

UNION OF SCIENTISTS IN BULGARIA – PLOVDIV



BOOK OF ABSTRACTS

**VIIIth International Conference of Young Scientists –
Plovdiv 2020**

23-26 July 2020, Plovdiv

Union of Scientists in Bulgaria – Plovdiv
6 Metropolit Paisii St., 4000 Plovdiv, Bulgaria

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The conference is an initiative of the Club of the Young Scientists at the Union of Scientists in Bulgaria – Plovdiv. The main goal is to provide an opportunity for young scientists from different countries to express themselves and to gain more experience and confidence in reporting scientific ideas and results.

Due to the complication of the epidemic situation in the country in recent weeks, the governing body of USB – Plovdiv decided to hold the Eighth International Conference of Young Scientists in online format.

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CONTENTS

PRENARY SESSION

- 3D-Bioprinting and Colorectal Cancer – **Yordan Sbirkov, Iliya Bodurov, Diana Molander, Nikolay Belev, Victoria Sarafian**.....15
- Autoimmune/Autoinflammatory Adjuvant Associated Syndrome (ASIA). Is it a new or an old syndrome? – **Stefka G. Radenska-Lopovok**.....17

NATURAL AND TECHNICAL SCIENCES

Section *Biology and Agrobiolgy*

- Landscape “Pattern-process” Interconnections and Interactions in the Lowland Part of the Catchment Areas of the Stara and the Vacha Rivers – **Ilija Tamburadzhiev**.....19
- Climate Transformation – a Factor for Change Agricultural Crops in Bulgaria – **Michaela Mihailova, Vassil Stoychev, Petar Marinov**20
- Adaptation of ISAP Technique for Genotyping Tomato – **Sibel Aziz, Nasya Tomlekova, Daniela Ganeva**.....21
- Applicability of SSR Markers Developed in Cowpea in Common Bean and Garden Pea – **Sibel Aziz, Nasya Tomlekova, Tsvetanka Dintcheva, Slavka Kalapchieva, Hriska Boteva**.....22
- Isolation of Lactic Acid Bacteria, Producers of Glycosyltransferases from Honey Bees – **Veselin Bivolarski, Mariana Nikolova, Stepan Bodlev, Daniela Mollova-Doshkova, Tonka Vasileva, Ilija Iliev**.....23
- Ex Situ Conservation and Comparative Determination of Radical Scavenging Activity of Two Balkan Endemic Species from Genus *Stachys* – **Desislava Mantovska, Veneta Kapchina-Toteva, Zhenya Yordanova**.....24
- Morphological Characteristics of Carrot Seeds Depending on the Fertilization Regime and Umbel Orders – **Alexander Trayanov, Nikolay Panayotov**.....25
- On the de Martonne Index in some Regions of Southeastern Bulgaria – **Nadezhda Shopova**.....26

Section *Technics and Technology, Mathematics and Informatics*

- Intelligent Agriculture – **Daniel Rusev, Mihaela Rusev, Stanimir Stoyanov**....27
- Application of Arithmetic and Logic Operations for Objects Extraction in Imagej – **Angel Danev, Atanaska Bosakova-Ardenska, Magdalina Kutryanska, Ivaylo Ivanov, Vladimir Karparov**.....28
- Selected Software Technologies for Building Interactive Interface – **Detelina Milkoteva**.....29

Formation on Higher-Order Thinking Skills Through Training in Graph Databases – Maria Borisova	30
Students Preferences for Delivery Modes of Content in E-Learning – Lambri Yovkov	31
Changes Occurring to Fruits (Strawberries, Raspberries, Cherries) after Storage in the Refrigerator Service – Leonita Salihu, Lorika Salihu, Egzon Salihu, Dilaver Salihu	32
Sensor Data Fusion and Filtering Techniques - Plamen Nikovski, Nikolay Doychinov	33
Section <i>Physics and Chemistry</i>	
Application of Polarization in Field Studies of Blood Samples in the Field of Veterinary Medicine - Vanya Slavova	34
Radioactivity in Tobacco – Anka Georgieva, Todorka L. Dimitrova, Stefka Kirkova	35
In vitro biological activity of new synthesized isocholine substance measured by isometric method – Vera Gledacheva, Valeri Slavchev, Stoyanka Nikolova, Iliyana Stefanova	36
Design of an Infrared Optical System for Dual-band MWIR/LWIR Uncooled Detector – Todorka L. Dimitrova, Radoslav Raychev	37
Liquid-Liquid Extraction-Chromogenic Systems for Azo Dye {4-(2-thiazolylazo)orcinol and Some Transition Metals – Magdalena Boradjieva, Siana Chobanova, Angel Mollov, Ivelina Koicheva, Zornitsa Jekova, Galya Toncheva	38
Determination of Mineral Content of Some Oriental Tobaccos from Plovdiv Tobacco Area – Ecotype Srednogorska Yaka and Ecotype Ustina – Desislava Kirkova, Margarita Docheva, Yovcho Kochev	39
Modification of Cyclic Terpens by Reaction of α -amidoalkylation – Desislava Kirkova, Sasha Minkova, Yordan Stremski, Stela Statkova-Abeghe, Plamen Angelov, Ilian Ivanov	40
Synthesis and Structural Characterization of Novel Ferrocenyl Benzothiazoles – Ilknur Ahmed, Yordan Stremski, Desislava Kirkova, Stela Statkova-Abeghe, Plamen Angelov, Iliyan Ivanov	41
Evaluation Of The Effects Of Reproductive Factors In Women With Non-Small Cell Lung Cancer - Petar Uchikov, Milena Sandeva	42
MEDICAL SCIENCES	
Section <i>Clinical Medicine</i>	
Laparoscopy in Colorectal Peritonitis – Nikola Kovachev, Boyko Atanasov	43
Surgical Treatment of Endoscopic Iatrogenic Perforations – Nikola Kovachev, Boyko Atanasov	44

New Prognosis Biomarkers for Systemic Lupus Erythematoses – Mariela Geneva, Stanislava Popova, Petja Gardzeva	45
Chemokines in Primary Sjogren’s Syndrome – Mariela Geneva, Stanislava Popova, Petja Gardzeva	46
Rare Venous Tumors: Raising GPs Awareness – Bogomila Cheshmedzhieva, Lyubima Despotova-Toleva	47
Rare Venous Tumors: Teaching with Cases – Bogomila Cheshmedzhieva, Lyubima Despotova-Toleva	48
Beneficial Prostate Hyperplasia in Men's Life. Role of Opl. – Dimitar Kalinov, Todor Goranov, Jan Chitalov, Lubima Despotova-Toleva, Ivan Dechev	49
Effect of Varicocelectomy on Sperm Concentration, Depending on Various Factors in Infertile Men – Stoil Tomov, Pepa Atanasova, Ivan Dechev	50
Analysis of the Method of Financing and the Effectiveness of the Diagnosis and Treatment of Occupational Bronchial Asthma in Inpatient Settings – Stefania Krasteva, Svetlan Dermendzhiev, Nikolai Atanasov	51
Angioneurotic Edema in Immunopathology and Allergology – Nikoleta Dimitrova, Svetlan Dermendzhiev	52
Specific Forms of Hypertension – Definitions, Prognosis and Therapeutic Approach – Nevena Ivanova	53
Rising The Knowledge of the General Practitioner about Male Infertility – Todor Goranov, Dimitur Kalinov, Jan Chitalov, Lubima Despotova-Toleva, Ivan Dechev	54
Allergic Rhinitis – Etiology, Epidemiology, Pathogenesis, Classifications – Svetlan Dermendzhiev, Vladimir Bozhilov	55
Clinical Manifestation, Forms and Social-Economic Aspects of Allergic Rhinitis – Svetlan Dermendzhiev, Vladimir Bozhilov	56
Sarcosine in Urine – a New Possibility for Potential Biomarker of Clinical Progression of Prostate Gland Vancer - Dimitar Delkov, Lyubka Yoanidu, Yordanka Uzunova, Ivan Dechev, Desislav Tomov	57
Atrial Fibrillation Complication – a Case Report - Nevena Ivanova	58
Resistant Hypertension - Nevena Ivanova	59
Diabetes and Diabetic Retinopathy – Current Diagnostic and Therapeutic Aspects – Emanuela Vasileva, Mariyan Batashki, Radiana Staynova	60
Sjögren’s Syndrome, Oral Microbiome and Probiotics – Maria Panchovska-Mocheva, Vladimir Andonov, Georgi Tomov, Irina Zdravkova	61
Membranous Nephropathy in a Patient with Autoimmune Thyroiditis - Irina Zdravkova, Eduard Tilkiyan, Iovko Ronchev	62

Sjögren’s Syndrome – Clinical and Preclinical Consideration – Sonia Kukusheva, Georgi Tomov, Maria Panchovska-Mocheva	63
Flexible Ureteroscopy for the Diagnosis of Chronic Unilateral Hematuria – Atanas Ivanov	64
Management of the Distal Ureter in Open Nerproureterectomy – Comparison between Endoscopic Ureteral Detachment and Bladder Cuff Excision – Atanas Ivanov	65
Laparoscopic Decortication of Simple Renal Cysts – A Single Institution Experience – Atanas Ivanov	66
Prostate Cancer Screening – From Beginning to the Future – Ivaylo Getsov	67
Flexible Ureteroscopy for Kidney Stones – Efficacy and Safety – Ivaylo Getsov	68
Treatment of Interstitial Cystitis/Painful Bladder Syndrome by Intravesical Instillation of Sodium Hyaluronate – Petar Antonov	69
Paraurethral Skine’s Duct Cyst – A Rare Finding after Puberty – Petar Antonov	70
Urethral Caruncle: Management and Rewiew of the Literature – Petar Antonov	71
Development of Angioedema in Patients with Rheumatological Diseases Threatened with TNF-A Blockers – A Prospective Study – Stanislava Popova, Nikoleta Dimitrova	72
Section Preclinical Medicine	
Health-related Quality of Life and Its Determinants among Women with Type 2 Diabetes Mellitus – Boryana Levterova	73
Osteoporosis in Rheumatoid Arthritis – Silvia Tsvetkova, Katya Doykova	74
High Resolution Ultrasound as a New Diagnostic Tool of Larynx – Katya Doykova, Silvia Tsvetkova	75
How to Interpret the Hypodense Splenic Lesion – Silvia Tsvetkova, Katya Doykova	76
Nurse Physician Relationship and Quality of Care – Boryana Levterova	77
Therapeutic Benefits of Plants in the Treatment of Non-alcoholic Fatty Liver Disease (Nafld) – Mihaela Popova, Merlin Esad, Anelia Bivolarska	78
Biochemical Aspects of Kynurenic Pathway in Schizophrenia – Ivelina Avramova, Zdravko Ivanov, Anelia Bivolarska, Katerina Koleva	79
Dietary Habits and Health Status of Medical Students – Elka Toseva, Iliyana Toseva, Desislava Bakova	80

Tobacco Use and Alcohol Consumption among Medical Students – Elka Toseva, Piya Toseva	81
Spect Tomography Image Quality Control – Plamena Enikova, Peter Trindev, Todorka L. Dimitrova	82
Ghrelin and Its Involvement in the Pathogenesis of Obesity and Gallstone Disease – Petar Hrishev, Nadya Penkova, Pepa Atanassova, Vladimir Penkov, Elias Antalis	83
The Opinion of Health Professionals about Telemedicine in Bulgaria – Kristina Kilova, Stanka Uzunova	84
Distance Learning in the Conditions of a Pandemic through the View of the Students from Medical University – Plovdiv – Kristina Kilova	85
Social Aspects of Distance Learning During the COVID-19 Pandemic – Tanya Kitova	86
Контрол на Legionella spp. в денталната практика в Англия и в България – сравнителен анализ – Велина Стоева, Искра Томова, Александър Атанасовски, Ани Кеворкян, Йорданка Стоилова	87
Противовъзпалително действие на растения от рода Sideritis. Обзор – Николай Янчев, Делян Делев	88
Distribution and Use of Silver Birch (Betula Pendula, Roth) – Dimityr Penkov, Margarita Kassarova	89
Application of Information Technology in Human Resource Management in Primary Healthcare – Emilija Harizanova, Teodora Dimcheva, Gergana Foreva	90
Health Status, Quality of Life and Psycho-Climate in Health Care Specialists – Survey - Zlatka Lozanova, Stefka Stoilova, Tanja Roleva, Miroslava Todeva, Teodora Dimcheva, Nonka Mateva	91
Stress in the Work of the Pharmacist in a COVID-19 Pandemic – Anna Mihaylova, Petya Kasnakova, Bozhidarka Hadzhieva, Daniel Argilashki	92
Vortioxetine a Multimodal Antidepressant with a Potential Analgesic Activity (Review) – Ilin Kandilarov, Natalia Vilmosh, Delian Delev	93
Cariprazine – a New Hope for Psychiatric Patients – Maria Georgieva-Kotetarova, Hristina Zlatanova, Vasil Kotetarov	94
Anxiolytic and Neuroprotective Effects of Cannabidiol: Review – Maria Georgieva-Kotetarova, Delian Delev, Ilia Kostadinov	95
Atomoxetine – an Alternative in the Treatment of Attention Deficit Hyperactivity Disorder – Natalia Vilmosh, Ilin Kandilarov	96

Section Dental Medicine

The Necessity of Diagnosing and Treating Chronic Periapical Periodontitis with 3D Cone-beam Computed Tomography – Bogdan Krastev	97
Nonsurgical Ultrasonic Periodontal Endoscopy. Effect on Bone Healing in Infraossal Defects – Bogdan Krastev	98
Clearing Technique as Educational Tool for Exploration of Root Canal System - Kostadin Georgiev, Aleksandra Pecheva	99
Transparency Changes of Ultratranslucent Multi-layered Zirconia – Aleksandra Pecheva, Snezhana Tsanova, Ralitsa Raycheva	100
Device for Mechanical-Cyclic Loading of Test Specimens – Magdalena Urumova, Rangel Todorov, Stefan Zlatev, Svetlin Aleksandrov	101
Parents’ Knowledge about Children’s Caries and Early Prevention – Mariyana Alexandrova, Kristina Kilova	102
Step by Step Defining Two Impression Techniques Using Quality Control Software – Mariela Tsanova-Stamatova, Neshka Manchorova-Veleva	103
Degree of Awareness of the Dental Practitioners according to Work Experience and Specialty about the Impact of Removable Dentures on Speech Function (Questionnaire Study) – Majed Hussein, Atanas Doshev	104
Volumetric Changes of Chronic Periapical Lesions Following Endodontic Treatment – Teodora Karteva, Ekaterina Karteva, Donka Keskinova³, Padostina Kanazirska, Georgi Yordanov, Neshka Manchorova-Veleva	105
Confocal Laser Scanning Microscopy for Visualizing the Adhesive Hybrid Layer – Pilot Study – Nikolay Simeonov, Vesela Stefanova	106
Investigation of the Attitude of Dentists in Plovdiv Region towards the Usage of Bioceramic Endodontic Sealers – Kostadin Zhekov, Vesela Stefanova, Stela Nicheva	107
Cephalometric Assessment Based on Schwarz Analysis Among Bulgarian Population – Katya Todorova-Plachiyska, Mariya Stoilova-Todorova, Manoela Kalaydzhieva, Konstantin Georgiev	108
Ултразвукова диагностика на долночелюстни стави при пациенти с краниомандибуларни дисфункции – Мариана Димова-Габровска, Десислава Димитрова, Димитър Йовчев	109
Профилактично постурологично изследване на деца на осемгодишна възраст – Мариана Димова-Габровска, Мариета Мандова	110
A Survey of the Patients’ Opinion regarding Their Oral Health Problems – Sonya Nencheva, Marieta Todorova, Stoyanka Velinova	111
Problems of Oral Health of Elderly Patients in Terms of Occupational Therapy – Marieta Todorova, Sonya Nencheva, Stoyanka Velinova, Veselina Todorova	112

Methods for Diagnostics of Early Proximal Caries Used by Bulgarian Dentists – Veselina Todorova, Ivan Filipov	113
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HUMANITIES AND SOCIAL SCIENCES

Section *Linguistics*

About Some Disagreements in Science Connected with the Lexico-grammatical Category of Gender in Bulgarian – Radostina Koleva	114
Observations on Some Cases of Gender Variability in Derivative Nouns – Diana Markova	115
To the Question of the "Receptivity" Category in Modern Bulgarian – Vasil Stamenov	116
On Some Constituency Tests in Dependency Grammar in English and Bulgarian – Nikolay Zhelyazkov	117

Section *Economics*

Challenges which Business Organizations Face in International Business – Ivelina Kulova	118
Global Branding – Applying Strategies to Win Customers – Ivelina Kulova	119
Regional Development of Industrial Crops Foundation for Innovative Bioeconomy in Bulgaria - Vassil Stoychev, Mihaela Mihailova, Peter Marinov	120
Sustainable Development of the World until 2030 – Mihail Mihaylov	121
R&D as a Factor for the Competitiveness of Higher Education – Gergana Dimitrova, Megi Dakova	122
Opportunities for Creating New Generation Chains with Added Value Adapted to Organic Food Processing – Mariyana Kovacheva	123

Section *Social Sciences, Art and Culture*

The Contradiction Between Traditional (Intellectual and Moral) and Basic Natural (Bodily and Hedonistic) Values as Part of the Process of Value Transformation in Bulgaria in the Years 2001-2009 of the Transition – Vanya Uzunova	124
Role and Functions of Municipalities in the Implementation of the State Health Policy – Mariyana Anastasova-Tumbakova	125
Didactic Technologies for Interdisciplinary Ecological Education – Zlatka Vakleva, Temenuga Pavlova	126
Education for Sustainable Development – Application in Biology and Health Education – Zlatka Vakleva, Svetla Ivanova	127
Environmental Education in the Digital Environment – Practical Aspect in Teaching Biology and Health Education – Zlatka Vakleva, Polina Djambazova	128

Metrorythme and Composition – Interpreter Profile in Jacques Casterede’s First Movement of His Sonatine for Trombone and Piano – Tzvetana Gigova	129
The Government during the first Bulgarian Empire – Radoslav Smailov	130
Comparing the Geometrical, Mechanical, and Christian Dualisms – Krassimir Tarkalanov	131

3D-BIOPRINTING AND COLORECTAL CANCER

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3D-bioprinting is a modern technology, which combines cells, growth factors and biomaterials to create spatially organized tissues and organs with structure and function closest to the normal ones.

The application of this method in medicine is basically in the field of transplantation, regenerative and personalized medicine. It is successfully used to model diseases, to design drugs and to check their efficacy.

The popular animal models pose serious ethical problems and lead to incorrect extrapolation of data and false positive results. Monolayer cell cultures also have significant limitations.

3D cultures and bioprinting, especially in oncology, offer optimal patient stratification and personalization of the treatment by establishing the individual response to therapy. Thus, the toxicity and resistance to antitumor agents could be determined for each patient.

The ideal *in vitro* model includes several cell types, allows the growth of blood and lymph vessels and mimics the metastatic process. In 3D *in vitro* cell systems (3D tumor organoids), obtained by self-organized stem cells, the *in vivo* architecture, the function and genetics of the tumor are restored. Individual modelling of the disease and drug screening is thus possible.

