51-4.

Exploring the Relationship between CDKN2A/B (rs10811661) Gene Polymorphism and Type 2 Diabetes Mellitus: A Meta-analysis

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Background: The meta-analysis aimed to investigate CDKN2A/B (rs10811661) gene polymorphism and its association with type 2 diabetes mellitus (T2DM) in Asian and Caucasian population.

Methods: The research cited in this article was gathered through the utilization of online databases. We conducted searches on platforms such as Scopus, Web of Science, Embase, and PubMed to identify case-control studies concerning the CDKN2A/B polymorphism and T2DM. MetaGenyo was employed to assess the statistical significance of the association between CDKN2A/B polymorphism and T2DM by calculating 95% confidence interval and odds ratio.

Results: This meta-analysis comprised six articles, revealing a significant association between the CDKN2A/B (rs10811661) gene polymorphism and susceptibility to T2DM with a $P = 0.01$. Subgroup analysis was performed.

Conclusion: The results of this meta-analysis provide a strong association between CDKN2A/B (rs10811661) gene variations and susceptibility to T2DM across allelic, recessive, dominant, and overdominant models. Analysis of subgroups indicated that both individuals of Asian and Caucasian exhibited statistically significant findings.

Keywords: CDKN2A/B, cyclin-dependent kinase inhibitor 2A/B, gene polymorphism, meta-analysis, type 2 diabetes mellitus

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Investigation of Degradation Mechanism on Dental Biomaterials Exposed to Chewing Cycle Process

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Background: Chewing movement is a mechanism that occurs during human survival. This mechanism can cause various degradation mechanisms in natural teeth and biomaterials subsequently placed in the human mouth. These damage mechanisms can sometimes prevent the mechanical, chemical, and esthetic sufficiency of natural teeth and dental materials. Therefore, it can appear as a factor that reduces the comfort of human life. The chewing movement has a continuous and complex structure depending on individual differences. **Methods:** This study aims to contribute to the analysis of test methods by defining the mechanisms that occur during the chewing process. In addition, it is to create a guide for parameter selection of laboratory testing experiments. Wear, fatigue, and corrosion mechanisms occur during the chewing mechanism. These mechanisms are divided into

many subgroups depending on their properties (for example two-body wear, three-body wear, fatigue wear, etc.). While these mechanisms can occur singly, they can also occur in combination. For example, while wear, corrosion, and fatigue mechanisms occur alone in the time axis, they can also occur in combination such as the formation of an acidic environment from food particles and the formation of biting force. Researchers have developed various *in vivo*, *in vitro*, and finite element analysis method experiments in the literature that can realize many degradation mechanisms.^[1-5] **Results:** Figure 1 show schematic representation of *in vitro* and finite element analysis chewing cycle simulation. These methods can produce successful test results depending on their ability to model living tissue. For example, if the wear behavior of teeth and dental materials during chewing is to be analyzed, transferring the conditions in the oral environment to the experimental environment is of great importance to the stability of the test results. For this reason, laboratory testing experiments must have high live tissue modeling ability. In addition, the applicability of changing living tissue conditions in the laboratory environment will affect the accuracy of the test results. As a result, all three test methods have advantages and disadvantages compared to each other for the chewing test process (for example; while the *in vivo* test method takes a very long time, the *in vitro* and three-dimensional finite element analysis test methods can be completed in a short time. **Conclusions:** Researchers should analyze whether the important parameters of the test method they design are suitable for which test method. In addition, designing test methods based on international standards will contribute greatly to the comparison of test results with each other.

Keywords: Chewing cycle process, degradation mechanism, dental biomaterial

DOI: 10.4103/bbrj.bbrj_77_24

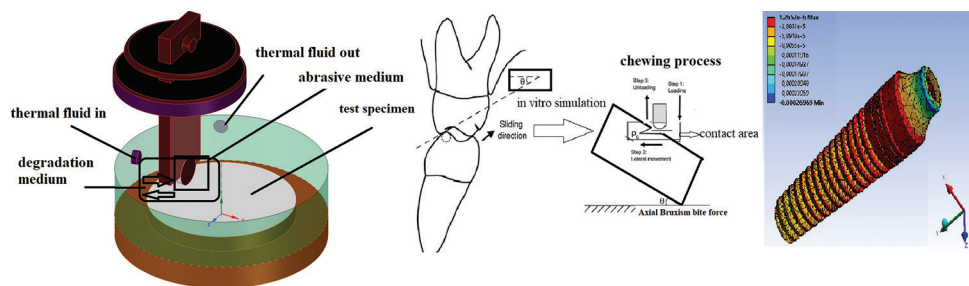


Figure 1: Schematic representation of *in vitro* and finite element analysis chewing cycle simulation

Saliva as a Diagnostic Tool: Oral Health and Disease

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Background: Saliva has emerged as a valuable diagnostic tool for both oral and systemic diseases due to its ease of collection, noninvasive nature, and abundance of biomarkers. Saliva, although commonly associated with digestion and oral hygiene, is increasingly recognized as a valuable diagnostic tool for assessing oral health

and detecting various diseases. **Methods:** Studies have shown that saliva contains a wide range of molecules, including DNA, RNA, proteins, and metabolites, which can provide valuable information about an individual's health status. Using saliva as a diagnostic tool offers several advantages. Recent advances in salivary diagnostics have shown promise in diagnosing various conditions such as autoimmune diseases (Sjogren's syndrome, cystic fibrosis), cardiovascular diseases, diabetes, HIV, oral cancer, caries, and periodontal diseases. **Results:** Saliva contains a complex composition of biomarkers including genetic material, proteins, urea, ammonia, uric acid, glucose, cholesterol, and various ions from the serum, making it a rich source for disease detection. Salivaomics, a field encompassing genomics, transcriptomics, proteomics, metabonomics, and microRNA analysis, has further enhanced the potential of saliva as a diagnostic medium. **Conclusion:** The use of saliva for disease diagnosis is expected to become more prevalent in clinical settings, offering a simpler, noninvasive alternative to traditional serum or urine tests.

Keywords: Diagnosis, disease, oral health, saliva

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Unraveling the Complexities of Tuberculosis and Sarcoidosis: Insights into Diagnosis and Differentiation

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Background: Unlike tuberculosis (TB), which is an illness caused by the bacterium *Mycobacterium tuberculosis*, sarcoidosis is an autoimmune disorder of unknown origins that can impact various body systems. Despite their distinct etiologies and pathophysiological mechanisms, these conditions share certain commonalities that

can lead to diagnostic confusion. **Methods:** Understanding the similarities and differences between sarcoidosis and TB is crucial for accurate diagnosis and appropriate management. Nonspecific systemic symptoms such as fever, tiredness, general discomfort, and weight loss are observed in approximately one-third of patients. **Results:** Typical findings on chest X-ray include enlargement of the lymph nodes in the chest and the area between the lungs. Histopathological features alone may not suffice for a definitive diagnosis of sarcoidosis. Distinguishing between sarcoidosis and TB can be particularly challenging in regions where TB is prevalent. Both diseases result in the formation of granulomas; TB is characterized by caseating granulomas, while sarcoidosis is typified by noncaseating granulomas. **Conclusions:** Recent research has shed light on the genetic underpinnings of sarcoidosis and how genetic makeup influences the clinical features and characteristics of patients. The diagnosis of sarcoidosis in areas with a high burden of TB can pose significant difficulties. Improved diagnostic methods, including genetic testing, hold promise in enhancing our understanding and differentiation of these two conditions. In this article, we explore the common features of these two diseases, shedding light on the complexities of their presentation and highlighting key points for differentiation in clinical practice.

Keywords: Diagnosis, sarcoidosis, tuberculosis

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Understanding Research Ethics: Perspectives of Faculty and Postgraduate Students in Medical and Dental Professional Institutions

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Background: Research ethics plays a crucial role in the entire research process, encompassing the collection, analysis, reporting, and publication of data, with a particular emphasis on respecting participants' rights to privacy, confidentiality, and informed consent.

This study aims to evaluate the knowledge, awareness, and attitudes regarding research ethics among faculty and students in medical and

dental colleges and to ascertain the necessity for regular instruction on research ethics within these academic institutions.

Methods: A cross-sectional study was conducted, and 39 specific questions related to knowledge, awareness, and attitudes about research ethics were framed. A total of 415 faculty members and postgraduate students from medical and dental institutions in Karnataka state participated. An online questionnaire was developed using Google Forms and categorized into five sections. Chi-square tests were employed to analyze the association of independent variables, while Student's *t*-tests were used to assess respondents' scores on a 5-point Likert scale ranging from 1 to 5. The average scores were compared across variables such as specialty and academic position using ANOVA tests.

Results: A total of 415 responses were collected, revealing significant deficiencies in understanding research ethics across various sections. The significance level (*P* value) for this study was set at 0.05.

Conclusion: Participants in the survey indicated the potential utility of institutional ethics committees in promoting health research and emphasized their essential role in evaluating health research projects. The necessity for regular instruction on research ethics among faculty and students in medical and dental colleges was underscored. Further investigation in this area is warranted.

Keywords: Awareness and attitudes, faculty, knowledge, professional college, research ethics, students

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Be Prepared for Infectious Disease Crisis

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Background: Several studies have indicated that health-care systems are not adequately prepared or resilient to COVID-19. This

study aims to identify issues that may, if left unaddressed, result in organizational vulnerability. This may result in poor hospital performance before a crisis and a lack of preparedness for future crises. Patient capacity management, deficiencies in communication and medical education, problems with physical infrastructure, bed shortages, and defects in the provision of medical equipment and personal protective equipment are challenges that have already embroiled health-care systems in organizational crises even before the emergence of novel health crises. This study was conducted using the content analysis method, and data were collected through structured interviews. The snowball sampling method was employed, and the specialists involved in this study were actively present during the COVID-19 pandemic outbreak.

Results: The final model proposed in this study comprises three main dimensions: psychological resources, human resources, and financial resources. Subdimensions include job burnout, psychological pressure, empowerment, staff training, staff retention, staff deployment, medical tariffs, provision of medical equipment and personal protective equipment, and provision of physical infrastructure for resource storage.

Conclusion: Strengthening health-care systems' psychological, human, and financial dimensions will allow them to develop innovative crisis management strategies. Hospitals must enhance organizational flexibility to increase resilience and minimize challenges during crises.

Keywords: Crisis management, epidemic, health systems

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Investigating the Effect of Polymacrocycles on the Specific Absorption of the COVID-19 Virus in Surgical, Three-layer, and Fabric Masks

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Background: Masks have been recommended as a potential tool to combat the COVID-19 pandemic since the initial outbreak. It is highly recommended by the WHO and CDC that face masks should be used for susceptible and infected patients with COVID-19. The aim of the present investigation was to assess the effect of polymacrocycles on the specific absorption of the COVID-19 viruses on fabric, three-layer, and surgical masks.

