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30 August - 01 September, 2023

6th International Conferences on Science and Technology Budva, Montenegro

Natural Science and Technology

Abstracts & Proceedings Book



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International Conferences on Science and Technology

Natural Science and Technology August 30 - September 1, 2023 in Budva, MONTENEGRO

ABSTRACTS & PROCEEDINGS BOOK

International Conferences on Science and Technology

Natural Science and Technology

August 30 - September 1, 2023 in Budva, MONTENEGRO

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ICONST 2023

International Conferences on Science and Technology Engineering Science and Technology Life Science and Technology Natural Science and Technology August 30 - September 1, 2023 in Budva, MONTENEGRO

Dear Readers;

The sixth of ICONST organizations was held in Budva/Montenegro between August 30 - September 1, 2023 with the theme of '*science for sustainable technology*' again. In recent years, weather changes due to climate change have reached a perceptible level for everyone and have become a major concern. For this reason, scientific studies that transform technological progress into a sustainable one is seen as the only solution for humanity's salvation. Here we ask ourselves "which branch of science is responsible for sustainability?". Sustainability science is an interdisciplinary field of study that covers all basic sciences with social, economic, ecological dimensions. If we consider technology as the practical application of scientific knowledge, the task of scientists under these conditions is to design products that consume less energy, require less raw materials, and last longer.

ICONST organizations organize congresses on sustainability issues of three main fields of study at the same time in order to present different perspectives to scientists. This year, 136 papers from 22 different countries presented by scientists in **ICONST Organizations**.

89 papers from 14 countries presented in our **International Conference on Engineering Science and Technology** organized under ICONST organizations. Türkiye leads the way with 48.8% of the participants, followed by Poland with 17.9%, Kosovo with 8.3%, Algeria, Azerbaijan and Montenegro with %4.8, Hungary with 2.4, Italy, Iraq, North Macedonia, Netherland, Iran, Bangladesh and South Africa with 1.2%.

25 papers from 11 countries presented in our **International Conference on Life Science and Technology** organized under ICONST organizations. Türkiye leads the way with 40% of the participants, followed by North Macedonia with 13%, Kosovo and Poland with 8.7%, Sweden, Finland, United Kingdom, Czech Republic, Portugal, Iran and Slovakia with 4.3%.

Finally, 22 papers from 9 countries presented in our **International Conference on Natural Science and Technology** organized under ICONST organizations. Türkiye leads the way with 45.5% of the participants, followed by Kosovo, Russia, Poland and Azerbaijan with 9.1% and India, Ethiopia, Serbia and Albania with 4.5%.

As ICONST organizations, we will continue to organize organizations with the value you deserve in order to exchange ideas against the greatest threat facing humanity, to inspire each other and to contribute to science. See you at your future events.

ICONST Organizing Committee

International Conferences on Science and Technology

Natural Science and Technology

August 30 - September 1, 2023 in Budva, MONTENEGRO

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On the convergence rate of collocation methods for Volterra integral equations with weakly singular oscillatory trigonometric kernels

Lakshmi Narayan Mishra*1

Abstract: This study offers effective collocation techniques for weakly singular, strongly oscillatory linear Volterra integral equations. The fundamental difficulty of the problem is to calculate the weakly singular oscillatory integrals, which is done using the generalized Gauss-Laguerre rule and the numerical steepest descent approach. Additionally, we develop the appropriate error estimation formula in terms of frequency and step size. This formula somewhat captures the method's global convergence. However, numerical illustrations demonstrate the method's high effectiveness and confirm the accuracy of the theoretical findings.

Keywords: Volterra integral equation, Oscillatory kernel, Generalized Gauss–Laguerre rule, Weak singularity, Collocation methods.

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INVESTIGATION OF ABSORBANCE VALUE THE EFFECT OF PECTINASE AND AMYLOGLUCOSIDASE ENZYME MIXTURE ON CLARIFICATION OF APPLE JUICE

Cengiz Cesko^{*1}, Jaser Veseli¹, Hatice Paluzar²

Abstract: Fruit juices contain polysaccharides (pectin, cellulose, hemicellulose and starch), proteins, tannins, etc. They cause a cloudy appearance due to the presence of components. One of the main problems in processing fruit juices in industrial applications is the high pectin content. Although particles are removed from the pulp by filtration, the presence of pectin makes filtration difficult. Pectolytic enzymes, which have been used in industrial applications since 1930, overcome this problem. Pectinolytic enzymes are used to assist in the extraction and clarification of juice from many fruits. In this study, the effect of the enzyme mixture obtained by mixing pectinase and aminoglycosidase enzymes at different concentrations on the clarification of apple juice was investigated. In addition, the effects of parameters such as time and temperature on the clarification capacity of the enzymes were also investigated. For this purpose, pectinase/aminoglycosidase (mg/L) enzyme mixtures were prepared at the ratios of 5/13.2, 10/26.4, 50/60 and 100/120. In order to examine the effect of temperature, applications were made at 38-40 °C and 50-55 °C. In order to examine the effect of time, the application was carried out in two different time periods, 1 hour 30 minutes and 2 hours. In the study, eight apple juice samples were subjected to enzymatic treatment and the results obtained were compared with apple juice without enzyme treatment. When the data obtained were analyzed, it was determined that the absorbance values were higher in the samples treated with a high concentration of pectinase/aminoglycosidase enzyme at 50-55°C for 1 hour and 30 minutes.

Keywords: apple juice, enzyme, absorbance.

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Cardiac Amyloidosis Models: in vitro, in vivo, in silico

Svetlana Morozkina*^{1,2}, Petr Snetkov*^{1,2}, Anastasiya Gorbunova¹, Mayya Uspenskaya¹

Abstract: The formation of amyloid fibrils may result into the serious incurable cardiovascular diseases, leading to some cases to death. The understanding of its structure and formation mechanism are key points for the development of therapeutic agents against cardiac amyloidosis.

Various models of amyloid formation have been developed: *in vitro*, *in vivo*, as well as *in silico*. In this paper we discuss the scope and limitation of such approaches.

The problem of amyloid formation models includes the fact, that *in vitro* technique may not be reproducible in the *in vivo* models. Many factors such as pH change, presence of other molecules, water structurization, polar environment effect on the folding process of peptide chains and its conformations.

The time of the fibril formation may differ from seconds to weeks in the *in vivo* and *in vitro* models, that is at least seven orders of magnitude greater than it may be done by all-atom molecular dynamic.

In silico models are quite useful approach to minimize and speed-up the pharmaceutical agents discovery process, because they illustrate a pharmacologic or physiologic process. The advantages of *in vivo* and *in vitro* experiments may be combined in the *in silico* approach. In silico modeling of disease is quite challenging. Results based on experiments using animal and human tissue may be quite different, and many considerations that cannot be applied. The selection of appropriate assumptions is key step in the model creation.

The factors which have to be considered during *in silico* models development based on the results of the *in vitro* and *in vivo* models are discussed in the present paper.

This research was funded by the Russian Science Foundation, project number 21-74-20093. Link to information about the project: https://rscf.ru/en/project/21-74-20093/

Keywords: cardiac amyloidosis, amyloid fibrils, models, in vitro, in vivo, in silico

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Nanotechnology and Textiles: Transformation for the Clothing Industry of the Future

Zofia Żurek *1

Abstract: The clothing industry is undergoing a major transformation thanks to the creative potential of nanotechnology. The study examines the applications of nanotechnology in the textile industry and discusses how it is used to increase the durability of textile products, improve their functionality, add modifications and reduce their environmental impact.

First, the study explains how nanotechnology is integrated into the textile industry. Nanocore fibers add properties such as durability, water repellency and stain resistance to textile products. At the same time, nanomaterials that block sunlight and kill bacteria enable the production of sun protection clothing and antibacterial textiles. The study highlights the value nanotechnology adds to the clothing industry. Nano-enabled clothing offers a wide range of applications, from performance-enhancing clothing for athletes to work clothes with fire extinguishing properties. It also notes that nanotechnology can offer innovations that help increase environmental sustainability in the textile industry. For example, using nanoparticles to clean polluted waters could reduce the environmental impacts of textile production. Finally, the study considers how nanotechnology may affect the textile industry in the future. Smart textiles can have a wide range of applications, from the fabric's ability to change color to temperature and humidity regulated fabrics. Additionally, nanotechnology can make clothing production processes more efficient and environmentally friendly.

This intersection between nanotechnology and textiles has the potential to make the clothing industry more functional, durable and environmentally friendly. This study aims to examine this interesting transformation more closely by emphasizing the importance of nanotechnology in the textile industry and its possible future applications.

Keywords: Nanotechnology in textiles, textile industry transformation, nano-enabled clothing, environmental sustainability, future textile innovations.

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Numerical Simulation of the Oil-Water Flow in a Horizontal Pipe in a Stratified Flow Regime

Dariusz Asendrych *1

Abstract: Multiphase flows are widely encountered in industrial applications, just to mention chemical and process industries, food and pharmaceutical processing, and hydraulic and pneumatic transport. Among various multiphase flow configurations, 2-phase oil-water flow with two immiscible liquids plays a quite important role in reflecting the oil extraction technology. Stratified and fully dispersed flow regimes are of the most importance, as they are commonly encountered in extraction installations. A variety of parameters like flow structure, flow velocity, mixture composition and material properties make the prediction of pressure drop difficult and consequently lead to an uncertain estimation of energy demand. That is why extraction installations are usually oversized as they are based on empirical formulas derived for a limited range of operating conditions and physical properties.

In the present paper, the oil-water flow in a horizontal pipe of diameter 50mm in a stratified flow regime is investigated with the use of computational fluid dynamics (CFD). The flow was simulated using Ansys Workbench commercial software package with the use of a 3-dimensional Eulerian approach combined with a Volume of Fluid (VOF) method allowing for a reconstruction of an oil-water interface in a stratified regime. Surface tension was included in the momentum equation as a source term. Water and paraffin oil were used as working fluids.

The model was verified by conducting a series of simulations following the flow conditions of the experimental-numerical work presented in a reference paper devoted to the 2-phase oil-water flow. The predicted pressure drops in test simulations showed very good agreement with reference data, proving the relevance of the applied numerical approach. The verified model was employed to carry out a parametric study for a stratified flow regime, with the following ranges of operating parameters: flow velocity 0.3-1.0m/s, oil volume fraction 0.06-0.6 and temperature $5-45\Box$ C. The results of the calculations allowed us to collect a database and show how oil volume fraction, flow velocity and temperature influence flow resistance. The predicted pressure drops turned out to vary in a quite wide range with its minimum value around 20Pa/m and exceeding 200Pa/m for the worst conditions (high velocity, low temperature, high oil volume fraction). It shows how important the choice of operating conditions can be to optimise energy consumption. The collected data allowed us to propose a functional dependence of pressure drop on 3 independent variables investigated in the present research. The proposed correlation, although limited to paraffin oil and pipe diameter, can be effectively used in managing oil transport in pipeline systems.

Acknowledgements: The present research work was supported by statutory research funds of the Częstochowa University of Technology under grant BS/PB-1-100-301/2023/P. The PL-Grid Infrastructure is gratefully acknowledged for providing its computational resources.

Keywords: Oil extraction, multiphase flow, stratified flow regime, computational fluid dynamics (CFD), temperature-dependent viscosity, volume of fluid (VOF).

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The New Future of Chemistry: Green Chemistry

Cengiz Çesko *1

Abstract: Today, the discipline of chemistry is experiencing a major transformation with a focus on sustainability and environmental protection. Green chemistry represents a significant paradigm shift shaping the future of chemistry by combining traditional chemistry principles with environmentally friendly and sustainable approaches. Our work addresses the fundamental concepts, principles and applications of green chemistry and examines how chemistry can contribute to a sustainable future.

At the heart of green chemistry is the reduction of environmental impacts in the design and implementation of chemical processes and the development of green products. Minimizing waste and by-products, using environmentally friendly solvents, increasing energy efficiency and material synthesis based on renewable resources are the key principles of green chemistry. Green chemistry also encourages the development of ingredients that are less harmful to the environment and human health, instead of toxic and harmful chemicals. This approach allows industrial sectors to produce more sustainable and safer products. The study also addresses the economic and social dimensions of green chemistry and highlights the benefits that green chemistry provides to business and society. The impacts of green chemistry on innovation, jobs and sustainable development are examined and are intended to serve as an important guide for future chemistry research and industrial applications.

As a result, green chemistry has an important role as a transformation tool that shapes the future of chemistry. This article aims to address the environmental and social responsibility of chemistry by highlighting the basic principles and potential of green chemistry. The new future of chemistry is being shaped based on sustainability and green principles

Keywords: Green chemistry, sustainability, environmental protection, sustainable chemistry,

environmental impact reduction

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Effect of Magnetic Biocomposite Doped with Agricultural Waste on The Removal of Synazol Blue Khl Textile Dye

Sibel Bişgin¹, Aslıhan Arslan Kartal^{1*}

Abstract: A significant portion of global trade consists of textile products. In countries where the textile industry is developed, the production primarily focuses on finished goods rather than raw materials. This requires a series of chemical processes, especially dyeing, which plays a significant role in the production of textile products. In order to ensure the continuity of aquatic life, control environmental pollution, and maintain the natural life cycle of the environment, there is a need for methods that remove and eliminate dyes released into water. In this study, the aim was to investigate the preparation of a new biocomposite material using natural renewable resources that reduce the negative effects on the environment, and to examine the conditions for the removal of Synazol Blue Khl textile dye from an aqueous solution. The agricultural waste powder and magnetite were encapsulated in alginate beads in an aqueous calcium chloride solution to prepare the biocomposite material. The parameters affecting adsorption and removal efficiency of dye from the aquatic solution such as pH, temperature, extraction time, biocomposite quantity, and type of agricultural waste, were evaluated using the batch technique and presented in the report.

Keywords: Removal, agricultural waste, alginate, textile dye.

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RBF Solution of MHD Flow and Heat Transfer with Hall and Viscosity Parameters

Merve Gürbüz Çaldağ*1

Abstract: Two dimensional, steady, laminar flow of a viscous, incompressible and electrically conducting fluid is studied in a square cavity under the impact of a uniform applied magnetic field. The viscosity of the fluid is assumed to vary exponentially with the temperature. Polynomial radial basis function (RBF) approximation is developed for solving the non-dimensional magnetohydrodynamic (MHD) flow equation coupled with the energy equation including variable viscosity and the Hall effect terms. In this method, particular solution, which is approximated by RBFs to satisfy both differential equation and boundary conditions, becomes the solution of the partial differential equation itself. Numerical results are depicted in terms of axis flow velocity (w) and temperature (T) profiles for several values of physical parameters such as Hartmann number (Ha), Brinkman number (Br), Hall (m) and viscosity (B) parameters. It can be obtained that as the intensity of magnetic field increases, the magnitude of the flow decreases due to the retardation effect of Lorentz force. However, the velocity of the fluid increases with an increase in Hall parameter. The rise in the viscosity parameter causes the average Nusselt number to increase but the increase in Hall parameter decreases the temperature of the flow because of the reduction of the Joule dissipation.

Keywords: RBF approximation, MHD flow, Hall effect, Viscosity parameter.

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The Search of Small Peptides by Molecular Docking for Development of Highly Effective Blockers of Cardiac Systemic Amyloidosis ATTR

Michael Petukhov¹, Petr Snetkov², Svetlana Morozkina², Mayya Uspenskaya²

Abstract: Cardiovascular diseases continue to be the most serious global problem in the World. One of the most difficult illnesses belong to cardiomyopathies, which are attributed with stretching, thinning, and induration of the walls of the heart chambers or heart muscle. Such alterations result in serious changes in cardiac and vessel function, that could result in the death of the patient.

