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# Scripta Scientifica Pharmaceutica

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**ORAL PRESENTATIONS**

## MOTIVATION TO STUDY IN AN ELECTRONIC ENVIRONMENT FOR STUDENTS OF THE 1-ST YEAR IN PHARMACY AT THE MEDICAL UNIVERSITY OF VARNA

Joanna Koleva

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**INTRODUCTION:** Motivation is an internal state that supports, directs and stimulates human behavior and occupies a leading place in the structure of individual behavior. Various forms of training at the Medical University of Varna are aimed at improving the quality of teaching, providing knowledge and information through advanced technologies, developing technological skills, online training and face-to-face training.

**AIM:** The aim of the study is to analyze innovative models of distance learning in an electronic environment at the Medical University of Varna for the first-year students in the Pharmacy program, revealing the advantages and limitations of using e-learning.

**RESULTS:** The results of the conducted survey of students show more than 80% satisfaction with the training conducted in an electronic environment, which provides various opportunities for active participation of students in the learning process. The last year and a half has revealed new opportunities for the medical university education system, which has provided an adequate environment for teaching its students in various specialties and has quickly moved to a virtual online mode. The initiatives carried out at the interactive meetings of the PharmCafe, presented various points of view of the leading teachers, and increased the interest of students in the possibilities of future implementation.

**CONCLUSION:** In conclusion, distance learning includes various types of interactive learning (synchronous and asynchronous forms of e-learning; training in simulation centers, and much more).

**Keywords:** *motivation, learning, electronic environment, students*

## ANALYSIS OF PHD OPPORTUNITIES IN BULGARIA

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**INTRODUCTION:** The educational and scientific degree Doctor of Philosophy (PhD) is internationally recognised. Acquiring a PhD is a step for academic career development and a valuable advantage for professional advancement, both in Bulgaria and abroad. In Bulgaria, doctoral programs are distributed in 9 different areas of higher education consisting of 51 professional fields.

**AIM:** The principal objective of this work is to find the number of doctoral programs, the average score of each area and field, average score of all accredited programs, the number of new and dropped programs and the highest scoring programs in all universities, higher education institutions and scientific organisations and then to compare them.

**MATERIALS AND METHODS:** We analysed the public data from the official website of the National Evaluation and Accreditation Agency of all accredited doctoral programs in all universities, higher education institutions and scientific organisations in Bulgaria with a focus on 7. Health and Sport area of higher education. The comparison was made using the Z score method.

**RESULTS AND CONCLUSION:** The obtained results showed that in Bulgaria there are PhD programs available in all 9 areas of higher education with the possibility for them to be acquired in 44 universities (52 in total, 8 of which are without accreditation) and in 18 scientific organisations. The highest number of accredited doctoral programs are in the 7.1 Medical Sciences professional field. This leads us to the conclusion that higher percentage of doctoral students are directed towards medical specialities.

**Keywords:** *PhD, doctoral programs, universities, scientific organisation, accreditation*

## THE EVOLUTION OF THE MEDICINE PACKAGING— CASE STUDY FOR THE BULGARIAN DRUG ISODINIT

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**INTRODUCTION:** Secondary packaging of medicines serves as the barrier for the drug to the environment, establishing their suitability and quality. The patient leaflet is intended to provide additional regulatory approved information to the product.

**AIM:** The aim of this article is to show the difference between the two packagings and the legal requirements about the information written on the packaging and in the medicinal leaflet.

**MATERIALS AND METHODS:** We have compared the secondary packaging and the leaflets of a medicine produced in 1999 and the another one—in 2021. A comparative analysis was made of both products and, in addition, the legal requirements for the information written in the patient leaflet were studied.

**RESULTS AND CONCLUSION:** Secondary packaging of the medicines produced with more than 20 years between them significantly differed. The comparative analysis showed serious difference in both patient leaflets. The one from 1999 contained very brief information about the drug's composition, effects, side effects, indications, contraindications and usage, versus the present leaflet of the medicine, which contained more information that was comprehensive.

In conclusion, the differences were due to the fact that the pharmaceutical regulation and practice has evolved, legal requirements have changed ensuring mainly the safety of the medicament. The patient has to be well informed so that the problem with wrong usage will be avoided.