Methods: A model of polymacrocycle compounds was developed for fabric, three-layer, and surgical masks to assess mask effectiveness in reduction of COVID-19 spread, at the time of first outbreak

occurrence. The model was examined by sensitivity analysis of the most influential factors. When the first outbreak of the epidemic occurs, if social distancing is not compulsory, the effective number of treatments <1 can only be reduced by 100% coverage of highly efficient masks. By implementing social distancing, the transmission rates would be significantly reduced, and hence, 80% effective masks would be capable of reducing the disease prevalence <1 , while they would fail to do so when people do not comply with social distancing protocols. As a matter of fact, the use of masks with 100% coverage is not economical for the consumption of the general public in large communities. Therefore, spraying the polymacrocycles on commercial masks, through covalent binding to the spike protein of the COVID-19 virus, can limit the virus from entering the respiratory system and hence, the commercial masks resemble the highly efficient masks for prevention of COVID-19 virus.

Results: Results of the present investigation indicated that the application of polymacrocycles on fabric, three-layer, and surgical masks meaningfully improved the outcomes. Spraying polymacrocycles increased the binding of COVID-19 virus to the surface of the mask, up to 160 times, compared to the masks without polymacrocycles, using scanning electron microscopy (SEM).

Conclusion: According to the results, homogeneous mixing is recommended for providing a higher limit for the masks containing polymacrocycles to be more efficient and effective. Although even masks with lower coverage levels can contribute to the prevention of COVID-19 and the reduction of its spread, in particular, their effectiveness can be strikingly enhanced by the use of polymacrocycle compounds.

Keywords: COVID-19, mask, polymacrocycle, prevention, social distancing

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Design and Manufacture of Bioartificial Liver

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Background: Acute liver failure is a severe life-threatening disease with a high rate of mortality. The prevalent treatments for this fatal condition are liver transplantation and artificial liver support systems, including bioartificial liver. The aim of the present investigation was to design and manufacture the bioartificial liver.

Methods: Herein, the progressive advances in the design and manufacturing processes of bioartificial liver support systems are

discussed. In particular, various kinds of cell sources and different bioreactors for the manufacture of bioartificial liver, as well as the advances in pioneering technologies for the construction of bioreactors and hepatocyte culture, are elaborated. Moreover, the existing challenges and feasible future trends in the enhancement of the next generation of bioartificial liver for clinical application are explained. In addition, scale-up processes are also discussed in detail.

Results: In comparison with the artificial liver, the bioartificial liver consists of functional liver cells, which are required for the proper function of the liver and chiefly contribute to the synthesis of metabolites and detoxification. In addition, bioartificial livers are considered an appropriate alternative therapy for liver transplantation and might be supportively involved in spontaneous recovery of acute liver failure patients.

Conclusion: The present study sheds light on influential aspects of liver support systems and describes advances in the development of vital parts of these systems, including cell sources as well as circulation circumstances to keep and enhance specific functions of the liver.

Keywords: Acute liver failure, bioartificial liver, bioreactor, transplantation

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Investigating the Effect of Oral Dispersible Films in Patients with Erectile Dysfunction

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Background: The conventional coated tablets for the treatment of erectile dysfunction (ED) demonstrate some drawbacks for consumers. To address these problems, innovative formulations, particularly oral dispersible films (ODFs), have been recently introduced. The purpose of the present investigation was to provide a brief overview of the beneficial effects of dispersible films on patients with ED.

Methods: A descriptive systematic review of ED patients was performed. By the use of the information collected from published documents including hormonal evaluations, self-report questionnaires, and patient medical history, the effects of ODF formulations were assessed. Moreover, the Index of Erectile Function (IIEF-15) questionnaire was administered. IIEF-15 scores within the ranges of ≤ 10 , 11–16, and 17–25 were used to classify the erectile function as severe, moderate, and mild.

Results: The results of the present investigation based on collected information demonstrated that ODFs significantly enhance erectile function, sexual desire, orgasm function, as well as intercourse satisfaction based on reported differences in IIEF average scores, and the overall satisfaction score was predominantly beneficial for 50-mg sildenafil DFs.

Conclusion: The present investigation is the first study to describe the benefits and effectiveness of the newly emerging ODFs for ED patients. The study suffered from restrictions due to the used method, namely, the study was not performed as a control-case, but a systematic descriptive one. In general, the results of this study revealed that ODFs can safely and efficiently provide a suitable alternative for more accurate treatments of ED.

Keywords: Erectile dysfunction, oral dispersible film, sildenafil

DOI: 10.4103/bbrj.bbrj_97_24

Alterations in Iron Parameters in Relation to Inflammation in People Living with Human Immunodeficiency Virus: Implications for Human Immunodeficiency Virus Treatment in Resource-limited Setting

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Background: There is an intricate relationship between human immunodeficiency virus (HIV), inflammation, and iron metabolism. While HIV is primarily recognized as an immune-suppressive viral infection, it is known to cause chronic inflammation and a number of

physiological complications, including changes in iron metabolism. Differences in the levels of some iron and inflammatory parameters in persons living with HIV (PLWH) and persons without HIV and its implication for HIV treatment were assessed in this study.

Methods: This cross-sectional study was carried out at the HIV clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi, southeastern Nigeria, from February to July 2023. The study involved 100 subjects comprising 50 adult persons living with HIV (PLWH) and on anti-retroviral treatment and 50 age- and gender-matched control (persons without HIV). Serum levels of iron and total iron-binding capacity (TIBC) were measured spectrophotometrically, while packed cell volume (PCV) and erythrocyte sedimentation rate (ESR) were measured using the Microhematocrit and Westergren methods, respectively. Statistical Package for Social Sciences (SPSS) version 23 was used for data analysis. Ethical approval was obtained as well as informed consent of the participants before the commencement of the study. **Results:** The findings show a significant decrease in the mean levels of total iron ($\mu\text{g/dl}$), TIBC ($\mu\text{g/dl}$), and PCV (l/l) among persons living with HIV in comparison to the controls ($P < 0.001$). Conversely, there were significantly elevated ESR (mm/h) levels in PLWH compared to the controls ($P < 0.001$). However, transferrin saturation levels did not differ between the two groups ($P > 0.05$).

Conclusions: The findings show a significant decrease in the mean levels of total iron ($\mu\text{g/dl}$), TIBC ($\mu\text{g/dl}$), and PCV (l/l) among persons living with HIV in comparison to the controls ($P < 0.001$). Conversely, there were significantly elevated ESR (mm/h) levels in PLWH compared to the controls ($P < 0.001$). However, transferrin saturation levels did not differ between the two groups ($P > 0.05$). This indicates a decrease in iron level in the presence of an increased inflammation.

Keywords: Human immunodeficiency virus, inflammation, iron, persons living with human immunodeficiency virus

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Antibiotic Susceptibility and Genetic Diversity of *Helicobacter pylori* from a Tertiary Care Hospital in North India

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Background: This study aimed to assess the antibiotic susceptibility of drugs commonly used for *Helicobacter pylori* (*H. pylori*) eradication and understand the interplay between genetic diversity of *H. pylori* virulence genes and antibiotic resistance in North India.

Materials and Methods: A total of 58 *H. pylori* strains isolated from

patients with various gastrointestinal diseases were analyzed. The minimum inhibitory concentrations of antibiotics were determined using the agar dilution method. Statistical analysis was performed using the Chi-square test and Fisher's exact test, with significance set at a *P* value of 0.05. Data visualization was conducted using RStudio 4.0. **Results:** The prevalence of antibiotic resistance was observed as follows: metronidazole (MTZ) (39.6%), tetracycline (TET) (20.7%), clarithromycin (CLA) (17.2%), amoxicillin (AMX) (20.7%), furazolidone (FZD) (34.4%), levofloxacin (LVFX) (70.7%), and rifabutin (RIF) (17.2%). Resistance patterns included cases with no resistance (10.3%), single-drug resistance (24.1%), dual resistance (32.7%), triple resistance (12%), and multidrug resistance (MDR) (19%). The resistance rates in MTZ, CLA, and RIF were significantly higher in females compared to males (*P* = 0.005, *P* = 0.002, and *P* = 0.02, respectively). 48.27% of *H. pylori* strains were *cagA* positive, while 51.7% were *cagA* negative. The *vacA* s2m2 allele predominated in 50% of *H. pylori*-positive patients, followed by s1m1 (29.31%), s1m2 (17.2%), and s2m1 (3.4%). Although we did not find any significant difference in the prevalence of antibiotic resistance with *H. pylori* virulence genes. **Conclusion:** TET, AMX, CLA, and RIF were effective against *H. pylori* infections, while further studies are needed on LVFX resistance. Gender differences showed females with higher antibiotic resistance than males. However, no clear association was found between antibiotic resistance and *H. pylori* virulence genes.

Keywords: Antibiotic resistance, antibiotics, *Helicobacter pylori*, multidrug resistance, virulence genes

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Information and Information Technology Needed by Adults, Families, and Managers of Elderly Centers

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Background: The elderly are the largest group that use information technologies the least, while these technologies are the most useful for them. Therefore, the purpose of this study was to investigate information and information technologies needed by elderly, family, and managers of elderly centers.

Methods: The research was descriptive and was conducted cross-sectionally in 2023. The research population were 234 elderly people and the sampling was done by census. The data were collected using a researcher-made questionnaire and validity and reliability were determined. Finally, the data were analyzed with SPSS23 and mean, standard deviation, percentage, and correlation coefficient tests.

Results: The average age of the elderly was 68 years. The percentage values of elderly and families needed mobile phones were 47.1% and 89.3% and video communication were 47.1% and 45.5%, respectively. Managers also considered mobile phones, video communication, and television necessary for the elderly with 38.1%, 85.7%, and 71.14%, respectively. Information technology had a significant relationship with education ($P = 0.038$), occupation ($P = 0.001$), and gender ($P = 0.04$) of the elderly.

Conclusions: The rapid growth of information technology and its impact on life makes it necessary to teach it to the elderly and to provide the necessary infrastructure for this purpose.

Keywords: Elderly, elderly center, information, information technology

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Evaluation of Warfarin-associated Major Hemorrhage in Hospitalized Patients

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Background: Warfarin has been the most common anticoagulant prescribed by physicians in recent decades; however, it needs to be

managed due to unwanted complications. Therefore, the study aimed to investigate major bleeding caused by warfarin administration in hospitalized patients.

Methods: The study was a descriptive analysis conducted in 2023. The research resources were 120 records of hospitalized patients due to major bleeding complications caused by warfarin administration from 2017 to 2021. The samples were selected by census based on research criteria. The data were collected via a researcher-made checklist and analyzed using SPSS 23.