Our research interest is focused on colorectal cancer (CRC) as a disease with multifactorial etiology due to progressive accumulation of genetic and epigenetic events. The lethality in these tumors hold the third position among cancer cases and they affect more and more young individuals.

The aim of our pilot study is the setting of lab protocols for processing, culturing and 3D bioprinting of primary CRC followed by biological characterization of 3D tumor organoids and *in vitro* testing the effect of chemotherapeutics.

After disintegration of tumor tissue from CRC, the cell monolayer is cultured on polypropylene plates. Using special bioinks 3D cultures are generated which are then analyzed for cell vitality in dynamics.

By Calcein AM / Propidium Iodide labelling the number of live / dead cells is counted. Cell morphology is examined and immunohistochemical detection is performed. The antibodies for the immunohistochemical study are validated by staining for cytokeratins 7,20 and vimentin on both standard cell cultures and on the bioprinted CRC tissue.

Our results prove that 3D bioprinting of primary CRC is an innovative and reliable technique which allows maintaining the *ex vivo* cell morphology and biology and opens new horizons for personalizing the therapy.

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AUTOIMMUNE/AUTOINFLAMMATORY ADJUVANT ASSOCIATED SYNDROME (ASIA). IS IT A NEW OR AN OLD SYNDROME?

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Y. Shoenfeld and N. Agmon-Levin first described autoimmune / inflammatory syndrome induced by adjuvants (ASIA) in 2011 [1]. The adjuvants are substances or complex of substances inducing or intensifying the immune reaction to immunogene in healthy people. They are not used to modify or correct the defective immune answer in illness. The development of ASIA is associated with the hyperergic reaction of the human immune system. ASIA gave the chance to understand and to revise many autoimmune conditions. The development of autoimmune inflammation is preceded by contact with internal or external trigger factors (silicon, alum, and other adjuvants) of immune disorders. Silicon is a resin having Si in its molecule. The chain contains SiO; the length and the branches define different properties of the silicon.

There are five possible options for the impact of adjuvants in the pathogenesis of autoimmune disorders [2]. The first one is the depot's effect at the injection site. They provide slow antigen release to stimulate the immune system and activate antigen-presenting cells (APCs). The second theory concerns the innate immunity. Some adjuvants act by inducing the innate immunity by targeting the APCs via Toll-like receptors (TLRs), NOD-like receptors (NLRs), RIG-I-like receptors (RLRs) and C-type lectin receptors (CLRs). The third hypothesis concerns the members of NOD-like family, such as NLRP3 and NLRC4. The formation of the inflammasome is triggered. At the same time, authors discuss that the adjuvants can directly support antigen presentation by the major histocompatibility complexes (MHC). And at last, the adjuvants initiate adaptive immunity. They are essential for enhancing and directing the immune response to vaccine antigens. This response is mediated by B and T lymphocytes. ASIA is associated with an individual genetic predisposition that is probably associated with the carriage of HLA-DRB1 or HLA-DQB1.

There are several syndromes which are included in ASIA: Gulf War syndrome; Macrophagic myophasciitis; Postvaccination syndrome (A list of the vaccines are more likely associated with autoimmune diseases: HBV,

Anthrax, Influenza, Rabies, Rubella, HPV, Swine flu); Sick building syndrome [1, 3-5].

We described two cases of silicon breast implants and granulomatosis with polyangiitis associated with adjuvants according to the Diagnostic criteria of ASIA [1, 6]. The women had myalgia, arthralgia, pyrexia and the laboratory tests showed acute inflammation. These symptoms appeared after the implantation of silicon implants. The spectrum of morphological changes in ASIA was extensive. In the tissues were found signs of immune inflammation, such as lymphohistiocytic infiltration, granulomatous inflammation, fibrinoid necrosis in soft tissues and small vessels. We saw the amount of silica deposits in the breasts muscle and fascia. One of the patients agreed to remove the implants and she achieved stable remission. The other patient refused to delete them and she died with a polyorganic failure. So there were fulfilled 6 major criteria of ASIA (silicone implants prior to clinical manifestation, myalgia, arthralgia, pyrexia, typical tissue involvement and removal of inciting agent induced improvement) and one minor criteria (clinical manifestation of systemic vasculitis – granulomatosis with polyangiitis). A characteristic feature is the regression of clinical, laboratory, and morphological manifestations after adjuvant removal, as it was seen in one of our patients [6, 7].

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LANDSCAPE „PATTERN-PROCESS” INTERCONNECTIONS AND INTERACTIONS IN THE LOWLAND PART OF THE CATCHMENT AREAS OF THE STARA AND THE VACHA RIVERS

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In order to clarify the peculiarities of the spatial-temporal heterogeneity and dynamics of landscapes, it is important to specify the interconnections and the interactions between the landscape pattern and the ecological processes occurring both within the landscape and at the inter-system level. The versatile manifestation of these interconnections and interactions is directly related to the anthropogenic effect exerted on systems of different rank. Thus, we have chosen a representative territory, part of the Pazardzhik-Plovdiv lowland area, which includes different by their nature landscape patterns, different ecological processes and intensive anthropogenic activity. The study area covers the lowland part of the catchment areas of the Stara and the Vacha rivers. The landscape mosaic is dominated by agricultural landscapes characterized by a diverse spatial-temporal pattern. The basic principles and approaches of the landscape-ecological research have been respected. Results for the spatial and temporal pattern of the landscapes in the study area were obtained.

CLIMATE TRANSFORMATION – A FACTOR FOR CHANGE AGRICULTURAL CROPS IN BULGARIA

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Climate change is a factor in the transformation of a number of biospheres globally. Changing its elements (temperature, rainfall and heavy cover) at regional level will lead to the replacement of crops with others and a change in the appearance of agriculture and typical practices. The article deals with the change of the climate processes in Bulgaria in the last 20-30 years, which has undoubtedly influenced the socio-economic life. The change affecting specific area crops and the introduction of new species to respond to new climate change will be addressed using a graphical and analytical method. The aim of the study is to demonstrate how climate change is leading to changes in the industry and the socio-economic impacts of these processes.

Keywords: climate, agriculture, climate change

ADAPTATION OF ISAP TECHNIQUE FOR GENOTYPING TOMATO

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Tomato (*Solanum lycopersicum* L.) is one of the most widely grown and economically important vegetable crops in the world. In modern breeding, the use of molecular marker systems enables us to overcome a number of limitations of the conventional selection and helps to optimize the selection process.

The purpose of the present work is to adapt ISAP (Inter-SINE-Amplified Polymorphism) technique to conduct ISAP-PCR analyses in tomato. The adaptation of the technique, based on transposable SINE-elements, was conducted with previously analyzed seven SINE-families in potatoes (*Solanum tuberosum* L.). ISAP amplifications of DNA sequences between two retroelements from the same or from different SINEs families were conducted in one tomato genotype. In the single-family and multiplex reactions, gradient PCR is conducted with programs to identify reproducible specific profiles that generate the most fragments. In single-family reactions, the most productive profiles were generated by *Sol* IIIaF/R primer pair, and the multiplex – by *Sol* Ib F/R *Sol* IIIa F/R; *Sol* Ib F/R *Sol* IIIb F/R; *Sol* Ib F/R *Sol* II F/R *Sol* IIIa F/R, and *Sol* IIIa F/R *Sol* IIIb F/R.

In the present study, the ISAP technique was adapted in tomato that can be used to detect polymorphic loci to study genetic variability, identify varieties and species, and characterize mutants, establishing hybrids.

Keywords: molecular technique, ISAP, SINE transposable elements, *Solanum lycopersicum*, tomato

APPLICABILITY OF SSR MARKERS DEVELOPED IN COWPEA IN COMMON BEAN AND GARDEN PEA

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Common bean (*Phaseolus vulgaris* L.) is one of the widely grown pulse crops in the world, as well as in Bulgaria. Pea (*Pisum sativum* L.) is a widely grown pulse crops in the world, however in Bulgaria its production is limited. The widely used cowpea (*Vigna unguiculata* L.) in Africa is not grown in Bulgaria. Both representatives of pulses are characterized with large genetic diversity. The use of suitable molecular markers facilitates the breeding process.

The purpose of the present work is the application of SSR (Simple Sequence Repeats) markers, designed for the genome of *Vigna unguiculata* L. in the genome of *Phaseolus vulgaris* L. and *Pisum sativum* L.

In a bioinformatics search in NCBI (National Center for Biotechnology Information) it was established that the primers designed for *V. unguiculata* SSR reaction possess 100% identity in the genomes of *P. vulgaris* and *P. sativum*. In the present study, we report the 10 successful markers (SSR-6273, SSR-6275, SSR-6276, SSR-6278, SSR-6279, SSR-6280, SSR-6284, SSR-6289, SSR-6300, SSR-6301) used for common bean, variety “Evros” and garden pea, variety “Paldin”. In garden pea, the selected markers are linked to different genes, which encode proteins.

The use of microsatellite markers provides opportunities for genotyping in the molecular selection of varieties and induced mutants. SSR technique can be used for investigation of populations and assessment of the origin of local varieties from different plant species.

Keywords: *Phaseolus vulgaris*, *Pisum sativum*, microsatellite markers, PCR, Agarose electrophoresis

ISOLATION OF LACTIC ACID BACTERIA, PRODUCERS OF GLYCOSYLTRANSFERASES FROM HONEY BEES

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Honeybee's crop presents an ecological niche rich in sugars that plays a significant role in the health of the bees by conferring symbiotic interactions between the specific microflora of the gut and the insect [1]. In addition, honeybee's crop can be a source of microorganisms having specific properties, including production of valuable biomolecules, such as polysaccharides and oligosaccharides with prebiotic potential.

We report isolation of fructophilic lactic acid bacteria (FLAB) from gastrointestinal tract of *Apis mellifera*. From the obtained 20 FALB isolates from honeybee's crop, only 4 (AG8, AG9, AG10, AG11) produced exopolysaccharides on sucrose medium. On the basis of their fermentation profiles (API 50 CH), the isolates were identified as strains of FLAB *Lactobacillus kunkeei*. The performed *in situ* electrophoretic analysis of enzyme fractions from the strains showed production of high-molecular-weight glycosyltransferase enzymes with mass ~300 kDa. The enzyme production by the studied strains was optimized, and after partial purification enzyme preparations were obtained with activity ranging from 1.25 U/mg to 2.69 U/mg.

Acknowledgements: This work was supported by Department for Scientific Research – PU, grant № MY19-БФ-019/2019.

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EX SITU CONSERVATION AND COMPARATIVE DETERMINATION OF RADICAL SCAVENGING ACTIVITY OF TWO BALKAN ENDEMIC SPECIES FROM GENUS STACHYS

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Stachys thracica, and *Stachys bulgarica* are Balkan endemic species included in The Red Data Book of Bulgaria with conservational status: endangered. Plants from *Stachys* genus have been widely used in the ethnomedicine for treatment of different inflammatory conditions including infected wounds. There is no available data on *ex situ* conservation of the species and little is known about their chemical composition and biological activity. The aim of the present work is to develop an effective protocol for *ex situ* conservation of *S. thracica* and *S. bulgarica* and comparative determination of the radical scavenging activity and phenolic compositions of extracts isolated from *in situ*, *in vitro* and *ex vitro* adapted plants. *In vitro* shoot cultures were induced from ripe dried seeds, collected from *in situ* growing wild plants and multiplied on basal MS medium. *Ex vitro* adaptation was accomplished in greenhouse and experimental field with 100% survival for *S. thracica* and 96% for *S. bulgarica*. The highest phenolic quantity as well as antioxidant activity was established in *in situ* plants from both species followed by *ex vitro* adapted *S. thracica* plants and *in vitro* cultivated *S. bulgarica*. The maximum inhibition of DPPH free radical was 80% in *in situ* plants from both species at concentrations 60 µg/ml for *S. thracica* and 150 µg/ml for *S. bulgarica*. Different growth conditions affect the phenolic quantity and antioxidant activity of both endemic species. A collection of *in vitro* cultivated and *ex vitro* adapted plants was established, which is an alternative approach for the preservation of *Stachys thracica* and *Stachys bulgarica*.

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MORPHOLOGICAL CHARACTERISTICS OF CARROT SEEDS DEPENDING ON THE FERTILIZATION REGIME AND UMBEL ORDERS

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The main aim of the present study was to establish the changes in morphological characteristics of carrot seeds such as linear sizes, weight of one seed and weight of 1000 seed under different fertilization regime and depending on umbel orders. Two times of fertilization were tested: once – phosphorus and potassium were applied in autumn and nitrogen in transplanting time, and twice – half of phosphorus and potassium in the autumn, while other half and nitrogen in soil spring and half nitrogen in flowering. The length, width, thickness and weight of seeds from central umbel and umbels from I, II and III orders were determined, as well as the weight of 1000 seed. Umbel order has a significant impact on 1000 seed weight and linear dimensions. The higher values of 1000 seed weight and linear dimensions were determined after application of $N_{50}P_{90}K_{100}$, $N_{50}P_{90}K_{200}$ and $N_{90}P_{90}K_{200}$.

Keywords: *Daucus carota L.*, seed size, fertilization, umbel, morphological

ON THE DE MARTONNE INDEX IN SOME REGIONS OF SOUTHEASTERN BULGARIA

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In recent years, there has been an increase in the frequency of extreme events of meteorological origin. For the cultivation of spring crops, the most important of them are the periods of drought and the aridity conditions during the growing season.

The territory of Southeastern Bulgaria, the subject of this publication, is one of the driest in our country, which makes it risky for growing major crops, especially under conditions of no irrigation.

The subject of research in this paper are conditions and a type of climate in relation to water availability in some agricultural areas according to the De Martonne aridity index I_{DM} (1926) [1]. The study covers the period between 1961 and 2019 by analyzing and comparing the values of two thirty-year periods (1961-1990 and 1991-2019).

[1] De Martonne, E. *Aréisme et Indice d'aridité*. Comptes Rendus de L'Academy of Science, Paris, 1395-1398 (1926).

INTELLIGENT AGRICULTURE

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In Bulgaria, so far no scientific studies have been carried out and no scientific publications have been opened for the application of intelligent agriculture. Several companies offer and implement precision agriculture, which is the first stage of the intelligent farming system. The fourth industrial revolution, which is becoming more and more tangible, opens up untold opportunities to improve people's lives so far by using integrated technologies based on the achievements of artificial intelligence, the Internet of Things, the integration of the physical and virtual worlds. We live in an ever-changing world, populated more and more by autonomous objects such as drones, robots, and remote-controlled machines, where virtual environments and physical spaces are increasingly integrated. Modern integrated technologies are increasingly entering agriculture, offering solutions for what is called "smart agriculture". Intelligent agriculture is an extremely vast area where a wide range of tasks can be solved. Despite the enormous scope, the tasks can be summarized in three broad classes: Optimal use and saving of water resources; Protection and minimum environmental burden of harmful substances; Weed prevention and early detection of diseases of winter wheat.

We are the 1st who use Intelligent Internet of Things to collect environmental data such as temperature, humidity, rainfall, wind speed, soil moisture, etc. and use those data to improve the quality and quantity of harvest, while minimizing the risk and waste.

APPLICATION OF ARITHMETIC AND LOGIC OPERATIONS FOR OBJECTS EXTRACTION IN IMAGEJ

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Arithmetic and logic operations are simple images processing operations, which involve two or more images [1]. There are a lot of applications of arithmetic and logic operations such as motion detection, objects extraction and etc. The open source software ImageJ implements two types of arithmetic and logic operations: one for an image and a constant value and a second one for two images.

ALOImagePro (Arithmetic Logical Operations for Images Processing) application is developed as Java plugin for the open-source software ImageJ [2]. The proposed plugin has one main window, which contains one or twelve images, which are results of arithmetic and logic operations performed on two images selected by the user. Images of bread and cheese are used for the evaluation of ALOImagePro functionalities. Every image is duplicated and some manipulations are performed on the duplicated one in order to emphasize some features of the object. Then the plugin ALOImagePro is used for selection of appropriate operation for objects extraction.

The results show that the developed plugin allows fast and easy testing of arithmetic and logic operations in order to choose appropriate operation as a step in process of image analysis.

[1] R. Gonzalez and R. Woods, Digital Image Processing, (Third Edition), 2008, Prentice-Hall, ISBN 978-93-325-7032-0

[2] Developing Plugins for ImageJ, ImageJ, [www], Available from: https://imagej.net/Developing_Plugins_for_ImageJ_1.x, Accessed on: 20.05.2020

SELECTED SOFTWARE TECHNOLOGIES FOR BUILDING INTERACTIVE INTERFACE

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“Miracles do happen, but one has to work hard for that.”

The present development aims to present the most modern technologies for building a dynamic information presentation in an attractive way with an interactive web approach called interactive interface.

The Internet is a wonderful place with all kinds of information, entertainment, games, texts filled with pictures, sound and animation; connection speed should be high, web page design – attractive, navigation – easy, finding information – instant. An interface is that part of a tool or technology that the user communicates with.

The interactive presentation aims to clarify the web content, and to “present” it rationally in the absolutely perfect form.

Web design should be user oriented.

Site planning is always done before any development.

Some principles are also mentioned during development; the principles of responsive design are respected, but the main goal is a sample of the most preferred software technologies: **HTML, CSS, XHTML, XML, Flash** – for dynamic content in web pages, rich interactive interfaces, **PHP** – embedding in HTML, **Java applets, DHTML, ASP.NET MVC 5**, Web content management systems and more. And for a unique logo, banner or button – **CorelDraw, Photo Shop, Adobe Illustrator**.

Interactivity and the ability to provide quick feedback are key benefits of virtual space.

FORMATION OF HIGHER-ORDER THINKING SKILLS THROUGH TRAINING IN GRAPH DATABASES

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Nowadays, education is not enough for a successful career. Quality training is needed, which forms higher-order thinking skills. This includes the ability to apply knowledge and skills in practice, adapt old knowledge and use it in new situations, create new knowledge, and more.

This paper presents Bloom's taxonomy and its relationship to higher- and lower-order thinking skills. The basic knowledge of graph databases, which are subject to compulsory study, is listed. The possibilities for formation of higher-order thinking skills through the training in graph databases have been studied.

A learning task for creating a graph database and many specific tasks are presented. They are classified according to the Bloom's levels. They aim to stimulate creative thinking in learners and to train the development of various higher-order thinking skills.

STUDENTS' PREFERENCES FOR DELIVERY MODES OF CONTENT IN E-LEARNING

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The form of presentation of information in e-learning is important for facilitating knowledge dissemination. A survey was conducted online via Google forms in 2019 and 2020 among 99 students from several Bulgarian universities who studied different specialties. Only 8% of them were not satisfied with the quality of e-learning, and 1% did not want to study in a distant form further. The students' wish to use e-learning in their further studies was affected by their satisfaction with e-learning quality. About 67% of students preferred both forms of study instead of only a traditional classroom with personal attendance (preferred by 2% of the students participating in the survey) or only e-learning (preferred by 31% of the studied students). Among the various forms of delivery of online content, the most preferred were the interactive tests (91%), followed by presenting images of studied objects (89%), video (87%), online discussion (77%), PowerPoint presentations (76%), audio files (74%), and text files – pdf (69%) or Word (63%) files. The students preferred diverse online lecture formats that included audio-visual and interactive components. The research findings revealed the importance of flexibility and variability in delivering knowledge in e-learning, and the preference for interactive forms of learning process and visualization of content to just listening information or reading it.