Cardiac amyloidosis, being an incurable disease, is caused by the formation of the abnormal protein amyloid layers in the myocardium and surrounding tissues. Nowadays the number of medications against amyloidosis is extremely limited, and the probability of the disruption of cardiac structure and function is very high, which results in heart failure syndrome. The clinically used pharmaceutical agents have nonselective modes of action and significant adverse effects.

Molecular docking of small peptides into the central cavity of the amyloid TTR protein fibrils allows the selection of several peptide molecules, which may lead to the effective therapy with less side effects.

Based on molecular docking, the most promising structures of peptide molecules (8 structures) were selected as the potential highly effective blockers of systemic amyloidosis ATTR. Although some dipeptides showed sufficiently high values of Δ ICM-Score for effectively blocking the attachment of the next TTR protein chains, their primary binding on minimal size amyloids is probably not high enough.

In comparison with dipeptides, tripeptides (38 molecules) have on average higher binding characteristics with the germline amyloid structures for growth phase of amyloid structure, and different characteristics for blocking of the growth phase of TTR amyloidosis, and therefore represent set are preferable candidates for the development of pharmaceutical substances against systemic amyloidosis ATTR.

WWK tripeptide seems to be one of the most interesting candidates, and takes the third place in the list of the most promising ultra-short peptides, according to ICM-Score value for minimal size binding to amyloid. However, the difference between the first two molecules (NWR and HRS) is insignificant (~0.5). Moreover, WWK peptide consists of the most extensive amino acids and has a symmetrical conformation, where the hydrophobic side chains of Trp residues are oppositely directed against the amyloid in the areas which has high level of TTR protein hydrophilic residues. It may prevent the binding of new chains of TTR protein to the amyloid.

Even in the case of binding of the largest tripeptides, there is still a lot of free space in the central cavity of the TTR amyloid. Therefore, some increase in TTR size, such as tripeptides with blocking groups at the N-and C-terminal and/or containing unusual amino acids, could be provided.

Among these, four peptides were selected, synthesis methods were chosen, synthesis was performed, purification was made, and structure evaluation at each synthesis step was carried out. The synthesis design was developed using the approaches that exclude racemization and minimize the formation of reaction by-products.

This research was funded by the Russian Science Foundation, project number 21-74-20093. Link to information about the project: https://rscf.ru/en/project/21-74-20093/

Keywords: cardiac amyloidosis, cardiomyopathies, molecular docking, protein fibrils, ultrashort peptides

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Assessing removal methods for controlling *Dichrostachys cinerea* encroachment and their impacts on plant communities in an East-African savannah ecosystem

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Abstract: Woody plant encroachment is known to adversely affect the biodiversity and functioning of savannah ecosystems, yet removal strategies have been shown to have variable success. Here we evaluated the effectiveness of three woody removal methods or treatments for controlling the leguminous thorny shrub Dichrostachys cinerea, and assessed plant community responses following removal in the savannah plains of Nech Sar National Park, South-Ethiopian rift valley. Based on a total of 72 10 x 10 m² experimental plots spread across six blocks, we carried out (i) stump burning, (ii) stump application with glyphosate herbicide, and (iii) manual uprooting on D. cinerea, and monitored the number, height, and thickness of resprouts and the number of resprouting stumps for two consecutive years. Additionally, we surveyed all vascular plant species per plot for each removal method and control. We found that the uprooting treatment resulted in a higher number of resprouting stumps and lower number of resprouts, and a smaller resprout height and diameter. The fire treatment showed the largest reduction in the number of resprouting stumps and resprouts, while the glyphosate treatment showed intermediate results although resprout height and diameter were significantly larger compared to the uprooting treatment. Whereas plant species richness and diversity were higher in the fire treatment, they were adversely affected in the uprooting treatment. Our results demonstrate that none of the woody removal methods were effective enough to completely eradicate D. cinerea from the field trials after only one intervention, suggesting the need for follow-up management actions considering their impacts on both woody encroachment and biodiversity restoration.

Keywords: Fire, glyphosate herbicide, Nech Sar National Park, resprouting, savannah plains, uprooting

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Blood Flow Measurement by Laser Doppler

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Abstract: Laser Doppler flowmetry (LDF) is non-invasive technique that measures average velocity of blood flow in a microcirculation. This technique is based on a Doppler shift, a phenomena of frequency change that light undergoes after being reflected by moving objects such as erythrocytes in a microvascular bed. LDF is commonly used for the analyses of blood flow parameters in various tissues, such as skin, mucose, gastrointestinal tract, microvascular grafts, and it also has a broad range of applications in the field of dentistry (i.e. LDF is the most accurate and reliable method for verification of dental pulp vitality, and can be also used for measurements of gingival, masticatory muscles, and alveolar bone perfusion). Modern Laser Doppler flowmeters emit near infrared light, at 780-820 nm wavelength, which enables deep penetration of a light wave into the examined tissue. Light source probe projects a wave beam through the tissue that strikes on immobile and moving objects and then reflects to the detector (the portion of light scattered from erythrocytes undergoes a Doppler shift). The detector converts total reflected light into electrical current and computer software transforms electrical impulses in perfusion units (PU) that represent the amount of blood flow in the tissue. The main disadvantages of this method are small volume of tissue that can be examined (1 to 2 mm3), possible artifacts due to movement of a patient or a probe, and unwanted signals collected from surrounding structures that can be solved by proper probe stabilization and isolation of the examined field.

Keywords: Laser Doppler, blood flow, perfusion units.

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Effect of Global Warming on Plant Genetics

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Abstract: Global warming is a serious environmental problem that leads to significant changes in climatic conditions around the world. Our study examines the potential effects of global warming, particularly in the field of plant genetics. Global warming can affect the adaptation mechanisms of plant species, creating potential risks for plant diversity and ecosystems.

The study highlights the importance of genetic research to understand how plant species respond to warming. Analysis of plant genomes is a powerful tool for determining the impact of warming on plant adaptation. It is shown that global warming can affect plant populations by causing or forcing certain gene variations in plant species. Our study also addresses the effects of global warming on plant productivity, plant diseases and pests. While examining how warming affects plant phenotypes and growth cycles, it discusses how strategies such as genetic engineering and selective breeding can be used to deal with these problems.

In conclusion, this study highlights the importance of genetic research to understand the effects of global warming on plant genetics and highlights the importance of a better understanding for the sustainability of plant species. This is an important issue for plant breeders, conservationists, and geneticists, guiding future research and policymaking.

Keywords: Global warming, plant genetics, climate change, genetic research, biodiversity conservation.

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Effect of Capparis ovata Treatment on the Gene Expression Levels of Ceramide Synthase 2 and 5 in Experimental Autoimmune Encephalomyelitis Model of Multiple Sclerosis in C57BL/6 Mice

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Abstract: It has been reported that Capparis ovata, which is widely used in the treatment of various diseases in traditional medicine, may also be useful in the treatment of neurodegenerative diseases such as Multiple Sclerosis (MS). Recent studies have shown that sphingolipid metabolism is important in neurodegenerative diseases and that sphingolipid metabolism may change in MS. This study was designed to determine the effect C. ovata treatment on the gene expression levels of ceramide synthase 2 (CerS2) and ceramide synthase 5 (CerS5), which are subclass of sphingolipids, in experimental autoimmune encephalomyelitis (EAE) model of MS in C57BL/6 mice. For this, female mice were allocated into three groups: group 1, healthy control group; group 2, control group with EAE model of MS; group 3, group with EAE model of MS treated with C. ovata water extract (COWE). COWE was prepared from the fruit, bud and flower parts of the plant using a rapid extraction system and lyophilized. To establish EAE model of MS, the mice in groups 2 and 3 were injected with MOG35-55/CFA. The mice in group 3 were treated with COWE at a daily dose of 500 mg/kg for 21 days. The qRT-PCR method was used to determine the CerS2 and CerS5 gene expression levels in the groups. It was observed that the CerS2 and CerS5 gene expression levels were significantly increased in group 2 compared to group 1 and significantly decreased in group 3 compared to group 2. The decrease in the gene expression levels of CerS2 and CerS5, which are considered inflammatory mediators, in group 3 indicates that COWE treatment can suppress the development of EAE and reduce inflammation.

Keywords: Capparis ovata, Multiple Sclerosis, Ceramide synthase, Experimental autoimmune encephalomyelitis, Sphingolipid.

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Enhancing Ballistic Impact Resistance of Twaron® Aramid Fabrics through Impregnation of PEG/Lead Metaborate-Silica as an Innovative Shear Thickening Fluid

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Abstract: The development of protective materials to meet the increasing needs of nuclear technology is crucial due to the high neutron and gamma radiation capture capabilities of lead borates. This study focuses on investigating the ballistic impact performance of Twaron® aramid fabrics impregnated with PEG/lead metaborate-silica as a new shear thickening fluid. Previous studies have explored the use of lead borate compounds for radiation protection, but there is limited research on their ability to capture gamma and neutron radiation. Additionally, the ballistic performance of lead borate has been found to be inferior to silica nanoparticles. This project aims to address these limitations by increasing the solid particle ratio, optimizing the preparation of lead borate/silica/polymer systems, synthesizing nano-sized lead borate, and performing modifications to enhance ballistic performance. Rheological tests will be conducted to evaluate the chosen systems, and ballistics tests will be performed according to standard protocols. The results will provide insights into the effectiveness of the modified flexible armor in meeting minimum performance standards. Furthermore, radiation tests will be conducted to assess the gamma and neutron radiation absorption properties of the materials. This research will contribute to the development of improved protective materials for various applications, including nuclear technology.

Keywords: lead borate, ballistic performance, aramid fabrics, shear thickening fluid.

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Impact of Climate Change on Ecosystems and Species

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Abstract: This academic study examines the profound effects of global climate change on natural ecosystems and species. Climate change manifests itself through changes in temperature, precipitation regimes, sea levels and other important climate factors on Earth. These changes cause direct and indirect impacts on many ecosystems.

The study brings together scientific research and quantitative data from different disciplines to understand the effects of climate change on ecosystems. The effects of climate change on ecosystems are based on statistical data such as temperature increase, changes in the water cycle, rise in sea levels and extreme weather events. The results of the research explain how climate change affects biodiversity, species distribution and ecological balance in ecosystems. These effects are observed in forests, oceans, polar regions and other ecosystems. For example, water levels in the oceans rise by 1-3 mm every year. Additionally, the article emphasizes the policies and strategies that need to be developed to combat climate change and protect ecosystems.

As a result, this study considers the effects of climate change on ecosystems and species from a broad perspective, providing an important resource for researchers and policy makers who want to direct efforts to combat climate change and develop measures against this important threat to the natural world.

Keywords: Climate change effects, ecosystem impact, biodiversity, species distribution, climate change policies.

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Social Aspects of Job Satisfaction among nurses in Hospital Settings

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Abstract: In the healthcare system, nurses play a crucial role. Recognizing aspects like job satisfaction and working conditions is one of the fundamental actions one can do to improve someone's happiness. As a result, the current study's objective was to investigate the relationship between nursing staff members' levels of happiness, work-life quality, and job satisfaction.

In the context of nursing work, social support is a vital resource with a positive impact on well-being (e.g., lowering role stress) and job satisfaction.

The study demonstrates the importance of having a skilled health workforce and the importance of certain organizational factors, such as numbers (the amount that is available), skill mix (the balance of health teams), distribution (urban/rural), and working conditions (compensation, nonfinancial incentives, and workplace safety). This study has shown that rules for retaining the nursing workforce need to be changed. Simple actions needing better management techniques could greatly enhance the working environment and, as a result, increase nurse retention.

Keywords: Healthcare system, nursing, job satisfaction.

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Viscum album Induces the Concentration of cAMP and Activity of the cAMP Response Element in Human Kidney HEK-293 Cells

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Abstract: cAMP response element-binding protein (CREB) is a protein that regulates the expression of several genes. Studies have shown that the activation of CREB may be responsible for the survival of cells. In this study, the concentration of cAMP and activity of the cAMP response element (CRE) in human kidney HEK-293 cells at a non-cytotoxic dose of Viscum album were investigated. For this purpose, first of all, the non-cytotoxic dose of V. album in HEK-293 cells was determined by crystal violet method. The concentration of cellular cAMP was measured using the cAMP Immunoassay Kit, and the regulation of the CRE activity by V. album was determined using the pGL4.29 luciferase reporter assay. It was observed that V. album significantly increased both the concentration of cAMP and the activity of the CRE. Based on these findings, it can be suggested that V. album may initiate signaling pathway activation by increasing the amount of cAMP significantly at the transcriptional level. Further studies are needed to identify the downstream genes activated by the CREB.

Keywords: Viscum album, cAMP, cAMP response element, HEK-293, luciferase.

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Moduli Space For Invariant Solutions Of Seiberg-Witten Equations

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Abstract: In this work, we study the *G* -invariant solutions of the Seiberg-Witten equations when *G* is a cyclic group acting on a manifold *M*, preserving the metric and the orientation. *G* is assumed to have a lift to the principle $Spin^c$ bundle which gives rise to Seiberg-Witten equations in question. It was shown that when the dimension b_+^G of the *G*-fixed points of harmonic two forms is positive, for a generic choice of an element in this fixed point set, the moduli space of invariant solutions of Seiberg-Witten equations is a compact, smooth and oriented manifold. In case b_+^G is zero, it was shown that there exist a unique singularity which has a compact neighborhood homeomorphic to a cone on a certain projective space. Using the latter case, a version of the theorem of Fintushel and Stern which gives a necessary condition for a Seifert homology 3-sphere occurs as the boundary of a negative definite four manifold whose first cohomology contains no 2-torsion, is proven. In this work we prove that If $b_+^G > 0$ then for a generic perturbation $\Phi \in \Omega_+^G$, the moduli space M_{Φ}^G of Seiberg-Witten equations perturbed by Φ is an oriented smooth manifold of dimension $d^G = ind(D_A^G) - b_+^G - 1$, where $ind(D_A^G)$ denotes the index of dirac operator.

Keywords: Equivariant Seiberg-Witten theory, Equivariant Seiberg-Witten moduli space

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1. INTRODUCTION

In the fall of 1994, Edward Witten (Witten, 1994) introduced a set of equations which give the main results of Donaldson Theory in a much simpler way. These equations are now known as the Seiberg-Witten equations. These equations are associated to a $Spin^{c}(4)$ structure on the manifold in question and they are invariant under the group of bundle automorphisms of the determinant line bundle associated to this $Spin^{c}$ structure. This group is called Gauge group. As in Donaldson theory gauge equivalence classes of solutions of Seiberg-Witten equations forms a moduli space and gives important information about the differential topology of the manifold. In fact, a diffeomorphism invariant, called Seiberg-Witten invariant, is introduced using this moduli space. The moduli space of Gauge equivalence classes of the solutions of the perturbed Seiberg Witten equations is compact and in some cases, for a generic perturbation, it is a zero dimensional manifold and

hence consists of finitely many points. In this case, Seiberg-Witten invariant is defined to be the algebraic sum of the points in the moduli space counted with the multiplicities according to the orientation. In this work we prove that If $b_+^G > 0$ then for a generic perturbation $\Phi \in \Omega_+^G$, the moduli space M_{Φ}^G of Seiberg-Witten equations perturbed by Φ is an oriented smooth manifold of dimension $d^G = ind(D_A^G) - b_+^G - 1$, where $ind(D_A^G)$ denotes the index of dirac operator.