Results: The results showed that 49.3% of bleeding occurred in the gastrointestinal in the age group of 51 to 60 years in men. The most common reason for using warfarin was to treat deep vein thrombosis. The average international normalized ratio of the patients was 4.57 for the main complaint and 4.74 for the reason for using warfarin. There was no statistically significant relationship between the international normalized ratio due to the use of warfarin and the main complaint of the patients ($P = 0.53$).

Conclusions: Deep vein thrombosis was the most common cause of warfarin use, causing bleeding complications in middle age. Patients with an international normalized ratio lower than the therapeutic range also presented with complaints of bleeding. Thus, it can be concluded that by replacing direct oral anticoagulants in some patients and without the need for repeated international normalized ratio testing, the bleeding complications of warfarin are reduced.

Keywords: Bleeding, complications, hospitalized patient, warfarin

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Investigating the Inhibitory Effect of the Fractions of Extracellular Secretions (Postbiotic) in *Limosilactobacillus reuteri* Probiotic Bacteria on Gastrointestinal Cancer

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Introduction: According to the 2020 World Health Organization report, cancer is the second leading cause of death globally, responsible for nearly 10 million deaths each year. Colorectal cancer contributes significantly to this statistic, with about 2 million cases and 1 million deaths annually. Recent studies have shown that microorganisms in the gastrointestinal tract play a crucial role in regulating human homeostasis and the immune system. Consequently, manipulating the microbiome and the general metabolism of intestinal microflora are effective strategies for cancer treatment, including probiotics and postbiotics. Although probiotics are beneficial, postbiotics are considered a safer alternative with fewer side effects. Given the promising potential of postbiotics in enhancing health and their emerging role in cancer prevention and

treatment, it is essential to explore postbiotics as an anticancer agent further. **Methods:** The current study employed a postbiotic derived from bacterial strains to investigate its inhibitory and anticancer effects on colon cancer cells. Initially, strains of *Limosilactobacillus reuteri* were isolated in the laboratory. Subsequently, the cell-free supernatant (CFS), known as postbiotic, was extracted using the lyophilization method. The cytotoxic effect of the postbiotic sample was evaluated on the HCT-116 colon cancer cell line at concentrations of 50, 100, 250, 500, and 750 µg/ml. Cytotoxicity was assessed through an methylthiazolyldiphenyl-tetrazolium bromide (MTT) or 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay at 24, 48, and 72-h intervals, and the IC50 value was calculated. Based on the IC50, flow cytometry and real-time polymerase chain reaction (PCR) analysis were conducted to examine apoptosis, necrosis, cell cycle arrest, reactive oxygen species (ROS) analysis, and the expression of the ATG5, BCL2, BAX, and mTORC1 genes.

Results: The anticancer properties of postbiotics were studied based on the preparation of isolated strains. The determination of statistical significance was made with two-way ANOVA. The MTT assay findings have clarified that postbiotics can able to induce cytotoxicity in HCT-116 cells, depending on concentration and time. There is a significant difference in the evaluated results of postbiotics with a concentration of 750 µg/ml. The reduced cell survival result after 72 hours for CFS of *Limosilactobacillus reuteri* (CFSR) was obtained as 53%. According to the results, treatment of cancer cell lines with determined IC50 increased the percentage of cells in early and late apoptosis phases compared with the negative control. The rate of induced apoptosis (late apoptosis) was $30.6 \pm 4\%$. In comparison to the untreated control cells, treatment with CFSR at a concentration of 750 µg/ml for 48 hours led to an increase in the sub-G1 phase of cells. CFSR treatment was associated with the highest sub-G1 phase of $11.89 \pm 2\%$ compared to the negative control. In examining the expression of studied genes, the expression of the mTORC1 gene was significant compared to the control in treatment with postbiotics, which indicates the induction of apoptosis in cells. Overall, the analysis of results indicates that postbiotics possess notable anticancer properties. **Conclusion:** The findings indicated that the laboratory-produced postbiotic, specifically the CFS, could exhibit inhibitory and lethal effects on colon cancer. Further research and investigations will be required to obtain more conclusive results.

Keywords: Anticancer therapy, cell-free supernatant, colorectal cancer, postbiotic, probiotic

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Clinical Use of Bioartificial Skin Produced by a 3D Bioprinter with the Ability to Create Langer's Lines

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Abstract

Background: The skin is the large organ covering the body, which protects it from environmental factors (such as UV light, pathogens, and toxins) and maintains the body's hemostasis. As a revolutionary strategy, which has been recently introduced to the scientific world, bioprinting is capable of producing three-dimensional structures of skin through the deposition of the scaffolds and the cells by a computer-controlled program. The aim of the present study was to

investigate the capability of the 3D bioprinter to produce bioartificial skin and to evaluate the possibility of creating Langer's lines in the skin for clinical applications.

Methods: The designed hood Class IIb chamber consisted of two parts: (1) the electrospinning set-up by which the nanofiber mat is formed on the cylinder-shape collector; and after separation of the produced mat from collector, (2) printing the fibroblasts and keratinocytes in combination with tissue culture medium enriched with recipient plasma on the pattern of Langer's lines. This pattern is implemented by our software.

Results: The present investigation revealed that 3D bioprinter device is capable of producing multi-layer vascularized skin graft, which is appropriate for clinical and biomedical applications and triumphs over the drawbacks and restrictions of the ordinary skin substitutes being currently utilized. This novel technology successfully provides a promising approach to treating acute skin wounds, particularly chronic skin injuries and severe burns.

Conclusion: As an inventive alternative, the produced bioartificial skin by 3D bioprinting provides the opportunity for skin reconstruction. The present study demonstrated the capability of 3D bioprinter to create Langer's lines in the produced bioartificial skin to inhibit the formation of scar in burn wounds, and discusses the existing challenges in its manufacturing processes, as well as the related clinical and medical uses.

Keywords: 3D bioprinter, bioartificial skin, reconstruction, scaffold, vascularized graft

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Investigating the Effect of Cold Atmospheric Plasma on Patients with Asthma

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Abstract

Background: Over the last four decades, the global prevalence of asthma has been strikingly increased in such a way that an urgent need for its effective control is perceived. Herein, the effect of cold atmospheric plasma (CAP) treatment on patients suffering from asthma was evaluated.

Methods: In the present investigation, the effectiveness of CAP on serum samples of allergen-sensitive individuals and the feasible involved mechanisms were elaborated. Patients were divided into two groups, which were nearly identical regarding age, gender, and clinical manifestations. All the patients received the same standard treatment protocol. However, for the first group, the patient room was treated with CAP every night for 3 h during the autumn season.

Results: The present study indicated that CAP was significantly effective in the reduction of allergenicity of the environmental allergenic aerosols. Air particle suction system showed a reduction in airborne antigen levels after 3 h of CAP exposure. According to the observed reduction in serum immunoglobulin E levels, it was revealed that CAP changes the immune system response.

Conclusion: The observed decrease in allergenicity was related to the produced free radicals from CAP. The obtained results confirmed that this novel technology successfully fights against asthma and other allergic diseases. Preclinical and clinical investigations verified the therapeutic effects of CAP. Overall, several suggestions are presented in this work which might be helpful to guide directions toward future treatments.

Keywords: Allergen, asthma, cold atmospheric plasma, free radical

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Isolation and Immunogenicity Assessment of Facultative Anaerobic Microorganisms from the Caseum of Tuberculosis Foci

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Background: Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), is a common respiratory infection. Granulomatous inflammation in the lungs and the formation of caseous necrosis are key aspects influencing the disease outcome. Satellite microbiota present in the caseum may play a role in both the chronic progression of the infection and the formation of the organism's immune response. This study aimed to isolate and assess the immunogenicity of representatives of satellite microbiota from the caseum of tuberculosis foci. **Methods:** A microbiological screening for satellite microbiota was conducted on 30 caseum samples from surgically excised tuberculomas. Isolated pure cultures of microorganisms were identified by whole-genome sequencing. Cell lysates of the isolated strains were used as antigens to assess the immunogenicity. The study assessed immunoglobulin G (IgG) levels among 87 TB patients and 86 healthy donors using enzyme-linked immunosorbent assay (ELISA). T-cell response was evaluated among 15 TB patients and

16 healthy donors with interferon gamma release assay (IGRA)-test using STANDART E TB-Feron IGRA kit (SB BIOSENSOR) and antigens obtained in the study. The innate immunity response was studied in an *in vitro* model of Mtb-induced granulomogenesis using peritoneal macrophages and splenocytes from C57BL/6 male mice, Beijing B0/W148 Mtb strain, and cell lysates of isolated strains.

Results: Three pure cultures of facultative anaerobic lipophilic microorganisms were isolated from two samples of caseum and identified as two strains of *Staphylococcus epidermidis* (2206/1 and 2206/2) and *Corynebacterium kefirresidentii*. The concentration of IgG against *S. epidermidis* 2206/1 was higher in TB patients, although not statistically significant. Despite this, the average IgG concentration against *S. epidermidis* in TB patients was higher, and two TB patients had significantly higher signal values. Interferon-gamma levels increased similarly in TB patients and healthy donors when treated with *C. kefirresidentii* antigens, reaching around 2 IU/mL. TB patients had significantly higher interferon-gamma release (2.5 IU/mL) when treated with Mtb antigens compared to healthy individuals (0.1 IU/mL). Seven TB patients showed stronger responses to *C. kefirresidentii* antigens than Mtb antigens. Adding cell lysates of *S. epidermidis* and *C. kefirresidentii* at different concentrations increased cell recruitment into granulomas and the number and size of granulomas. For example, *C. kefirresidentii* antigens doubled the number of granulomas and led to the emergence of very large granulomas on the 7th day, whereas it enhanced the bactericidal activity on the 14th day. *S. epidermidis* antigens had similar effect on granuloma numbers. **Conclusion:** The active immunogenic components of *S. epidermidis* and *C. kefirresidentii* isolates likely affect innate immunity responses more than adaptive ones. Further studies will aim to uncover the mechanisms of action of these microorganisms and their active components for potential optimization of the immune response in TB infection.

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Keywords: Antibody, granulomas, IGRA, lung microbiota, tuberculosis

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Outer Inflammatory Protein A Coding Gene of *Helicobacter pylori* and Its Associated Pathogenesis

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Objective: Understanding the pathophysiology and disease component of the *Helicobacter pylori*'s outer inflammatory protein A (oipA) coding gene is the main goal of this study.