CHANGES OCCURRING TO FRUITS (STRAWBERRIES, RASPBERRIES, CHERRIES) AFTER STORAGE IN THE REFRIGERATOR SERVICE

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Fruits are important for human health, as they are rich in vitamins, minerals, and fiber (R. Kongoli, I. Boci 2007). In this research, we analyzed the organoleptic, physicochemical, sugar and pH changes in fresh and stored refrigerated fruits at 6-8 °C for 28 days. (M. Vokshi, I. Pallushi, 2018; M.A. Jankovic, 2002). Organoleptic changes in strawberries occurred after day 14, whereas in raspberries changes began to occur after day 21, and in cherries, changes occurred around day 26-28. (D. Prifti, 2006). Determination of pH was done through the pH meter, where the pH value of fresh strawberries was pH = 3.66, during storage there was a decrease where on day 28 it reached pH = 3.41. The pH value of fresh raspberries was pH = 3.35, where a decrease was observed during storage, where on day 21 it obtained pH = 3.21. The pH value of the fresh dress was pH = 3.71, with a decrease during storage, where on the 28th day it received a pH value of 2.01. (Ljubo O. Vracar 2001, B. Zilatkovic 2003). The quantification of sugar in these fruits was done by refractometer, where the sugar content in fresh strawberries was 6.5%, and during storage there was a decrease, where on day 14 it reached 2.4%, and the appearance of molds began. In raspberries, the amount of sugar in the beginning was 8.5% and during storage there is an increase, where on day 28 it reaches 11.8%. In the early days, the amount of sugar in the cherry was 15.1% and during storage there is an increase, where on the 28th day it reaches 17.2% (Ljubo O. Vracar 2001, B. Zilatkovic 2003).

Keywords: Fruits, Acidity, Sugar, Organoleptic

SENSOR DATA FUSION AND FILTERING TECHNIQUES

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Originating and developed in the evolution of living forms, the fusion of information is an effective mechanism through which modern measuring systems can be created not only with better, but also with qualitatively new features. To realize such systems, first of all it is important to choose and apply mathematical procedures for processing the information received from the sensors. In the present work, an overview of the known fusion methods is made and the possibility for their implementation in the form of digital filters is evaluated. This approach allows sensor data fusion to be performed in real time, saving resources and time to execute the fusion algorithm in a computing device.

APPLICATION OF POLARIZATION IN FIELD STUDIES OF BLOOD SAMPLES IN THE FIELD OF VETERINARY MEDICINE

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The application of polarization in field research in veterinary medicine provides direct experimental methods for the analysis of blood samples. An important application of methods using this effect of light is the use of the rotation of the plane of polarization by blood cells for early diagnosis of diseases [1].

The investigation is based on the Salzman method, which proves that lymphocytes, monocytes and granulocytes can be distinguished in concentrated blood solutions by measuring the levels of polarized light intensity, mainly due to differences in orthogonal light scattering [2].

During the investigation, new results were obtained for the viral composition of the blood samples. The existence of BVDV virus was detected by extracting information on the cell morphology of 30 g of blood samples from ruminants, by analyzing the level of polarization of the scattered light passed through them.

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RADIOACTIVITY IN TOBACCO AND TABACO PRODUCTS

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The health damages caused by tobacco products consumption are well known. So far, the belief has been that the increased morbidity of smokers is due to the smoke, nicotine, tar and carbon monoxide. However, scientists consider that the naturally occurring radioactive isotopes in cigarettes are one of the most significant cause of the lung cancer of smokers. This new theory has pushed the researchers to study the radioactive components content in tobacco, the mechanisms of transmission of the radioactive isotopes through the smoke and the relative dose obtained by smokers.

The significance of the health problems caused by tobacco radioactivity led to inserting the natural isotope ^{210}Po in the Established List of the Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke in the Federal register of the United States Government [1].

The present work is an attempt to present an overview on the radioactivity in tobacco, tobacco products and cigarette smoke on the base of scientific literature published in Bulgaria and abroad.

[1] <https://www.federalregister.gov/documents/2012/04/03/2012-7727/harmful-and-potentially-harmful-constituents-in-tobacco-products-and-tobacco-smoke-established-list>

IN VITRO BIOLOGICAL ACTIVITY OF NEW SYNTHESIZED ISOCHOLINE SUBSTANCE MEASURED BY ISOMETRIC METHOD

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Purpose: The study of the biological action of newly synthesized molecule [1- (2-chlorophenyl) -6,7-dimethoxy-3-methyl-3,4-dihydroisoquinoline] on the smooth muscle preparations from circular muscle layer of a rat stomach-corpus [1].

Methods: Parameters of contractile activity was registered isometrically by detectors Tenzo "Swema" - Sweden. Substance-caused reactivity of smooth muscle preparations was counted and registered by gain stage "Microtechna" - Czech Republic and recorded on a paper recorder "Linseis" - Germany [2].

Results: The test substance significantly alters the phasic component of the tonic and phasic activity at a concentration range of $5 \cdot 10^{-5} \text{M}$ to $1 \cdot 10^{-4} \text{M}$.

Conclusions: The method used to establish biological activity convincingly demonstrates the demonstrated one and gives grounds to use it for future studies of newly synthesized substances.

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DESIGN OF AN INFRARED OPTICAL SYSTEM FOR DUAL-BAND MWIR/LWIR UNCOOLED DETECTOR

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Thermal imaging technology was initially developed for military purposes. Nowadays thermovision cameras with uncooled detectors are also found in different industrial and civil applications. The design of the infrared optical systems is related to the development of the detector's technique. The electromagnetic radiation of atmosphere and of ground in MWIR and LWIR ranges is different and depends on the weather and on the landscape. The use of two-band infrared detectors allows observation of both ranges, thus combining different advantages such as high sensitivity, penetration in dust, fog, smoke etc. Vanadium oxide (VOx) detectors take 70% from all uncooled detectors on the market due to their specific characteristics.

Here we present the design and ZEMAX optimization of an optical system for uncooled detector working at both infrared bands: from 3 μm to 5 μm (MWIR) and from 8 μm to 14 μm (LWIR). We have opted for a BIRD 640 Wide Band 640 x 480, 25 μm pitch, VOx Microbolometer, produced by SCD.USAInfrared.

The basic parameters of our optical system are as follows: referent wavelength of 10.6 μm , equivalent focal length $f=100$ mm and focal ratio $F/\#$ =of 1,2.

The first criterion for the selection of optical materials was transparency for both MWIR and LWIR ranges, and the second – the chromatic aberrations minimization. A three-lens optical system was designed, any of them from different materials: Ge, ZnS and IRG26 respectively. Different combinations of lenses were optimized via Zemax Optics Studio software. The MTF analysis have shown best quality image for optical system including aspherical and diffractive elements.

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LIQUID-LIQUID EXTRACTION-CHROMOGENIC SYSTEMS FOR AZO DYE {4-(2-THIAZOLYLAZO)ORCINOL AND SOME TRANSITION METALS

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The ion-pairing between some transition metals, azo dye {4-(2-thiazolylazo)orcinol, TAO}, quaternary ammonium salt (Aliquat 336) and low-toxic organic solvent (isobutanol) were studied. The difference in the formed complexes for nickel(II), vanadium(V), and copper(II) was studied.

The optimum conditions for extraction of the mentioned metal ions were found. The following extraction and spectrophotometric characteristics were determined: absorption maxima, molar absorptivities, Sandell's sensitivities, constants of extraction, constants of distribution, fractions extracted, and Beer's law limits. The stoichiometry of the extracted binary and ternary complexes was established by different methods.

Acknowledgements: This work was supported by the Plovdiv University Scientific Fund (grant No SP19-009).

DETERMINATION OF MINERAL CONTENT OF SOME ORIENTAL TOBACCOS FROM PLOVDIV TOBACCO AREA – ECOTYPE SREDNOGORSKA YAKA AND ECOTYPE USTINA

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The minerals are important for the consumer qualities of tobacco [1]. Macroelements were affected by the combustibility of tobacco. The content of microelements was related to its environmentally friendly material [2]. The aim of this study was to investigate the content of the minerals in Bulgarian oriental tobacco in Plovdiv tobacco region.

A three-year comparative study of the control varieties and perspective breeding lines of oriental tobaccos of ecotype Srednogorska yaka and ecotype Ustina were performed. The content of macroelements Ca, P, K, N, P, Cl and Mg and microelements Cd, Pb, Zn, Cu in tobaccos was established. The highest amounts of macroelements were Ca, K, N, while the smallest – P, Cl, Mg. The content of microelements was relatively low, indicating that the raw material was environmentally friendly material. The content of basic macro- and microelements in the investigated tobacco samples did not exceed the conventionally accepted limit values for tobacco. The obtained data has been applied in assessing the smoking qualities of tobaccos and the breeding practice in making decisions on promising lines.

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MODIFICATION OF CYCLIC TERPENS BY REACTION OF α -AMIDOALKYLATION

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Terpenoids are the largest and most structurally diverse class of natural products. They possess potent and specific biological activity in multiple assays against various diseases, including cancer and malaria as distinguished examples.^[1] In recent years, hybrid molecules have been widely synthesized. Hybrid molecules containing a combination of two natural or synthetic biologically active fragments often exhibit unexpected pharmacological bioactivities. 2-aryl substituted benzothiazoles show a wide spectrum of chemotherapeutic activity, including their use as antitumor and antibacterial agents. In earlier scientific report, a new one-pot approach for the synthesis of *Camalexin* and its derivatives via α -amidoalkylation reactions was showed.^[2] The purpose of this study was to expand the scope of this method for the synthesis of modified cyclic terpenes. A series of new molecules were obtained with good yields (80% – 96%). In the next step, the compounds were purified by column chromatography and their structure was characterized by spectral ¹H- ¹³C-NMR analysis.

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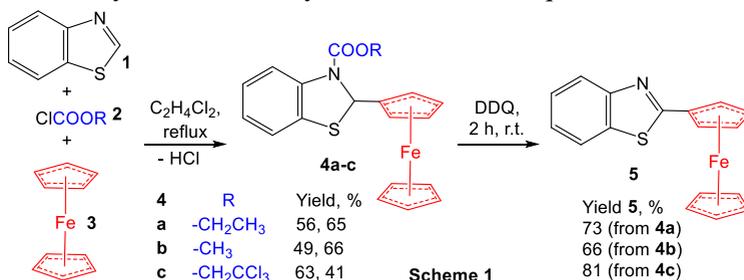
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SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF NOVEL FERROCENYL BENZOTHAZOLES

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Ferrocene and its synthetic derivatives have attracted interest nowadays because of their wide range of applications.^[1] The aim of this research is the synthesis and subsequently spectral characterization of some new ferrocenyl benzothiazoles by an α -amidoalkylation-oxidation sequence (**Scheme 1**).



New one-pot synthetic approach to *N*-acyl-2-(1-ferrocenyl)-benzothiazole derivatives was evaluated. The amidoalkylated products **4a-c** were obtained with yields (49%–63%) involving equimolar ratio of the starting reagents for 6 hours. The double excess of benzothiazole **1** and alkyl chloroformate **2** (for 12 hours) led to increased yields of **4a** (65%) and **4b** (66%). Compounds **4a-c** were successfully oxidized with DDQ for the obtaining of **5** with rearomatized benzothiazole ring, with yields from 66% to 81%. The synthesized products were purified by column chromatography and spectral characterized by ¹H-¹³C-NMR and IR analysis. Furthermore, the structure of product **4c** was confidently confirmed via X-ray crystallography.

Acknowledgements: This research was funded by the University of Plovdiv (Grant MU19-HF-012), Bulgarian National Science Fund (Grant DN09/15-2016). Yordan Stremski expresses his gratitude for the financial support by National Program "Young Scientists and Postdoctoral Researchers" (PMC 577/2018).

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EVALUATION OF THE EFFECTS OF REPRODUCTIVE FACTORS IN WOMEN WITH NON-SMALL CELL LUNG CANCER

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Introduction: After 1985 Lung cancer is the most frequently diagnosed and with the highest mortality rate (24.6%) among all oncological diseases. Differences between men and women regarding the frequency, mortality rates, histological variability of tumor, and the survival rates can be associated with the influence of the sex hormones on both physiological and pathological processes in the lung tissue.

Methods and materials: A retrospective and prospective case-control study has been conducted at the Clinic of Thoracoabdominal Surgery in “St. George University Hospital” – Plovdiv, on 90 women, all non-smokers, divided into two groups: “Cases” – 49 women with *NSCLC* and “controls” – 41 women.

Results: The mean age of women with *NSCLC* is 65.90 ± 12.02 , with the youngest woman being 37 years old, and the oldest – 87. The risk of developing lung cancer is almost three-fold increased in women who gave birth to their first child under 25 years of age (OR = 2.71; 95% CI (1.02-7.15)). A correlation was found between the number of births and the likelihood of lung cancer (Multiple R = 0.364).

Conclusions: The age of the first birth under 25 and the number of births are most likely a risk factor for non-small cell lung cancer.

LAPAROSCPY IN COLORECTAL PERITONITIS

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During the last few decades, medicine has achieved a remarkable progress in diagnostics and surgical opportunities. Apart from that, the colorectal peritonitis remains frequently met and has a severe outcome. For the patients with this kind of condition, the morbidity and mortality rates are very high [1]. Through the years, the minimally invasive techniques, have had a major development and now are becoming the method of choice. With the improvement of the surgical experience and skills with the laparoscopic approach, these procedures are finding a wider application even in the emergency surgery. There are still discussions about the place of the laparoscopy in the treatment of patients with colorectal peritonitis [2,3]. In the present research, we analyzed our experience with treating this kind of conditions by using minimally invasive techniques. For this purpose, we studied all the patients diagnosed and operated in UMHAT “Eurohospital” Plovdiv with colorectal peritonitis for the last 5 years.

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SURGICAL TREATMENT OF ENDOSCOPIC IATROGENIC PERFORATIONS

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Colonoscopy remains the main choice of diagnostics of colon diseases. Observed complications are generally rare. The iatrogenic perforation of the colon is the most severe one of them [1]. By many sources, the frequency of this complication varies between 0.14% and 0.65% for diagnostic colonoscopies, and around 3% for the performed therapeutic procedures [2]. Because of the great bacterial contamination, the perforation quickly leads to development of peritonitis. This explains the high morbidity and mortality rates among patients with this kind of condition. Surgery is usually the main method of treatment. Different studies from the last years have shown that the laparoscopic approach is fully applicable in these situations and can offer many advantages over the conventional techniques [3]. In the present paper, we describe and analyze our experience in the diagnostics and treatment of this type of endoscopic complication.

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NEW PROGNOSIS BIOMARKERS FOR SYSTEMIC LUPUS ERYTHEMATODES

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Introduction: Haematological abnormalities are a common manifestation of SLE, characterized by leukopenia, lymphopenia, thrombocytopenia, anemia, and abnormalities in the coagulation status. Therapeutic management of haematological abnormalities in systemic lupus has improved in recent decades, but there is still a need to seek new biomarkers to assist in this process. One such option is the study of certain cytokines, which can be studied dynamically over time and their level to predict the development of hematological abnormalities. **The aim** of the study was to evaluate the predictive role of chemokines in the development of hematological abnormalities in patients with systemic lupus.

Materials and methods: The study included 26 patients with systemic lupus with haematological abnormalities (leukopenia, lymphopenia, thrombocytopenia, anemia, abnormalities in the coagulation status). All patients met the criteria for diagnosis. The control group included 12 healthy individuals, similar in sex and age. We studied the SLEDAI and BILAG activity indices for systemic lupus. We tested chemokines CCL2, CCL19, CXCL10 dynamically with through triple samples by ELISA method, by kits of the company Diaclon, France, observing all the requirements of the manufacturer. For statistical processing we used SPSS at significance $p = 0.05$.

Results: Serum levels of CCL2, CCL19, CXCL10 were higher than controls. High serum levels of CCL2, CCL19, CXCL10 correlated with low levels of leukocytes, platelets, lymphocytes, and erythrocytes. Patients who responded adequately to treatment with corticosteroids 5-10 mg/kg initially had higher levels of cytokines tested; with improvement, their levels returned to normal. **Conclusion:** Chemokines are a new, unexplored unit of humoral immunity in patients with rheumatic diseases. Future studies will show the importance of their use as biomarkers for patients with systemic lupus and Sjögren's syndrome. Chemokine levels can be used as a prognostic biomarker in patients with systemic lupus.

CHEMOKINES IN PRIMARY SJÖGREN'S SYNDROME

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Chemokines are a large family of small cytokines and usually have a low molecular weight ranging from 7 to 15 kDa. Chemokines and their receptors are able to control the migration and residence of all immune cells. Some chemokines are considered inflammatory and their release may be induced during an immune response at the site of infection, while others are considered homeostatic and are involved in controlling cell migration during tissue development or maintenance. The physiological importance of this family of mediators is due to their specificity – to participate directly in inflammation or to cause migration of immune cells to the target organ associated with the disease. The aim of the study was to investigate chemokines that are important for inflammation and chemotaxis in patients with newly diagnosed primary Sjögren's syndrome and patients with haematological manifestations of systemic lupus and to look for a correlation between their level and disease activity. The study included 14 patients with Sjögren's syndrome and 26 patients with systemic lupus with haematological abnormalities (leukopenia, lymphopenia, thrombocytopenia, anemia). All patients met the criteria for diagnosis. The control group included 10 healthy individuals, similar in sex and age. We studied the SLEDAI and BILAG activity indices for systemic lupus and Schirmer's test, CRP, and erythrocyte sedimentation rate for Sjögren's syndrome. We tested chemokines CCL2, CCL19, CXCL10 dynamically with through triple samples by ELISA method, with kits of the company Diaclon, France, observing all the requirements of the manufacturer. For statistical processing we used SPSS at significance $p = 0.05$. Serum levels of CCL2, CCL19, CXCL10 were higher than controls. Serum levels of CCL2 and CCL19 were higher in patients with systemic lupus than in patients with Sjögren's syndrome ($p < 0.0001$). Patients with systemic lupus have lower CXCL10 levels than patients with Sjögren's syndrome ($p < 0.0001$). CXCL10 levels remained stable during the study period. Activity indices correlated with elevated levels of CCL2 and CCL19 in patients with systemic lupus. Chemokines are a new, unexplored unit of humoral immunity in patients with rheumatic diseases. Future studies will show the importance of their use as biomarkers for patients with systemic lupus and Sjögren's syndrome.

RARE VENOUS TUMORS: RAISING GPs AWARENESS

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Introduction: Venous tumors are rare and often present with unusual symptoms, but are very aggressive and with a high degree of local recurrence and early haematogenous metastases. Therefore, it is necessary to raise the GPs' awareness of the likelihood that the complaints of some of their patients could be caused by such a rare pathology and, respectively, they should promptly refer their patients for diagnosing by relevant specialist – vascular surgeon.