2. MATERIAL AND METHOD

A gauge transformation on a line bundle *L* is a bundle over a 4 dimentional smooth manifold *M* is a homomorphism $h: L \to L$ commuting with the action of the structure group U(1). That is $h(g \cdot a) = g \cdot h(a)$ for all $g \in U(1)$. The set of all gauge transformations of *L* form a group G(L), under composition, and we have an isomorphism $G(L) \cong Map(M, S^1)$. After fixing a base point $P_0 \in M$, for $G_0(L) = \{g \in G(L); g(P_0) = 1\}$, we hav the isomorphism $G(L) \cong G_0(L) \ge S^1$.

Let *M* be oriented, Riemannian 4-manifold with a $Spin^{c}(4)$ structure. We consider the pairs (d_{A}, ψ) where d_{A} , is a connection on the line bundle L^{2} and $\psi \in \Gamma(W_{+} \otimes L)$. Let $A = \{d_{A_{0}} - ia, \psi\}$ denote the configuration space. Seiberg Witten equations are defined as

$$D_A^+ \psi = 0$$

$$F_A^+ = i\sigma(\psi)$$

Where $F_A^+ \epsilon \Gamma \left(\Omega^2 \left(T^* M \otimes iR \right) \right) = \Omega^2(M)$. Let $M(L) \cong M(L)/S^1$ denote the moduli space of $G_0(L)$ equivalence classes of the solutions of the Seiberg Witten equations. Similarly for a generic perturbation $\Phi \in \Omega_+^G$, we define $M_{\Phi}(L) = \{(A, \psi) \epsilon A(L) \ x \ \Gamma(W_+ \otimes L); \ D_A^+ \psi = 0 \ and \ F_A^+ = i\sigma(\psi) - \Phi \}/G$ as the moduli space of gauge classes of the perterbed Siberg Witten equations. We use the cobordism theory and group actions to compute the dimension of moduli space.

2.1. Simulation

It has been proven (Uguz, 1999) that Seiberg Witten equations are invariant under *G* action, and hence one can consider *G*-fixed solutions of the perterbed Seiberg Witten equations. It has also been proven that when $b_+^G > 0$ the moduli space of the solutions of Seiberg Witten equations with a generic perterbation is a smooth manifold. These results combined with a cobordism theory and group actions ware the main techniques for the proof of the theorem stated in the next section.

3. RESULTS

The result of this work can be summarized by the following theorem

Theorem: Let *M* be a closed, simply connected smooth 4-manifold with a $Spin^{c}(4)$ structure. If $b_{+}^{G} > 0$ then for a generic perturbation $\Phi \in \Omega_{+}^{G}$, that is a self dual *G* fixed two form, the moduli space $M_{\Phi}^{G}(L)$ of Seiberg-Witten equations perturbed by Φ , is an oriented smooth manifold of dimension $d^{G} = ind(D_{A}^{G}) - b_{+}^{G} - 1$, where $ind(D_{A}^{G})$ denotes the index of dirac operator.

Proof: The existence of a reducible solution in $\widetilde{M_{\Phi}^G(L)}$, which causes singularity in $M_{\Phi}^G(L)$, depends on the condition that the first chern class $c_1(L)$ of the line bundle contains a connection with $F_A^+ = 0$, in turn which occurs only if ϕ is an element of a subspace of Ω_+^G of codimension b_+^G . Since, by the assumption $b_+^G > 0$, these singularities are avoidable. Hence as a subgroup of the gauge group, S^1 acts freely on $\widetilde{M_{\Phi}^G(L)}$. Therefore $M_{\Phi}^G(L)$ is an oriented smooth manifold with dimension equal to $\dim(\widetilde{M_{\Phi}^G(L)}) - 1 = ind(D_A^G) - b_+^G - 1$. The orientation of $M_{\Phi}^G(L)$ is induced from the orientation of $\widetilde{M_{\Phi}^G(L)}$.

As a final remark, the moduli space $M_{\Phi}^{G}(L)$ depends on the choice of *G*-invariant Riemannian metric and *G*-fixed perturbation ϕ .

4. DISCUSSION AND CONCLUSIONS

For the cases when the assumption on the dimension of self dual *G* fixed 2 forms, that is $b_+^G > 0$ is not satisfied, the structure and dimension of the moduli space $M_{\Phi}^G(L)$ of Seiberg-Witten equations perturbed by Φ , should be studied and we will focus on this as a future work.

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REFERENCES

Donaldson S.K. and P.B.Kronheimer. The Geometry of Four-Manifolds. Clarendon Press- Oxford, 1990.

Freedman M. The topology of four dimensional manifolds. J.Diff.Geo., 17:357-454, 1982.

Morgan John W.The Seiberg-Witten Equations and Application to the Topology of Smooth four-Manifolds. Princeton University Press, 1996.

Uğuz Muhiddin, "Moduli space for invariant solutions of Seiberg-Witten equations" No 82424.

Witten, Edward (1994), "Monopoles and four-manifolds.", Mathematical Research Letters, 1 (6): 769–796, arXiv:hepth/9411102, Bibcode:1994MRLet...1..769W, doi:10.4310/MRL.1994.v1.n6.a13, MR 1306021, S2CID 10611124, archived from the original on 2013-06-29



The Effect of Nutrition on Metabolic Parameters in Mice with Type II Diabetes

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Abstract: Diabetes mellitus (DM) is a metabolic disease in which the metabolism of energy source molecules such as carbohydrates, lipids and proteins is impaired as a result of chronic hyperglycemia due to decreased insulin secretion, damage to the pancreatic β -cell or insulin resistance, and which tends to increase dramatically worldwide. Genetic causes, immunological factors, malnutrition, sedentary life, and other environmental factors play a role in the etiology of the disease. Many pathological changes such as nephropathy, retinopathy and cardiovascular complications occur with the progression of the disease. Mice are widely used in type II diabetes research as they give similar metabolic responses to humans with diabetes. Mechanisms such as reducing insulin production, inducing insulin resistance, or damaging pancreatic cells are aimed to induce experimental diabetes in mice. Experimental diabetes induction in mice is done with chemical agents such as alloxan and streptozotocin (STZ), nutrition, genetic modifications, viruses, and surgical methods. The majority of DM patients are obese or obesity itself causes insulin resistance. Dietary and non-alcoholic fatty liver disease causes various metabolic diseases such as obesity, dyslipidemia, and diabetes mellitus. In this study, it is aimed to determine which of the different nutrition models such as low carbohydrate diet, low fat diet, vegetarian/vegan diet, Mediterranean type diet and intermittent fasting is more effective in patients with diabetes. In this way, it is thought that the nutrition model to be selected will make an important contribution to the treatment strategies of DM patients, whose number is increasing day by day.

Keywords: Diabetes mellitus, type 2 diabetes, diabetic mice, nutrition, metabolism.

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1. INTRODUCTION

Type II diabetes (T2D) is a disease characterized by hyperglycemia that occurs as a result of complete or partial insufficiency or deficiency of insulin hormone secretion from the pancreas, which regulates the use of blood sugar. Chronic hyperglycemia due to diabetes causes long-term damage, especially in the eyes, kidneys, heart and vessels. These damages lead to various complications such as neuropathy, nephropathy and cardiovascular complications (ADA, 2014).

In type II diabetes, insulin production becomes irregular due to dysfunction of beta cells in the pancreas and cells develop insulin resistence. This prevents the plasma glucose concentration from being kept within the normal range as a result of the mechanisms that regulate the activity of insulin (Ozougwu et al., 2013). Insulin resistance refers to a condition in which the normal biological response to insulin in the body's target tissues (liver, muscle and adipose tissue) is impaired. Insulin resistance is a condition in which body cells become less sensitive to insulin. Normally, the hormone insulin allows glucose to be taken up into cells in the body and used as energy. However, in the case of insulin resistance, the cells are less responsive to insulin, which leads to insufficient glucose uptake by the cells and a high level of glucose accumulation in the blood, resulting in diabetes mellitus (Lin and Sun, 2010).

While T2D is mainly associated with lifestyle and genetic factors, aging, unbalanced diet, alcohol consumption and smoking are also important risk factors in the pathogenesis of T2D (Ozougwu et al., 2013).

The International Diabetes Federation (IDF) reported that individuals who are overweight, have an unhealthy diet, and have a family history of T2D have a greater risk of developing diabetes (IDF, 2003). It is extremely important to prevent

T2D in the pre-disease stage or to change unhealthy diets during the treatment process of the disease and to improve nutritional models (Jannasch et al., 2017).

One of the most important goals for individuals with type 2 diabetes is to keep blood glucose under control. Proper nutrition is an important factor in preventing fluctuations in blood glucose levels. Excess weight increases the risk of T2D, thus low-calorie, low-fat and high-fiber foods should be preferred. Carbohydrates directly affect blood glucose. For a controlled and balanced carbohydrate intake, complex carbohydrates (whole grains, vegetables) that pass slowly into the blood should be consumed. High-fiber foods slow down digestion, increase the feeling of fullness and have a blood glucose regulating effect. For the body's fat needs, saturated fats should be avoided, mono and polyunsaturated fats (olive oil, avocado, fish) should be preferred. Protein intake should also be balanced.

Mice are important models of choice in medical and scientific research, as they can be kept in controlled conditions in a laboratory environment and better control over nutrition, environmental factors and genetic changes. Mice have a shorter life span compared to humans, allowing researchers to obtain faster results and advance their experiments faster. Mice with Type II diabetes may exhibit features similar to those observed in humans with insulin resistance, high blood glucose levels, and other metabolic changes. Therefore, mice have an important role in understanding Type II diabetes in humans and in the development of treatment strategies.

In recent years, different nutritional models and dietary approaches have gained popularity. These dietary models offer a variety of strategies to improve people's health and lifestyle. In this study, the most recommended nutritional models for T2D patients are emphasized.

1.1. Experimental Methods of Inducing Diabetes in Mice

1.1.1. Inducing Diabetes with Chemical Agents

Streptozocin (STZ) and alloxan are the most commonly used chemical agents to induce experimental diabetes in animal models. These substances functionally target beta cells in the islets of Langerhans in the pancreas, causing hypoglycemia (low blood glucose) and hyperglycemia (high blood glucose). Intraperitoneal, subcutaneous, intravenous or parenteral administration of these agents causes diabetes.

Alloxan monohydrate is a uric acid derivative. It causes insulin-dependent diabetes by damaging pancreatic beta cells. Streptozotocin (STZ) is in the form of N- (Methylnitrosocarbamoyl)- α -D-glucosamine. It is a diabetogenic agent that causes hyperglycemia by causing damage to the insulin-producing β -cells of the pancreas through oxidative stress, resulting in a decrease in the insulin-producing capacity of these cells (Szkudelski, 2001).

1.1.2. Inducing Diabetes with Nutrition

Long-term consumption of sucrose (glucose + fructose) in mice causes weight gain, hyperglycemia, glucose intolerance and insulin resistance. Studies showed that high fructose nutrition causes weight gain and impairs the lipid profile and glucose metabolism (Nomura and Yamanouchi, 2012).

Animal and human studies show that a high-fat diet significantly impairs the effects of insulin, reduces skeletal muscle glucose metabolism, and reduces the ability of insulin to suppress hepatic glucose production. Specifically, intracellular glucose transport, use of glucose for lipogenesis, and decreased insulin receptor kinase activity have been reported to be associated with high-fat diet. Consistently high intake of saturated fatty acids causes insulin resistance (Park et al., 2010).

1.1.3. Inducing Diabetes with Surgical Methods

In this method, part or all of the pancreas of mice is removed. Specifically, the insulin-producing beta cells of the pancreas are targeted. In addition, as another method, fat cells can be surgically injected into the abdomen of mice, and these fat cells can increase insulin resistance and cause metabolic changes (Erbaş, 2015).

1.1.4. Inducing Diabetes Through the Virus

The M variant of the Encephalomyocarditis virus, a member of the Picarno virus family, has the ability to cause diabetes in mice. Coxsaki viruses, Rubella virus, Reovirus are also viruses that cause diabetes. Pancreatic insulinitis that develops after the virus is administered to mice causes hyperglycemia and glucose tolerance disorders (Burke et al, 2020).

1.1.5. Geneticially Engineered Diabetic Mice

Ob/ob mice, db/db mice, and Zucker fa/fa rat are the most characteristic examples of the monogenic T2D model. These diabetic patterns are caused by mutations in the leptin gene (ob/ob) or the leptin receptor (db/db and fa/fa).

The ob/ob mice have an abnormal leptin deficiency as a result of a mutation of leptin encoded on chromosome 6. This results in hyperphagia, reduced energy expenditure and obesity. db/db mice have mutations in the hypothalamic leptin receptor gene on chromosome 4 and the receptor cannot respond to leptin (Pickup and Williams, 2002).

1.2. The Effect of Nutrition Models on Type II Diabetes

1.2.1. Low-Carb Diet Model

In normal nutrition, at least 45-50% of the energy comes from carbohydrates. In carbohydrate-restricted diets, less than 45% of energy comes from carbohydrates (Bolla et al., 2019). The American Dietetic Association (ADA) defined a low-carbohydrate diet as a diet containing carbohydrates less than 130 g/day or 26% of total energy.

A low-carb diet aims to encourage the body to burn fat by limiting daily carbohydrate intake. In this type of diet, the consumption of carbohydrate foods is reduced, while the intake of protein and fat is increased. Low-carb diets cause weight loss and help stabilize insulin levels.

In a very low carbohydrate diet (ketogenic diet), 5% to 10% of daily calorie intake is usually from carbohydrates, while protein and fat intake are increased. In the ketogenic diet, the liver converts fats into fatty acids and ketone bodies for energy. The aim of this diet model, which results in ketosis, is to use fats as an energy source (Turton et al., 2018).

Studies have shown that the ketogenic diet increases insulin sensitivity, provides glycemic control, reduces HbA1c level and fasting glucose in T2D patients, and diabetes is not observed in mice even after STZ injection (Westman et al., 2008). However, this diet can also lead to dyslipidemia and a high number of hypoglycemic indices in the long term (Leow et al., 2018). In T2D mice, hepatic steatosis, increase in total cholesterol, triglyceride, ALT and AST levels were observed as side effects in the ketogenic diet groups for more than 6 weeks. The negative aspect of this diet is that long-term ketogenic diet can cause different health problems.

1.2.2. Intermittent Fasting Nutrition Model

Intermittent fasting diets are a broad nutritional approach that includes different fasting programs, with the aim of promoting overall health and improving body composition by interrupting eating for a specified period of time.

Intermittent fasting basically aims to lower insulin levels by limiting energy intake and changing food intake times. Intermittent fasting nutrition model has different application methods. The most preferred ones are 16/8 (16 hours fasting, 8 hours normal eating), 5:2 (fasting 2 days a week, normal eating 5 days), alternate-day fasting (fasting for one day, normal eating period the next day) model (Harris et al., 2018).

The application of intermittent fasting nutrition model has positive effects on weight loss and metabolic health. This diet has potential benefits in controlling insulin resistance and high blood glucose levels by increasing fat burning, especially in patients with T2D (Zang et al., 2022).

It has been reported that intermittent fasting in mice significantly reduces IL6, TNF- α , IGF-1 and leptin levels in the circulation and adipose tissue compared to ad libitum feeding (Doğan et al., 2017). Fasting has been found to improve immune disorders associated with dysregulated leptin signaling, including obesity, metabolic syndrome, and autoimmunity (Longo and Mattson, 2014; Kim et al., 2017; Cignarella et al., 2018).

Studies show that intermittent fasting diet increases insulin sensitivity by suppressing fasting glucose levels and fasting insulin, and decreases HOMA-IR values reflecting insulin resistance in mouse models with T2D (Liu et al., 2020).