Background: A Gram-negative bacterium called *H. pylori* inhabits the human stomach and is linked to a number of digestive disorders, including gastritis, peptic ulcer disease, and gastric cancer. One important virulence component of *H. pylori* that is important to the pathophysiology of these disorders is the oipA. The present state of research on oipA and the pathogenic pathways linked to it, is compiled in this abstract. The region of genome plasticity in *H. pylori*, where oipA is found, is prone to genetic changes. It produces a surface-expressed protein called outer inflammatory protein 'A', which interacts with host cells and sets off a series of inflammatory reactions. Conflicting data, however, point to a complicated

interaction between oipA and other bacterial variables in the course of the disease. The oipA is linked to a higher risk of gastrointestinal diseases that include severe gastritis, peptic ulcer disease, and gastric cancer, underscoring its significance in the pathophysiology of *H. pylori*. The oipA stimulates the generation of pro-inflammatory cytokines generated primarily by stimulated macrophages. These comprise, granulocyte-macrophage colony-stimulating factor, interleukins (IL-1, IL-6, IL-12, and IL-18), interferon-gamma, and tumor necrosis factor-alpha, which draws the immune cells to the region of infection and worsens the tissue damage. In addition, OipA alters the signaling pathways linked to cell survival and proliferation.

Method: Using keywords associated with OipA, *H. pylori*, and pathogenesis, systematic searches of electronic databases, such as PubMed, Scopus, and Web of Science, produced pertinent material.

Results: The *H. pylori* genome's plasticity area contains the oipA gene, which has a significant genetic variation between strains. In order to induce pro-inflammatory cytokines and break tight junctions, which in turn contribute to the development of gastric inflammation, ulceration, and maybe carcinogenesis, OipA is essential for *H. pylori*'s adherence to gastric epithelial cells.

Conclusion: This gene contributes to *H. pylori*'s colonization and persistence in the host by facilitating the bacterium's adhesion to gastric epithelial cells through the encoding of the outer membrane protein OipA. OipA has also been linked to the loss of gastric epithelial cell integrity. Targeted therapy approaches against *H. pylori* may benefit from additional studies into the mechanisms underpinning oipA's involvement in the pathogen's pathogenesis.

Keywords: Cytokines, gastritis, *Helicobacter pylori*, inflammatory reactions, outer inflammatory protein A, pathogenesis

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Morphological and Improvement of Human Adipose Stem Cells Derived Retinal Pigment Epithelium using Extracellular Matrix and Neural Retina Co-culture

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Background: Differentiation of human mesenchymal stem cells into retinal pigment epithelium is challenging, so the aim of this study is investigation of morphological improvement and melanin granules production in differentiated cells.

Methods: In this study, human adipose stem cells were used following lipoaspiration from the abdominal area. First, adipose stem cells extracted in the third passage were differentiated into neurosphere cells by neural differentiation medium. In the next step, neurospheres were cultured on insert plates containing the extracellular matrix of ARPE-19 cells and induced with retinal differentiation medium to retinal pigment cells were differentiated. Finally, for better differentiation, the cells were placed in proximity to the neural retina isolated from C57 mice for 2 days. The amount of changes in the appearance of cells differentiated into hexagons, as well as the amount of melanin pigment production was calculated by Image J software.

Results: The results of adipose stem cell culture showed that more than 90% of them expressed mesenchymal stem cell markers. Furthermore, the expression of more than 80% of the specific markers of neural stem cells showed that neurospheres derived from adipose tissue were differentiated into neural stem cells. In addition, the expression of more than 80% of specific markers of retinal pigment cells showed that these cells were differentiated into retinal pigment cells. In the examination of the morphological results, it was shown that the pigmented cells obtained were hexagonal in shape with sharp borders close to other cells. The amount of melanin production in the cytoplasm of these cells was increased during the time in the culture medium.

Conclusions: The results of this study showed that the use of human adipose stem cells can lead to the production of retinal pigment cells with an appearance similar to normal cells and the ability to produce melanin pigment. The findings of this study can be used in cell studies for cell therapy in the retina.

Keywords: 3D culture, adipose stem cells, neural retina co-culture, neurosphere, retinal pigment epithelium

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Diagnostic Impact of P53, P16, Retinoblastoma, and Bcl-2 Proteins in Human Papillomavirus-Associated Squamous Cell Carcinoma Cervical Lesions

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Background: Cervical cancer is the third most prevalent disease among women and mostly associated with the human papillomavirus with significant number of mortalities. It accounts for more than 95% of cases diagnosed late.

To investigate the involvement of tumor protein 53 (P53), tumor suppressor protein 16 (P16), retinoblastoma (Rb), and B-cell

lymphoma 2(BCL-2) as diagnostic factors in tumor suppression in cervical lesions.

This was a case-control study that used 160 cervical tissue blocks selected from the pathology archives. All blocks used were confirmed cases of cervical samples.

Methods: Hematoxylin and eosin staining and immunohistochemical technique were used to treat samples with the matching antibodies for P53, P16, retinoblastoma, and B-Cell Lymphoma (BCL-2) expression as described by Camacho-Urkaray. Statistical analysis done by analysis of the data obtained from the study was carried out using photomicrographs, charts, graphs, and tables.

Results: There was a positive association between the expression levels of P53, P16, Rb, and BCL-2 with the progression of cervical lesions. It was revealed that P53 had a higher diagnostic effect for squamous cell carcinoma of the cervix, with a positive rate of 100% and a reactivity rate of around 96%. P16 had a complete positivity rate of 100% and a reactivity rate of around 72%. The retinoblastoma exhibited a positivity rate of 100% and a reactivity rate of 82%. BCL-2 showed a positivity rate of 100% and a reactivity rate of 62%.

Conclusion: The research shows that the P53, P16, Rb, and BCL-2 proteins are expressed in malignant lesions with moderate-to-severe intensities accordingly and are also closely related to the progression of cervical oncogenesis. However, to get optimal and precise outcomes, it is advisable not to rely only on individual Immunohistochemistry (IHC) markers.

Keywords: BCL-2, biomarkers, cervical cancer, immunohistochemistry, P53, P63, retinoblastoma, Squamous cervical carcinoma

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Indian Siblings with Waardenburg Syndrome Living Beyond the Age of 40 Years – Diagnosis and Management

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Background/Objectives: The hallmark features of Waardenburg syndrome (WS) are pigmentary defects, dysmorphic craniofacial features, upper limb abnormalities, neurological defects, and intestinal anomalies, while some individuals may exhibit sensorineural hearing loss. Based on the phenotypic variations, WS is divided into four subtypes, Waardenburg syndrome 1 to 4 (WS1 to WS4) and confirmed by genetic testing. There are limited cases reported in India. This article aims to report the rare WS siblings' diagnosis, treatment, and genetic counseling to their family members.

Methods: We present our first case of a 47-year-old woman born as the first child to a nonconsanguineous couple, without any pregnancy complications. She presented with severe developmental delay, short stature, microcephaly, intellectual disability, dystopia canthorum, syndactyly, skeletal disabilities, language deficits, patch of white hair at the frontal area, light-colored eyes, and Hirschsprung disease. The second case of a 44-year-old male sibling born as a second child showed intellectual disability, aphasia, hypotonia, sensorineural hearing loss, hyperkeratotic papules over limbs, brachydactyly, dislocated shoulders, hiatus hernia, and gastroesophageal reflux disease.

Results: Magnetic resonance imaging studies showed cortical malformations and ventriculomegaly in both patients. There was no similar history in their parents or other siblings. According to Read and Newton, the first case was diagnosed with WS type 4 (Shah WS) and the second case was diagnosed with WS type 3 (Klein WS). The genetic testing confirmed the missense variant C>T at exon 7 of paired box 3 gene (PAX3) on chromosome 2 in both patients caused WS. (NM_181458:exon7:c.C1003T:p.P335S). This finding extends the prevailing knowledge of mutations of the PAX3 gene in WS3 and WS4 patients. This is considered the first case report of type 4 WS associated with PAX3 mutation in India.

Conclusion: As it is a genetic disease, there is no definitive treatment for WS, but symptomatic treatments like surgery for skeletal abnormalities and intestinal disabilities. Since it is an autosomal dominant disorder, other unaffected two siblings were undergoing carrier screening test and were provided with genetic counseling.

Keywords: Exome sequencing, global developmental delay, Hirschsprung disease, PAX3 gene, Waardenburg syndrome

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Multistage Investigation of Gene Expression Pattern in Colorectal Cancer and Gene Silencing of Pyroxd1 in HTC116 Colon Cancer Cell Line

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Background: The purpose of this study was to investigate the expression profile of *Foxm1*, *Mctp1*, *Slc6a11*, *Bmi1*, *Ppara*, *Pim3*, and *Pyroxd1* genes in patients with colorectal cancer and small

interference RNA (siRNA) inhibition of Pyroxd1 in HTC116 colon cancer cell line.

Methods: Real-time reverse transcription–polymerase chain reaction was carried out to analyze the expression patterns of genes in Stage I to IV colorectal cancer patients. siRNA was designed against the Pyroxd1 gene. Flow cytometric technique was used to investigate the possible role of Pyroxd1 on the cell division and apoptosis cycle after treatment of HCT-116 colon cancer cells with Pyroxd1 siRNA.

Results: The expression level of *Foxm1*, *Pyroxd1*, and *Mctp1* genes was significantly increased in the tumor tissue of colorectal cancer patients compared to adjacent normal tissue. Suppression of *Pyroxd1* gene expression by siRNA inhibited cell cycle and induced apoptosis in HCT-116 colon cancer cell lines.

Conclusion: Our study suggests that the expression profiles of these genes individually or together can be used as potential biomarkers for the prognosis of colorectal cancer. *Pyroxd1* also plays a critical role in regulating cell cycle and apoptosis and possibly demonstrates its therapeutic potential for targeting colorectal cancer models.

Keywords: Colorectal cancer, gene expression profile, gene expression suppression, HCT-116 cell line

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Possible Method for Detection of Iron in Retinal Pigment Epithelium Cells using Image J Software

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Background: There are many factors involving in RPE degeneration and eye diseases. Today, one of the most interesting factors is iron. Hence, the quantification and qualification of iron in RPE flat-mount were the main goal of this study.

Methods: In this study, the eyes of a healthy rat were enucleated and following removing the anterior segments, vitreous body, and the retina, the RPE layer was relaxed on a glass slide and captured by a fluorescent microscope. Then, the iron signal was detected by Fiji plugin at image J software to split from other active signals. Finally, the number of iron particles was counted and the intensity was measured.

Results: The results of this study showed that there were three active signals in RPE flat-mount for lipofuscin, melanin, and iron. The strong mean color histogram and intensity were for lipofuscin, while the weakest signal was for iron. In addition, the iron signal was successfully separated from other channels.

Conclusions: Detection of iron in RPE cells is very important in the diagnosis of degenerative eye disease. In this study, for the first time, we quantified and qualified the iron in RPE flat-mount.

Keywords: 3D, image J, Iron wavelength, RPE

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Gene Expression Data Analysis Leads to Better Characterization of Pathways Which Are Involved in Colorectal Cancer

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Background: Bioinformatics analysis was applied based on previous transcriptomic data to characterize better pathways and gene sets involved in colorectal cancer.

Methods: The cross-shaped co-expression pattern, gene regulatory network, and gene set enrichment analysis (GSEA) were applied in this study.