Aim: To raise the GPs' awareness of the problems of rare venous tumors and to acquire knowledge and competencies necessary to manage patients with probable venous tumors in general practice setting.

Methods: The authors present part of a study (bibliographic review) on rare venous tumors. The problems are discussed in the context of general practice specificity of tasks and responsibilities.

Results and discussion: A brief overview and analysis of publications on rare venous tumors focusing on general practice and primary care, aimed at raising GPs' awareness of the rare venous tumors, are presented.

Conclusions: The topic is very important and up-to-date because these problems are not included in the curriculum of the general practice specialty. GPs definitely need basic knowledge and skills to manage, in time and properly, patients with rare vascular/venous tumors, thus contributing to early diagnosis, better treatment and improved quality of life for the patients and their families and enhancing the patient compliance and trust in their GPs.

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RARE VENOUS TUMORS: TEACHING WITH CASES

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Introduction: Medical knowledge and achievements of modern medicine increase continuously, thus posing a number of challenges for doctors of all medical specialties. Training GPs with cases is effective, develops critical thinking and improves their skills. It has significant advantages over other teaching methods, as decision-making in clinical practice depends on experience, and case study training is **experience training**, which mobilizes and expands both theoretical knowledge of trainees and problem-solving skills, stimulates the use of all accumulated previous experience and develops abilities for complex analysis and search for optimal clinical solutions.

Objective: Enhancing the knowledge and skills of GPs on the problems of rare vascular tumors through case studies.

Methods: case studies

Results and discussion: A case of a rare venous tumor (leiomyosarcoma of the mouth of the saphenous vein magna dextra vein, vena femoralis communis dextra and the distal part of the vein) is presented.

Conclusion: Teaching with cases is a dynamic, inductive, interactive method, the value of which is growing in the context of lifelong learning, as well as in light of the growing role of e-learning. GPs develop the ability to think clearly, think carefully and identify hidden hypotheses. We would also like to emphasize that the role of the teacher's personality/charisma as a university professor and as an experienced doctor is very important in the process of motivating, in stimulating trainees/GPs to acquire new knowledge, strengthening their desire for self-improvement and high professional achievements.

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BENEFICIAL PROSTATE HYPERPLASIA IN MEN'S LIFE. ROLE OF OPL

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BPH is a histological diagnosis and prostate enlargement is one of the most commonly diagnosed clinical conditions in urology [1]. Many studies have shown that the initial treatment of BPH may vary between the urologist and the general practitioner. A study by Wei [17,19] and colleagues showed that the percentage of men undergoing active treatment was significantly higher than those observed by an urologist, regardless of the severity of the disease. According to studies, GPs play an important role in the process of early detection, diagnosis and treatment of BPH. For optimal management of the patient's health problems related to BPH, close cooperation between the GP and the urologist is required, and in our view this type of care can and should be provided by the general practitioner.

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EFFECT OF VARICOCELECTOMY ON SPERM CONCENTRATION, DEPENDING ON VARIOUS FACTORS IN INFERTILE MEN

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Varicocele is the most common disease in the general male population. The surgical intervention (varicocelectomy) is the most common treatment approach. The purpose of this study is to determine the effect of varicocelectomy on the values of sperm concentration depending on age, diagnosis, harmful working environment and smoking.

Patients (n = 48) were examined at the Urology Clinic at the University Hospital “St. George” in Plovdiv, Bulgaria with proven varicocele - gr. II and III with established diagnoses - oligoasthenozoospermia (OA), asthenoteratozoospermia (AT) and oligoasthenoteratozoospermia (OAT). Patients signed an informed consent. The men were separated in four groups according to their age, diagnosis, harmful working environment, and smoking. By a spermogram, sperm concentrations were monitored before and three months after varicocelectomy. The results were processed statistically -descriptive statistics, t-test for statistically significant differences before and after surgery (at $p < 0.05$), total percentage change after surgery.

Sperm concentrations improved after varicocelectomy, with percentage change of 26.93% ($p < 0.001$). Better results were observed for ages between 22-26 and 27- 31 years. The established positive effect in diagnoses OA, AT and OAT showed no trend of percentage change, while for smokers we observed a decline in the rate of change as the number of cigarettes per day increases. Overall, the surgical intervention has a lesser effect on drivers, foundrymen and others, as well as patients working under the influence of dust, paints, etc. compared to those working in a non-harmful environment. Three months after varicocelectomy, sperm concentration levels improved. Working environment and smoking can reduce the effect of treatment.

ANALYSIS OF THE METHOD OF FINANCING AND THE EFFECTIVENESS OF THE DIAGNOSIS AND TREATMENT OF OCCUPATIONAL BRONCHIAL ASTHMA IN INPATIENT SETTINGS

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Introduction: The “Working conditions” fund operates in the structure of the Ministry of Labor and Social Policy. Its strategy is concentrated on the increase of the working conditions quality, development of projects and programs concerning safety and health at work, improvement of the working conditions, reduction of the professional and health risks at the working place, and prevention of the occupational diseases.

Materials and methods: To achieve the given goals and tasks, I used the patient data registered in official records from the following sources: Book for patients admitted to the hospital, Alphabetical list of the patients admitted to the ward, Medical history of each of the examined patients with the results of the performed clinical and paraclinical procedures attached to them.

Results: The patients hospitalized with BA with occupational character by the fund “Working conditions” are 12.67% (95 patients) of the total number of patients admitted by the fund “Working conditions” (750 patients). At the same time, patients by CP diagnosed with bronchial asthma are 30.86% of the total number of patients admitted by CP for the whole 5-year period of the study (2 048 patients).

Conclusions: After observing the main characteristics of the clinical pathways and the “Working conditions” fund, we found that the aim of the clinical pathways is to increase the quality of the health care by improving the clinical results and by optimal consumption of health resources, and the aim of the “Working conditions” fund is to support the financing of activities for diagnosis and prevention of occupational diseases. Within the examination period, the expenses for diagnosing occupational diseases as part of the prevention and their early detection are characterized by a low implementation percent.

ANGIONEUROTIC EDEMA IN IMMUNOPATHOLOGY AND ALLERGOLOGY

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Angioneurotic edema is a common disease in allergologic practice. Leading in etiology and pathogenesis of the disease are immunoallergic factors and processes, despite the interdisciplinary characteristics of the issue. Special attention is paid having in mind the fact that the hereditary angioneurotic edema (HAE) is a rare disease with specific etiology and pathogenesis. It becomes clear that the interest in the problem is significant.

The aim of our presentation is to focus on some of the current aspects of etiology, epidemiology, clinical course, diagnostic and therapeutic algorithms of angioedema, including HAE. This assists clinicians of different specialties in adequate diagnosis and therapy of the disease.

SPECIFIC FORMS OF HYPERTENSION-DEFINITIONS, PROGNOSIS AND THERPEUTIC APPROACH

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Hypertension is defined as office systolic blood pressure (SBP) values ≥ 140 mmHg and/or diastolic BP (DBP) values ≥ 90 mmHg. Auscultatory or oscillometric semiautomatic or automatic sphygmomanometers are the preferred method for measuring BP in the doctor's office. These devices should be validated according to standardized conditions and protocols. Out-of-office BP measurement refers to the use of either home monitoring blood pressure (HBPM) or ambulatory monitorin blood pressure (ABPM), the latter usually over 24 h. It provides a larger number of BP measurements than conventional office BP in conditions that are more representative of daily life. Although the prevalence varies between studies, white-coat hypertension can account for up to 30-40% of people (and $>50\%$ in the very old) with an elevated office BP. It is more common with increasing age in women and in non-smokers. White-coat hypertension have increased adrenergic activity, a greater prevalence of metabolic risk factors, more frequent asymptomatic cardiac and vascular damage, and a greater long-term risk of new-onset diabetes and progression to sustained hypertension and left ventricle hypertrophy (LVH). Masked hypertension can be found in approximately 15% of patients with a normal office BP. Masked hypertension is associated with dyslipidaemia and dysglycaemia, hypertension-mediated organ damage (HMOD), adrenergic activation, and increased risk of developing diabetes and sustained hypertension. Treatment may be considered in white-coat hypertensive people with a higher cardiovascular (CV) risk profile, such as those with HMOD. In masked hypertension, lifestyle changes are recommended to reduce CV risk, with regular follow-up, including periodic out of office BP monitoring.

Keywords: hypertension, white-coat hypertension, masked hypertension, CV risk, HMOD

RISING THE KNOWLEDGE OF THE GENERAL PRACTITIONER ABOUT MALE INFERTILITY

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Introduction: Infertility is a major health problem affecting 10-15 per cent of couples and a male factor can be identified in half of the cases. Male factor contributes to almost 50 per cent of the infertile cases.

Materials and methods: Fifty English-language articles were read in total and analyzed.

Results: The literature search shows that there are no articles in Bulgarian about male infertility and worldwide the problem is not widely discussed.

Conclusion: The review shows that the information about male infertility in general practice is very sufficient not only in Bulgaria. The textbooks for general practitioners are not sufficient. There is a need of making standardized diagnostic algorithm for the needs of the general practice.

Keywords: male infertility, general practice, general practitioner

ALLERGIC RHINITIS – ETIOLOGY, EPIDEMIOLOGY, PATHOGENESIS, CLASSIFICATIONS

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Allergic rhinitis is the most common allergic disease in clinical practice. The great diversity of etiological factors and pathophysiological mechanisms are the leading cause for the different endotypical and phenotypical manifestations of the disease. The allergic rhinitis comorbidity and more specifically the association found between it and bronchial asthma are the circumstances affecting the clinical presentation of the allergic rhinitis, hindering the achievement of an efficient therapeutic control. Hence studying the etiology and pathogenesis of the allergic rhinitis have a key role in its treatment.

CLINICAL MANIFESTATION, FORMS AND SOCIAL-ECONOMIC ASPECTS OF ALLERGIC RHINITIS

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The persistent allergic inflammation of the nasal mucosa, being the distinctive pathophysiological feature of the disease, often leads to more pronounced symptoms and deterioration of patients' quality of life. The substantial overall cost of the direct and indirect expenses regarding the treatment and the control of the disease is another major socially important factor proving the definition of allergic rhinitis as "A disease of our time".

SARCOSINE IN URINE – A NEW POSSIBILITY FOR POTENTIAL BIOMARKER OF CLINICAL PROGRESSION OF PROSTATE GLAND VANCER

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Prostate gland cancer is one of the most common cancers and takes the third place in Bulgaria among the oncological diseases in men (Cancer incidence in Bulgaria 2013). It is most common in the age over 50. The nonspecific or absent symptomatology leads to late diagnosis in which case the treatment is not effective. At the moment, PSA (prostate specific antigen) is usually used in practise as a biomarker for screening and early detection of prostate gland cancer. The normal levels in serum are 0-4 ng/ml. However, this marker is an organ-specific, not a tumor-specific. The increased levels in serum are not always connected with malignant tumor; they can be caused even by benign prostate hyperplasia or prostatitis. For mass of opportunistic screening, it is recommended to make DRE (digital rectal investigation) and investigation of PSA-levels. In 20 % of cases of PSA-negative patients (not increased levels) prostate gland cancer is detected. For that reason, the search for new biomarkers is very important for early detection and clinical development of the disease. Prostate gland cells produce a lot of aminoacids (sarcosine, uracil, cinurenine, levcine) and metabolites and they are very often detected with increased levels in patients with prostate cancer, mostly in urine.

Chromatographic methods are the most appropriate for detecting aminoacids and metabolites produced by prostate gland cells, mostly in urine. The most common of them is sarcosine. The increased levels of these metabolites is detected in cases of prostate gland cancer.

The act of detecting aminoacids and metabolites of prostate gland cancer cells in urine and their increased levels is a new possibility for using them as biomarkers for early detection of prostate gland cancer. For the progression of the disease, they can be used as a panel.

Keywords: Prostate cancer, oncometabolites, sarcosine

ATRIAL FIBRILATION COMPLICATION – A CASE REPORT

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Despite good progress in the management of patients with atrial fibrillation (AF), this arrhythmia remains one of the major causes of stroke, heart failure, sudden death, systemic embolism and cardiovascular morbidity in the world. Furthermore, the number of patients with AF is predicted to rise steeply in the coming years. AF is independently associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men (Benjamin EJ, et al., 1998, Stewart S, et al., 2002, Andersson T, et al., 2013). Death due to stroke can largely be mitigated by anticoagulation, while other cardiovascular deaths, for example due to heart failure and sudden death, remain common even in AF patients treated according to the current evidence base. AF is also associated with increased morbidity, such as heart failure and stroke (Wolf PA, et al., 1991, Krahn AD, et al., 1995). Contemporary studies show that 20-30% of patients with an ischaemic stroke have AF diagnosed before, during or after the initial event (Kishore A, et al., 2014, Henriksson KM, et al., 2012, Grond M, et al., 2013).

RESISTANT HYPERTENSION

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Hypertension is a socially significant disease. Hypertension is defined as resistant to treatment when the recommended treatment strategy fails to lower office systolic blood pressure and diastolic blood pressure values to <140 mmHg and/or <90 mmHg respectively, and the inadequate control of blood pressure is confirmed by ambulatory or home blood pressure monitoring in patients whose adherence to therapy has been confirmed. Appropriate lifestyle measures and treatment with optimal or best-tolerated doses of three or more drugs. The recommended treatment strategy should include a diuretic, typically an angiotensin converting enzyme inhibitor (ACE) or an angiotensin receptor blocker (ARB), and a calcium channel blocker (CCB). Reasons for resistant hypertension are large gains in weight, excessive alcohol consumption, high sodium intake, intake of vasopressor or sodium-retaining substances, drugs prescribed for conditions other than hypertension, obstructive sleep apnoea (usually, but not invariably, associated with obesity), undetected secondary forms of hypertension. Effective treatment combines lifestyle changes (especially the reduction of sodium intake), discontinuation of interfering substances, and the sequential addition of antihypertensive drugs to the initial triple therapy. Addition of low-dose spironolactone or if not tolerated eplerenone, amiloride, a higher dose thiazide/thiazide-like diuretic, or a loop diuretic or bisoprolol or doxazosin.

Keywords: resistant hypertension, lifestyle changes addition of antihypertensive drugs to the initial triple therapy.

DIABETES AND DIABETIC RETINOPATHY – CURRENT DIAGNOSTIC AND THERAPEUTIC ASPECTS

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Diabetes mellitus, also referred to just as diabetes, is a chronic, social metabolic disease, characterized by a variety of complications, which affect different aspects determining the patients' quality of life. Hardly is there a medical care provider who does not come across a case involving diabetes in their everyday practice. Although the basis of establishing the diabetes diagnosis, as well as its pathogenesis, has been formulated for a long time, the focus of nowadays treatment is put not only on early treatment, but mainly on the patient-centered approach.

Although doctors have numerous medications as options for treatment at present, few of the patients do not develop any consequence caused by the “ominous” or deadly octet in the pathogenesis of the disease. Therefore, having in mind that diabetes is a common pathology in the population of working age, it is not only a matter of personal medical care, but an economic and social matter of interest as well.

Diabetic retinopathy is one of the complications requiring multidisciplinary approach. In the article, current tendencies of morbidity and treatment of diabetes are pointed out and there is a special focus on the need for medical standards dealing with diabetic retinopathy prevention, diagnosis and treatment in order to protect the eyesight of diabetic patients.

SJOGREN'S SYNDROME, ORAL MICROBIOME AND PROBIOTICS

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Sjogren's syndrome is an autoimmune disease that affects the exocrine glands. Lymphocytic infiltration of the salivary and lacrimal glands determines the manifestations of "sicca" syndrome (dry eyes and dry mouth). Clinical symptoms due to the development of autoimmune epitheliitis may originate from the kidneys, lower digestive tract, lungs, other organs and systems. Sjogren's syndrome is a heterogeneous and multifactorial disease that can affect any age, with a female-to-male ratio of 10:1 (1). Lately, modern technology has focused on the study of microbial communities in the human body, as well as the diversity of genes in the human microbiome (2). Microbiome bacteria are related to the immune system of the mucous membranes (oral, intestinal). In a state of dysbiosis in the course of the autoimmune inflammatory process and under the action of the applied therapy, the inflammation and disturbed mucosal barrier allow bacterial antigens to penetrate the systemic circulation and induce an immune process. In this aspect, studies on the oral and intestinal microbiome in Sjogren's syndrome, the state of dysbiosis and the inclusion of probiotics in therapeutic regimens are of logical interest of scientific and practical significance (3). Recovery of microbial populations and their ratios in the digestive tract could reduce some of the symptoms of the disease and reduce the overall activity.

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MEMBRANOUS NEPHROPATHY IN A PATIENT WITH AUTOIMMUNE THYROIDITIS

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Abnormalities of thyroid function are common in patients with kidney diseases. There are limited number of studies on how thyroid dysfunction affect the kidney. The most common renal disease observed in autoimmune thyroiditis is membranous nephropathy [1]. Membranous nephropathy is a common cause of nephrotic syndrome in adults. It usually occurs secondary to underlying disease processes such as autoimmune disorders, malignancy, infection, and drugs. Primary membranous nephropathy in 70-80% is autoimmune disease with positive antibodies against APLA2R.

We present a case of a man with postoperative hypothyroidism due to Graves' disease, nephrotic syndrome and membranous nephropathy revealed from kidney biopsy. The case is of interest because of the rare positivity to APLA2R, ANCA, Anti-Tg and ANA on the background of severe hypothyroidism and nephrotic syndrome, both of them barely responsive to treatment.

Membranous nephropathy associated with thyroiditis is well described in the literature, but membranous nephropathy associated with ANCA antibodies in the presence of thyroiditis is very rare [2].

We reconsider the connection between autoimmune thyroiditis and glomerulopathies.

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SJÖGREN'S SYNDROME – CLINICAL AND PARACLINICAL CONSIDERATIONS

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Sjögren's syndrome is a disorder of the immune system identified by its two most common symptoms – dry eyes and a dry mouth. Xerostomia itself is an unsatisfactory diagnostic criterion for the salivary component of Sjögren's syndrome. The clinician needs to identify the possible cause(s) and to provide the patient with appropriate treatment. In the presented clinical case, the patient is suspicious for Sjögren's syndrome but also for physical activities (sport) – induced xerostomia. The presence of focal sialadenitis in labial salivary gland biopsy specimen was compared with measurements of parotid flow rate, and the presence or absence of symptomatic xerostomia, major salivary gland enlargement, keratoconjunctivitis sicca and other connective tissue diseases. Following the ACR/EULAR criteria, the patient was diagnosed with primary Sjögren's syndrome deteriorated by extreme dehydration during regular sport activities.

FLEXIBLE URETEROSCOPY FOR THE DIAGNOSIS OF CHRONIC UNILATERAL HEMATURIA

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Chronic unilateral hematuria is characterized by intermittent or continuous gross hematuria that cannot be diagnosed using standard radiology and hematology methods.