 β cells in the pancreas produce insulin in the body. Insulin is important for regulating blood glucose levels. β -cell function includes insulin secretion and release. Irregularities in β cells of the autophagy-lysosome pathway can affect the function of β cells and impair insulin production. Ngn3 is a protein that expresses a gene that plays an important role during pancreatic development. The increase in Ngn3 levels may have an effect on the maturation and functionality of β cells. In T2D mouse models undergoing intermittent fasting, an increase in β cells and the Ngn3 gene was seen, as well as an improvement in insulin sensitivity (Muñoz-Hernández et al., 2020).

However, studies on the long-term effects and side effects of intermittent fasting are limited, and more research is needed to fully understand its potential benefits and risks.

1.2.3. Vegetarian/Vegan Nutrition Model

Individuals on a vegetarian diet consume all of the plant foods and some or all of the animal foods such as eggs, honey and dairy products (Demir and Seran, 2017). The vegetarian diet is classified according to the food groups consumed. Lacto-ovo vegetarian diet, in which no meat products from killed animals are consumed; pesco-vegetarian diet, in which only seafood from the meat group of animal origin is consumed; There are varieties of vegetarianism such as lacto-

vegetarian, in which only the foods produced while the animal is alive, such as honey, milk and dairy products, are consumed (Özcan and Baysal, 2016).

In a vegan diet, the consumption of all animal foods is rejected. Vegan nutrition is divided into groups such as fruitarian, zenmacrobiotic, ravist. In the fruitarian vegan diet, all fruits and vegetables that are in the botanical fruit group such as tomatoes and cucumbers are consumed. In the zenmacrobiotic vegan diet, grain plants and cereals are consumed, while in the ravist vegan diet, foods are consumed only raw (Akpınar et al., 2019).

Because both vegan and vegetarian diets are generally low in calories and low in fat, they cause short-term weight loss in patients with T2D. Because of its high fiber content, a plant-based diet plays an important role in regulating blood glucose. Studies have reported that there is a significant decrease in daily calorie intake, weight, HbA1C, CRP, and total cholesterol levels in both dietary models (Barnard et al., 2009). However, although it varies according to the varieties preferred in vegan/vegetarian nutrition, muscle loss and changes in body composition were observed in mice as a result of insufficient protein intake. Since continuous plant-based nutrition leads to deficiencies of nutrients such as vitamin B12, iron, zinc, calcium and omega-3 fatty acids, these deficiencies cause adverse effects on general health and diabetes.

1.2.4. Mediterranean Diet

The Mediterranean diet is characterized by high consumption of plant foods such as legumes, nuts, cereals, fresh vegetables/fruits, seeds and olives to support a healthy lifestyle. At the same time, this diet emphasizes low consumption of red meat, moderate consumption of wine, moderate consumption of milk and its derivatives, and fish. Olive oil is the main source of fat in the Mediterranean diet.

The Mediterranean diet contains a variety of nutrients such as healthy monounsaturated fats, omega-3 fatty acids, polyphenols, flavonoids, phytosterols, vitamins with antioxidant and anti-inflammatory effects (e.g. β -carotene, vitamin C and vitamin E) and minerals (e.g. selenium). It is rich in nutrients (Lacatusu et al., 2019; Barrea et al., 2021). As a result, an increase in insulin sensitivity, insulin resistance and a decrease in cellular oxidative stress are observed in patients with T2D fed a Mediterranean diet.

Studies have shown that epigallocatechin gallate and resveratrol, which are polyphenols found in high amounts in the Mediterranean diet, prevent insulin resistance and improve mitochondrial biogenesis with the activation of PGC-1 α and SIRT-1 in mice with T2D (Baur et al., 2006; Wang et al., 2013).

In particular, some specific nutrients in the Mediterranean diet, such as olive oil, fish, walnuts and hazelnuts, are very important in reducing the risk of Type 2 Diabetes. Olive oil contains antioxidants and anti-inflammatory compounds and reduces insulin resistance. Fish contains omega-3 fatty acids. Nuts, almonds and walnuts are foods rich in healthy fats, protein and fiber. These foods have a blood glucose regulating effect (Martín-Peláez et al., 2020).

The Mediterranean diet is very rich in terms of melatonin content as well as various phytochemicals. Melatonin is found in olive oil, wine, which is the main source of the Mediterranean diet, and walnuts and almonds, which are the most consumed nuts in the Mediterranean diet. It was observed that melatonin administration in experimentally diabetic mice decreased body weight, adipocyte inflammation, blood glucose and proinflammatory factors in mice, and also had a protective effect on enzymes that regulate glucose metabolism in liver tissue (Yüzüak and Aybak, 2014; Favero et al., 2015).

1.3. Effects of Vitamins on Type II Diabetes

Vitamins are organic compounds that take part in various metabolic activities and are important for the healthy functioning of the body. A healthy lifestyle and a balanced diet are important for the body to get the vitamins it needs. Some metabolic problems may occur in the deficiency of vitamins (Valdés-Ramos et al., 2015).

Some vitamins that have a role in T2D include:

Vitamin D

Vitamin D has an important role in regulating calcium metabolism. It also increases insulin sensitivity and helps reduce the risk of type 2 diabetes (Valdés-Ramos et al., 2015).

Vitamin D deficiency has adverse effects on insulin secretion and β -cell function in experimental animals and humans. Studies have shown that vitamin D deficiency is associated with the risk of type 2 diabetes. Vitamin D deficiency can increase insulin resistance and impair glucose metabolism by negatively affecting β -cell function. Since vitamin D receptors are located in pancreatic β -cells and immune system cells, the decrease of vitamin D in serum reduces intracellular calcium level in adipocytes, which stimulates lipogenesis and causes more weight gain. Vitamin D can directly stimulate β -cells to secrete insulin or facilitate the conversion of proinsulin to insulin by increasing intracellular calcium concentration (via Ca channels) (Mitri and Pittas 2014). Experimental studies indicate that vitamin D

supplementation increases insulin production in mice with T2D and causes improvement in hyperglycemia (Robinson, 2011).

Vitamin C

Vitamin C, also known as ascorbic acid, acts as a cofactor in many enzymatic reactions, including collagen synthesis. Humans cannot synthesize vitamin C due to a deficiency of the enzyme L-gulonolactone oxidase, which catalyzes the final step in ascorbic synthesis. Therefore, people must take vitamin C through external foods.

It is thought that high blood glucose levels (hyperglycemia) in patients with T2D prevent the cellular uptake of dehydroascorbic acid (DHA), an oxidized form of vitamin C that can be transported into the cell, therefore, intracellular vitamin C deficiency occurs (Christie-David et al., 2015).

Vitamin C helps prevent cell damage due to its antioxidant properties and supports immune system functions. Therefore, it may help reduce oxidative stress caused by abnormalities in glucose metabolism in individuals with T2D (Valdés-Ramos et al., 2015). As a result of experimental studies, it is seen that vitamin C supplementation to mice with T2D causes significant decreases in food intake, plasma glucose, HbA1c levels, plasma glucose levels and insulin concentrations (Abdel-Wahab et al., 2002; Christie-David et al., 2015).

Vitamin E

As a fat-soluble vitamin, Vitamin E ,has antioxidant properties and plays an important role in many biological processes such as protecting cell membranes and preventing cellular damage caused by free radicals. Tocopherols and tocotrienols are compounds that make up the vitamin E complex. However, only α -tocopherol is found in human plasma. Vitamin E also plays an important role in the function of protein kinase C, which plays a role in cellular communication and signal transduction, and in the activity of microsomal enzymes (Colombo, 2010). At the same time, vitamin E provides the stability of the cell membrane to maintain the integrity and function of the cell.

Decreased plasma tocopherol levels have been observed in individuals with T2D. This reduction is thought to be related to lipid peroxidation. Lipid peroxidation means that cell membranes are damaged by free radicals, which contributes to T2D complications. T2D is a metabolic disease in which oxidative stress and free radicals increase. It is thought that vitamin E reduces cellular damage by protecting cells against oxidative stress caused by free radicals (Valdés-Ramos et al., 2015).

2. CONCLUSION

T2D is an endocrine disorder that continues to increase in prevalence all over the world. It has been widely accepted that nutrition plays an important role in the clinical management of T2D. Diabetes treatment requires an interdisciplinary treatment process in which nutrition, physical activity and pharmacological treatment are carried out together (Via and Mechanick, 2016).

To reduce cardiometabolic risk in patients with T2D and obesity, the primary goal is to promote moderate and sustained weight loss. In this context, the benefits of dietary changes that result in weight loss and the associated positive metabolic effects cannot be denied.

Nutrition in type II diabetes is extremely important for a diabetic individual to be protected from acute and chronic complications of diabetes, to provide glycemic control and to lead a quality life. Proper nutrition habits should become a lifestyle in diabetic patients.

Adopting a balanced diet and healthy lifestyle is an important way to get all the vitamins needed for the body and to minimize potential deficiencies since vitamin deficiencies can cause various metabolic problems. For this reason, it will be possible to take the vitamins that the body needs with a balanced diet, by choosing a healthy diet that contains enough vitamins and minerals.

This study examined the effects of different dietary regimens on blood glucose levels, insulin sensitivity, fat metabolism and other metabolic indicators in mice. The results suggest that certain types of nutrition can have positive or negative effects on the metabolic health of mice with Type 2 diabetes.

Studies with experimental animals and humans have shown that the ketogenic diet and vegetarian/vegan diet are effective in promoting weight loss and may have beneficial effects on glycemic control, triglyceride levels, and high-density lipoprotein cholesterol levels in diabetic patients. However, although there are studies supporting this diet to be beneficial in the short term, there is limited information supporting its long-term effectiveness, safety and health benefits.

Intermittent fasting and the Mediterranean diet are more preferable diets than other nutritional models in the treatment and/or prevention of T2D. However, the long-term effects of intermittent fasting are not well known.

The Mediterranean Diet is recognized as a high-fiber, low-fat and low-sugar diet. This diet includes healthy foods such as whole grains, vegetables, fruits, legumes, nuts, walnuts, seeds, olive oil, fish and small amounts of red meat. These foods are rich in fiber, vitamins, minerals and antioxidants. In particular, some specific nutrients in the Mediterranean diet, such as olive oil, fish, walnuts and hazelnuts, are very important in reducing the risk of Type 2 Diabetes. Olive oil contains antioxidants and anti-inflammatory compounds and reduces insulin resistance. Fish contains omega-3 fatty acids and has a regulating effect on blood glucose levels. Hazelnut contains healthy fats, protein and fiber and has a blood glucose regulating effect.

The Mediterranean diet can be preferred since it has numerious features such as containing various antioxidants and antiinflammatory components that protects the body against free radicals, helping control inflammation, having immunomodular properties thanks to the rich omega 3 fatty acids in this diet and having immunomodular properties.

REFERENCES

- Abdel-Wahab, Y. H., O'Harte, F. P., Mooney, M. H., Barnett, C. R., & Flatt, P. R. (2002). Vitamin C supplementation decreases insulin glycation and improves glucose homeostasis in obese hyperglycemic (ob/ob) mice. Metabolism-Clinical and Experimental, 51(4), 514-517.
- Akpınar A, Erk G, Seven A. (2019). Vegan ve vejetaryen beslenmede probiyotik bitkisel bazlı süt ürünlerinin yeri. Gıda, 44: 453-462.
- American Diabetes Assosiation, (2014). Diagnosis and classification of diabetes mellitus, Diabetes Care, 7: 81-82.
- Barnard, N. D., Cohen, J., Jenkins, D. J., Turner-McGrievy, G., Gloede, L., Green, A., & Ferdowsian, H. (2009). A lowfat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74wk clinical trial. The American journal of clinical nutrition, 89(5), 1588S-1596S.
- Barrea L, Muscogiuri G, Frias-Toral E, Laudisio D, Pugliese G, Castellucci B, Garcia-Velasquez E, Savastano S, Colao A. (2021). Nutrition and immune system: from the mediterranean diet to dietary supplementary through the microbiota. Crit Rev Food Sci Nutr, 61: 3066-3090.
- Baur, J.A.; Pearson, K.J.; Price, N.L.; Jamieson, H.A.; Lerin, C.; Kalra, A.; Prabhu, V.V.; Allard, J.S.; Lopez-Lluch, G.; Lewis, K. (2006). Resveratrol improves health and survival of mice on a high-calorie diet. Nature, 444, 337– 342.
- Bolla, A.M., Caretto, A., Laurenzi, A., Scavini, M., Piemonti, L. (2019). Low-Carb and Ketogenic Diets in Type 1 and Type 2 Diabetes. Nutrients, 11(5), 962.
- Burke RM, Tate JE, Jiang B, Parashar UD.. (2020). Rotavirus and Type 1 Diabetes-Is There a Connection? A Synthesis of the Evidence. J Infect Dis. Sep 1;222(7):1076-1083.
- Christie-David, D. J., Girgis, C. M., & Gunton, J. E. (2015). Effects of vitamins C and D in type 2 diabetes mellitus. Nutrition and Dietary Supplements, 21-28.
- Colombo, M. L. (2010). An update on vitamin E, tocopherol and tocotrienol-perspectives. Molecules, 15(4), 2103-2113.
- Demir H, Seran SC. (2017). Vejetaryenlerde enerji alımı. İnsan Topl Bil Araş Derg, 6: 3193-3202
- Erbaş, O. (2015). Deneysel diyabet modelleri. İstanbul Bilim Üniversitesi Florence Nightingale Tıp Dergisi, 1(1).
- Favero G, Stacchiotti A, Castrezzati S, Bonomini F, Albanese M, Rezzani R, Rodella LF. (2015). Melatonin reduces obesity and restores adipokine patterns and metabolism in obese (ob/ob) mice. Nutrition Research., 35(10):891–900.
- Harris L, Hamilton S, Azevedo LB, Olajide J, De Brun C, Waller G, Whittaker V, Sharp T, Lean M, Hankey C, Ells L. (2018). Intermittent fasting interventions for treatment of overweight and obesity in adults: a systematic review and meta-analysis. JBI Database System Rev Implement Rep, 16: 507-547.
- International Diabetes Federation, (2003). Available online: http://www.idf.org/diabetesatlas (accessed on 22 July 2020).
- Jannasch, F., Kröger, J., & Schulze, M. B. (2017). Dietary patterns and type 2 diabetes: a systematic literature review and meta-analysis of prospective studies. The Journal of nutrition, 147(6), 1174-1182.