Results: We found that the pair of genes – (IL2R, CYFIP2), (FOXMI, PPARA), (MCTP1, CTSC), and (PYROXD1, CYFIP2) – are functionally related. In addition, the pair of genes – (IL2R, CYFIP2) and (FOXMI, PPARA) – simultaneously were involved, respectively, in “vascular endothelial growth factor signaling pathway” and “ribonucleotide diphosphate metabolic process.” These two pathways are considered important biological processes in colorectal cancer.

Conclusion: This research shows that the combination of bioinformatics analysis and functional investigations provided the opportunity to discover the feasible pathways and gene sets related to tumorigenicity.

Keywords: Bioinformatics, bioinformatics analysis, colorectal cancer, gene regulatory network, gene set enrichment analysis, genetics

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The Diagnostic Value of the Italian Score for Predicting Extended-spectrum β Lactamase-producing *Enterobacterales* Infection in Sepsis Patients at Dr. M. Djamil Central General Hospital Padang, Indonesia

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Background: Infections caused by extended-spectrum β lactamase-producing *Enterobacterales* (ESBL-PE), especially *Escherichia coli*-producing ESBL and *Klebsiella pneumoniae*-producing ESBL, require adequate management. Globally and within the community, the number of ESBL-PE carriers has likewise sharply surged. Even if their impact on mortality is still debatable, ESBL-PE infections are linked to extended hospital stays and expensive medical care. Giving definitive antibiotics according to culture results is so important, but it takes a long time. Therefore, a clinical scoring system is needed

to predict ESBL-PE bacterial infections, one of which is the Italian score. This research aims to determine the diagnostic value of the Italian score in predicting ESBL-PE infection in sepsis patients at Dr. M. Djamil Central General Hospital, Padang.

Methods: This research used a cross-sectional design and was conducted in the inpatient room of Dr. M. Djamil Central General Hospital Padang from September to December 2023. The samples in this research were sepsis patients who underwent culture examination at Dr. M. Djamil Central General Hospital Padang and who met the research inclusion criteria (age >18 years, sepsis patients with culture results for *E. coli* or *K. pneumoniae*, and were willing to take part in the research) and exclusion criteria (patients whose Italian score cannot be calculated and sepsis patients with carbapenem-resistant culture results). Phenotypic analysis for ESBL-PE using a Vitek-2 machine that can only identify *E. coli* and *K. pneumoniae*. Sampling was carried out using consecutive sampling, and the total sample obtained was 34. The selected samples will have the Italian score calculated using auto-anamnesis in patients with Glasgow Coma Scale (GCS) 15, alloanamnesis to family members in patients with GCS <15, and secondary data analysis in the patient's medical records to determine the components of the Italian score. Specimens will be also taken for clinical culture examination. The culture results and Italian score calculations were then analyzed and processed using a 2 × 2 table.

Results: The diagnostic test between the Italian score and the culture results of the source of infection from the 34 samples examined obtained sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the Italian score in predicting ESBL-PE infection in sepsis patients at Dr. M. Djamil Central General Hospital were 80.77%, 87.5%, 95.45%, 58.33%, and 82.35%, respectively.

Conclusions: The Italian score has a good enough ability to be used as a tool in predicting the risk of ESBL-PE bacterial infection.

Keywords: Diagnostic value, extended-spectrum β lactamase-producing *Enterobacterales*, Italian score, sepsis

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***CACNA1B* Gene Mutation Associated with Typical Rett Syndrome Patients from India**

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Background/Objectives: *CACNA1B* encodes the alpha-1-subunit of a voltage-dependent N-type calcium channel Cav2.2 expressed in the brain. The heterozygous variants of *CACNA1B* have been previously reported in association with Autism Spectrum Disorder (ASD) and other neurodevelopmental disorders. Here, we report the rare familial case series of three Rett syndrome siblings with intellectual disability (ID).

Methods: After signing informed consent from the patients/parents this study was conducted in accordance with the principles of the World Medical Declaration of Helsinki. The phenotypic

characteristics were recorded and for the genotypic analysis whole blood of 3 ml was collected and the DNA was extracted and purified using Qiagen kit. Genomic DNA with high integrity, as checked by nanodrop-based spectrophotometric and Qubit-based fluorometric method, was used as the input material for exome sequencing library preparation using TruSeq DNA Exome Library Prep Kit (Illumina). HaplotypeCaller of Genome Analysis Toolkit (GATK v4.1.4.1) was used for the germline variant calling.

Results: Three profound patients showed the phenotypic characteristics of microcephaly, short stature, loss of communication, gait abnormalities, apraxia, hypoalgesia, and repetitive movements. We had found the pathogenic heterozygous variant of rs4422842 (*CACNA1B*) associated with Rett syndrome in three ID patients. There was a correlation of microcephaly and short stature with the *CACNA1B* variants found in three siblings.

Conclusion: The phenotype of rare neurological disorders often overlaps. For proper genetic counseling and treatment, both phenotype and genotype information should be used to make the diagnosis. Whole exome sequencing studies showed that the genetic variants in *CACNA1B*, increasing the risk of intellectual disability. Screening of calcium voltage-dependent genes is inevitable for the ID patients.

Keywords: *CACNA1B* gene, calcium channel, exome sequencing, intellectual disability, Rett syndrome

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Morphological Improvement of Human Adipose Stem Cells Derived Retinal Pigment Epithelium Using Extracellular Matrix and Neural Retina Co-culture

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Background: Differentiation of human mesenchymal stem cells into retinal pigment epithelium is challenging, so the aim of this study is investigation of morphological improvement and melanin granules production in differentiated cells.

Methods: In this study, human adipose stem cells were used following lipoaspiration from the abdominal area. First, adipose stem cells extracted in the third passage were differentiated into neurosphere cells by neural differentiation medium. In the next step, neurospheres were cultured on insert plates containing the extracellular matrix of ARPE-19 cells and induced with retinal differentiation medium to retinal pigment cells were differentiated. Finally, for better differentiation, the cells were placed in proximity to the neural retina isolated from C57 mice for 2 days. The amount of changes in the appearance of cells differentiated into hexagons as well as the amount of melanin pigment production was calculated by Image J software.

Results: The results of adipose stem cell culture showed that more than 90% of them expressed mesenchymal stem cell markers. Furthermore, the expression of more than 80% of the specific markers of neural stem cells showed that neurospheres derived from adipose tissue were differentiated into neural stem cells. In addition, the expression of more than 80% of specific markers of retinal pigment cells showed that these cells were differentiated into retinal pigment cells. In the examination of the morphological results, it was shown that the pigmented cells obtained were hexagonal in shape with sharp borders close to other cells. The amount of melanin production in the cytoplasm of these cells was increased during the time in the culture medium.

Conclusions: The results of this study showed that the use of human adipose stem cells can lead to the production of retinal pigment cells with an appearance similar to normal cells and the ability to produce melanin pigment. The findings of this study can be used in cell studies for cell therapy in the retina.

Keywords: Adipose stem cells, neural retina co-culture, neurosphere, retinal pigment epithelium, three-dimensional culture

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Unraveling the Etiological Profile of Recurrent Miscarriages at a Genetic Unit in India

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Background: Recurrent miscarriages are more than two consecutive pregnancy losses before 20 weeks of gestation in women. The objective is to evaluate the association of consanguinity and miscarriages in our genetic unit.

Methods: The present case-control prospective study was performed between January 2021 and December 2023 on 82 couples, who had two or more consecutive miscarriages before 20 weeks of gestation. We subjected the patients to conventional cytogenetic analysis, chromosomal microarray, and whole exome sequencing.

Results: Chromosomal abnormality was detected in 36 cases, most of which were structural abnormalities such as addition (43%), deletion (22%), carrier reciprocal translocation (13%), and balanced chromosomal translocations (11%). Chromosomal microarray analysis revealed the presence of copy number variations in 16% of cases. Whole exome sequencing explored the rare genetic syndromes in 8% of cases. Consanguinity was predominantly found in 76% of the cases. Chromosomal abnormalities such as 46XY, 9qh + and 46, Xyqh – were commonly found in male cases. Likewise, 46, XX, +21ps + and 46XX, 15pstk + were common in most of the female cases being evaluated for miscarriages.

Conclusion: Consanguinity has a significant effect on the etiology of miscarriages and these patients should undergo prenatal genetic diagnosis and genetic counseling.

Keywords: Chromosomal abnormality, consanguinity, exome sequencing, genetic counseling, recurrent miscarriages

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Inspecting the Allelic Frequency of SNPs of Solute Carrier Organic Anion Transporter Family Member 1B1(*SLCO1B1*) Gene in the Metabolic Pathway of Proposed Drugs in the Treatment of Pulmonary Tuberculosis in Iranian Population by Using Whole Exome Sequencing Technique

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Background: Clinical application of pharmacogenetics has led to a worthy progress in the context of our understanding of genetic factor roles in drug response. One of the concerns in the tuberculosis (TB) treatment is anti-TB drug side effects in some patients. Many studies have shown that toxicity related to anti-TB drugs is associated with genetic changes, and these changes may also affect the achievement of maximum drug concentrations. Rifampin is one of the first-line antibiotics for TB treatment. Previous studies indicated the role of solute carrier organic anion transporter family member 1B1 (*SLCO1B1* gene) in transporting and the concentration of rifampin in blood.

Materials: In this research, the influence of pharmacogenetics marker of human *SLCO1B1* Gene, especially rs4149056, in TB treatment by whole exome sequencing method was studied.

Results: Our result revealed that the allelic frequency of rs4149056 was 12.9% in Iranian population.

Conclusion: Previous researches showed that the presence of polymorphism rs4149056 might cause a decrease in gene expression of *SLCO1B1* Gene resulting in reduce uptake of organic anion-transporting polypeptide 1B1 which leads to upper levels of rifampicin in the bloodstream. Since in this study allelic frequency of rs4149056 was 12.9% in Iranian population, investigation genetic variation of human *SLCO1B1* Gene, especially rs4149056, in TB treatment is recommended.

Keywords: rs4149056, solute carrier organic anion transporter family member 1B1 gene, tuberculosis treatment, whole exome sequencing technique

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Investigating the Expression Level of miR-302/367 Plasmid and the Signaling of Related Genes in Breast Cancer Cell Line: The Effect on the Signaling Pathway

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Abstract

Background: Breast cancer cells are incurable tumor cells that affect women during their life. The aggressiveness of this cancer has been attributed to grow and/or spread quickly which causes a poor prognosis. MiRNAs are small noncoding RNA molecules which have a critical role in posttranscriptional gene regulation in numerous biological pathways. Various researches examined the miR-302/367 cluster as a tumor suppressor in many human cancers. The main focus of this study was inspecting the role of miR-302/367 cluster in cell-based therapy by using miR-302/367 expression plasmid in breast cancer cells.