In a total of 23 patients who presented with chronic unilateral hematuria, in whom radiologic and laboratory tests failed to reveal the source of bleeding, flexible ureteroscopy was performed. In the cases in which the lesion was identified, after complete inspection of the collecting systems, the bleeding site was treated ureteroscopically with a holmium-YAG laser.

During the follow-up of the 23 patients, 21 remained symptom-free, with only one session of flexible ureteroscopy necessary. Relapse occurred in two patients after 4 months and 6 months, respectively; during a second session of flexible ureteroscopy, the bleeding site was successfully identified and cauterized with a holmium:YAG laser. No surgical complications occurred.

Conservative treatment of patients with chronic unilateral hematuria should always be considered. Laser ureteroscopic treatment is an excellent method and should be considered as the first option for the management of chronic unilateral hematuria.

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MANAGEMENT OF THE DISTAL URETER IN OPEN NEPHROURETERECTOMY – COMPARISON BETWEEN ENDOSCOPIC URETERAL DETACHMENT AND BLADDER CUFF EXCISION

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Radical nephroureterectomy with complete removal of the ipsilateral ureter is considered mandatory in patients with upper urinary tract urothelial carcinoma.

In this study we compared differences after endoscopic ureteral detachment and open bladder cuff excision in nephroureterectomy.

A total of 69 patients underwent open nephroureterectomy for upper urinary tract transitional cell carcinoma – 45 with endoscopic ureteral detachment and 24 with bladder cuff excision.

Demographic, perioperative and oncological outcome data were collected and analysed in all cases.

Endoscopic ureteral detachment reduces operative duration and is associated with equivalent oncological outcomes compared with open bladder cuff excision in nephroureterectomy.

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LAPAROSCOPIC DECORTICATION OF SIMPLE RENAL CYSTS – A SINGLE INSTITUTION EXPERIENCE

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Simple renal cyst is a relatively common disease of renal parenchyma, with the reported incidence of about 10% in the general population

The aim of this study is to present our experience with laparoscopic management of symptomatic simple renal cysts.

20 patients underwent laparoscopic decortication for simple renal cysts at our department and were included in the analysis. All procedures were carried out using a transperitoneal approach. Patients underwent a radiological follow-up with computerized tomography and/or ultrasonography. Procedural success was defined as no recurrence of the cyst and complete pain relief. Symptomatic success was defined as a significant pain decrease.

Laparoscopic transperitoneal decortication represents an effective and safe treatment option in the management of symptomatic renal cysts.

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PROSTATE CANCER SCREENING – FROM BEGINNING TO THE FUTURE

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Prostate cancer is one of the most common malignancy and the second most common cause of cancer death in men (1).

Even though prostate cancer screening with PSA test has been studied with several large, well-funded studies, the evidence does not provide a clear recommendation to screen or not to screen patients.

PSA screening leads to overdiagnosis (i.e. diagnosis of prostate cancer in men who have indolent cancers, which otherwise would never come to clinical notice) and overtreatment (2,3).

Based on the current knowledge, prostate cancer screening by any method other than PSA is not supported. Multiple biomarkers have been shown to refine risk stratification with independent added value. Biomarkers can be considered only for selected men to improve decision of management.

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FLEXIBLE URETEROSCOPY FOR KIDNEY STONES – EFFICACY AND SAFETY

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The aim of this study is to present the efficacy and safety of flexible ureteroscopy for renal calculi with a burden of <2 cm, as well as the prevention and treatment of complications.

A total of 38 patients treated with flexible ureteroscopy and laser lithotripsy were retrospectively analyzed. Evaluation of the stone-free rate, effectiveness, safety, surgical technique, incidence of complications, and relevant treatments was carried out.

All patients underwent only one lithotripsy procedure. The success rate of flexible ureteroscopy was 94.7% (36/38). Among the 36 cases, the total lithotripsy success rate was 97.2% (35/36). The total stone-free rate after 8 weeks post-operation was 94.4% (34/36), the stone-free rate of the lower calyx was 77.7% (7/9); it was 94.1% (16/17) in the middle–upper calyceal and renal pelvis. The incidence of complications was 13.1% (5/38). None of the patients had serious adverse outcomes.

Flexible ureteroscopy represents an optimal treatment option for selected renal calculi with burden of <2 cm.

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TREATMENT OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME BY INTRAVESICAL INSTILLATION OF SODIUM HYALURONATE

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Interstitial cystitis/painful bladder syndrome (IC/BPS) is a chronic bladder condition characterized by frequent urination, urgency and pain, in the absence of any identifiable cause, such as bacterial infection, bladder out obstruction, or carcinoma (1). IC pain, when present, may be in different areas – pelvic, suprapubic, or perineal, and these urinary symptoms may involve both motor and/or sensory bladder dysfunction. The diagnosis of IC is difficult and made based on symptomatology, cystoscopy examination, and exclusion of other bladder disease. This disease seriously impacts the quality of life (2).

The ineffectiveness of IC/BPS therapies in part results from a poor understanding of the underlying pathogenesis and etiology. Due to the lack of fixed diagnostic measures and variety of clinical presentation, IC/BPS is challenging to treat (3).

Intravesical infusions of Sodium Hyaluronate in patients' with IC/BPS, in our view, is a good challenge for improving the symptoms and quality of life.

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PARAURETHRAL SKINE'S DUCT CYST – A RARE FINDING AFTER PUBERTY

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Benign cystic lesions of the external female genitals are relatively frequent encounters in routine gynecology practices. The prevalence of vaginal cysts has been estimated at one in 200 women, but this number is likely an under-representation, as many of them are asymptomatic and do not come to clinical symptoms (1).

The paired periurethral, or Skene's, glands, which are homologous to the prostate in men, enter the vestibule as paired gland openings adjacent to and below the urethra.

Paraurethral cyst (also commonly known as Skene duct cyst) is a rare cause of vaginal mass in neonates, with an incidence of 1 in every 2000-7000 live births and represents less than 0.5% of congenital malformations of the urinary tract (2,3).

Management of paraurethral cysts is controversial and include observation, aspiration, incision and drainage, excision, unroofing, and marsupialization

On a clinical note, complete urological evaluation should be undertaken to exclude all other lesions, such as urethral diverticulum, ureterocele, and paraurethral tumours.

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URETHRAL CARUNCLE: MANAGEMENT AND SHORT REVIEW OF THE LITERATURE

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Urethral caruncle is a benign lesion in postmenopausal women, pedunculated, or sessile polypoid lesion of the urethra [1], typically presenting as a fleshy, easily friable nodule of the posterior urethra near the external meatus.

Although women are sometimes asymptomatic at diagnosis, some patients experience pain or bleeding. As many as 5% of cases clinically suspected to be urethral caruncle may be represented as true neoplasms, of which half are malignant (2,3).

Although various treatment strategies have been reported and proposed, there is a lack of consensus amongst the gynaecologists and the urologists on the best management and treatment of the condition.

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DEVELOPMENT OF ANGIOEDEMA IN PATIENTS WITH RHEUMATOLOGICAL DISEASES TREATED WITH TNF-A BLOCKERS – A PROSPECTIVE STUDY

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Introduction: In recent years, there has been a significant increase in the number of drugs used and, accordingly, those that trigger directly or indirectly are associated with the development of angioedema. In women, the angioedema is characterized by a more severe course, which according to some authors is due to deterioration from periods of hormonal changes in the body – puberty, pregnancy, menstruation. TNF-a blockers have been used daily in rheumatology for inflammatory joint disease. Despite their undoubted role in controlling the disease process, with the accumulation of knowledge about these drugs, we are increasingly seeing side effects associated with them. **The aim** of the study was to evaluate the development of angioedema as a side effect in patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, receiving biological therapy with TNF- α blockers. **Materials and methods:** 96 patients were prospectively studied – 50 of them women and 46 patients receiving various TNF- α blockers – 35 patients – adalimumab, 30 etanercept, 24 infliximab, 5 golimumab, 4 certolizumab. All patients received additional slow-acting disease modifiers – methotrexate 7.5 to 15 mg / week, leflunomide 20 mg / day, sulfasalazine 2x1000 mg daily. Patients were followed for 24 months. For statistical processing we used SPSS at significance $p = 0.05$. **Result and conclusion:** All patients were questioned about the presence of signs of angioedema – during the approach of the medication and days after. No signs of angioedema were observed in any woman. Three men (6.52%) reported transient itching and a feeling of swelling in the face and neck. One man who was being treated with infliximab on the second application of the drug showed swelling in the face and neck, difficulty speaking and swallowing, increasing shortness of breath. He started treatment with corticosteroids and antihistamines, but due to the persistence of shortness of breath and edema, the patient consulted a toxicologist. After examination of C1 and C4, which turned out to be low, it was assumed that the patient had hereditary angioedema and treatment with a TNF-a-blocker was stopped. Although rare, treatment with TNF- α blockers can trigger angioedema.

HEALTH-RELATED QUALITY OF LIFE AND ITS DETERMINANTS AMONG WOMEN WITH TYPE 2 DIABETES MELLITUS

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During the past decades, many researchers have paid attention to health-related quality of life (HRQoL) and its determinants, especially in chronic diseases [1]. Diabetes mellitus is one of the chronic diseases, which causes a significant morbidity and mortality worldwide [2]. The International Diabetes Federation estimated that the number of diabetic patients would increase from 463 million in 2019 to 700 million in 2045 [3]. The current study aimed to evaluate HRQoL and its determinants among females with type 2 diabetes mellitus referred to outpatient clinics in Plovdiv. This cross-sectional study was carried out on a sample of female patients with type 2 diabetes mellitus (T2DM) in Plovdiv, the second largest city of Bulgaria. Inclusion criteria were female gender with duration of T2DM at least six months, willingness to participate in the study and age over 18 years old. The results showed the total AWI score of QoL to be -3.04 ± 1.45 ($p=0.2$). The highest and the lowest mean scores were observed in ‘freedom to eat’ and ‘people’s reaction’ domains (-3.86 ± 2.41) and (-1.79 ± 2.34) respectively. The mean score of quality of life in females with T2DM was far from desirable condition. In conclusion, these findings can help physicians and healthcare providers to design suitable interventions to improve the female patients QoL.

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OSTEOPOROSIS IN RHEUMATOID ARTHRITIS

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Osteoporosis (OP) is a frequent complication of rheumatoid arthritis (RA) with local and systemic bone loss which affects both trabecular and cortical bone. The etiology and pathogenesis of OP in these patients are complex and include life-style risk factors and disease-related determinants such as high levels of inflammation, low levels of physical activity and use of corticosteroids.

The purpose of our study is to determine the frequency of low bone mass as well as the influence of disease duration and corticosteroid use on bone mass in patients with RA.

Material and methods: the study includes 62 patients with RA and 88 age matched controls. Bone densitometry was performed by dual energy X-ray absorptiometry equipment in the lumbar spine (LS) and femoral neck (FN). The mean age of patients and controls were 53.4 and 54.8 years respectively. The mean disease duration was 6.3 years and 81.1% of patients were taking corticosteroids for a mean period of 4.3 years. At the FN, 46% of patients had OP compared to 28.2% in the controls ($P < 0.05$). At the LS the frequency of OP in patients was non-significantly lower than in the controls. OP was more frequent in corticosteroids treated patients as compared to non-corticosteroids treated patients both at the FN (42.8% vs 38.4%) and LS (27% vs 22.6%) but the differences were not significant. Disease duration longer than 10 years in comparison to disease duration of less than two years was associated with bone mineral density change of -10.6% at the FN ($P = 0.05$) and -10.1% at the LS ($P=0.05$).

Conclusion: OP is frequent in patients with RA both at the FN and LS. Fortunately, the clinicians can employ several antiosteoporotic medications to prevent OP fractures.

HIGH RESOLUTION ULTRASOUND AS A NEW DIAGNOSTIC TOOL OF LARYNX

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The larynx is located between hypopharynx and trachea. It has a small size and mobility in different planes, and it has complex anatomy. The diagnostics of the normal anatomy and pathological changes of the larynx is very difficult. The main imaging modalities for laryngeal evaluation are computed tomography (CT) and magnetic resonance (MRT), but both have a lot of limitations.

High Resolution Ultrasound (HRUS) is a noninvasive, cheap, easily available method of diagnostics with no radiation exposure. It could be used as an additional imaging modality or as an alternative to flexible fiberoptic-laryngoscopy in unresponsive patients. As a proven method for diagnostics of cervical lymph nodes, HRUS could be used for staging patients with laryngeal cancer.

The aim of the study is to present the normal parameters and sonographic anatomy of the larynx. 30 patients were observed by HRUS, using high frequency linear transducer of Esaote MyLabTM9 eXP. We visualized and examined significant structures in neck region: thyroid gland; thyroid, cricoid and arytenoid cartilages; pre-epiglottic space; vocal cords – true and false; lymph nodes.

Because of the good visualization of all these components by HRUS, HRUS could be used as an alternative and complimentary method of evaluation and follow-up.

HOW TO INTERPRET THE HYPODENSE SPLENIC LESION

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Focal hypodense splenic lesions could be found relatively often during standard computed tomography (CT) examinations of the abdomen for different abdominal pathological conditions. Although most hypodense lesions of the spleen can be considered benign, the interpretation of a hypodense lesion can be challenging. CT can offer different morphological criteria that can be applied to differentiate hypodense lesions of the spleen. The aim of this presentation is to review and discuss the characteristic CT imaging findings of hypodense lesions of the spleen.

Material and methods: The study includes 336 patients with hypodense splenic lesions with different origin for the period 2008-2019 year. We present the most common splenic pathologies leading to hypodense appearances on CT images and discuss the key CT morphologic imaging findings together with the clinical history of the patients. We discuss CT morphological criteria that can be applied to differentiate hypodense lesions of the spleen, such as the appearance of the lesion, borders, attenuation, presence of calcifications, cystic or solid components.

Conclusion: The most common benign lesions of the spleen are the cystic lesions, followed by haemangiomas. The most common malignant tumour is lymphoma, followed by splenic metastases. Most hypodense splenic lesions on CT represent benign lesions. Hypodense splenic lesions need to be evaluated in the clinical context.

NURSE PHYSICIAN RELATIONSHIP AND QUALITY OF CARE

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Nurses and midwives play a vital role in providing health services [1]. The world needs 18 million more health workers to achieve and sustain universal health coverage by 2030. That is why the World Health Assembly has designated 2020 the International Year of the Nurse and the Midwife [2]. Doctors and nurses make up the largest groups of individuals within the healthcare practice environment. Collaboration between physicians and nurses is key to improving patient care [3]. We know very little about the collaboration and interdisciplinary practice in the Bulgarian healthcare settings.

The purpose of this study was to examine the relationships between nurses' perceptions of their practice environment and nurse-physician communication. Physicians and nurses were questioned regarding the nature of their relationship, areas of disagreement related to patient care, and how disagreement gets resolved. Seventy percent of the physicians and 69% of the nurses described relationships as mostly positive. In conclusion, the need for greater collaboration between nurses and physicians in clinical practice is essential to improve patient care and worker satisfaction.

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THERAPEUTIC BENEFITS OF PLANTS IN THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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The liver plays a central role in the body's metabolism and detoxification [1]. Non-alcoholic fatty liver disease (NAFLD) is one of the socially significant diseases. The liver is the major organ that regulates lipid metabolism through various processes and disorders in them leading to abnormal lipid accumulation and the development of steatosis. If left untreated, steatosis can lead to cirrhosis and liver cancer [2]. Herbs have a number of positive effects (antioxidant, anti-inflammatory, anti-adipogenic, etc.), which is why the attention to them is increasing.

They combine beneficial action with no side effects. The aim of the review is to consider plants as a potential therapeutic agent in the treatment and alleviation of symptoms of NAFLD. We examine some herbs such as goji berry, green tea, coffee, turmeric, etc. that can be used in NAFLD treatment. Studies have shown that they affect non-alcoholic steatosis in various ways – they increase antioxidant enzyme activity and reduce insulin resistance and liver inflammation. They also regulate lipid metabolism by enhancing PPAR α (peroxisome proliferator-activated receptor α) expression, reducing SREBP (Sterol regulatory element-binding protein) activation, inhibiting the Fatty acid synthase, activate AMPK (5' adenosine monophosphate-activated protein kinase), etc. [3]. However, more research and clinical trials are needed to clarify their full potential.

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BIOCHEMICAL ASPECTS OF KYNURENIC PATHWAY IN SCHIZOPHRENIA

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There has been growing evidence that a relation exists between schizophrenia and the kynurenine pathway (KP) of tryptophan degradation in which several neuroactive compounds are generated. Of those, kynurenic acid (KYNA) draws most attention when exploring the biochemical mechanisms of schizophrenia as the elevation of its levels shows a correlation in patients diagnosed with this mental disorder. The KYNA is known to serve as a N-methyl-D-aspartate (NMDA) and alpha-7 nicotinic (α7ACh) receptor antagonist in the brain and agonist for several receptors related to inflammation in the periphery [1]. Both NMDAR and α7AChR are expressed on the cell membrane of astrocytes, which are the primary source of cerebral KYNA. KYNA tightly controls cortical neurotransmission, most notably the glutamatergic and dopaminergic systems. This is supported by the fact that elevated brain levels of KYNA appear associated with cognitive impairments and psychotic symptoms. The increase of pro-inflammatory cytokines induces elevated synthesis of the neuroactive KYNA. Evidence on the association between increased plasma levels of KP metabolites during prenatal development and long-term cognitive deficits has been discovered. Pharmacological methods of normalizing cortical kynurenine pathway metabolism are being explored [2]. The presented data aims to support the idea that the recognition of KYNA's role in the pathophysiology of schizophrenia might turn kynurenic acid into target for diagnostics and potential therapeutic strategies.

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DIETARY HABITS AND HEALTH STATUS OF MEDICAL STUDENTS

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Healthy dietary habits among medical students today are important to promote the consumption of quality food among their patients in the future. The main **aim** of this research is to assess dietary habits, body mass index (BMI), and self-assessment of own health of medical students. **Methods:** A questionnaire study was conducted among 107 students at the Medical University of Plovdiv in 2019. Weight and height were measured using a *Tanita* body analyser. **Results:** At home, the students prefer to eat/consume cooked meals, meat, fish, milk, vegetables and fruits. This type of eating has deteriorated outside sharply ($p < 0.001$) – they consume more dry foods and sandwiches. Students who have breakfast are predominant ($p < 0.001$). 69.2% of the students have a BMI within the normal range (18.5-24.99). 88.8% of students define their own health as *very good* or *good*. **Conclusion:** Medical students endeavour to observe principles of healthy eating including breakfast, and most of them have a normal range of BMI. Most students evaluate their own health positively.