- Lacatusu CM, Grigorescu ED, Floria M, Onofriescu A, Mihai BM. (2019). The mediterranean diet: from an environmentdriven food culture to an emerging medical prescription. Int J Environ Res Public Health, 16(6): 942.
- Leow, Z. Z. X., Guelfi, K. J., Davis, E. A., Jones, T. W. and Fournier, P. A. (2018). The glycaemic benefits of a verylow-carbohydrate ketogenic diet in adults with Type 1 diabetes mellitus may be opposed by increased hypoglycaemia risk and dyslipidaemia. Diabetic Medicine, 35(9), 1258-1263.
- Lin Y, Sun Z. (2010). Current views on type 2 diabetes, Journal of Endocrinology, 204: 1-11.
- Liu, Z., Dai, X., Zhang, H., Shi, R., Hui, Y., Jin, X., ... & Liu, X. (2020). Gut microbiota mediates intermittent-fasting alleviation of diabetes-induced cognitive impairment. Nature communications, 11(1), 855.
- Martín-Peláez, S., Fito, M., & Castaner, O. (2020). Mediterranean diet effects on type 2 diabetes prevention, disease progression, and related mechanisms. A review. Nutrients, 12(8), 2236.
- McNally, M. A., Pyzik, P. L., Rubenstein, J. E., Hamdy, R. F., & Kossoff, E. H. (2009). Empiric use of potassium citrate reduces kidney-stone incidence with the ketogenic diet. Pediatrics, 124(2), e300-e304.
- Mitri, J. and Pittas, AG. (2014) Vitamin D and diabetes. Endocrinol. Metab. Clin. North. Am., 43(1), 205-32
- Muñoz-Hernández, L., Márquez-López, Z., Mehta, R., & Aguilar-Salinas, C. A. (2020). Intermittent fasting as part of the management for T2DM: from animal models to human clinical studies. Current Diabetes Reports, 20, 1-10.
- Nomura K, Yamanouchi T. (2012). The role of fructose-enriched diets in mechanisms of nonalcoholic fatty liver disease. The Journal of nutritional biochemistry; 23(3):203-8. Epub 2011/12/02.
- Ozougwu J.C., Obimba K.C., Belonwu C.D., Unakalmba C.B. (2013). The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus, Journal of Physiology and Pathophysiology, 4: 46-57.
- Özcan T, Baysal S. (2016). Vejetaryen beslenme ve sağlık üzerine etkileri. Uludağ Üniv Zir Fak Derg, 30: 101-116.
- Pickup JC, Williams G. (2002). Textbook of Diabetes. 2nd ed. Vol. 1. Oxford: Blackwell Science Inc.
- Szkudelski T. (2001). The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. Physiol Res; 50:537-46.
- Turton, J.L., Raab, R., Rooney, K.B. (2018). Low-carbohydrate diets for type 1 diabetes mellitus: PLoS One, 13(3), 0194987.
- Valdés-Ramos, R., Ana Laura, G. L., Beatriz Elina, M. C., & Alejandra Donaji, B. A. (2015). Vitamins and type 2 diabetes mellitus. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders), 15(1), 54-63.
- Via, M. A., & Mechanick, J. I. (2016). Nutrition in type 2 diabetes and the metabolic syndrome. Medical Clinics, 100(6), 1285-1302.
- Westman, E. C., Yancy, W. S., Mavropoulos, J. C., Marquart, M., & McDuffie, J. R. (2008). The effect of a lowcarbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutrition Metabolism, 5(1), 1-9.
- Yüzüak H, Aybak M. (2014). The possible protective effect of melatonin on streptozotocin induced experimental diabetes. Journal of Clinical and Experimental Investigations., 5(4): 592–598.
- Zang, B. Y., He, L. X., & Xue, L. (2022). Intermittent fasting: potential bridge of obesity and diabetes to health?. Nutrients, 14(5), 981.

How to do Haplotype Analysis in Sea Turtles

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Abstract: Understanding the genetic structure of sea turtles is important both for threatened species and has an important place in understanding their relatedness and inter-population distribution. It is important to carry out conservation studies to master the genetic structures of sea turtles and to keep the environmental conditions. Gene transfer from mitochondrial DNA (mtDNA) genetically transferred from females can provide important information based on the knowledge that sea turtles return to the beaches where they were born to reproduce. We explain how it can be achieved by haplotype analysis, which is important in understanding genetic diversity. Any available tissue sample is collected and stored in the appropriate fixative solution. DNA was isolated from the collected samples and DNA levels were measured with the Qubit Flex Fluorometer device. Then, primers commonly used in sea turtles samples are designed and Polymerase Chain Reaction (PCR) analysis is performed. After checking the PCR product with gel electrophoresis, DNA purification and Sanger sequencing analysis are performed. Samples from the array are analyzed with appropriate software for alignment and evaluation of gene quality. The aligned sequences are then edited with the appropriate programs if they need to be edited. Sequences are compared to haplotypes provided via GenBank BLAST. In addition to common haplotypes, rare haplotypes can be found as a result of haplotype analysis. Deductions about the populations then can be made by performing network analysis and mixed stock analysis. The aim of the study is to emphasize the importance of genetic diversity in conservation of sea turtles and to guide further studies.

Keywords: Sea turtle, haplotype, DNA isolation, PCR, squencing

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1. INTRODUCTION

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Utilization of genetic markers has emerged as a valuable mechanism for comprehending the distribution patterns of migratory marine populations (Bolten et al., 1998). Haplotype analysis constitutes a pivotal genetic tool that centers on the scrutiny of mitochondrial DNA (mtDNA), an inheritance exclusively maternally-derived genetic material devoid of recombination processes (Bowen & Karl, 2007). This genetic feature renders mtDNA a potent marker for elucidating maternal lineages, thereby illuminating migratory trajectories and population dynamics inherent to sea turtles. The identification of haplotypes, characterized by distinct linked genetic variations, offers the potential to infer distribution patterns among populations, interconnectivity among divergent groups, and discern the impacts of environmental shifts (Ferrera et al., 2021)

Haplotype analysis is employed primarily to determine the nesting beach linked to an observed turtle. Distinct haplotypes exhibit varying prevalence across specific coastal sites due to the natal homing of nesting females to particular locales (Bolten et al., 1998). This fidelity results in distinct genetic populations, serving as demographic and management units, bearing implications for tailored conservation strategies and effective management practices. This can guide conservation efforts, as understanding genetic diversity and migration patterns can lead to the establishment of protected areas and the implementation of effective management strategies (Bolten et al., 1998).

This study provides information about how haplotype analysis is done in sea turtles. In the details of the study, the loggerhead sea turtle (*Caretta caretta*) was used as a sample organism.

2. MATERIAL AND METHOD

2.1. Sample collection and DNA isolation

Any available tissue sample (eg: blood, muscle, skin, etc.) is collected and stored in the appropriate fixative solution.

Standard DNA isolation methods may be preferred to extract total DNA. For example; DNA isolation can be done by salt/chloroform method (Hsieh et al., 2006; Sambrook JF, 2001). Another method for DNA isolation is the method in which the phenol chloroform protocol is applied (Kaska et al., 2001).

Measuring DNA levels is crucial for the PCR (polymerase chain reaction) procedure. DNA levels can be measured with the appropriate method. For example; DNA levels can be measured with a Qubit Flex Fluorometer (Life Technologies, Thermo Fisher Scientific, USA).

2.2. DNA Amplification

For DNA amplification, the approximately 800 basepair (bp) fragment of the mtDNA control Region is amplified by polymerase chain reaction using primers. Commonly used primers LCM15382 (5'-GCTAACCCTAAAGCATTGG-3') and H950 (5'-TCTCGGATTTAGGGGTTTG-3') for loggerhead sea turtle were designed by (Abreu-Grobois et al., 2006). DNA samples are amplified using the appropriate PCR procedure. One of the most common methods of PCR, the procedure followed by (Rees et al., 2017); Initial denaturation at 98°C for 5 min. This step was followed by 40 cycles of 5 seconds at 98°C. Then 20 seconds at 60.6 °C and 72 °C and a final 1 minute at 72 °C. The product quality of the PCR product needs to be evaluated by gel electrophoresis. (Loisier et al., 2021); separated PCR products by 1% agarose gel electrophoresis using 0.5X TBE buffer. Then visualized with ethidium bromide in UV light.

2.3. Sequencing and Alignment

DNA purification and Sanger sequencing of PCR products should be performed. Thus, the reverse and forward directions are sequenced. It is necessary to use appropriate software to align the sequences such as SeqScape3 software (Figure 1.) Sequentially the sequences are analyzed for alignment and evaluation of gene quality.

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Figure 1. Loading sequences into SeqScape 3 software

Certain programs can be used for sequences that are aligned later, and for those that need to be edited. The program that is used to demonstrate is BioEdit version 7.2.5 (Hall TA., 1999), in which the sequences can be edited. The difference between 350-360 bp can be seen in the figure below, where differences in nucleotides indicate different haplotypes (Figure 2).



Figure 2. Display of sequences in Bioedit program.

2.4. Haplotype determination

Sequence comparison tool for haplotype detection is performed by comparing sequences with existing haplotypes in GenBank BLAST (http://ncbi.nlm.nih.gov/Blast.cgi). If new haplotypes are detected, they are named according to the ACCSTR standard nomenclature and submitted to GenBank (Shamblin et al., 2014).

2.5. Network Analysis and Mixed stock analysis

Once haplotypes are determined, haplotype networks can be created to show the relationship between different haplotypes. For example; PopART version 1.7 (Leigh & Bryant, 2015) program can be used to generate haplotype networks. PopART uses the median merging algorithm. Kaska et al. (2023) have visualized the haplotype mtDNA network for loggerhead sea turtles from different management units using PopART (Figure 3). In Figure 3, a network illustrating the mtDNA haplotypes of loggerhead sea turtles from distinct management units is presented. Lines linking haplotypes depict single nucleotide mutations. The size of haplotype circles corresponds to the sample size bearing that specific haplotype.

Using DnaSP version 5.10.01 (Librado & Rozas, 2009), haplotype diversity (Hd), nucleotide diversity (π), haplotype number (k) can be learned. Mixed stock analysis (MSA) is used to predict origins and foraging areas in rookies (Bass AL, Epperly SP, 2004; Bjorndal KA, 2008; Bowen & Karl, 2007) Analyzes mtDNA sequences from mixed population in MSA by comparing them with baseline haplotypes from rookies. MSA can be done using different packages. One of them is to use the Bayesian approach in the MIXSTOCK package in R studio (Bolker B. Okuyama T., 2014).

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Figure 3. Haplotype network representation. The circle areas of the haplotypes are visualized in proportion to the sample size carrying the haplotype. Link lines indicate single mutations (Kaska et al., 2023).

3. DISCUSSION AND CONCLUSIONS

Haplotype analysis is a genetic technique used to determine the particular nesting population of a sea turtle encountered outside its nesting period. This methodology relies on probabilistic computations to deduce the likely origin of the turtle within a nesting population. The significance of haplotype analysis rests in its capacity to elucidate the complex population dynamics of sea turtles, a critical undertaking due to their dual status as both endangered and extensively motile species (Tolve et al., 2018).

Illustratively, Tolve et al. (2018)'s investigation centers on the foraging population of loggerhead turtles inhabiting the Adriatic region. The application of haplotype analysis have unveiled variances in genetic diversity across regions of Adriatic. By leveraging this analytical approach, Tolve et al. computed the probabilities associated with diverse nesting sites contributing to the Adriatic Stock. Evidently, the nesting locations in Greece and Crete emerged as the preeminent rookeries contributing to the foraging populace in the Adriatic domain.

Turkozan et al. (2018) applied haplotype analysis to examine the habitat utilization of loggerhead sea turtles in the eastern Mediterranean. Their study revealed that loggerhead turtles foraging along the eastern Mediterranean coastline of Turkey predominantly trace their origins to Cyprus.

In their 2023 study, Kaska et al. has also employed haplotype analysis, revealing five haplotypes at Turkish nesting sites, with one novel haplotype shared by two individuals. Variability in polymorphic traits was observed across Mediterranean management units, particularly higher in Libya despite fewer samples. Furthermore, Libya disclosed two previously unrecorded haplotypes. The study enhances the understanding of loggerhead sea turtle dynamics, highlighting the presence of haplotypes in other rookeries within the Mediterranean population that were previously thought to be site-specific (Kaska et al., 2023).

In conclusion; Haplotype analysis provides insight about the complex population dynamics of sea turtles. By enabling the identification of nesting populations with greater genetic diversity, haplotype analysis facilitaties targeted conservation efforts focused on safeguarding nests within these specific nesting regions. It is critical protect the genetic diversity of sea turtles through haplotype analysis.

REFERENCES

- Abreu-Grobois, F. A., Horrocks, J. a., Formia, A., Dutton, P. H., LeRoux, R. a., Velez-Zuazo, X., Soares, L. S., & Meylan, A. B. (2006). New mtDNA D-loop primers which work for a variety of marine turtle species may increase the resolution of mixed stock analysis. Proceedings of the 26th Annual Symposium on Sea Turtle Biology, Book of Abstracts, January, 179.
- Bass AL, Epperly SP, B.-M. J. (2004). Multi-year analysis of stock composition of a loggerhead turtle (Caretta caretta) foraging habitat using maximum likelihood and Bayesian methods. Conserv Genet, 5, 783–796.
- Bjorndal KA, B. A. (2008). Annual variation in source contributions to a mixed stock: implications for quantifying connectivity. Mol Ecol, 17, 2185–2193.
- Bolker B. Okuyama T. (2014). Mixed stock analysis in R: getting started with the mixstock package.
- Bolten, A. B., Bjorndal, K. A., Martins, H. R., Dellinger, T., Biscoito, M. J., Encalada, S. E., & Bowen, B. W. (1998). Transatlantic developmental migrations of loggerhead sea turtles demonstrated by mtDNA sequence analysis. Ecological Applications, 8(1), 1–7. <u>https://doi.org/10.1890/1051-0761(1998)008[0001:TDMOLS]2.0.CO;2</u>
- Bowen, B. W., & Karl, S. A. (2007). Population genetics and phylogeography of sea turtles. Molecular Ecology, 16(23), 4886–4907. <u>https://doi.org/10.1111/j.1365-294X.2007.03542.x</u>
- Ferrera, A., Formia, A., Ciofi, C., Natali, C., Agyekumhene, A., & Allman, P. (2021). Genetic structure of olive ridley sea turtles (Lepidochelys olivacea) in Ghana, West Africa. Journal of Experimental Marine Biology and Ecology, 544(August), 151614. <u>https://doi.org/10.1016/j.jembe.2021.151614</u>
- Hall TA. (1999). BioEdit: a user-friendly biological sequence alignment editor and analysis program for Windows. Nuclear Acids Symposium Series, 41, 95–98.
- Hsieh, H. M., Huang, L. H., Tsai, L. C., Liu, C. L., Kuo, Y. C., Hsiao, C. T., Linacre, A., & Lee, J. C. I. (2006). Species identification of Kachuga tecta using the cytochrome b gene. Journal of Forensic Sciences, 51(1), 52–56. https://doi.org/10.1111/j.1556-4029.2005.00004.x
- Kaska A, Bagci H, K. Y. (2001). Genetic material collection of sea turtles and PCR amplifications. In: Margaritoulis D, Demetropoulos A (eds) Proceedings of the First Mediterranean Conference on Sea Turtles. Barcelona Convention-Bern Convention-Bonn Convention (CMS). Nicosia, Cyprus., 147–150.
- Kaska, A., Koç, G., Sözbilen, D., Salih, D., Glidan, A., Elsowayeb, A. A., Saied, A., Margaritoulis, D., Theodorou, P., Rees, Al. L., Snape, R., Broderick, A., Godley, B., Beton, D., Ozkan, M., Jribi, I., Ismail, M. Ben, Hmida, A. Ben, Badreddine, A., ... Kaska, Y. (2023). Increased sample size provides novel insights into population structure of Mediterranean loggerhead sea turtles. Conservation Genetics Resources, 15(1–2), 67–75. https://doi.org/10.1007/s12686-023-01303-9
- Leigh, J. W., & Bryant, D. (2015). POPART: Full-feature software for haplotype network construction. Methods in Ecology and Evolution, 6(9), 1110–1116. <u>https://doi.org/10.1111/2041-210X.12410</u>
- Librado, P., & Rozas, J. (2009). DnaSP v5: A software for comprehensive analysis of DNA polymorphism data. Bioinformatics, 25(11), 1451–1452. <u>https://doi.org/10.1093/bioinformatics/btp187</u>
- Loisier, A., Savelli, M. P., Arnal, V., Claro, F., Gambaiani, D., Sénégas, J. B., Cesarini, C., Sacchi, J., Miaud, C., & Montgelard, C. (2021). Genetic composition, origin and conservation of loggerhead sea turtles (Caretta caretta) frequenting the French Mediterranean coasts. Marine Biology, 168(4), 1–15. <u>https://doi.org/10.1007/s00227-021-03855-6</u>
- Rees, Al. F., Carreras, C., Broderick, A. C., Margaritoulis, D., Stringell, T. B., & Godley, B. J. (2017). Linking loggerhead locations: using multiple methods to determine the origin of sea turtles in feeding grounds. Marine Biology, 164(2), 1–14. <u>https://doi.org/10.1007/s00227-016-3055-z</u>
- Sambrook JF, R. D. (eds). (2001). Cold Spring Harbor Laboratory Press, Cold Spring Harbor. Molecular Cloning: A Laboratory Manual.