Methods: The overexpression of miR-302/367 cluster and its effect on *Foxm1* gene expression level was investigated by real-time polymerase chain reaction method in SKBR breast cancer cell line.

Result: The expression level of *Foxm1* gene was decreased significantly in SKBR breast cancer cell line transfected by miR-302/367 expression plasmid.

Conclusion: This study results indicate that miR-302/367 clusters have a significant effect on the signaling pathways which are involving in cancer progress and can be considered an efficient tool for cancer treatment.

Keywords: Breast cancer cell line, expression level, miR-302/367, signaling pathway

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Investigating the Activity and Level of Telomerase Gene Expression in Nonsmall-cell Lung Cancer Treated with miR-302/367

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Abstract

Background: MiR-302 cluster has been described as a tumor suppressor in various human cancers. Furthermore, in most cancers, cancer cells have high levels of telomerase enzyme. With the help of the telomerase enzyme, these cells compensate for telomere shortening that occurs after successive divisions. So far, various methods, such as direct inhibition of telomerase and telomerase immunotherapy, have been proposed to inhibit this enzyme.

Methods: In this study, we intend to investigate the effect of miR-302/367 cluster on telomerase gene expression level using A-549 cancer cells by overexpression of miR-302/367 cluster using expression plasmid.

Results: Our results indicate that the miR-302/367 cluster has the potential to modulate oncogenic properties of cancer cells through suppression of telomerase gene expression level in these cells.

Conclusion: These results suggest that the miR-302/367 cluster may act as a lung cancer suppressor through negative regulation of telomerase gene expression. Therefore, targeting the miR-302/367 cluster may provide a novel strategy for the treatment of patients with lung cancer.

Keywords: Gene expression, miR-302/367, nonsmall-cell lung cancer, telomerase, treated

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Nepeta macrosiphon Essential Oil Chemical Composition and Antioxidant Activity

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Background: The genus *Nepeta* belongs to the *Lamiaceae* family and famous as pune-say in Iran. This genus comprises about 280 species in the world and 67 species that are found all over of Iran. In folk medicine, some species are used as a bacteriostatic, disinfectant, fortifier, and treating eczema type disorders.

Methods: In this study, the aerial parts of *Nepeta macrosiphon* Boiss. were collected from its wild habitat in Zonoz, Tabriz, East Azerbaijan province, Iran, and then its essential oil was extracted by hydro-distillation method. The essential oil components were analyzed by Gas chromatography (GC) and Gas chromatography–mass spectrometry (GC–MS).

Results: Twenty-one compounds consisting 96.4% of the total components were identified from the oil obtained with a yield of 0.21%w/w. The results indicated that 4 α , 7 α , 7 β -nepetalactone (47.2%) and 4 α β , 7 α , 7 β -nepetalactone (35.9%) were the main constituents of essential oil. Furthermore, the antioxidant activity of essential oil was investigated by 2,2-Diphenyl-1-picrylhydrazyl (DPPH). 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay. The results confirmed that the IC₅₀ value was 95.45 μ g/mL, and it had moderate antioxidant activity compared to ascorbic acid.

Conclusion: In addition, it was concluded that *N. macrosiphon* is a source of bioactive compounds.

Keywords: Antioxidant, *Lamiaceae*, *Nepeta*, nepetalactone

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Investigating Intracellular Signaling Pathway and Telomerase Gene Expression in Nonsmall Cell Lung Cancer Treated with miR-302/367

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Background: Increasing the expression of telomerase enzyme is found in most of the cancers and suppressing the expression of this gene as a therapeutic candidate in cancer treatment has attracted the attention of many scientists. Previous reports have been described MiR-302/367 cluster as a tumor suppressor in many human cancers. In this research, the expression levels of miR302/367 and its potential role in targeting telomerase gene expression in human lung cancer were examined.

Methods: Quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) was performed to evaluate miR-302/367 cluster and telomerase gene expression levels in A549 lung cancer cell.

Results: MiR-302/367 expression levels were significantly increased in A549 lung cell line ($P < 0.05$). The overexpression of miR-302/367 cluster and its effect of modulating on transcription levels of telomerase were subsequently confirmed via qRT-PCR.

Conclusion: Our results showed that MiR-302/367 may have significant implications in controlling cancer progression and invasion and can be a good candidate for cancer treatment. Tuberculosis (TB) treatment.

Keywords: Intracellular, miR-302/367, signaling pathway, telomerase

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Gene Expression in Bronchoalveolar Lavage Cells: Identifying Targets and Pathways in the Tumor Microenvironment of Non-small Cell Lung Cancer

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Background: Bronchoalveolar lavage is frequently used to evaluate inflammation and to detect the pathogens causing lung diseases. Analyzing bronchoalveolar lavage fluid is a promising strategy for assessing the microenvironment of tumor progression. Bronchoalveolar lavage cells are a crucial resource for identifying clinically significant predictive and prognostic biomarkers, which can assist in making informed treatment decisions for lung cancer. The aims of this study were to analyze and identify the core genes associated with expression and prognosis in non-small cell lung cancer (NSCLC), using bioinformatics technology, and to explore potential therapeutic targets.

Methods: In this prospective study, the gene expression profile GSE103888 was downloaded from the Gene Expression Omnibus database. Differentially expressed genes (DEGs) were obtained from the microarray dataset using R software (Institute for Statistics and Mathematics-Wirtschaftsuniversität Wien -Vienna, Austria). Following the screening of DEGs, functional enrichment analysis and KEGG analysis were performed on the upregulated DEGs. Protein–protein interaction (PPI) networks among DEGs were constructed using the STRING database and analyzed with Cytoscape. The Kaplan–Meier method was employed to assess survival linked to hub genes, while the GEPIA webserver was utilized for validating gene expression.

Results: From the PPI network analysis of bronchoalveolar lavage cells in lung adenocarcinoma data, seven hub genes with a high degree of connectivity were identified. These genes are EPCAM, ERBB2, KRT19, MET, MMP9, SPP1, and FOXA1. Further examination of these hub genes through KEGG pathway analysis revealed their association with pathways including the role of proteoglycans in cancer, the calcium signaling pathway, and the PI3K-Akt signaling pathway. From the PPI network analysis of bronchoalveolar lavage cells in lung squamous cell carcinoma data, five hub genes with a high degree of connectivity were identified. These genes are EGFR, SMAD2, CCND1, SPP1, and COL1A1. Further examination of these hub genes through KEGG pathway analysis revealed their association with pathways including the PI3K-Akt signaling pathway, focal adhesion, and the role of proteoglycans in cancer.

Conclusions: Analysis of gene expression data from microarray of bronchoalveolar lavage cells identified key genes and biological processes that play a significant role in the development of NSCLC. The identified genes have potential to be valuable diagnostic biomarkers and open up new possibilities for the development of targeted therapies for NSCLC.

Keywords: Bronchoalveolar lavage, differentially expressed genes, lung adenocarcinoma, lung squamous cell carcinoma, pathway

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Correlation of Genetic Mutation in Rv0676 and Drug Susceptibility Patterns in Tuberculosis Isolates

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Background: Multidrug-resistant tuberculosis (MDR-TB) is a significant public health concern, with rising cases of drug-resistant strains. The overexpression of efflux pumps (Eps) has been reported to contribute to MDR-TB. This study investigated the association of the mycobacterial membrane protein (MmpS5-MmpL5) Ep and its gene regulator (Rv0678) in MDR-TB isolates.

Methods: *Mycobacterium tuberculosis* (MTB) strains were isolated from patients with persistent symptoms despite treatment. Sputum specimens underwent molecular testing, susceptibility testing, and whole-genome sequencing (WGS) on two isolates per patient.

Results: WGS documented genetic mutations in the transmembrane transport protein MmpL5 (Rv0676) of Eps, including a unique deletion mutation and a large insertion mutation. The majority of isolates (92.3%) showed specific deletion mutations, while one isolate (7.6%) had no deletion. All isolates exhibited a large insertion mutation. Thirty-eight substitutions in Rv0676 were detected, with 92.3% being identical in the studied isolates. No differences were observed in MmpS5-MmpL5 and its gene regulator (Rv0678) between isolates collected at different intervals.

Conclusions: Significant genetic mutations in the MmpL5 (Rv0676) transporter protein can alter the functional balance of Eps and contribute to reduced drug susceptibility. This is the first report documenting unique amino acid mutations in Rv0676 among drug-resistant MTB. The changes in MmpL5 appear to be stable and persist in subsequent culture-positive specimens.

Keywords: Efflux pumps, multidrug-resistant tuberculosis, Rv067, Rv0676, Rv0677

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Virulence Determinants of Russian *Helicobacter pylori* Clinical Isolates

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Background: *Helicobacter pylori* infection is recognized as an important public health concern in more than 50% of the world's population and may be associated with such gastrointestinal diseases as chronic gastritis (G), gastric/duodenal ulcers (DUs), and stomach cancer. Based on the assessment of virulence-associated *cagA* and *vacA* genes, we aimed to determine *H. pylori* genotypes associated with the clinical outcomes in patients with *H. pylori* infection in St. Petersburg, Russia.

Methods: In total, 122 biopsies from both the corpus and antral mucosa taken during endoscopy from 61 patients were available (2014–2022). All strains were isolated from the separate adult patients with G ($n = 37$), DU ($n = 21$), and gastric cancer (GC) ($n = 3$). The study group included 28 men (45.9%) and 33 women (54.1%). The median age was 44 years (range = 17–88 years). The total DNA of *H. pylori* isolates was extracted using the QIAamp DNA Mini Kit. The polymerase chain reaction for the detection of *cagA* and *vacA* genes in the DNA samples was performed in the BioRad C1000 Thermal Cycler.

Results: As a result, 41/61 (67%) *H. pylori* isolates were *cagA* positive. The proportion of *cagA*-positive isolates was higher in patients with DU (17/21, 80.9%) compared to G group (21/37, 56.7%). However, the difference was not statistically significant ($P = 0.06$). The *vacA* gene in various s, m, and i allelic variants was detected in all isolates, while 7 isolates (11.5%) were positive for mixed allele combinations, which may indicate the presence of mixed infection. Allelic variants of *vacA* gene were grouped into five genotypes, among them *vacA* s1/m1/i1 was dominant (41%). Noteworthy, a rare s2/m1 genotype was not detected in our study. The proportion of *H. pylori* isolates carried *vacAs1* allele in the DU (95.2%) group was significantly higher than that in the G group (64.9%) ($P = 0.01$). The m1 and i1 *vacA* alleles in isolates from patients with G and DU were found in almost equal proportions ($P > 0.05$). All isolates from patients with GC were *cagA* positive and possessed s1/m1/i1 alleles. Analysis of the correlation between *vacA* allelic variants and the *cagA* gene revealed a relationship between *cagA*-positive status and the *vacAs1* allele. 39 out of 41 *cagA*-positive isolates (95.1%) carried the *vacAs1* allele, while none of the *vacAs2* isolates had the *cagA* gene. Noteworthy, all *vacAs2* isolates had m2 allele. The proportion of *cagA*+/ *vacAs1* isolates in patients with G reached 51% compared to DU (81%) and GC (100%) ($P > 0.05$). Only one isolate in the DU group (4.7%) had *cagA*-/*vacAs2* genotype.