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TOBACCO USE AND ALCOHOL CONSUMPTION AMONG MEDICAL STUDENTS

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Unhealthy personal behavior doesn't have only a high personal price, but also a high public one. The **aim** of this study is to analyze the frequency and severity of the using of alcohol and smoking among medical students and their opinion on these unhealthy habits. **Methods:** The survey was conducted among 107 students at the Medical University of Plovdiv in 2019. **Results:** Most students do not consider acceptable behaviour and do not tolerate habits such as smoking ($p<0.001$), over drinking with alcohol ($p<0.001$), marihuana/cannabis use ($p<0.001$), but they consider acceptable risk habits such as hookah use ($p<0.001$) and consumption of small quantity of alcohol ($p<0.001$). 30.8% of students consider acceptable over drinking with alcohol or smoking of marihuana/cannabis (18.7%). 65.4% of students do not smoke; 27.1% are smoking with varying intensity of the risk habit: once a day or more often; ex-smokers are 7.5% of students. 16.8% of medical students do not use alcohol, 22.4% consume alcohol less than once a month, 17.8% consume alcohol once a month, 29.0% consume alcohol several times per month and 14.0% consume alcohol once a week or more often. **Conclusion:** Most medical students do not use tobacco, but most of them use alcohol and tolerate unhealthy habits. Therefore, the effectiveness of health education needs to be increased in the medical education system.

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SPECT TOMOGRAPHY IMAGE QUALITY CONTROL

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In the single-photon emission computed tomography (SPECT), the detector rotates around the patient's body and registers from 60 to 90 planar images. Afterwards, from them are reconstructed tomographic images of sections of the studied object in the three main planes.

Tomography imaging contains valuable diagnostic information that is the basis for follow-up therapy of the investigated patient. It is therefore critically important that these images accurately represent the true distribution of radiopharmaceuticals in the human body. Possible malfunction of the camera can add so-called artifacts that may lead the physician to a wrong diagnostic conclusion. Regular control of main parameters such as homogeneity, resolution and contrast of the tomographic image obtained using Jaszczak phantom guarantees the accuracy of the obtained diagnostic information. According to the requirements of the NEMA standard, homogeneity and resolution are evaluated visually, while the tomographic contrast is evaluated quantitatively.

In this work, we propose a new approach for evaluation of the output parameters involved in the computation of the tomographic contrast in order to ensure the uniformity and repeatability of the quantitative indicator.

GHRELIN AND ITS PARTICIPATION IN THE PATHOGENESIS OF OBESITY AND GALLSTONE DISEASE

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Obesity is a health problem that corresponds to a number of diseases, including cholelithiasis. It is one of the most common diseases of the digestive system – it occurs in 15% of adults. The pathogenesis of gallstone disease is closely related to lipid and pigment metabolism in hepatocytes. Cholesterol stones are 10% of cases of cholelithiasis, 15% bilirubin stones, and 75% mixed stones. Ghrelin is involved in the regulation of hepatocyte lipid metabolism by stimulating hepatic lipogenesis directly through GHS-R. There is a direct relationship between the level of ghrelin in the blood and that of high-density lipoprotein (HDL). Our aim is to investigate the role of ghrelin in the pathogenesis of gallstone disease accompanied by obesity in human individuals and an experimental rat model.

Material and methods: 10 patients from University Hospital "Evrohospital", Plovdiv with a clinical diagnosis of cholelithiasis are examined by ultrasound, biliary endoscopy and biochemical methods. The liver of rats with proven metabolic syndrome and obesity was immunohistochemically tested for ghrelin receptors in hepatocytes.

Results: 10 of the patients with cholesterol stones have disorders of lipid metabolism. 7 are overweight and three are not obese. In the liver of obese rats, we detect presence of ghrelin receptors.

Conclusion: Through its receptors in hepatocytes, ghrelin directly interferes with their metabolism. As a hunger hormone, it plays a key role in controlling body weight, and the formation of gallstones is associated with obesity. The formation of gallstones is a multifactorial process. Various aspects of lipid metabolism are affected: the synthesis of cholesterol, phospholipids, bile salts, as well as mucoid secretion from the gallbladder wall and biliary tract motility. Ghrelin also has a role to play in these complex mechanisms, which needs to be clarified.

THE OPINION OF HEALTH PROFESSIONALS ABOUT TELEMEDICINE IN BULGARIA

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The development of information and communication technologies play an important role in the transformation of healthcare. In times of global emergencies such as COVID-19, telemedicine can provide a high-quality service that increases the access to quality health care.

The main **aim** of this study is to examine the attitudes among medical professionals to offer distance medical services in Bulgaria.

Material and methods: 92 medical professionals were surveyed. Own tools were used – a questionnaire containing questions related to the opinion of health professionals about the possibilities of offering telemedicine services. Statistical processing of the data was performed using the software product SPSS v.17.

Results: The majority of the respondents are positive about offering telemedicine services (71.7%). Approximately half of the respondents (45.6%) do not agree to consult a patient they do not know by phone or computer. There was a statistically significant difference in the answers to the question related to the concerns about the use of medical services at a distance ($P < 0.05$), as the respondents with higher education are more worried about the misuse of personal information. The analysis of the results shows a dependence on the concerns of medical professionals about the legal regulation.

Conclusions: The telemedicine service for consultation on a health problem is well received by health professionals. The application of telemedicine services would also increase the satisfaction among patients – it saves time, there is no need to travel and wait in front of a doctor's office. In the context of the COVID-19 pandemic and physical distancing, the telemedicine solutions would protect patients and healthcare professionals from spreading the infection.

DISTANCE LEARNING IN THE CONDITIONS OF A PANDEMIC THROUGH THE VIEW OF THE STUDENTS FROM MEDICAL UNIVERSITY – PLOVDIV

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During the COVID-19 pandemic and following the WHO recommendations for physical distancing, distance learning became extremely relevant and important for Bulgaria. This demanded conducting exercises, lectures, tests and exams in a remote electronic environment.

The **aim** of the present study is to examine the student's opinion about distance learning during the COVID-19 pandemic.

Material and methods: An anonymous online survey was conducted among students from the Medical University – Plovdiv in the period from 23.05.2020 to 30.05.2020. It involved a total of 406 students from English and Bulgarian programs.

Results: The positive factors from the introduction of distance learning are that it provides more free time and according to the two studied groups – taught in Bulgarian (54.2%) and taught in English (46.9%) – it gives a good opportunity for self-development and new knowledge. Most often students communicate with teachers through the Microsoft Teams platform or via email. Among both study groups the most commonly used distance learning device is a laptop. In second place among those trained in Bulgarian is the smartphone (18.6%), and among those trained in English is the tablet (14.2%).

Conclusions: The opinion of the students is crucial for the management of each university. Their assessment of the effectiveness and quality of distance learning in the context of the COVID-19 pandemic should encourage the communication with their teachers. The distance learning in medical universities cannot completely replace the traditional one, but it can upgrade it.

SOCIAL ASPECTS OF DISTANCE LEARNING DURING THE COVID-19 PANDEMIC

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The aim of the present study is to examine some social aspects of distance learning (DL) during the COVID-19 pandemic.

Material and method: An anonymous online survey was conducted among students from Medical University – Plovdiv from all courses and specialties, which was spread with the help of Google forms.

The questionnaire is in Bulgarian and English and it has two panels. The first panel consists of questions related to the specialty, course, gender, age and permanent residence of the respondents. The second panel has 2 questions with more than one answer, 5 – open answers related to the overall satisfaction with distance learning, teaching methods, the quality of assessment of student knowledge, communication with teachers and recommendations.

Results: 288 foreign and 118 Bulgarian students completed the questionnaire. Most often the students communicate with their teachers through the Microsoft Teams platform (92.4%; 88.9%) or by email (31.4%; 34.4%) in both groups. English-speaking students prefer instant messaging (8.5%; 24.3%), while Bulgarian students rely more on telephone contacts in order to communicate with their teachers (9.3%, 3.5%). Opinions among students are very different when problems arise. Most often they seek solutions directly from the lecturer (57.6%; 47.9%) or the head of the department (9.35; 4.2%). About 11.9% of the Bulgarian students and 34.4% of the foreign students express a pessimistic opinion: there is no point in dealing with problems as they do not solve them. The answers to the open-ended questions prove how demanding the students to their teachers are, to the way the exercises and lectures are presented.

Conclusions: Students are the most logical evaluators of the quality of education. Their assessment should encourage their communication with teachers. This can lead to joint participation in the teaching and learning process, which will increase the quality of the learning process.

КОНТРОЛ НА LEGIONELLA SPP. В ДЕНТАЛНАТА ПРАКТИКА В АНГЛИЯ И В БЪЛГАРИЯ – СРАВНИТЕЛЕН АНАЛИЗ

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В денталната практика е лесно да се разпространят инфекции, причинени от *Legionella* spp. и други като *Pseudomonas*, spp. и атипични микробактерии, при работа с множество устройства, които използват вода и генерират фин воден аерозол, както и продължителните периоди на застой на водата във водните пътища на денталния юнит (напр. през нощта). Всичко това, както и липсата на мерки, или недостатъчните такива, водят до образуване на биофилм по вътрешната повърхност на водните пътища – среда, която осигурява на бактериите оптимални условия за живот. Целта на тази работа е се сравнят прилаганите в България мерки за мониторинг и за контрол на водата в денталния кабинет с добрите медицински практики в Англия и извеждане на препоръки за оптимизиране качеството на водата за дентално лечение у нас. Инструктивните материали за превенция и контрол на бактериалната контаминация и качеството на водата в денталната практика според Code of Practice: Legionnaire disease; The Control of Legionella Bacteria in Water Systems (L8); НТМ 01-05 (England and Northern Ireland) и WNTM 01-05 (Wales) и НТМ 04-01 в Англия са сравнени с реално приложимите инструктивни материали в България в денталните практики. Изследвани са 56 водни проби от юнити и водопреносната мрежа в денталната практика. От извършваните превантивни дейности в Англия: използване на питейна вода; продухване на водните пътища за 2 мин в началото на работния ден и за 20-30 сек между пациентите; задължителна дезинфекция на бутилката на денталния юнит; промиване на водните пътища на столове, които се използват рядко поне 2 пъти в седмицата; тест за бактериална контаминация на водата; прибавяне на биоцид към водата в бутилката и промиване на водните пътища, в България единствено се осъществява използването на питейна вода за лечение. От 56 водни проби от дентални юнити и водни пътища от различни обекти 18(32,14%) са положителни за *Legionella* spp.

ПРОТИВОВЪЗПАЛИТЕЛНО ДЕЙСТВИЕ НА РАСТЕНИЯ ОТ РОДА *SIDERITIS*. ОБЗОР

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В биологичната таксономия се споменават повече от 100 растения от рода *Sideritis*, като разпространението им обхваща широк ареал, от Мароко през Средиземноморието и Балканите до източна Азия и Китай. В последните години се наблюдава все по-интензивен интерес към тези растения и те се откриват все по-често в композицията на хранителни добавки, напитки, козметични продукти. Събирани и използвани като билки от древността, представители на този род се прилагат в етнофармакологията за различни индикации, много от които са придружени с възпаление. Съставът от биологично активни вещества се различава значимо при отделните видове, но при почти всички се откриват редица дитерпени, полифеноли, флавоноиди, иридиоиди, органични киселини, а повечето се характеризират с изразена на актиоксиданта активност [1,2].

Целта на настоящия обзор е да обобщи и съпостави резултати от изследвания и експерименти, показващи изявената противовъзпалителната активност на екстракти от различни видове от рода *Sideritis*, както и изолирани вещества от състава им като монопрепарати.

Представяйки редица трудове с различни *in vivo* и *in vitro* методи, авторите се стремят да се създадат научна основа, която обяснява етнофармакологична употреба на растенията от рода *Sideritis* и да подчертае потенциала им за по-нататъшна работа по разработването на терапевтични продукти за лечение на множество заболявания.

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DISTRIBUTION AND USE OF SILVER BIRCH (*BETULA PENDULA*, ROTH)

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Modern phytotherapy is a successful combination of the traditional knowledge about the use of medicinal plants and a modern scientific approach to the detailed study of the composition and mechanisms of action. The interest in the therapy with pharmaceutical products derived from medicinal plants grew exclusively in the second half of the last century, for a number of reasons. They are a rich source of biologically active substances, offering potential opportunities for the development of new drugs. In addition, they show good tolerance by the human body and the absence (or much less frequent manifestation) of side effects compared to synthetic products.

Products containing extracts from different parts of white birch (*Betula pendula*, Roth) are known and used in traditional medicine and phytotherapy in various forms. The diuretic action as well as the beneficial effect of alcoholic extracts from the buds, leaves and bark in chronic eczema and other skin diseases are well known and described. Birch tar is included in a number of ointments with pronounced antiseptic and keratolytic action. This review covers some aspects of the broad therapeutic potential of birch products, with emphasis on birch leaves, their chemical composition and some of the effects of derivative products, such as anti-inflammatory, antiproliferative, cytotoxic, antioxidant and others.

APPLICATION OF INFORMATION TECHNOLOGY IN HUMAN RESOURCE MANAGEMENT IN PRIMARY HEALTHCARE

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Objective: This study aims to explore the availability of human resources management tools among Primary Care Information System. **Material and method:** Analysis of the most commonly used Primary Care Information Systems. **Results:** With the beginning of the healthcare reform in Bulgaria, also begin the development and use of medical software in primary medical practice. About 20 Bulgarian and international providers of information technology develop and implement over 50 software products for healthcare purposes. The information systems are oriented to the needs of different groups of users – general practitioners, specialists, diagnostic and consulting centers (DCC), hospitals, medical laboratories, pharmacies. The existing medical software products provide automation of the reporting of the medical services and give an opportunity to reduce the time of the medical specialists for work with paper documents. The available Primary Care Information System does not have a tool for human resources management. **Conclusion:** The implementation of new technologies in human resource management processes is necessary to optimize the management and quality of health care, at two levels – primary care, as part of the healthcare system and each outpatient practice for primary care. Targeted research and analysis of human resources and their management should be an integral part of the information technology used in primary care.

Keywords: primary care, human resources management, software, information systems.

HEALTH STATUS, QUALITY OF LIFE AND PSYCHO-CLIMATE IN HEALTH CARE SPECIALISTS – SURVEY

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Abstract: This study **aims** to evaluate the health status and quality of life of healthcare professionals regarding the workplace psycho-climate.

Material and Methods: A survey was conducted in the period 2018-2019. Among 304 (284 women and 20 men) healthcare professionals selected randomly from the University Hospitals, District Hospitals, Oncology Center-Plovdiv, Diagnostic and Consultation Centers in Plovdiv and the region and the Specialized Rehabilitation Hospital, Hisarya. The object of the study was the health status and quality of life of health professionals, and the subject – their physical and mental health.

Results: Almost half (48.74%) of the respondents suffer from chronic diseases, mostly diseases of the blood and blood-forming organs. Healthcare professionals working in larger healthcare facilities report uncomfortable work environments and irrational daily routines, while impacts of psychological and personal character report those working in smaller healthcare units.

Conclusions: The study showed that the health status and quality of life of health care professionals are independent of factors such as gender, age and work experience, and chronic illnesses are strongly affected by the workplace psycho-climate. It was found that with increasing work experience, healthcare professionals not only are not susceptible to side effects, but cope with them significantly better, relying on established personal and professional qualities characteristic of the profession.

Keywords: healthcare professionals, health status, quality of life, psycho-climate

STRESS IN THE WORK OF THE PHARMACIST IN A COVID-19 PANDEMIC

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The WHO and public health authorities around the world are taking action to limit the spread of COVID-19 [1]. This period created stress, insecurity, fear and panic in society. In March, a state of emergency was declared in Bulgaria in order to limit and slow down the spread of COVID-19. Authorities have introduced a number of measures and called for people to work from home and stay at home whenever possible.

Pharmacists worldwide continue their mission amid the pandemic and the state of emergency. They are fulfilling their official duty on the first line to deal with the growing number of patients coming to pharmacies. Pharmacists may experience additional stressors during a pandemic, such as working with at-risk patients, insufficient personal protective equipment, the need for constant vigilance, increased working hours, the need for constant training and changes in rules and requirements of MH and NHIF, reduced social support, insufficient personal capacity for self-care, insufficient medical information about the long-term effects of the infection, fear of infecting the family and loved ones.

During a pandemic, recognizing the symptoms of stress is necessary in order to take steps to build resilience and deal with the crisis. Strategies need to be developed to reduce fear and anxiety among front-line workers by providing clear, concise and accurate information on COVID-19, including how to access assistance when needed [3].

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VORTIOXETINE A MULTIMODAL ANTIDEPRESSANT WITH A POTENTIAL ANALGESIC ACTIVITY (REVIEW)

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Vortioxetine is a new multimodal antidepressant drug, which inhibits the high affinity serotonin transporter and also modulates different subtypes of serotonin receptors. The drug is a full agonist of 5-HT_{1A} receptors, a partial agonist of 5-HT_{1B} receptors and an antagonist of 5-HT_{1D}, 5-HT₃ and 5-HT₇ receptors. Vortioxetine has good profile of safety and does not increase body weight and sexual dysfunction like SSRIs nor leads to adverse cardiovascular effects like SNRIs. It also improves the quality of life for depressive patients due to its effectiveness on the cognitive dysfunction that often occurs in unipolar depression.

Its analgesic effect is not fully known yet although preclinical studies show that the drug reduces neuropathic pain in mice [1]. Serotonin induced hyperalgesia is related to the activation of 5-HT₃ receptors while the activation of 5-HT₇ receptors leads to analgesic effect. In a dose of 10mg/kg b.w. Vortioxetine will efficiently antagonize 5-HT₃ receptors leaving the nearly 80% of 5-HT₇ receptors unoccupied and ready to be activated by serotonin [2].

More studies need to be conducted regarding the antinociceptive effects of the drug on different type of pain models in animals.

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CARIPRAZINE – A NEW HOPE FOR PSYCHIATRIC PATIENTS

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Schizophrenia and bipolar disorder are severe and debilitating psychiatric disorders. Despite the availability of numerous antipsychotic drugs, many patients still experience poor outcomes and treatment-limiting adverse side effects. Cariprazine is a novel antipsychotic with unique pharmacodynamic and pharmacokinetic properties, approved by FDA in 2015. It is both a dopamine type 2 and dopamine type 3 partial agonist and is similar to other atypical antipsychotics in exhibiting antagonistic activity at serotonin type 2A receptors. Cariprazine exhibits higher affinity for the D3 versus the D2 receptor. Initially cariprazine was indicated for the treatment of schizophrenia and acute manic or mixed episodes [1]. In clinical trials cariprazine have demonstrated enhanced efficacy for negative symptoms, compared with other antipsychotics, in patients with high negative symptom scores [2]. In preclinical studies cariprazine showed antidepressant action [3] and recently FDA approved it for the treatment of depression in patients with bipolar I disorder. The objective of the present review is to describe the pharmacokinetic and pharmacodynamic properties of cariprazine, its efficacy, therapeutic potentials and tolerability in the management of psychiatric disorders.

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ANXIOLYTIC AND NEUROPROTECTIVE EFFECTS OF CANNABIDIOL: REVIEW

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The therapeutic benefits of cannabis have been known since ancient times. In traditional Chinese medicine, cannabis has been used to treat asthma, malaria and gout, and in India for neuralgia, convulsions and migraines. Cannabidiol (CBD) is the major non-psychotomimetic phytocannabinoid present in *Cannabis sativa*.