- Tolve, L., Casale, P., Formia, A., Garofalo, L., Lazar, B., Natali, C., Novelletto, A., Vallini, C., Bužan, E., Chelazzi, G., Gaspari, S., Fortuna, C., Kocijan, I., Marchiori, E., Novarini, N., Poppi, L., Salvemini, P., & Ciofi, C. (2018). A comprehensive mitochondrial DNA mixed-stock analysis clarifies the composition of loggerhead turtle aggregates in the Adriatic Sea. Marine Biology, 165(4). <u>https://doi.org/10.1007/s00227-018-3325-z</u>
- Turkozan, O., Yılmaz, C., Uçar, A. H., Carreras, C., Ergene, S., Aymak, C., & Karaman, S. (2018). Local differentiation in the origin of stranded loggerhead turtles, Caretta caretta, within an eastern Turkey foraging area. Ocean and Coastal Management, 153(July 2017), 70–75. <u>https://doi.org/10.1016/j.ocecoaman.2017.12.011</u>

Evaluation of Final Consumption Expenditures in Turkey by Quantile Regression and Polynomial Regression Methods

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Abstract: In economics, the term consumption is a key concept, meaning the use of goods and services for the satisfaction of the individual or society. Expenditures made by households on final goods and services represent final consumption. Statistics allows to obtain important outputs in economic matters such as consumption expenditures. The main objectives of this study are to determine the factors affecting final consumption expenditures in Turkey, to analyze the effects of these factors on consumption expenditures by Quantile Regression Method and to make forward-looking predictions with Polynomial Regression Method. In this study, the determinants of consumption expenditures in the Turkish economy and their relationship with other variables are explained. By analyzing the changes in consumption expenditures at different levels, data forecasts for the future are made on a certain variable. For this purpose, the unemployment rate, inflation, income inequality, Gross Domestic Product (GDP), population density, exchange rate and interest rate variables between the years 2002-2021 created the data set. In addition to the quantile regression model, the effects of the variables were examined comparatively by using the least squares model. The results showed that the variables had different effect levels in the quantile regression analyzes performed at 0.25, 0.50 and 0.75 quantile points. Compared to least squares model estimates, quantile regression analyzes provided a more detailed explanation. When the results are examined, the only variable found to be significant for the consumption expenditures variable according to the least squares model is the exchange rate variable. In this context, estimated values for the exchange rate variable until 2030 were obtained with the polynomial regression method, and a different perspective is presented for decision makers.

Keywords: Final Consumption Expenditures, Polynomial Regression Analysis, The Least Squared Method, Turkey, Quantile Regression Analysis.

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1. INTRODUCTION

Expenditures made for goods and services that directly meet the needs of individuals are called consumption expenditures. Some of the main factors affecting consumption expenditures in the literature; national wealth and national income level, market interest rates, inflation rates, sociocultural factors (Altan and Göktürk, 2007). Economists take the view that final consumption expenditures are generally a function of income. However, the type of income that affects the consumption expenditures in question in the economy or the absolute situation contains uncertainty (Almasifard, 2013).

One of the most important goals in globalizing economies is to ensure the production of effective policies in order to increase the welfare level of the society. The concept of public size is important in the policy making process of decision makers. As the needs of individuals increase, the size of public expenditures should be well planned. For example, when the unemployment rate is high, the state may try to increase the level of total demand by giving importance to current expenditures and thus prevent unemployment. In addition, increased public expenditures may lead to an increase in taxes and the unemployment level may increase. In this context, it is clear that final public consumption expenditures have an impact on the general price stability and economic policies of countries (Bölükbaş, 2018).

There are many studies in the literature that statistically examine the relationship between the factors affecting public final consumption expenditures. One of the advanced regression methods, which is one of the important subjects of statistics, "quantile regression" is frequently used in the literature. Some of the studies using the quantile regression method are summarized:

Awosusi et al. (2022) proposed an Sustainable Development Goal framework for BRICS economies and suggested that this framework could be used as a model for other regions. The analysis, carried out using Moment Quantile Regression with fixed effects, investigates the impact of biomass energy use on the ecological footprint between 1992 and 2018, taking into account the role of gross capital formation, natural resources and globalization. The findings of the research

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show that globalization and use of biomass energy at all quantile levels (from 10% to 90%) are effective in reducing environmental degradation. The study by Wei and Ullah (2022) examines the role of tourism and Information and Communications Technology industry in economic development and their effects on environmental quality in 37 Asian economies between 1996-2019 using Fully-modified Ordinary Least Squared (FMOLS), Dynamic Ordinary Least Squared (DOLS) and quantile regression techniques. In FMOLS and DOLS models, it has been seen that tourism and digitalization improve environmental quality. In the quantile regression model, tourism arrivals and tourism income estimations have a positive effect from low quantiles to high quantiles, while it turns into a negative effect in higher quantiles. The predicted coefficients of the digital infrastructure in the robust quantile regression model, on the other hand, show that it has a negative effect in different quantile ranges. Bilgili et al. (2022) examines the impact of energy access on the environment using panel quantile regression method, using panel data for 36 Asian countries for the period 1997-2017. The findings reveal that CO_2 damage decreases with economic development. It has also been found that increased access to electricity reduces CO₂ damage, the use of renewable energy reduces CO₂ damage, and agricultural activities increase CO₂ damage. Liu et al. (2022) focus on the re-evaluation of technology policies for E-7 countries in their study. The effect of various factors on CO₂ emissions was investigated by least squares, panel quantile regression and variance decomposition analysis methods. According to the findings of quantile regression, technological innovation negatively affects carbon emissions in medium and high quantiles, institutional quality is significantly and negatively related to carbon emissions between the 40th and 80th quantiles, renewable energy consumption reduces carbon emissions, and economic growth is in the 40th to 90th quantiles. It has been seen that it has a statistically significant and positive effect on carbon emission among the population, while the population has a statistically significant effect on the 10th and 30th quantiles and has a positive effect on environmental pollution. Li et al. (2022) applied the panel quantile regression method using 1991-2019 data in BRICST economies to examine the factors of renewable energy consumption and to investigate the effect of green environmental policy on renewable energy consumption. The panel quantile regression results confirm that economic growth and non-renewable energy have positive effects on renewable energy consumption. However, the consumer price index and CO₂ emissions negatively affect renewable energy consumption. Estimates of the environmental tightness index were determined as positive in low quantiles and negative in high quantiles. Huo et al. (2022) examines the relationship between globalization and high carbon emissions for a sustainable environment in the UK during the period 1970-2019. Analyzes using wavelet consistency and quantile regression methods reveal a significant positive relationship between CO₂ emissions and globalization, economic growth and coal consumption. Liu et al (2023) investigated the effect of crude oil price volatility on stock markets in the economic sectors of China, Japan, USA, France and Germany between 2000 and 2020 by using quantile-quantile regression and double quantile regression methods. The findings show that the volatility of crude oil prices has a negative effect on stock returns. Demir et al. (2022), examined the effects of FinTech on financial inclusion and income inequality. The relationship between financial market imperfections and new financial technologies has been discussed with the quantile regression method for the years 2011, 2014 and 2017 of 140 countries. The results show that FinTech indirectly reduces income inequality due to its effects on financial inclusion. Financial inclusion reduces income inequality across all quantiles. Opoku and Aluko (2021), using ecological footprint to represent environmental degradation, examined the heterogeneous effects of industrialization on the environment in 37 African countries between 2000 and 2016 by killer regression method. As a result of the study, it was observed that industrialization increased environmental degradation by 10%-30% in cantilevers and reduced it by 40%-90% in cantilevers.

In this study, the final consumption expenditures of the state are used to represent the public size. The determinants of consumption expenditures in the Turkish economy and their relationship with other variables are explained. For this purpose, quantile regression method is used. By analyzing the changes in consumption expenditures at different levels, data estimation for the future on a certain variable is made with polynomial regression. Differences from the methods used in the studies discussed and time series estimation provide new contributions to the literature.

2. MATERIAL AND METHODS

In this study, the determinants of final consumption expenditures in the Turkish economy and their relationship with other variables are explained. By analyzing the changes in consumption expenditures at different levels, data forecasts for the future are made on a certain variable. For this purpose, the unemployment rate, inflation, income inequality, Gross Domestic Product (GDP), population density, exchange rate and interest rate variables between the years 2002-2021 are considered as data set (The World Bank, 2023; CBRT EDDS, 2023).

Factors affecting final consumption expenditures in Turkey are determined and the effects of these factors on consumption expenditures are analyzed by least squares method and quantile regression method. In addition, according to the findings obtained as a result of the analysis, prospective data estimation is made with the polynomial regression method.

2.1. The Least Squares Method

The purpose of multiple linear regression analysis is to estimate the dependent variable with the help of independent variables and to determine the effects of independent variables on the dependent variable. In this analysis method, coefficient estimation is performed using the least squares method (Güven, 2021). The least squares method is an important technique that is frequently used among statistical analysis and regression models. Its main purpose is to maximize the performance of the model when the error terms have normal distribution and homogeneous variance. That is, it estimates the parameters of a linear model that minimizes the error between the observed and expected data (Cankaya et al., 2019).

The matrix form of the multiple regression model is as in Equation (1).

Υ=Χβ+ε

(1)In this equation, Y represents the dependent variable vector, X the independent variables vector, β the coefficients vector, and ε the error vector. In multiple regression analysis, Equation (2) is used to estimate the coefficient vector using the least squares method (Alpar, 2011).

 $\hat{\beta} = [X'X]^{-1}X'Y$

(2)

(3)

(4)

In order to successfully apply the least squares method, certain assumptions need to be fulfilled. Some important assumptions of the method can be listed as follows:

1. Linearity: The regression model should be linear in the coefficients.

2.Independence: Observation units should be independent from each other.

3. Constant variance (Homoscedasticity): The variance of the error terms should not change depending on the levels of the independent variables.

4. The mean of the error terms is zero: The expected value of the error terms should be zero, depending on the levels of the arguments.

5. There is no linear relationship between independent variables: There should be no multicollinearity between independent variables. That is, the independent variables should not be strictly related to each other.

6. Error terms are uncorrelated: The correlation between error terms must be zero.

Ensuring these assumptions is important to increase the accuracy and reliability of the analysis. The least squares method is the basis of regression analysis and is applied in many disciplines, from economics to engineering, from social sciences to physics and biology. Despite the popularity and wide use of the method, some problems are encountered in practice. In particular, it has high sensitivity to outliers. Robust techniques are used to overcome this problem and studies are continuing in this area (Abdi, 2007).

2.2. Quantile Regression Method

The quantile regression model proposed by Koenker and Bassett in 1978 is used to deal with some situations where the ordinary least squares method cannot cope. Although the ordinary least squares method is a widely used method in parameter estimation, its performance may be low in some data distributions and in the presence of outliers. The quantile regression method was developed to overcome this limitation of the Least Squares approach (Öztürk, 2023). Since it is a more flexible method, it does not need some assumptions and has the ability to make reliable and robust predictions. Outlier resilience provides the ability to more effectively deal with real-world data challenges. This approach allows to analyze various features of the distribution of the data, while also taking into account possible unobserved heterogeneities (Ponomareva, 2010). In addition to classical regression modeling, it can be used as a descriptive and graphical representation tool in the analysis of transformed data (Staffa et al., 2019). Quantile Regression is an alternative approach in the linear model to estimate the conditional quantities in the distribution of the dependent variable. Unlike other classical regression methods, this method models quantile values, not the mean value (Waldmann, 2018). Thus, a more comprehensive analysis opportunity is provided (Leping, 2005).

The functional form of the quantile regression is given in Equation (3).

 $y_i = x_i \beta_{\theta} + u_{\theta}$

In this equation, θ represents the quantile values, y the dependent variable vector, x the independent variables vector, u_{θ} the error vector, and $\theta \in (0, 1)$. We can estimate the dependent variable y_i using the conditional quantiles of the x_i independent variables. prediction can be made.

We can express the conditional quantile function as follows: It is given in Equation (4).

 $Q_{\theta}(y_i \mid x_i) = x_i \beta_{\theta}$

In the quantile regression model, the β_{θ} parameter is obtained as in Equation (5) by minimizing the objective function; $\min_{\beta} \frac{1}{n} \left\{ \sum_{i: y_i \ge x_i \beta} \theta | y_i - x_i \beta | + \sum_{i: y_i < x_i \beta} (1 - \theta) | y_i - x_i \beta | \right\}$ (5)

As can be clearly understood from the equations, coefficient estimates in quantile regression analysis generally vary between different quantiles (Erilli and Çamurlu, 2018). Different aspects of the data can be examined by selecting the desired quantile point. The use of this method can be an important analysis tool to obtain strong results, especially in data sets with outliers.

2.3. Polynomial Regression Method

The data set obtained by measuring one or more variables for a certain period or time interval is called time series. Using historical data with time series, future data can be predicted. One of the methods frequently used for time series is regression analysis (Nebati et al., 2021). The dependent variable, known as the response or outcome variable, is affected by the independent variable, which is the factor or explanatory variable. Apart from estimating the status of a dependent or independent variable in the future time interval with regression analysis, the relationships between variables can also be modeled mathematically (Yergök and Acı, 2019).

The polynomial regression method is essentially a special case of multivariate linear regression (Meyers et al., 2016). Only one independent variable (x) is considered in the polynomial regression analysis. For time series, the variable x is "period (day, month, year, etc.)". In this study, the variable x is taken as "year". For the polynomial regression model, when the degree of the independent variable x is "3", the relevant polynomial regression model is called the "cubic regression model". The cubic regression model is given in Equation (6) (Güler and Kandemir, 2022).

 $y_i = \beta_0 + \beta_1 x_i + \beta_2 x_i^2 + \beta_3 x_i^3 + \varepsilon$

(6)

In this equation, y is the dependent variable, β_0 is the regression constant, β_1 , β_2 , β_3 are the regression coefficients, x is the independent variable, ξ is the error term.

3. RESULTS

In this study, the indicators affecting consumption expenditures in Turkey are examined by least squares and quantile regression methods, and estimated values until 2030 are obtained with the polynomial regression method. The analysis is carried out with the annual data of the 2002-2021 period obtained from the Central Bank of the Republic of Turkey (CBRT) Electronic Data Distribution System (EVDS) and the World Bank (The World Bank) databases and the number of observations is determined as "20".



Figure 1. Final consumption expenditures in Turkey between 2002-2021 periods

The graph of change in final consumption expenditures for the period 2002-2021 in Turkey is presented in Figure 1. When the graph is examined, it is seen that there are fluctuations between 2002 and 2010 and consumption expenditures are at different levels every year. A continuous decreasing trend is observed in the 2010-2015 period. This may indicate an economic recession or an unsustainable restraint in consumption expenditures. However, it can be said that since 2015, consumption expenditures have changed into a similar structure with the fluctuations between 2002 and 2010. When the consumption expenditures rates are analyzed over the 20 years period, it is seen that the lowest rate is recorded in 2021.