Conclusions: Although Russia belongs to countries with a high prevalence of *H. pylori* infection, a relatively low proportion of the *cagA*-positive isolates were detected without association with DU. The significant correlation between *vacAs1* genotype and clinical manifestations of *H. pylori* infection has been established. This finding may serve as a potential predictor for the *H. pylori* disease progression in Russia.

Keywords: *CagA*, *Helicobacter pylori*, Russia, *vacA*, virulence

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Clarithromycin Resistance Patterns in Russian *Helicobacter pylori* Clinical Isolates

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Background: Clarithromycin (CLR) is a key antibiotic for the treatment of *Helicobacter pylori* infection, and resistance to CLR is the most relevant for first-line triple therapy failure. Point mutations A2146G and A2147G in V domain of the 23S rRNA gene are mainly responsible for *H. pylori* resistance to CLR. To date, Russia belongs to countries with a high prevalence of *H. pylori* infection; however, the data on CLR resistance patterns in Russia are underreported. The aim of our study was to determine the point mutations in 23S rRNA gene in *H. pylori* clinical isolates from Russia associated with phenotypic antimicrobial susceptibility testing.

Methods: In total, 50 *H. pylori* clinical isolates collected between 2014 and 2022 were retrieved from the bacterial strain collection of the St. Petersburg Pasteur Institute, St. Petersburg, Russia. All strains were isolated from gastric biopsy specimens taken during endoscopy

from the separate adult patients with chronic gastritis ($n = 35$), duodenal ulcer ($n = 13$), and gastric cancer ($n = 2$). The susceptibility of *H. pylori* isolates to CLR was determined by conventional disc diffusion method. The total DNA of *H. pylori* isolates was extracted using the QIAamp DNA Mini Kit. The polymerase chain reaction products (1402 bp) of the 23S rRNA gene were sequenced by Sanger approach. The DNA sequences were compared to the *H. pylori* 26695 reference using Unipro UGENE v. 38.1.

Results: As a result, 30 *H. pylori* isolates were determined as CLR resistant, while 20 were CLR susceptible. The A2147G point mutation was detected in 17 (56.7%) CLR-resistant isolates and 1 (5.0%) CLR-sensitive isolate ($P = 0.0002$). The other point mutation A2146G was found in 13.3% (4/30) of CLR-resistant isolates ($P = 0.14$). All CLR-susceptible isolates (100%; 20/20) possessed A2146 allele; none of the CLR-resistant isolates carried two A2146G/A2147G mutations simultaneously: all 2147G isolates carried the A2146 allele, while all 2146G isolates carried the A2147 allele. Nine (30.0%) CLR-resistant isolates had neither A2146G nor A2147G mutations. The agreement between genotypic and phenotypic susceptibility to CLR based on both A2146G and A2147G mutations was 70.0%. The other point mutations at positions 2146–2147, including G1567T, C1568A/T, A1825G, G1830A, T1834C, and T2186C, were identified. However, these mutations were not associated with phenotypic drug resistance ($P > 0.05$).

Conclusions: Our study showed that among all variants of nucleotide substitutions in the 23S rRNA gene, only one of them – A2147G – is significantly associated with phenotypic resistance *H. pylori* to CLR. Despite the low frequency of A2146G point mutation, combination of both A2146G/A2147G mutations can be used as a predictor of phenotypic resistance of Russian *H. pylori* clinical isolates.

Keywords: 23S rRNA gene, clarithromycin resistance, *Helicobacter pylori*, mutations, Russia

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Effect of Cold Atmospheric Plasma on Apoptosis of Lung Epithelial Cells Infected with Coronavirus Disease 2019

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic exerted strong pressure on the international community and caused supply chain shortages of personal protective equipment, disinfectants, and health-care resources globally. As an interesting novel strategy for disinfection, cold atmospheric plasma (CAP) provides the opportunity to remove pathogenic microorganisms without the requirement of any consumable reagents (hence, in comparison with the conventional disinfection methods, CAP addresses many of the above-mentioned problems). On the other hand, CAP is able to cause apoptosis in lung epithelial cells infected with virus and induces expression of aquaporin-1 gene which leads to water transportation from alveolar space to the capillary vessels.

Methods: In the present investigation, a novel instrument was designed, which was able to produce CAP inside the oxygen mask. For this purpose, helium gas (He) was passed between two electrodes (14 KV, 6 KHz) and the produced excited plasma was combined with oxygen, which was subsequently inhaled through the oxygen mask. In this study, 64 patients with confirmed COVID-19 by nasopharyngeal swabs, reverse transcription polymerase chain reaction (RT-PCR), and computed tomography (CT) scan were selected and treated with the standard method and simultaneous CAP treatment (three times daily, 5 min each time for 7 days) in Masih Daneshvari Hospital (Tehran, Iran). Then, their nasopharyngeal swabs were collected at the 4th day after administration of CAP and sent to the laboratory for RT-PCR. CT scan was performed at the time of reception and 7 days after CAP treatment. For a semiquantitative assessment of the extent of COVID-19 pneumonia on chest CT, the following criteria were used: (a) minimal or no pneumonia, <5%; (b) mild, 5%–25%; (c) moderate, 26%–75%; and (d) severe, >75% of lung involvement.

Results: The nasopharyngeal swabs were all positive by RT-PCR (100%) before CAP treatment, while 4 days after administration, 87% of cases were negative. In this study, the most common CT abnormalities of COVID-19 pneumonia were ground-glass opacity, crazy paving pattern, consolidation, and linear opacities, respectively. The results of CT scan showed significant reduction of scores in 75% of the patients after inhaling CAP.

Conclusion: CAP can significantly contribute to the control of viral pandemics globally (such as COVID-19) to help the medical community. This method is easy to implement, and the required equipment are simply deployable.

Keywords: Apoptosis, cold atmospheric plasma, coronavirus disease 2019, lung epithelial cells, pandemic

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Designing a Specific Electrospinning Device in a Hood Class IIb Cylindrical Chamber, along with a Novel Programmable Cell Jet Printer for Repair of Skin Defects

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Abstract

Background: Electrospinning technique is an evolving low-cost method for the fabrication of polymeric nanofibers. The produced electrospun nanofibers are able to mimic the functions of the native extracellular matrix, and for this reason, they are considered suitable scaffolds in tissue engineering. However, the proper collection of the produced

electrospun nanofibers is not simple, and hence requires a special design. The aim of the present work was to design a specific electrospinning device in a hood Class IIb cylindrical chamber, accompanied by a novel programmable cell jet printer, to repair skin defects.

Methods: In this research work, a specific electrospinning device was designed for the first time for the fabrication of nanofiber mat, accompanied by a novel three-dimensional (3D) cell jet printer, all inside the specific hood Class IIb. The fabrication of the nanofiber mat requires a high voltage zone, whereas a low voltage zone is required for cell printing. The combination of the two zones inside a specific hood Class IIb chamber, without any interactions between them (while being safe for the operator), is substantially difficult. In addition, the construction of 3D cell printing cartridge is the most challenging aspect of this design because during the process of cell printing, the cells undergo high pressures, which might lead to membrane damage and cell destruction.

Results: After electrospinning of polycaprolactone (PCL) mat on a cylindrical stainless steel collector, human infant foreskin fibroblasts were printed on the produced electrospun mat. Microscopic examinations demonstrated a parallel-aligned pattern of fibroblasts on the PCL mat. Fibroblast bioavailability was checked by supravital staining, which exhibited more than 80% of cell viability.

Conclusion: Results of the present investigation indicated that in comparison with commercial devices, the designed electrospinning system is simple and cost-effective, and is capable of repairing skin defects.

Keywords: Cell printer, electrospinning, fabrication, nanofiber, skin defect

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Construction and Application of a Novel Electrospinning Device in a Specific Hood Class IIb Cylindrical Chamber along with a Novel Programmable Cell Jet Printer for Repair of Skin Defects

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Abstract

Background: In recent decades, several studies have focused on the discovery of novel bioactive dressings to treat acute and chronic wounds. Thanks to acceptable porosity and desirable permeability to water and air, electrospun nanofibers would be considered effective barriers against external pathogens. They can also be suitable alternatives for skin regeneration and wound healing because their structure is highly similar to that of the extracellular matrix. The aim of this work was to construct a novel electrospinning device in a specific hood class IIb cylindrical chamber, accompanied by a novel

programmable cell jet printer to repair skin defects, and to investigate its clinical applications.

Methods: Human infant foreskin fibroblasts were introduced to the structure of the electrospun nanofibers (gelatin with Polycaprolactone (PCL)) using our designed specific three-dimensional cell jet printer in a specific hood class IIb cylindrical chamber. Then, the epithelial cells were printed on the produced electrospun mat (containing printed fibroblasts). For the experimental study, six adult albino rabbits were used, and in each rabbit, two circular total thickness wounds with dimensions of 2 cm × 2 cm were created on both sides of the dorsal middle line of rabbits at a distance of 6 cm. Rabbit plasma and keratinocyte cells were autologously printed on PCL-gelatin electrospun mat (containing printed fibroblasts and epithelial cells). Grafting of this biosynthetic skin was performed on the wounds on the right side of the head and on the left caudal side, whereas the wounds on the left side of the head and on the right caudal side were only bandaged with the gauze containing normal saline. A descriptive-comparative study was performed during the treatment: the structures of the wounds on the right side were subjected to microscopic examinations, and the wounds on the left side were evaluated for changes in the dimensions of the lesion.

Results: Results of the microscopic examinations on the dimensions of the lesion during the 21-day treatment indicated that the healing rate of the epithelial tissue in the grafted parts using this produced biosynthetic skin was obviously higher than the control parts in each of the rabbits. Moreover, microscopic examinations on days 7, 14, and 21 revealed that epithelialization was clearly evident in the transplanted sections compared to the control parts. Bacteria were observed in each of the control samples.

Conclusion: Electrospinning is a newly emerging advanced technology which offers prominent opportunities for production of efficient dressings and other wound care and healing products.

Keywords: Cellular printer, electrospinning, fabrication, nanofiber, skin defect

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Investigating the Effect of Novel Diclofenac Topical Formulation on Knee Pain Relief in Osteoarthritis Patients

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for the treatment of osteoarthritis patients. Topical formulations of NSAIDs reduce the side effects of oral administration. Diclofenac topical formulations (including gel and solution) are approved for knee pain relief in osteoarthritis. The purpose of this study was to investigate the effect of a novel diclofenac topical formulation on knee pain relief in osteoarthritis patients.