In clinical practice, the effectiveness of CBD has been proven only in a narrow range of medical conditions, such as epilepsy, chronic pain, nausea and vomiting caused by chemotherapy. Studies in animal models and in healthy volunteers clearly suggest an anxiolytic-like effect of CBD [1]. Studies show that cannabidiol reduces anxiety via 5-HT_{1A} and cannabinoid receptor activation. Existing preclinical evidence strongly supports CBD as a treatment for generalized anxiety disorder, panic disorder, social anxiety disorder and post-traumatic stress disorder when administered acutely [2].

In the last decade, CBD administration has emerged as a potential therapeutic strategy for the treatment of several neuropsychiatric conditions. A number of preclinical models of cognitive impairment suggest that CBD improves learning and memory. CBD has been proposed to exert neuroprotective effects in neurodegenerative conditions, including Alzheimer's and Parkinson's disease, epilepsy and multiple sclerosis [3]. The present review summarizes data for the anxiolytic and neuroprotective effects of CBD.

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ATOMOXETINE – AN ALTERNATIVE IN THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER

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Attention deficit hyperactivity disorder (ADHD) is a disease of the neurodevelopment, which affects the quality of life [1]. ADHD is usually diagnosed in childhood, but the number of adult patients suffering from this pathological condition has increased. More than half of the children and almost 90% of adults with ADHD have a comorbid psychiatric disorder [2].

Pharmacological treatment includes medicines that affect reuptake of norepinephrine. Atomoxetine is a new drug with the same mechanism of action. Despite that, it has been registered for the first time in Bulgaria in 2014; it becomes more popular in 2019. Atomoxetine can be used by comorbid psychiatric patients due to lack of exacerbation of accompanying disorders [2].

The inhibition of norepinephrine reuptake is associated with cardiovascular side effects. Atomoxetine increases diastolic and systolic blood pressure and heart rate in children and adolescent patients, which is similar to the effects of amphetamines (AMP), but in contrast to AMP Atomoxetine does not cause dependence [3].

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THE NECESSITY OF DIAGNOSING AND TREATING CHRONIC PERIAPICAL PERIODONTITIS WITH 3D CONE- BEAM COMPUTED TOMOGRAPHY

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Periapical periodontitis can be an acute or chronic disease. Research shows that there are 6 main causes that lead to asymptomatic or chronic apical periodontitis: persistent intra-radicular infection; intraradicular infection (actinomycosis); foreign body reaction caused by a root-obturing material, accumulation of endogenous cholesterol crystals true cystic lesions and tissue formed post treatment (scar) [1]. Chronic periapical periodontitis is usually asymptomatic and is most often diagnosed, treated and followed with two dimensional conventional, digital periapical or orthopantomograophical radiographs. They tend to have a lower ionising radiation but a lower sensitivity.

Teeth which have chronic periapical lesions tend to be difficult to treat even when endodontic treatments have been performed with the best possible care and up to the current standards. The size of the lesion and its histologic status determine their future prognosis. Three dimensional cone beam computed tomography has proven to be a valuable adjunct in locating and fully representing the size and relationships of such lesions to important anatomical structures [2]. They are invaluable in planning a future endodontic surgery procedure, prognosing the success or failure after treatment and following up the healing process. The information that 3D CBCT gives presents a totally different picture, which can completely change the diagnosis, treatment plan and prognosis. The information given may justify the increased ionising radiation dose [3].

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NONSURGICAL ULTRASONIC PERIODONTAL ENDOSCOPY. EFFECT ON BONE HEALING IN INFRAOSSAL DEFECTS

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Non-surgical periodontal therapy techniques are applied by hand, rotary, sonic, ultrasonic, laser, combined instruments and devices. Non-surgical treatment is performed by access through the entrance of the periodontal pocket [1].

Kwan J. used miniature ultrasonic tips to treat the root surface with the help of the periodontal endoscope and introduced the term ultrasonic periodontal endoscopy – UPE. The combined method with systemic antibiotics achieves a reduction in periodontal probing depth and radiographic filling of the initial infraossal defects. UPE is an endoscopically performed SRP that can be combined with intentional curettage of various types. The advantage is that there is the possibility of indirect visual access, which saves time and tissues due to minimally invasive removal of dental biofilm and calculus [2]. Studies show that ultrasonic treatment of the root surface under visual control achieves less removal of cementum and dentin, which improves healing results.

Nonsurgical therapy alone can result in improved bone healing, preservation of the supracortical tissues and total filling of the infraossal defect [3].

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CLEARING TECHNIQUE AS EDUCATIONAL TOOL FOR EXPLORATION OF ROOT CANAL SYSTEM

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Clearing technique is a simple and inexpensive technique for in vitro examination of root canal system and it renders the teeth transparent. The clearing technique is the simplest method for visualizing and exploration tree-dimensionally the comprehensive structural anomalies and variation of different teeth [1]. Transparent tooth model developed after clearing technique can be used to obtain information on various aspects of endodontic treatment like root canal configuration; canal instrumentation techniques; effect of post design and its influence on root fracture; penetration of human saliva through dentinal tubules; sealer placement techniques in curved canals; microleakage of root canal sealers; for obtaining information on the quality of root canal obturation [2]. The knowledge gained permits an increased appreciation of the anatomy of the root canal system.

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TRANSPERENCY CHANGES OF ULTRATRANSLUCENT MULTI-LAYERED ZIRCONIA

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The process of low-temperature degradation of zirconia occurs because of the spontaneous transformation of metastable tetragonal (t) phase into a monoclinic (m) phase [1]. Via CAD/CAM systems, 27 veneers of UTML zirconia are milled in 3 different thickness and 3 colors. Translucency is measured before and after hydrothermal ageing through the formula: $(L^*_B - L^*_w)^2 + (a^*_B - a^*_w)^2 + (b^*_B - b^*_w)^{2|1/2}$ [3]. Statistical analysis of the data is performed via IBM SPSS Statistics v. 22, level of significance $p < 0.05$. Results show statistical difference in the level of translucency with no clinical meaning and no change of the colour of veneers.

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DEVICE FOR MECHANICAL-CYCLIC LOADING OF TEST SPECIMENS

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Precision attachments have different design. During the chewing process, the elements of this type of constructions are repeatedly subjected to mechanical stress. In the case of precision attachments, the matrix-patrix design adheres to the cyclic repeated chewing cycle.

Purpose: Our aim is to design and provide a device for multiple mechanical and cyclic loading of various constructions of matrix and patrix precision attachments on a project implemented with the participation of lecturers from the Technical University, Department of Electronics.

Materials and Methods: The device concerns a cyclic laboratory examination of the retention of telescope crowns made by different methods. The unit has the following main parts: **the mechanical part** consists of upper, middle and lower plates connected by strictly parallel guiding axes. Each plate carries different activating elements. **The retentive part** secures the support element and has a reservoir and container for artificial saliva attached to it. **The electronic-processing** unit records the values the number of cycles, the time to complete one cycle and regulates the pressure forces.

Results: The constructive principle of the developed device, which detects multiple insertion and separation cycles, in artificial saliva, is used to test telescope crowns. There were prepared four groups test specimens in advance for various double crown modifications designed using CAD/CAM and produced using a 3D-printer.

Conclusion: Preliminary tests for working with the device, with the participation of professors from the Technical University of Plovdiv give us a reason to apply the repeated insertion-separation cycles approach to other prosthetic elements.

Keywords: telescope crowns, device, insertion-separation cycles

PARENTS' KNOWLEDGE ABOUT CHILDREN'S CARIES AND EARLY PREVENTION

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Tooth decay is one of the most common oral diseases among children. This requires prevention to start from an early age [1, 2]. Apart from dentists, the family environment and the personal example of the parents also play a crucial role in protecting the dental health of adolescents.

Aim: To establish the awareness of parents of children attending kindergartens about dental caries as a disease encountered among children, as well as their participation in the implementation of the necessary preventive measures.

Material and methods: A survey was conducted with 174 parents of children attending kindergartens in Plovdiv. The questionnaire developed by the authors contains questions related to the knowledge of parents about oral hygiene, the frequency of visits to the dental office for prevention and timely treatment of children.

Results: The role of pediatricians and GPs in the prevention of dental diseases among children is unsatisfactory. The first visit to a dentist is when children turn 1 year old or even later. There are parents who do not take their children for preventive examinations, and others neglect the timely treatment of their children's diseased teeth. Children prefer the most cariogenic carbohydrate foods.

Conclusions: The majority of parents neglect the early preventive measures needed to protect children from developing a tooth decay.

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STEP BY STEP DEFINING TWO IMPRESSION TECHNIQUES USING QUALITY CONTROL SOFTWARE

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Aim: To characterize qualitatively step by step two impression techniques using specially designed program 3Shape Convince™ Standard.

Materials and methods: Tooth 36 is prepared for indirect restoration. From the prepared tooth an impression was taken in two ways: with Trios 3Shape scanner intraorally and after taking a conventional cast using 800D scanner. The two casts were aligned and precise data in 2D and 3D projection was gathered, including vector deviation inquiry, colour mapping and statistical analysis.

Results: The successive steps using quality control software are specified: proper positioning of the two models, detailed plane and statistical analysis.

Conclusions: An accurate impression is fundamental to a successful dental treatment. The digital casts are better accepted by the patients, less time-consuming for the dental practitioner and reveal a great potential for obtaining precise biomimetic restorations.

Keywords: impression, digital, scanner

**DEGREE OF AWARENESS OF THE DENTAL
PRACTITIONERS ACCORDING TO WORK EXPERIENCE
AND SPECIALTY ABOUT THE IMPACT OF REMOVABLE
DENTURES ON SPEECH FUNCTION
(QUESTIONNAIRE STUDY)**

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Despite the advancement of medicine and the immense information flow, in scientific literature there is lack of contemporary studies on the effect that removable dentures exert on the speech function and adaptation.

Purpose: The awareness of the dental practitioners according to work experience and specialty about the impact of removable dentures on speech function

Material/Methods: 369 dental practitioners from 70 settlements (67 of which – towns and 3 – villages in Bulgaria) were part of the research. The participation of dental practitioners is random, without prior selection, which validates the representativeness of the sample.

Results: With the accumulation of work experience, medical professionals are more informed about the impact of removable prosthetics on speech function.

Specialist dental practitioners are defined as far better informed than their General dental practitioner (GDP) peers ($\chi^2=11.58$; $p < 0.01$); 69.50% of the specialist dental practitioners report excellent awareness of all the explored factors that influence the speech function.

The dental practitioners specializing in Prosthetic dentistry are those who are the most informed ones of the effect of treatment with removable dentures on the speech function. ($\chi^2=17.64$; $p < 0.01$)

Conclusions: Postgraduate specializations increase the level of awareness – dentists with a specialty are more informed, and those with a specialty in prosthetic dentistry are defined as well informed.

Keywords: complete dentures, speech function

VOLUMETRIC CHANGES OF CHRONIC PERIAPICAL LESIONS FOLLOWING ENDODONTIC TREATMENT

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Cone Beam Computed Tomography (CBCT) has been successfully implemented in the field of Endodontics as it has enhanced the diagnosis of periapical radiolucencies. The purpose of this study was to examine the preoperative volume of periapical lesions measured from CBCT images and its changes following non-surgical endodontic treatment.

The sample group comprised of teeth diagnosed with periapical radiolucencies of endodontic origin (n=31). The initial assessment of the lesions' volume was performed with limited-volume CBCT. All teeth underwent non-surgical endodontic treatment and were reassessed 10 months later following the same diagnostic protocol. The pre- and post-treatment volumes were compared.

Seventeen of the cases were healed, twelve of the cases were assessed as healing, in one of the cases the treatment was unsuccessful and one patient did not attend follow-up appointments. No correlation between lesion volume and the rate of the healing process was established.

Within the limitations of this study, CBCT is a useful method for the assessment of periapical lesions volume. Further research is required to assess the influence of the preoperative volume of the periapical lesion on the healing process.

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CONFOCAL LASER SCANNING MICROSCOPY FOR VISUALIZING THE ADHESIVE HYBRID LAYER – PILOT STUDY

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The aim of this pilot study is to give us information about the methodology for sample preparation, when using Confocal Laser Scanning Microscopy (CLSM). The unanswered questions are: Do dyes lose their fluorescence properties with time before and after mixing them with the adhesive system?; Is splitting a proper way for separation of samples?; Is classic tooth preparation convenient when using CLSM?; Is it possible to see the adhesive system in the dentinal tubules using magnification x10 and digital magnification? For this pilot study, we used 1 human freshly extracted tooth. Cavities were prepared using burs or Er:YAG laser. Fluorescence dyes were added to the adhesive systems that were used [1]. The samples were studied with CLSM. It was found that the fluorescent dyes maintain their fluorescence properties even 6 months after mixing them with the adhesive system. When splitting the samples, there were fracture line-like artefacts. The classic tooth preparation greatly limits the observed area when using CLSM. Using x10 magnification was not enough to study the adhesive system in the dentinal tubules even with digital magnification [2]. The methodology for sample preparation has to be optimized when using CLSM, which will give us more details in future studies about the micromorphology of the interface between the dentin and the adhesive system.

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INVESTIGATION OF THE ATTITUDE OF DENTISTS IN PLOVDIV REGION TOWARDS THE USAGE OF BIOCERAMIC ENDODONTIC SEALERS

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Introduction: Bioceramic endodontic sealers are presented in 2009 by the Canadian company Innovative BioCeramix, Inc [1]. One of the investigations prior to the release was performed in Bulgaria [2].

The **AIM** of the present research is to study the attitude of dental medicine practitioners in the Plovdiv region towards the usage of bioceramic endodontic sealers (BES) in their clinical practice.

Materials and methods: Anonymous questionnaires (n=200) were administered, 164 correctly filled were collected and statistically analyzed by licensed software Numbers 6.2 (Apple Inc.)

Results and discussion: The data shows high rate of endodontic treatments (ET) in the Plovdiv region (94%). Although most of the clinicians (70%) prefer obturation techniques, which are present in the indications for BES, the usage of the latter is generally low (16%). This is attributed mainly to the high price (40%) and the lack of sufficient information (32%).

Conclusions: It is necessary to increase the level of awareness of dental medicine practitioners in the Plovdiv region about the qualities of this new type of materials.

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CEPHALOMETRIC ASSESSMENT BASED ON SCHWARZ ANALYSIS AMONG BULGARIAN POPULATION

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Introduction: Distal malocclusion is one of the most common malocclusions in children: 32.1%. In order to establish an accurate diagnosis of class II subdivision 1 malocclusion in mixed dentition and proper therapy planning, it is necessary to perform the analysis of sagittal linear indicators of the jaws.

Aim: The aim of our research is to present orthodontics diagnosis based on cephalometric Schwarz analysis among Bulgarian subjects with class II subdivision 1 malocclusion in mixed dentition.

Material and Methods: We studied 140 lateral cephalometric radiographs of Bulgarian subjects with class II subdivision 1 malocclusion in mixed dentition. The following cephalometric indicators were estimated: S-N-linear measurement for assessment of the cranial base; A₁-PNS-linear indicator for assessment of the maxillary base; Go-Pog₁-linear indicator for assessment of mandibular base. The Schwarz method was used for the cephalometric analysis. The lateral cephalometric radiographs were calculated using the AudaxCeph software. Database were processed with statistical package SPSS 19.0. For the level of significance in rejecting the null hypothesis was chosen $p < 0.05$.

Results: The analysis of the lateral cephalometry showed that the mandibular base appears shorter and the maxilla is normal in 2 14% of the subjects; the mandible is of normal size but the maxillary base is longer in 34 29% of cases and the combination is observed in 63 57% of cases.

Conclusions: The position and size of the maxillary base and mandibular base require an individual assessment consistent with the type of growth to derive an optimal plan of orthodontic treatment. Proportional cephalometric analyses based on cranial base correlations are a significant predictor of interceptive treatment in mixed dentition.

УЛТРАЗВУКОВА ДИАГНОСТИКА НА ДОЛНОЧЕЛЮСТНИ СТАВИ ПРИ ПАЦИЕНТИ С КРАНИОМАНДИБУЛАРНИ ДИСФУНКЦИИ

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Цел: да се разработи и валидизира диагностичен алгоритъм за ултразвуково изследване на долночелюстните стави при пациенти с артропатии, вследствие на краниомандибуларни дисфункции, чрез анализ на референтни точки и съотношенията между тях.

Материал и методи: Проведено е ултразвуково изследване на долночелюстните стави на 30 пациенти (средна възраст 45 ± 3.5 г.) с артропатии, вследствие на краниомандибуларни дисфункции и на 30 здрави пациенти (средна възраст $46\pm 4,0$ г.). След период от шест месеца на лечение с оклузални посредници, на засегнатите пациенти е проведено повторно ехографско изследване. Получените данни са подложени на сравнение и статистически анализ.

Резултати: Създаден е диагностичен алгоритъм с помощта на три реперни точки, позиционирани върху *caput mandibulae*, от които са спуснати перпендикуляри към ставната ямка. Получени са цифрови измерения на ставното пространство в централна оклузия, които позволяват сравнение с възможните промени в етапите на проследяване на нарушенията и след терапевтичните манипулации.

Заклучение: Предложеният алгоритъм на изследване улеснява разчитането на ехографските изображения и диагностиката на нарушенията в долночелюстните стави.

Ключови думи: ултразвук, краниомандибуларни дисфункции, долночелюстни стави

ПРОФИЛАКТИЧНО ПОСТУРОЛОГИЧНО ИЗСЛЕДВАНЕ НА ДЕЦА НА ОСЕМ ГОДИШНА ВЪЗРАСТ

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Цел: след анализ на цялостното състояние на постуралната система на деца на осем годишна възраст да се определят насоките за по-широко постурологично проучване в ранна училищна възраст у нас.

Материал и методи: Изследвани са 30 деца (15 момчета и 15 момичета) на осем годишна възраст посредством съкратен протокол на постурологичен анализ, включващ определяне на цялостното състояние на постуралната система. Статистическата обработка на данните е извършена със софтуерен продукт SPSS Inc., IBM SPSS Statistics за Windows 15.0.

Резултати: Резултатите от определянето на общото състояние на постуралната система на изследваните, извършено чрез теста за хармония на постуралния тонус, показаха, че при над 1/3 няма данни за наличие на структурни увреждания (първични или компенсаторни), т.е. те са постурално хармонични и не се налага терапевтична намеса.

Заклучение: Получените резултати за изключително висок дял на пациентите с хармонични връзки между постуралните станции са индикатор за отсъствие на структурни увреждания (първични или компенсаторни).

Ключови думи: постурологично изследване, деца

A SURVEY OF THE PATIENTS' OPINION REGARDING THEIR ORAL HEALTH PROBLEMS

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Introduction: Demographic changes in the population have resulted in increase in life expectancy and increase in the percentage of retired adults.

Aim: To study patients' opinion regarding the problems of oral health.

Material and methods: 33 subjects completed an interview questionnaire consisting of 21 questions. The survey was conducted in a dental office in the town of Plovdiv in the period November 2019 – January 2020. Sociological and statistical methods were used. An alternative analysis was applied – indicators for relative share and graphical analysis – to visualize the data. Data processed with SPSS 19.