The dependent and independent variables used in the study and the descriptive statistics for these variables are given in Table 1.

Table 1. Descriptive statistics of the data set							
Variable	Number of Observations	Mean	Standard deviation	Min	Max		
Consumption Expenditures	20	74.644	2.409	68.351	77.904		
Unemployment rate	20	10.5	1.491	8.15	13.67		
Inflation	20	12.432	8.763	6.251	44.964		
Income inequality	20	40.93	1.414	38.4	42.9		
GDP	20	5.537	3.959	-4.823	11.353		
Population density	20	97.991	8.133	85.74	110.267		
Exchange rate	20	2.807	2.156	1.292	8.885		
Interest rate	20	21.435	10.579	11.797	54.682		

3.1. Results of The Least Squares and Quantile Regression Methods

In the study, the least squares method, which is one of the classical regression methods, and the quantile regression method are used to compare the performance of the least squares model. The quantile regression method is examined for three different quantile points (0.25, 0.50, 0.75) to analyze the change in consumption expenditures at different levels. The quantile regression method can determine the factors affecting consumption expenditures and allows us to determine how the factors affecting consumption expenditures change at different levels. Analyzes are performed using the STATA program.

In the table below, the results of the estimated Least Squares Model are given in Table 2.

Table 2. Results of the Least Squales Model				
Variables	The Least Squares Model			
Unemployment rate	0.605			
	(0.296)			
Inflation	0.042			
	(0.083)			
Income inequality	-0.127			
	(0.296)			
GDP	0.064			
	(0.094)			
Population density	-0.061			
	(0.103)			
Exchange rate	-1.078*			
-	(0.320)			
Interest rate	-0.036			
	(0.092)			

Table 2 Results of the Least Squares Model

¹ The first rows in each cell represent the estimated coefficients, while the second rows in parentheses show the standard errors. The * symbol indicates statistical significance at the 5% level.

After the least squares model, the final consumption expenditures, which are the dependent variable, are examined via the normality test. Kolmogorov-Smirnov and Shapiro-Wilk tests are commonly used in studies in the literature. In this study, the Shapiro-Wilk test is preferred for the normality test due to the small number of data, and the results are given in Table 3.

Table 3. Normality test						
	Shapi	iro-Wilk Test				
	Statistic	df	Sig.			
Consumption Expenditures	.964	20	.619			

The hypotheses tested here are.

H₀: The data are normally distributed.

H₁: Data are not suitable for normal distribution.

According to Table 3, the significance value (sig.) was obtained as 0.619. Since this value is greater than 0.05, H_0 cannot be rejected, and it can be said that the data conform to a normal distribution.

After the least squares method, the quantile regression method is applied and the results are given in Table 4.

Variables	Qu	antile Regression Mod	lel
variables	0.25	0.50	0.75
Unemployment rate	1.135*	0.869*	0.276
	(0.178)	(0.368)	(0.283)
Inflation	0.045	0.090	-0.030
	(0.050)	(0.103)	(0.079)
Income inequality	-0.531*	-0.143	-0.001
	(0.177)	(0.367)	(0.282)
GDP	0.219*	0.095	-0.087
	(0.056)	(0.117)	(0.090)
Population density	0.009	-0.096	-0.300*
	(0.062)	(0.128)	(0.098)
Exchange rate	-1.323*	-1.167*	-0.424
	(0.191)	(0.397)	(0.305)
Interest rate	-0.004	-0.100	0.063
	(0.055)	(0.114)	(0.088)

Table 4	Results	of the	Quantile	Regression	Model ¹

¹ The first rows in each cell represent the estimated coefficients, while the second rows in parentheses show the standard errors. The * symbol indicates statistical significance at the 5% level.

When the results are examined, the only variable found to be significant for final consumption expenditures according to the least squares method is the exchange rate variable. A negative relationship was found between final consumption expenditures and the exchange rate. When the behavior of final consumption expenditures at different quantile levels is examined, unemployment rate, income inequality, GDP and exchange rate variables were found to be statistically significant for years with low expenditures (at 0.25 quantile point). With the increase in unemployment rate, final consumption expenditures increase. Similarly, an increase in GDP increases final consumption expenditures. Income inequality and the increase in exchange rates have a negative effect on final consumption expenditures. For years with high final consumption expenditures (at 0.75 quantile point), the only statistically significant variable was population density, and population density affects final consumption expenditures negatively. While unemployment rate and exchange rate variables are statistically significant in years when final consumption expenditures are at medium levels (0.50 quantile point), other variables do not affect consumption expenditures. At this point, the increase in the exchange rate causes a decrease in final consumption expenditures. On the other hand, with the increase in unemployment rate, final consumption expenditures also increase.

3.2. Results of Polynomial Regression Method

In the analyzes within the scope of this study, the only variable found to be significant for the consumption expenditures variable according to the least squares model is the exchange rate variable. In this context, estimated values for the exchange rate variable until 2030 are obtained with the polynomial regression method. The exchange rate trend graph of the past data (2002-2021) is given in Figure 2.



Figure 2. Trend graph of exchange rate

In the polynomial regression analysis, the cubic regression model is created by taking the "k" value of 3. The equation of the model obtained in Excel is given in Equation (7).

$y' = 0,0027x^3 - 0,0485x^2 + 0,2459x + 1,1352$ (7)

 R^2 (Coefficient of Determination) shows what percentage of the change in the dependent variable is explained by the independent variable. As the R^2 value approaches 1, the fit of the model increases. The R^2 value for the polynomial regression model established in this study was calculated as 0.9952.

The graph with the model equation, R^2 value and trend lines is given in Figure 3.



Figure 3. Exchange rate polynomial regression equation, R^2 and trend lines

With the model equation obtained, the estimated exchange rate values for the future periods were calculated. The obtained values are given in Table 5.

Table 5. Estimated exchange rate values						
Years	Estimated Exchange Rate Value					
2022	9.9153					
2023	11.8206					
2024	13.9853					
2025	16.4256					
2026	19.1577					
2027	22.1978					
2028	25.5621					
2029	29.2668					
2030	33.3281					

Table	5.	Estimated	exchange	rate	values

The estimated values obtained with a high degree of accuracy in Table 5 are the standard values estimated at the current balance of final public consumption expenditures. Only "time dependence" is considered as the independent variable.

4. DISCUSSION AND CONCLUSIONS

Regression analysis is a statistical method used to understand the relationship between data, to express this relationship with a mathematical structure and to predict future values. It tries to determine the determinants of the dependent variable, to understand the relationships between the variables, and to reveal the degree and direction of these relationships. In this study, quantile regression method, one of the powerful regression methods that has become popular in recent years, was used to examine the factors affecting final consumption expenditures in Turkey, and the future values of the exchange rate obtained as a significant variable were estimated by polynomial regression method. In addition to the quantile regression model, the effects of the variables were examined comparatively by using the least squares model. The results showed that the variables had different effect levels in the quantile regression analyzes performed at 0.25, 0.50 and 0.75 quantile points. The results show that the direction and magnitude of the relationship between dependent and independent variables are different at different quantile points, and a variable that is significant at one quantile point may be meaningless at other points. In other words, it is seen that the factors affecting final consumption expenditures in Turkey provide different levels of influence at different quantile points.

In this study, the changes in final consumption expenditures are analyzed and a statistical perspective is presented to the decision makers. The scope of the study can be expanded by including different dependent and independent variables.

Conflict of Interest

The authors have no conflicts of interest to declare.

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REFERENCES

Abdi, H. (2007). The method of least squares. Encyclopedia of measurement and statistics, 1, 530-532.

- Almasifard, M. (2013). An econometric analysis of financial development's effects on the share of final consumption expenditure in gross domestic product (Master's thesis, Eastern Mediterranean University (EMU).
- Alpar, R. (2011). Multivariate statistical methods, third ed. Detay Press, Ankara.
- Altan, M., & Göktürk, İ. E. (2007). The Effect of Credit Cards on Total Private Final Consumption Expenditures in Turkey: A Multiple Regression Analysis. The Journal of Selcuk University Social Sciences Institute, (18), 25-47.
- Awosusi, A. A., Adebayo, T. S., Altuntaş, M., Agyekum, E. B., Zawbaa, H. M., & Kamel, S. (2022). The dynamic impact of biomass and natural resources on ecological footprint in BRICS economies: a quantile regression evidence. Energy Reports, 8, 1979-1994.

- Bilgili, F., Öztürk, I., Kocak, E., Kuşkaya, S., & Cingöz, A. (2022). The nexus between access to electricity and CO₂ damage in Asian Countries: The evidence from quantile regression models. Energy and Buildings, 256, 111761.
- Bölükbaş, M. (2018). The Causality Relationship Between Government Final Consumption Expenditures and Unemployment: An Analysis For Turkey. IV. International Conference on Applied Economics and Finance. Kuşadası, Turkey.
- CBRT EEDS (2023). Central Bank of the Republic of Turkey Electronic Data Delivery System. https://evds2.tcmb.gov.tr/ (accessed 10 May 2023)
- Çankaya, S., Eker, S., & Abacı, S. H. (2019). Comparison of Least Squares, Ridge Regression and Principal Component approaches in the presence of multicollinearity in regression analysis. Turkish Journal of Agriculture-Food Science and Technology, 7(8), 1166-1172.
- Demir, A., Pesqué-Cela, V., Altunbas, Y., & Murinde, V. (2022). Fintech, financial inclusion and income inequality: a quantile regression approach. The European Journal of Finance, 28(1), 86-107.
- Erilli, N., & Çamurlu, S. (2018). Bootstrap Estimation in Quantile Regression Analysis. Erciyes University Journal of the Institute of Science and Technology, 35(2), 16-25.
- Güler, E., & Kandemir, S. Y. (2022). Estimation of CO₂ Emissions by OECD Countries Using Linear and Cubic Regression Analyzes. European Journal of Science and Technology, (34), 175-180.
- Güven, E. (2021). Investigation of Least Squares Assumptions and Alternative Approach for Multiple Connections: Ridge Regression. https://www.istmer.com/en-kucuk-kareler-varsayimi-ridge-regression/ (accessed 22 Jul 2023)
- Huo, C., Hameed, J., Sharif, A., Albasher, G., Alamri, O., & Alsultan, N. (2022). Recent scenario and nexus of globalization to CO₂ emissions: evidence from wavelet and Quantile on Quantile Regression approach. Environmental Research, 212, 113067.
- Leping, K. O. (2005). Public-private sector wage differential in Estonia: evidence from quantile regression. University of Tartu Faculty of Economics and Business Administration Working Paper, (39).
- Li, X., Ozturk, I., Raza Syed, Q., Hafeez, M., & Sohail, S. (2022). Does green environmental policy promote renewable energy consumption in BRICST? Fresh insights from panel quantile regression. Economic research-Ekonomska istraživanja, 35(1), 5807-5823.
- Liu, F., Umair, M., & Gao, J. (2023). Assessing oil price volatility co-movement with stock market volatility through quantile regression approach. Resources Policy, 81, 103375.
- Liu, H., Anwar, A., Razzaq, A., & Yang, L. (2022). The key role of renewable energy consumption, technological innovation and institutional quality in formulating the SDG policies for emerging economies: evidence from quantile regression. Energy Reports, 8, 11810-11824.
- Meyers, L.S., Gamst, G., & Guarino, A.J. (2016). Applied multivariate research: Design and interpretation, first ed., SAGE Publications, New York.
- Nebati, E. E., Murat, T. A. Ş., & Ertaş, G. (2021). Demand Forecasting for Electricity Consumption in Turkey: Comparison with Time Series and Regression Analysis. European Journal of Science and Technology, (31), 348-357.
- Opoku, E. E. O., & Aluko, O. A. (2021). Heterogeneous effects of industrialization on the environment: Evidence from panel quantile regression. Structural Change and Economic Dynamics, 59, 174-184.
- Öztürk, K. N. (2023). Determining The Main Determinants of Happiness with Macroeconomic and Social Indicators (Master Thesis). Yıldız Technical University, Institute of Science, Istanbul, Turkey.
- Ponomareva, M. (2010). Quantile regression for panel data models with fixed effects and small T: Identification and estimation. University of Western Ontario.

Staffa, S. J., Kohane, D. S., & Zurakowski, D. (2019). Quantile regression and its applications: a primer for anesthesiologists. Anesthesia & Analgesia, 128(4), 820-830.

The World Bank (2023). https://databank.worldbank.org/source/world-development-indicators (accessed 08 May 2023)

Waldmann, E. (2018). Quantile Regression: A Short Story on How and Why. Statistical Modelling, 18(3-4), 203-218.

- Wei, L., & Ullah, S. (2022). International tourism, digital infrastructure, and CO₂ emissions: fresh evidence from panel quantile regression approach. Environmental Science and Pollution Research, 29(24), 36273-36280.
- Yergök, D. & Acı, M. (2019). An Alternative Approach for Daily Demand Prediction in Mass Meal Production: Regression Learner. European Journal of Science and Technology, (Special Issue), 64-73.

Green Synthesis of Lichen-Based Nanocomposites and Their Cytotoxic Activities

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Abstract: Green synthesis of nanoparticles is considered safe and environmentally friendly compared to traditional nanoparticle production methods. The synthesis of nanomaterials using lichen extracts is known as a promising and environmentally friendly, and cost-effective biological synthesis process. Lichens contain many secondary metabolites. These metabolites act as bioreducers to prevent the side effects of free radicals in the human body. It was concluded that the secondary metabolites in lichens, besides their medicinal effects, have a very good potential to reduce and stabilize metallic salts, as well as convert them into metal nanoparticles via an electron transfer mechanism. Therapies used in cancer treatment based on nanotechnology have attracted a lot of attention in recent years due to their small side effects and high specificity. The defensive nature of lichens and their excellent anti-cancer potential against a wide variety of cancers make lichens important from a pharmaceutical point of view. In line with these properties of lichens, lichen-based syntheses will be mentioned as a source of bioactive metabolites in the green synthesis of nanocomposites. The characterization methods used to determine the obtained nanoparticles were investigated. In addition, cytotoxic effects of lichen-based nanocomposites were mentioned. In studies, lichen extracts have been used as an effective reducing and capping agent for NPs (nanoparticles) due to the abundance of these organisms and their environmental sustainability. It has been stated that the functional groups of secondary metabolites obtained from lichen extracts are effective in preventing the aggregation of NPs, thus enabling the production and stabilization of NPs. Lichen-based NPs show great potential as therapeutic agents serving as antimicrobials, antidiabetics and antioxidants. Lichen-mediated nanoparticles studies show that lichens are stable, cost-effective, and biocompatible, making them ideal candidates for antimicrobial agents. Generally, studies are on antimicrobial activities. Studies on cytotoxicity are very limited.

Keywords: Green synthesis, Lichen, Nanocomposites, Cytotoxicity

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1. INTRODUCTION

Nanotechnology emerges as an interdisciplinary technology in which engineering-based fields such as materials science and medicine, especially basic sciences such as physics, chemistry and biology. The prefix nano is derived from the Greek word nanos meaning dwarf and means one billionth of something. The term nanoparticle describes particles with a length between 0.1 and 1000 nm in any spatial dimension (Narayanan et al., 2010).

Different methods have been developed for the synthesis of metallic nanostructures in solution environment. The aim of most of these methods is that the obtained nanostructures have a certain size and morphology. Biosynthesis is used in biology as a term denoting chemical processes in living organisms. These processes, carried out using energy, enable more complex products to be obtained from simple materials. Its definition in the field of nanotechnology is to synthesize nanoparticles by using living organisms or chemicals such as plant extracts, microbes, fungi, yeast, algae, and viruses. The classical synthesis methods of metal nanoparticles have many disadvantages such as being complex and expensive, using toxic substances, and not suitable for pharmacological and biomedical applications.