Methods: A randomized, double-blind, controlled study was performed on 86 patients (aged 40 to 80 years) using the novel topical formulation of diclofenac 1.5% solution which is under US Patent No. 9617562. Half of the patients were treated with diclofenac sodium 1.5% solution four times daily (20 drops equal to 1.5 mg diclofenac each time) for 5 days. The second group used high-intensity laser therapy (HILT) for alleviating knee pain. All patients completed self-administered pain scales during the experiment. The change from baseline to the last visit in the pain scales was evaluated. Skin irritation as a side effect was assessed throughout the study.

Results: The mean value of the pain scale in patients who received diclofenac 1.5% solution was significantly improved from baseline to the last visit (approximately 5 times). Moreover, a significant decrease in the mean pain scale at the final visit was observed for patients treated with diclofenac novel formulation in comparison with the second group treated with HILT (~2 times). The most commonly reported side effect was the cold sensation at the site of administration in all of the patients. However, skin petechiae were observed in five patients, and consequently, the treatment was stopped.

Conclusion: The results of this research study indicated that administration of the novel diclofenac sodium 1.5% topical solution significantly improved knee pain relief in osteoarthritis patients compared to HILT.

Keywords: Diclofenac solution, high-intensity laser therapy, knee pain relief, nonsteroidal anti-inflammatory drug, osteoarthritis, pain scale

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Case Series of Long COVID-19 among Patients with Good's Syndrome

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Introduction: Good's syndrome (GS) is an acquired rare adult immunodeficiency characterized by thymoma, hypogammaglobulinemia, and recurrent infections due to a weak immune response. Its manifestation can vary from mild bacterial infections to severe malignancies.

Investigations: The systematic analysis of 152 cases reveals a global distribution, with nearly half reported in Europe.

Case Presentation: Most cases happen in the 40–70 age range. Despite the GS was initially discovered in 1957, its pathogenesis remains unclear. Only 6%–10% of patients with thymoma develop GS.

Discussion: In cases of recurrent COVID-19 symptoms coupled with persistent positive PCR results, clinicians should broaden their diagnostic approach to include the evaluation of primary and secondary immune deficiencies.

Conclusion: Recently, relapsing COVID-19 has been reported as a manifestation of GS. Despite a few case reports of concurrent COVID-19 and GS, there are little data about the clinical features of COVID-19 and mutation analysis of SARS-CoV-2 in patients with GS. Persistent SARS-CoV-2 infections in immunocompromised patients have been implicated in the accumulation of mutations and consequently may result in the emergence of new variants. Prolonged SARS-CoV-2 infections in patients with a history of thymoma should provoke one to investigate for GS, accelerating early diagnosis and timely treatment. Here, we describe a case series of patients with GS and long COVID-19 in a referral center.

Keywords: Case series, Good's syndrome, long COVID-19

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Investigating the Effect of Cold Atmospheric Plasma on Early Glottic Cancer Using Laryngoscopy

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Abstract

Background: Although various approaches have been developed over the last decade toward the treatment of early glottic cancer, its mortality rate is also significantly increased. The standard method of care includes the larynx preservation approaches and selecting the appropriate treatment modality is of great importance. Prevalent treatment approaches for early glottic lesions are chemotherapy and

radiation therapy. The aim of this study was to evaluate the effect of cold atmospheric plasma (CAP) on early glottic cancer using laryngoscopy in accompany with the standard treatment method.

Methods: In the present investigation, a novel instrument was designed to produce CAP. First, the helium gas was passed between two electrodes (14 KV, 6 KHz) and the produced excited plasma was subsequently passed through a 2-mm PTFE nozzle to be focused on the laryngeal squamous cell carcinoma. This novel CAP-based method was simultaneously performed in accompany with the standard treatment method (including chemotherapy and radiation therapy) on five patients. Positron emission tomography scan was performed for the patient before treatment and subsequently after 12, 24, and 36 months after treatment, and the outcomes were compared.

Results: The results indicated that the standardized uptake value (SUV) of (^{18}F) 2-fluoro-2-deoxy-d-glucose (FDG) significantly decreased after 12 posttreatment months. Moreover, SUV reached 0 in the 24th and 36th month after CAP treatment accompanied by the chemotherapy and radiation therapy standard methods.

Conclusion: Although patients with high (^{18}F) FDG uptake often have a poor prognosis, in the absence of positive lymph nodes, adjuvant CAP treatment is recommended along with chemotherapy and radiation therapy standard treatments.

Keywords: Cold atmospheric plasma, glottic cancer, laryngoscopy, laryngeal cancer, squamous cell carcinoma

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Chimeric Antigen Receptor-T Cells Biotechnology as a Treatment Strategy for Malignancies and Nonmalignancies Diseases: Future Perspectives

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Abstract

Background: Chimeric antigen receptor (CAR) T cell therapy has shown remarkable success in treating various hematological malignancies, such as acute lymphoblastic leukemia, diffuse large B-cell lymphoma, and multiple myeloma. However, the application of CAR-T cells is expanding beyond oncology, with the potential for treating autoimmune disorders and viral infections.

Objective: This review discusses the current status, future perspectives, and potential applications of CAR-T cell technology in the treatment of both malignant and nonmalignant diseases.

Methods: The review provides an overview of the CAR-T cell structure, gene delivery methods, and the latest advancements in improving CAR-T cell efficacy and persistence. It also summarizes the clinical outcomes of CAR-T cell therapies in hematological malignancies and the emerging applications in autoimmune disorders and viral infections.

Results: CAR-T cell therapy has demonstrated impressive complete remission rates in patients with refractory or relapsed B-cell malignancies. The technology has also shown promise in the treatment of solid tumors, although challenges remain. Importantly, the application of CAR-T cells is being explored for autoimmune disorders and viral infections, with the aim of reducing autoreactive immune cells or modulating the T-cell phenotype from cytotoxic to regulatory.

Conclusion: While CAR-T cell therapy has made significant strides in the treatment of hematological malignancies, further optimization of CAR-T cell design and delivery is needed to expand its application to a wider range of diseases, including nonmalignant conditions. Ongoing research and clinical trials will continue to shape the future of this transformative technology in medicine.

Keywords: Biotechnology, chimeric antigen receptor-T cells, malignancies, nonmalignancies, treatment

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Antioxidant and Neuroprotective Effect of Triterpenoids from *Centella asiatica* Using U-87 MG Glioblastoma Cell Line: A Pilot Study

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Background/Objectives: *Centella asiatica* (L.) Urb. is a traditional Indian medicine that has many medical applications, including wound healing and antioxidation. This study was designed to evaluate the effects of triterpenoids, a major bioactive component of *C. asiatica*, on oxidative stress and neuroprotective effect using the human U-87 MG glioblastoma cell line.

Methods: The plant was collected from Coimbatore city and authenticated at the Herbarium of Botanical Survey of India (Authentication ID: CA - BSI/SRC/5/23/2018/Tech/538). Whole plant parts were dried, and nanoparticles (NPs) were prepared by a process based on a dry-milling technique and were characterized

by the narrow particle size distribution range of 1744 nm using a dynamic light-scattering technique. A known quantity of NPs was allowed to pass through the Soxhlet apparatus using petroleum ether, methanol, and ethyl acetate solvents. The methanolic extract of *Centella asiatica* consists of the highest content of triterpenoids when compared to other solvent extracts. The presence of triterpenoids was confirmed based on Thin layer chromatography (TLC), followed by anisaldehyde treatment and High-performance thin-layer chromatography (HPTLC). The triterpenoids were extracted and lyophilized, and its purity was confirmed in Ultra-High-Performance Liquid Chromatography (UHPLC). Various concentrations of triterpenoids (0, 20, 40, 60, 80, 100, 120, and 150 µg/ml) were treated in U-87 MG cell line. Cells (10^{-6} – 10^{-8} M) were pretreated with various concentrations (10^{-6} – 10^{-8} M) of the three plant extracts for 8 h, followed by exposure to 100 µM of H₂O₂ for 12 h. Cytotoxicity and neuroprotectivity of triterpenoids were measured using colorimetric assay for assessing cell metabolic activity (MTT) assay. Cells were imaged before and after treatment using Zeiss Axioscope 5. Dendrites and soma size were measured using Neuron J software. The neurite growth parameters of the average number of neurites per cell, the average length of neurites per cell, and the total outgrowth in all cells between control and treatments were compared using student *t*-test and one-way ANOVA in SPSS 22.0 (statistical software program).

Results: The effective concentration (EC₂₀) of triterpenoids was 80 µg/ml and conferred significant neuroprotectivity ($P < 0.001$) against 100 µM H₂O₂-induced oxidative stress at 40 µg/ml. In H₂O₂-induced oxidative conditions, triterpenoids inhibited dendrite retraction and improved neurites growth (165.02 ± 3.29 µm) and soma size significantly in a concentration-dependent manner. In conclusion, triterpenoids possess a considerable neuroprotective effect which might be used to overcome the abnormal oxidative stress found in most of neurological disorders.

Keywords: *Centella asiatica*, neuroprotectivity, soma size and U-87 MG, triterpenoids

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Hepatitis B and C Virus Epidemic in Libya: A Systematic Review

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Background: Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are among the most frequent viral infections in humans and important cause of morbidity and mortality. Worldwide, it is estimated that 350 million people have chronic HBV infection and 170 million people have chronic HCV infection. HBV and HCV represent a significant public health problem that leads to liver cirrhosis and hepatocellular carcinoma in developing nations. Libya is a developing country in the Maghreb region of North Africa. Due to the armed conflict and social obstacles, it is difficult to determine the prevalence of HBV and HCV, although there is consensus that it is increasing.

The objective of this study was to conduct a comprehensive review of the epidemiology of HBV and HCV in Libya.

Methods: A comprehensive search was performed on articles related to the prevalence of chronic HBV and HCV infection in Libya published in English language using electronic databases such as PubMed, ScienceDirect, and Google Scholar. The terms “Libya,” “HBV,” “HCV,” and “prevalence” were used as keywords in titles.

Results: Out of the 985 records that were initially recognized, 31 and 32 eligible studies related to HBV and HCV, respectively, were chosen for the study. The overall prevalence of HBV infection ranged from 0.1% to 67.3%. The highest prevalence of HBV infection was reported in hemodialysis patients, prisoners, and health-care workers. Moreover, the overall prevalence of HCV infection ranged from 0% to 64.8%. Hemodialysis patients, prisoners, and intravenous drug users have reported the highest prevalence of HCV infection.

Conclusions: Hepatitis B and C infection is clearly a significant public health issue in Libya, and the literature suggests that there is a high prevalence of HBV and HCV infection among high-risk groups in Libya. Implementing preventive methods, including health education, screening, and treatment, will assist in managing the illness to prevent a possible future sudden increase.

Keywords: Epidemic, hepatitis B virus, hepatitis C virus, Libya

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