Results: Only 12.12±5.68% of the patients defined their health as "excellent" and these were men under 65. The majority (84.84±6.24%) of them think that nutrition affects the general state of health. Only a quarter of the studied do not think that proper nutrition is associated with healthy teeth.

Conclusions: Provision of dental treatment should be based on the medical, cognitive and functional status of the patient.

Keywords: oral health, research, elderly patients

PROBLEMS OF ORAL HEALTH OF ELDERLY PATIENTS IN TERMS OF OCCUPATIONAL THERAPY

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Introduction: The dental health of the elderly is their basic need. The most common oral problems of people at retirement age are: loss of teeth, caries, parodontitis, xerostomia and oral lesions.

Aim: To present the problems of oral health of elderly people in terms of occupational therapy.

Material and methods: A review of the available and accessible scientific literature from the recent 20 years is conducted regarding oral pathology of the elderly patients and the development of occupational therapy.

Results: Changes in oral health associated with advanced age are discussed. Treatment guidelines for elderly patients with specific disabilities are given.

Conclusions: Aging is associated with physiological changes, systemic health issues, reduced physical activity and increased intake of medicines. Multidisciplinary approach in treatment plan determination and maintenance of optimum oral health is necessary.

Keywords: elderly patients, occupational therapy, oral health

METHODS FOR DIAGNOSTICS OF EARLY PROXIMAL CARIES USED BY BULGARIAN DENTISTS

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Proximal caries is both a diagnostic and therapeutic challenge. Early detection of caries lesions is crucial for their proper treatment. The aim of the study was to find out which methods for early proximal caries diagnosis are mostly used by Bulgarian dentists.

Materials and methods: A survey was conducted amongst 200 members of the Bulgarian Dental Union during different scientific events. Results: The most often used methods of proximal caries detection were radiography (83%) and visual-tactile examination (74.5%). The contemporary methods were poorly presented (FOTI/DIFOTI – 10.5%, fluorescence – 3%, transillumination – 1.5%, CBCT – 2.5%). From the radiographic methods, the bitewing radiography was the most widely used method (46%), followed by segment parallel radiography (40%).

Conclusion: The conventional methods for proximal caries detection, which are proved to have low sensitivity, are still most popular amongst Bulgarian dentists. The contemporary methods for early proximal caries detection are poorly used.

ABOUT SOME DISAGREEMENTS IN SCIENCE CONNECTED WITH THE LEXICO-GRAMMATICAL CATEGORY OF GENDER IN BULGARIAN

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The present paper is dedicated to some disagreements in science connected with the category of gender of nouns in contemporary Bulgarian, and namely with the number of the genders, on the one hand, and the availability or the lack of semantics with the category of gender, on the other. Those are actually the only points concerning that grammatical category about which the scientists argue. That is why their clarification is very important and it is obligatory for each explorer of that issue to take a clear stand on them. The standpoints of leading authors on the theme are commented, such as Petya Kostadinova and Stoyan Burov, among others. Some of their conclusions are questioned and our opinion about their positions is provided. We also offer our own position on the point and illustrate it by a scheme accompanied by an explanation. We try to prove that the question about the semantics of the category is a very complicated one and it is very difficult to answer it categorically.

OBSERVATIONS ON SOME CASES OF GENDER VARIABILITY IN DERIVATIVE NOUNS

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This paper aims to present some unusual instances of gender changes in the derivation of nouns in the Bulgarian language. An examination is conducted on nouns derived from a primary stem form, but containing various prefixes, exhibiting gender variability. Examples are presented to illustrate the difference in gender within the selection of derivative noun forms.

Keywords: Bulgarian morphology, noun, gender, derivation

TO THE QUESTION OF THE “RECEPTIVITY” CATEGORY IN MODERN BULGARIAN

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The article discusses different concepts of distinguished linguists who present a possible model of a morphological category, which includes forms of the verb in the Bulgarian language marked with the evidentiality feature. To refer to this specific category of the verb, we use the term “receptivity”. The opposite relations between the evidential, renarrative and conclusive forms are presented. On the basis of the comparative analysis a conclusion is formulated – forms of the type “*pisheshe : pishel*”, “*pisheshe : pishel e*” differ by more than one distinctive feature and therefore cannot be part of an independent morphological category.

ON SOME CONSTITUENCY TESTS IN DEPENDENCY GRAMMAR IN ENGLISH AND BULGARIAN

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In recent years, there is a conspicuous increase in the interest in dependency grammar (DG). On the one hand, after years of dominance by the phrase structure grammar (PSG), the founding fathers of DG, and Tesnière in particular, are brought to the forefront. For instance, the keystone in Tesnière's oeuvre, *Elements of Structural Syntax*, has finally been translated into English. On the other hand, the interest in DG is additionally boosted by its wide use in the field of computational linguistics and the latest technologies in the natural language processing.

First, the current paper provides a short review of the developments in DG recently. Then, it moves on to the topic of constituency testing. This is one of the mainstays of DG, where it collides with PSG, claiming that these tests, in certain cases, simply do not work for PSG. The study focuses on the matching of some phrases between English and Bulgarian in such testing from the DG point of view.

CHALLENGES WHICH BUSINESS ORGANIZATIONS FACE IN INTERNATIONAL BUSINESS

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Abstract: The global market is becoming more interconnected and accessible; hence, the risks involved in doing business abroad should not be underestimated. The purpose of this study is to outline and analyze the most significant challenges faced by international business. It also presents examples showing the experience and hurdles faced by different companies in international markets. As a result of the research, it is concluded that changes require actions to adapt to dynamics. The study will help companies to become the next generation of global business leaders, embracing the opportunities and challenges of international business.

Keywords: international business, international strategy, challenges, global market

GLOBAL BRANDING – APPLYING STRATEGIES TO WIN CUSTOMERS

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The purpose of this study is to explore how companies seeking to be multinational apply different international strategies to adapt to the local market in order to compete globally. A case study on the Oreo brand of Kraft Foods, currently renamed Mondelez International, has been examined. Faced with stagnation in the US domestic market, Kraft Foods has moved the Oreo brand to emerging markets. The strategies used to win clients in China and India have been surveyed. As a result, conclusions have been drawn about what can be learned from the experience of Kraft Foods in India and China.

Keywords: strategy, brand, globalization, adaptation

REGIONAL DEVELOPMENT OF INDUSTRIAL CROPS FOUNDATION FOR INNOVATIVE BIOECONOMY IN BULGARIA

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Transition to an economy based on biologically renewable resources is set in the strategy and action plan “Innovating for Sustainable Growth: A Bioeconomy for Europe” adopted by EC in 2012. They are updated in 2018 to accelerate the implementation of bioeconomy principles in practice and to reflect commitments made with other agreements, such as the Paris Agreement on Climate Change and to meet the UN Millennium Development Goals.

In this regard, the development of industrial crops in Bulgaria is of great importance in the context of ensuring a diverse raw material base for developing the full potential of a modern bio-based economy, covering not only its decarbonization through biofuel and bioenergy production, but also by production of fibers, biopolymers, medicinal plant drugs, building materials and special chemicals that have high economic and social value. The use of unutilized resources, the introduction of new processing technologies and their dissemination in production chains is expected to lead to new jobs, higher added value and overall greening of the Bulgarian economy.

The aim of the study is to present potential for development of modern bioeconomy at the regional level in Bulgaria. Data from MAFF, Eurostat and an EC observatory were used. The results show unevenly developed agricultural production for different industrial crops, due to both the soil and climatic characteristics of the regions, as well as available processing capacity and foreign investment in the agriculture and industry. The presence or absence of support measures in agricultural policy applied is another significant factor – while oilseeds and essential oils report significant production growth, traditional industries such as textile and industrial fibers output manifest serious decline. It is important to take into account uneven production development when the new EU’s CAP will be developed and to find a way to support these decaying agricultural productions, given that the current policy focus is on greening.

Keywords: industrial crops, bioeconomy, regions, support measures

SUSTAINABLE DEVELOPMENT OF THE WORLD UNTIL 2030

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The imbalance between economic growth, social well-being and the state of the ecological environment creates a desire to create a socio-economic model that will solve the problem. Thus, at the beginning of the 21st century, the concept of sustainable development of the world with a horizon of 2030 is created. The goals of the Sustainable Development Program outline the vision and priorities in the policy of each prosperous country. Its adoption as a strategy by every government and its study is a prerequisite for accelerated economic development, social welfare, improving the quality of life and protecting the environment of the planet – the home of humanity.

R&D AS A FACTOR FOR THE COMPETITIVENESS OF HIGHER EDUCATION

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Investment in research and innovation is one of the EU's top priorities. A leading moment in the field is R&D, with a focus on HEIs, due to their indisputable contribution to building a competitive knowledge-based economy. The subject of this publication is the financing and implementation of research activities by HEIs, as a factor in increasing their competitiveness. The possibilities for creating the added value for HEIs through their cooperation with the business, with a view to approbation and commercialization of the scientific developments in the economy of the state, are considered.

Keywords: R&D, innovation, higher education, competitiveness, collaboration between higher education and business

OPPORTUNITIES FOR CREATING NEW GENERATION CHAINS WITH ADDED VALUE ADAPTED TO ORGANIC FOOD PROCESSING

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The paper contributes towards improving the understanding over the potential of the organic sector for creating new generation chains with added value. Organic farming in Bulgaria is developed by small farms / family farms with an average farm size of 12 ha, which reasonably produce food, but in small quantities, in accordance with the season. How these farmers can be competitive in two ways, in terms of optimizing certification costs and in increasing sales revenue, is a key issue for the future development of the sector. The proposal is for the organization of branch cooperatives, for example in the dairy sector. Homogeneous raw material should be processed to final production, as well as to carry out logistical and marketing activities for its sale to the end customer.

This is a descriptive study that gives an idea of the current structure of the sector and the directions through which it can be optimized. Through conducting an analysis of empirical-causal models of a number of authors, the author's view about the structure of organic foods in Bulgaria is established. The study is realized by applying combinations of comparative analysis and deductive analysis.

The data indicators are based on the latest international publications and directories such as:

[1] Willer, H., Lernoud, J., (2019), The World of Organic Agriculture - Statistics and Emerging Trends 2019. Research Institute of Organic Agriculture (FiBL), Frick, and International Federation of Organic Agriculture Movements (IFOAM), Germany.

[2] Willer, H., Lernoud, J., (2018), The World of Organic Agriculture- Statistics and Emerging Trends 2018, Research Institute of Organic Agriculture (FiBL), Frick, and International Federation of Organic Agriculture Movements (IFOAM), Germany, pp.24-27,72.

[3] Eurostat database Organic Farming.

[4] USDA Organic Annual Report Bulgaria 2020.

THE CONTRADICTION BETWEEN TRADITIONAL (INTELLECTUAL AND MORAL) AND BASIC NATURAL (BODILY AND HEDONISTIC) VALUES AS PART OF THE PROCESS OF VALUE TRANSFORMATION IN BULGARIA IN THE YEARS 2001-2009 OF THE TRANSITION

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The scientific report examines the process of value transformation in Bulgaria as part of the transition to democracy. It studies the period 2001-2009. The contradiction between the traditional (intellectual and moral) and the basic natural (bodily and hedonistic) values is analysed. Conclusions are made about the Bulgarian people's psychology and morality in the course of the great social changes in our country, accompanying the democratic reorganization of the Bulgarian society and state. The study is based on the ideas of the Bulgarian researcher Vasil Prodanov about the value changes in our country during the transition period, and in particular on his concept of the choice of value [1]. Our aim is to apply this idea in the outlined research field of the contradiction between the traditional (intellectual and moral) and basic natural (bodily and hedonistic) values and to derive the obtained results.

[1] Prodanov, V. *Theory of the Bulgarian Transition*, Zahariy Stoyanov Publishing House, Sofia, 2012, p.348.

ROLE AND FUNCTIONS OF MUNICIPALITIES IN THE IMPLEMENTATION OF THE STATE HEALTH POLICY

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One of the fundamental human rights enshrined in a number of international universal and regional treaties is the right to health [1]. In the Republic of Bulgaria, the protection of health, defined in the international legal doctrine as "*a state of complete physical, mental and social well-being*" [2], is one of the main priorities of the power of the state. Achieving this priority requires, on the one hand, the adoption of adequate legislation in the field of health, and on the other hand, the existence of well-functioning bodies and institutions to properly implement the established legal norms. In this regard, a number of laws and regulations, health programs and strategies have been adopted in the Bulgarian legislation, which proclaim the basic principles applicable in the implementation of the national health policy. The legislation clearly defines the main state bodies that have powers in the field of healthcare. Next, in the Republic of Bulgaria a National Health Care System has been established. An important role for the successful implementation of the health policy in the Republic of Bulgaria play not only the central state bodies, but also the municipalities, which are part of the National Health Care System. Municipalities have an important role in providing quality and affordable medical care to the local population, for its awareness of various health issues, to support the activity of the providers of medical care through administrative and financial mechanisms and resources.

[1] Mavrov, M., & Hristozova, M. (2019). *International standards for the protection of the right to mental health*. Knowledge International Journal, 35(5), 1455-1460; Hristozova, M. (2018). *Children's right to health in the acts of the United Nations Organization*. Knowledge International Journal, 28 (6), 2051 – 2055.

[2] Mavrov, M. *The legal institute of informed patient consent*, Stovi Bulgaria Publishing House, 2018.

DIDACTIC TECHNOLOGIES FOR INTERDISCIPLINARY ECOLOGICAL EDUCATION

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The new State Educational Standards and Curricula establish integrative mechanisms for the implementation of environmental education. Effective environmental education is much more than a one-way transfer of knowledge about environmental laws and problems. It is a tool for positive change in attitudes, values, as well as commitment skills and practical actions for the protection, restoration and sustainable development of the environment. The way to achieve these results is multifaceted. Quality environmental education involves partnerships between many stakeholders. In the development, we present a variety of points of view of researchers. We identify resolved and unresolved issues on how to improve the quality of environmental education. The contribution of the present study is to contribute to maintaining relevance in the discussion of environmental education in Bulgaria. In order to better understand how positive results can be achieved in the field of environmental education, in view of the current environmental situation, we make a critical review of leading research on the topic and focus on a generalized model of pedagogical research to establish working mechanisms for effective environmental education.

EDUCATION FOR SUSTAINABLE DEVELOPMENT – APPLICATION IN BIOLOGY AND HEALTH EDUCATION

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Education for Sustainable Development (ESD) is a tool for achieving sustainability. It aims to prepare young people for a balanced, harmonious and sustainable world for present and future generations. The concept of sustainable development on the one hand is not easy to define, but on the other hand it is constantly evolving. Three components are taken as the basis for sustainable development: environment, society and economy. The paradigm for sustainable development is gaining popularity in the education system. It reflects the urgency set out in the 2030 Agenda for Sustainable Development to integrate the principles of education for sustainable development into all levels of education. One of the goals set in the program is the development of competencies for sustainable development. We use the methods of pedagogical research: systematic review of the literature, content analysis of curricula, pedagogical diagnostics, methodological modelling. In the research, we focus on: the relationship between the content of sustainable development, the formation of competencies for sustainability and tools for their assessment in the biological preparation of students, and the development of methodological models applicable in educational practice. The research is a contribution to the development of educational standards for sustainable development and operationalization of sustainability competencies in a specific subject area.

ENVIRONMENTAL EDUCATION IN THE DIGITAL ENVIRONMENT – PRACTICAL ASPECTS IN TEACHING BIOLOGY AND HEALTH EDUCATION

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Environmental education is designed to prepare young people to deal with environmental problems and build a harmonious relationship between people and their environment. It is an integrative component at all levels in the biological preparation of students. Environmental education is an emphasis in the methodology of teaching biology as a specific organization, implementation and evaluation of the quality of the learning process. The digitalization in education, which has been observed in recent months all over the world, influences the development of new perspectives in the ecological preparation of students. The transformation of environmental education with the tools of the electronic educational environment needs a theoretically substantiated and experimentally proven didactic model for organizing the lesson. This research is aimed at the process of methodical modelling of the biology lesson conducted in an electronic environment. The answers to the questions are sought: How to model the lesson in an electronic environment? What are the characteristics of verbalization and illustration of the learning process on environmental issues? The formation of skills for identification, solution and assessment of environmental problems, as well as behavior for protection and sustainable development of the environment, is also subject to rethinking as a methodological justification. The contribution in the present development is to contribute to the discussion on the researched problem, as well as to the development of a generalized methodical model of a lesson in ecological education for e-learning.

METRORHYTHME AND COMPOSITION – INTERPRETER PROFILE IN JACQUES CASTEREDE’S FIRST MOVEMENT OF HIS SONATINE FOR TROMBONE AND PIANO

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The following article analyses the first movement of Jacques Casterede’s Sonatine for trombone and piano in terms of compositional structure and interpretation. It examines briefly its form, meter signatures change, as well as some of the melodic outline, harmonic language, and counterpoint characteristics. In addition, some features of both the piano and the trombone parts with regard to ensemble problems are discussed. The modern sound and the jazzy rhythm, formed as a result of a complex meter pulsation within the first movement of the piece, challenge the performers with a constant intensity. The togetherness of the duo meets several obstacles when keeping through the changing pulsation of tonal and rhythmic patterns. Meanwhile, the first movement’s harmonic and polyphonic outline as well as the variety of intonations invite both the players to give way to their imagination and artistic creativeness. The Sonatine’s interpretation and style as a whole might be successfully defended if both the interpreters are enough experienced in their technical and musical mastership.

Keywords: meter dissonance, rhythmic patterns, ensemble unity

THE GOVERNMENT DURING THE FIRST BULGARIAN EMPIRE

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The article analyzes the period of the First Bulgarian Empire. An analysis of the period, its historical reconstruction and points of reference are given. The ruling institute is presented. Different interpretations of it and its structure are considered. Conclusions have been made.

Keywords: Bulgaria, history, rulers, First Bulgarian Kingdom, division, politics

COMPARING THE GEOMETRICAL, MECHANICAL, AND CHRISTIAN DUALISMS

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We introduce **a rule** for elevating the Hegel's [1] reflexive level of the cognitive process allowing adding a new law (property) as a postulate or negation of an acting law, or replacing with/adding new objects with or without negation of laws. We repeat our four geometrical levels reflected in [2] and determine such physical levels (classical mechanics, non-relativistic quantum mechanics, relativistic one, and general relativistic one) on the basis of this rule. The Euclidean-Lobachevsky's geometrical dualism and the corpuscular-wave dualism are disposed on the second indicated levels but applying different parts of the rule for elevating. An experiment from [3] can be interpreted as a modelling of the wave manifestation of the photons with the means of their corpuscular one but **a realization** of this experiment **in the reverse direction** – as a modelling of the corpuscular manifestation of the photons with the means of its wave one. These modellings are like analogs of the existence of models of each one of both geometries above into the other one. **A natural substitution of ours** with the components of the photo-electrical effect in the catholic Trinity diagram (c. 1208, [4]) leads to an analogically acting “quantum Trinity” diagram. The catholic Filioque clause is also confirmed. **This clause led** to East-West **schism** (1054)). If a person is accepting the Catholic Filioque clause, then he must be agreed with **the denouncing** the Holy Fire (1238) – much **later than the schism**.

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