Biosynthesis has become a frequently used method today due to its advantages such as being simple and economical, not requiring the use of toxic substances, and being suitable for pharmacological and biomedical applications. The synthesis method, also called green chemistry, is used in the synthesis of metallic nanoparticles. Substances such as fungi, yeast, bacteria, and plant extracts are used as reducing agents in the biosynthesis of metal nanoparticles (Bar et al., 2009, Philip et al., 2010, Dubey et al., 2010).

Bimetallic nanoparticles (NP) have enhanced properties such as antimicrobial, anticancer and photocatalytic activity due to the synergistic effects of their components. The unmet needs of current cancer treatments are spurring researchers to new treatment approaches, especially natural products.

It has been found that lichens have a potentially reducible activity to produce different types of nanomaterials as metal and metal oxide NPs (Hamida and Abdelmeguid, 2021).

2. SYNTHESIS OF LICHEN-BASED NANOPARTICLES

Lichens are natural resources used in the treatment of various diseases since ancient times. They are among the most fascinating organisms on earth and arise from the symbiotic relationship between fungi (ascomycetes) and green algae or blue-green algae (Bates et al., 2011). More than 1050 secondary metabolites have been isolated from lichens and these metabolites have been found to have antibacterial, antiviral, anti-analgesic, antipyretic and antiproliferative activities (Molnár and Farkas, 2010). The defensive nature of lichens is a crucial point from a pharmaceutical point of view, as they have excellent anti-cancer potential against a wide variety of cancers (Zambare and Christopher, 2012). Today, synthetic nanomaterials pose a great challenge to human life, mostly because they are not environmentally friendly and are produced in expensive and harsh conditions. In some cases, their application is limited due to their adsorption to the surfaces of chemicals and hazardous materials. Therefore, nowadays, researchers are trying to replace and improve traditional nanomaterial synthesis methods with green, economical and safe methods (Sajadi, Kolo, Abdullah, et al., 2018; Zhang et al., 2018). In studies on lichens, it has been determined that it synthesizes secondary metabolites with antioxidant properties. These metabolites act as bioreducers to prevent the side effects of free radicals in the human body. It was concluded that the antioxidant phytochemicals in lichens, besides their medicinal effects, have a very good potential to reduce and stabilize metallic salts, as well as convert them into metal nanoparticles via an electron transfer mechanism (Nugraha et al., 2019; Jayanthi, et al., 2012).

From the past to the present, lichens have been used to meet people's basic life needs and even to protect and improve health (Ranković et al., 2011; Walker and Lintott, 1997). In studies, lichen extracts have been used as an effective reducing and capping agent for NPs (nanoparticles) due to the abundance of these organisms and their environmental sustainability. It has been stated that the functional groups of secondary metabolites obtained from lichen extracts are effective in preventing the aggregation of NPs, thus enabling the production and stabilization of NPs. Lichen-based NPs show great potential as therapeutic agents serving as antimicrobials, antidiabetics and antioxidants (Hamida and Abdelmeguid, 2021). Studies of lichen-associated nanoparticles show that lichens are stable, cost-effective, and biocompatible, making them ideal candidates for antimicrobial agents.

In the studies, the characteristic light absorption point of the synthesized nanoparticles is determined by UV-Vis, and the hydrodynamic diameter is determined by DLS (Dynamic Light Scattering). Morphological imaging is determined by FE-SEM (Field Emission Scanning Electron Microscopy) and the presence of functional components is determined by FT-IR (Fourier-Transformed Infrared Spectroscopy). In addition, the presence of elements is determined by EDX (Energy Distribution X-ray Spectroscopy) and crystal plane analyzes are performed with XRD (X-Ray Diffraction) analysis (Koca et al., 2022).

3. ANTICANCER EFFECTS OF LICHEN-BASED NANOPARTICLES

Cancer is one of the leading causes of death in the world. The World Health Organization defines cancer as a broad spectrum of diseases characterized by the uncontrolled proliferation of abnormal cells that can invade adjacent parts of the body and/or spread to other organs (Piñeros et al., 2022).

Looking at current advances in anticancer drug development, there has been a shift from traditional non-specific cytotoxic agents to specific target-based therapies and immune-related modulators. However, the discovery of new anticancer drugs from nature remains important to modern cancer research, and many potential sources of natural products remain largely unexplored (Liu et al., 2017).

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Therapies used in cancer treatment based on nanotechnology have attracted a lot of attention in recent years due to their small side effects and high specificity. Especially, nanoparticles produced by synthesizing from plants draw attention due to their antimicrobial, antioxidant and anticancer effects (Sur et al., 2012; Singh et al., 2016). In recent studies, the ability of green silver nanoparticles to decrease cell viability and increase apoptosis in different cancer types has been reported (Vasanth et al., 2014). For this reason, research has focused on the selection of natural compounds with anticancer effects for the synthesis of new silver nanoparticles, which have high activity against cancer cells but low toxicity in normal cells. The defensive nature of lichens is a crucial point from a pharmaceutical point of view, as they have excellent anti-cancer potential against a wide variety of cancers (Zambare and Christopher, 2012). So far, although the role of lichens as natural factories to synthesize NPs has been reported, the production of NPs using lichens has remained largely unexplored. Lichens have potentially reducible activity to produce different types of nanomaterials, including metal and metal oxide NPs and bimetallic alloys and nanocomposites. These NPs exhibit promising catalytic and antidiabetic, antioxidant and antimicrobial activities (Hamida et al., 2021). Studies on cytotoxicity are relatively new.

In the study conducted in 2020, researchers used biogenic agents to synthesize stable and safe AgNPs. Their main purpose is to investigate the ability of lichens in AgNP formation, their cytotoxic activity as well as their ability to suppress bacteria. In the study, *Xanthoria parietina* and *Flavopunktelia faventior* species were used. Lichen methanolic extracts were prepared for the conversion of Ag ions to AgNPs. The prepared biogenic AgNPs were supported by physicochemical analyzes. The cytotoxic effect of biogenic AgNPs was tested against HCT116 (Human Colorectal Cancer cell), MDA-MB-231 (Breast cancer cell) and FaDu (Pharynx cancer cell) by MTT assay. Considering the current findings, it was determined that biogenic AgNPs mediated by lichens have positive antibacterial, synergistic and cytotoxic effects. Therefore, lichens can be considered as promising candidates to fight multi-drug resistant organisms and some cancer cells (Alqahtani et al., 2020).

In a study conducted in 2020, they investigated the antiproliferative effects of Ag@ZnO NP on the SH SY5Y human neuroblastoma cell line. The results showed that Ag@ZnO NP had antiproliferative effects on SH-SY5Y cells and increased cell proliferation at low dose. They stated that the effects at low doses depend on the activation of the stabilizing mechanisms in the cell, and it is important to investigate the anticancer potential on different cancer cell lines (Isik et al., 2020).

In a study conducted in 2021, bio-inspired nanoparticle synthesis has received great attention in the scientific community due to its environmentally friendly and non-toxic nature. In this study, silver nanoparticles (AgNPs) were synthesized using *Cladonia subradiata* lichen species and characterized using different techniques. In vitro cytotoxic results were found for A549 lung cancer cells treated with AgNPs. Therefore, the study demonstrates efficient and non-toxic synthesis of AgNPs using a discovered lichen extract as a promising anticancer agent in nanomedicine (Shanthi et al., 2021).

Again, in a review in 2021, they stated that Lichen-based NPs show great potential as therapeutic agents acting as antimicrobials, antidiabetics, anticancer and antioxidants. In studies conducted with *Xanthoria parietina* and *Flavopunctelia flaventior* species, both antibacterial and anticancer activities were determined (Hamida et al., 2021).

In a study conducted in 2022, the neuroprotective or neurotoxic effects of Pseudevernia furfuracea and Usnea florida lichen extracts and silver-based zinc oxide nanocomposites (Ag-ZnO NCs) were evaluated for the first time. As a result, it was predicted that Ag-ZnO Np based on *P. furfuracea* and *U. florida* extract could be synthesized in a cheap, short time and environment-friendly way and used in cytotoxic studies (Koca et al., 2022).

4. CONCLUSIONS

- Green synthesis of nanoparticles has been determined to be safer and an environmentally friendly and inexpensive alternative when compared to traditional NP production methods.
- These methods require natural resources and biomolecules such as lichens, algae, plants and fungi to reduce target metal salts to a nano-sized product.

- Synthesis of nanomaterials to be synthesized using lichen extracts is an environmentally friendly, simple and low-cost biological synthesis process.
- Studies so far have reported that lichens are natural factories to synthesize NPs. However, studies on the production of NPs using lichens are not sufficient.
- Lichens have a potentially reducible activity to produce different types of nanomaterials, including metals, metal oxide NPs, bimetallic alloys and nanocomposites. It has been determined that these NPs exhibit catalytic, antidiabetic, antioxidant and antimicrobial activities in studies (Hamida et al., 2021). It has also been determined that it has cytotoxic effects in recent studies (Işık et al., 2020).

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It should be written as short as possible and expressing the contribution made without giving the number.

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Author Contributions

Conceptualization: Z.K.; Investigation: Z.K., M.K.; Supervision: Z.K.; Writing-Original Draft: Z.K., M.K.; Writing-review & Editing: Z.K., M.K.; Other: All authors have read and agreed to the published version of manuscript.

Conflict of Interest

Confict of interest The author declares that are no conficts of interest to disclose.

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REFERENCES

- Alqahtani, M. A., Al Othman, M. R., Mohammed, A. E. (2020). Bio fabrication of silver nanoparticles with antibacterial and cytotoxic abilities using lichens. Scientific Reports, 10 (1), 16781.
- Bar, H., Bhui, D. Kr., G. P. Sahoo., Sarkar, P., De S. P., Misra, A. (2009). Green synthesis of silver nanoparticles using lateks of Jatropha curcas, Colloids and Surfaces A: Physicochem. Eng. Aspects, 339, 134–139.
- Bates, S. T., Cropsey, G. W., Caporaso, J. G., Knight, R., Fierer, N. (2011). Bacterial communities associated with the lichen symbiosis. Applied and Environmental Microbiology, 77, 1309–1314. <u>https://doi.org/10.1128/AEM.02257-10</u>
- Dubey, S. P., Lahtinen, M., Sillanpaa, M. (2010). Tansy fruit mediated greener synthesis of silver and gold nanoparticles. Process Biochemistry 45, 1065–1071.
- Hamida, R. S., Abdelmeguid, N. E. (2021). Lichens-Potential Source for Nanoparticles Fabrication: A Review on Nanoparticles Biosynthesis and Their Prospective Applications. Journal of Fungi, 1–42.
- Hamida, R. S., Ali, M. A., Abdelmeguid, N. E., Al-Zaban, M. I., Baz, L., & Bin-Meferij, M. M. (2021). Lichens—A potential source for nanoparticles fabrication: A review on nanoparticles biosynthesis and their prospective applications. Journal of Fungi, 7 (4), 291.
- Isik, Y., Unal, G., Koca, F. D., Halici, M. G. (2020). Anticancer activity of lichen extract (*Usnea sp.*) based synthesized Ag@ ZnO bimetallic nanocomposite. Multidisciplinary Digital Publishing Institute Proceedings, 40 (1), 51.
- Jayanthi, S., Priya, P., Monica Devi, D., Benila Smily, J. M. (2012). Lichens: Origin, types, secondary metabolites and applications, Journal of Academia and Industrial Research, 1, 45–49.
- Koca, F. D., Halici, M. G., Işik, Y., & Ünal, G. (2022). Green synthesis of Ag-ZnO nanocomposites by using Usnea florida and Pseudevernia furfuracea lichen extracts and evaluation of their neurotoxic effects. Inorganic and Nano-Metal Chemistry, 1–8.
- Liu, Z., Delavan, B., Roberts, R., & Tong, W. (2017). Lessons learned from two decades of anticancer drugs. Trends in pharmacological sciences, 38 (10), 852–872.

- Molnar, K., Farkas, E. (2010). Current Results on Biological Activities of Lichen Secondary Metabolites: a Review. Verlag der Zeitschrift für Naturforschung, 65, 157–173.
- Narayanan, K. B., Sakthivel, N. (2010). Biological Synthesis of Metal Nanoparticles By Microbes, Adu, Colloid Interface Sci.156, 1–13.
- Nugraha, A. S., Wangchuk, T., Willis, A. C., Haritakun, R., Sujadmiko, H., Keller, P. A. (2019). Phytochemical and pharmacological studies on four Indonesian epiphytic medicinal plants: Drynaria rigidula, *Hydnophytum* formicarum, Usnea misaminensis, and Calymperes schmidtii, Natural Product Communications, 14 (6), 1–6.
- Philip, D. (2010). Gren synthesis of gold and silver nanoparticles using Hibiscus rosa sinensis, Physica E 42, 1417–1424.
- Piñeros, M., Ginsburg, O., Bendahhou, K., Eser, S., Shelpai, W. A., Fouad, H., Znaor, A., Staging Survey Group (2022). Staging practices and breast cancer stage among population-based registries in the MENA region. Cancer epidemiology, 81, 102250. Advance online publication.
- Ranković, B. R., Kosanić, M. M., Stanojković, T. P. (2011). Antioxidant, antimicrobial and anticancer activity of the lichens *Cladonia furcata*, *Lecanora atra* and *Lecanora muralis*, BMC Complementary and Alternative Medicine, 11, 97.
- Sajadi, S. M., Kolo, K., Abdullah, S. M., Hamad, S. M., Khalid, H. S., Yassein, A. T. 2018. Green synthesis of CuO/ eggshell nanocomposite as a novel adsorbent nanocatalyst to efficient removal of aromatic containing compounds and reduction of 4-Nitrophenol at room temperature, Surfaces and Interfaces, 13, 205.
- Shanthi, S., Nallal, V. U. M., Anand, K., Ravindran, B., Chang, S. W., Chandrasekaran, M., ... Razia, M. (2021). Bio-Inspired Fabrication of Silver Nanoparticles Using High Altitude Squamulose Lichen Extract and Evaluation of its Antioxidant, Anticandida and Cytotoxic properties.
- Singh, P., Kim, Y. J., Wang, C., Mathiyalagan, R., El-Agamy Farh, M., Yang, D. C. (2016). Biogenic silver and gold nanoparticles synthesized using red ginseng root extract, and their applications. Artif Cells Nanomed Biotechnol, 44 (3), 811–6.
- Sur, I., Altunbek, M., Kahraman, M., Culha, M. (2012). The influence of the surface chemistry of silver nanoparticles on cell death. Nanotechnology, 23, 375102.
- Vasanth, K., Ilango, K., Mohan Kumar, R., Agrawal, A., Dubey, G. P. (2014). Anticancer activity of Moringa oleifera mediated silver nanoparticles on human cervical carcinoma cells by apoptosis induction. Colloids Surf B: Biointerfaces, 117, 354–9.
- Walker, J. L., Lintott, E. (1997). A phytochemical register of New Zealand lichens. New Zealand Journal of Botany, 35, 369–384. https://doi.org/10.1080/0028825X.1997.10410162
- Zambare, V. P., Christopher, L. P. (2012). Biopharmaceutical potential of lichens. Pharmaceutical Biology, 50 (6), 778–798.
- Zhang, J., Guo, W., Li, Q., Wang, Z., Liu, S. (2018). The effects and the potential mechanism of environmental transformation of metal nanoparticles on their toxicity in organisms, Environmental Science: Nano, 5, 2482.