**Keywords:** *medicines, medicine packaging, patient leaflet, Isodinit, legal requirements, medicinal safety*

## ANALYSIS OF FACTORS INFLUENCING THE CONSUMPTION OF MEDICINES IN THE CONTEXT OF THE COVID-19 PANDEMIC

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**INTRODUCTION:** The aim of this study was to determine the main factors influencing the consumption of medicines, OTC products, food supplements and medical devices when patients make purchases at a community pharmacy. Awareness and preferred purchasing behavior of patients for various medicines were studied.

**MATERIALS AND METHODS:** An anonymous online survey conducted in the period April–September 2021 among randomly selected patients in the Varna region. A sociological method was used—a direct anonymous online survey and the results were processed using Microsoft Excel 2010.

**RESULTS:** After analyzing the results, a variety of factors were found to have different influences on patients' decision to purchase various medicines, OTC products, supplements and medical devices in the Covid-19 setting.

**CONCLUSION:** The study shows that the role of the Internet and media is significant in the patients awareness regarding Covid-19. The leading factor in choosing an OTC product or dietary supplement is the pharmacist's recommendation. When purchasing prescription medicines, the role of the health professional is leading the way.

**Keywords:** *factors, influence, consumption, medicinal products, Covid-19, pandemic*

## METHODOLOGY FOR SEMI-QUANTITATIVE ANALYSIS OF THE VITAMIN D INTAKE OF UNIVERSITY STUDENTS

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**INTRODUCTION:** COVID-19 caused a pandemic situation worldwide, changing the global health and pharmacy systems. This novel disease has led to severe atypical pneumonia, causing more acute disease progression and higher mortality in patients with vitamin D deficiency compared to others with normal levels of vitamin D. These newly published facts focused our scientific interest on elucidating the nutritional status of young students and development of methodology for semi-quantitative analysis of food intake based on a questionnaire survey.

**AIM:** This study was focused on developing a research methodology for semi-quantitative analysis of students' food intake as a part of investigating their nutritional status in regard to vitamin D.

**Materials and Methods:** This study used a documentary method. It was based on a retrospective analysis of 25 articles published in the last 30 years in peer-reviewed journals. They were focused on social behavior, food safety, and knowledge of university students from different countries (Greece, Sweden, China, Slovenia, etc.)

**RESULTS:** The results from the study focused our attention on the factors that play a significant role in social behavior. A central role play their educational status, level of income, habitat, health status, and consumer culture.

**CONCLUSION:** These results can be used as a starting point for the design of a unique methodology, which, using a cross-sectional study, would allow the conduction of a semi-quantitative analysis of vitamin D in food intake.

**Keywords:** *COVID-19, vitamin D, university students, nutritional status*

**Acknowledgments:** *Special thanks for the financial support from Plekhanov Russian University of Economics (№655/07.06.2021)*

# THE CRITICAL ROLE OF CELLULAR PRION PROTEIN IN THE DEVELOPMENT OF NOVEL THERAPIES FOR TREATMENT OF ALZHEIMER'S DISEASE

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**INTRODUCTION:** Alzheimer's disease (AD) is a neurodegenerative disease presented pathologically by the assemblage of amyloid-beta ( $A\beta$ ) peptide and hyperphosphorylated tau protein in the brain. Symptoms include loss of cognitive function and memory. It is believed that the soluble pre-fibrillar  $A\beta$ -oligomers are the toxic form of  $A\beta$ -peptide rather than the senile plaques. The recent identification of the cellular prion protein as a cell surface receptor for  $A\beta$ -oligomers encouraged research regarding the identification of effectors that cause neuronal toxicity and synaptic dysfunction in AD.

**AIM:** The aim of the study was to gather information on recent projects that deepen the understanding of the mechanisms that cause AD and identify new ways to treat it.

**MATERIALS AND METHODS:** An analysis of 13 articles published in the time period between 2010–2021 was performed. We searched the following databases: Google Scholar, PubMed, as well as Social Science Research Network (SSRN), using a unique combination of keywords listed below. Results: PrPc is an extracellular protein attached by a GPI anchor to the cell surface that acts as a specific receptor for  $A\beta$ -oligomers and intervenes in the suppression of the long-term potentiation (LTP). There is a great interest to seek potential co-receptors or determine if the  $A\beta$ -mediated signalling pathways are also PrPc-dependent, building a fully finished network of AD connections.

**CONCLUSION:** Comprehending the  $A\beta$ -oligomer-mediated neurotoxic signalling pathways would be extremely beneficial to the development of new therapies for this devastating disease.

**Keywords:** Alzheimer's disease, PrPc,  $A\beta$ -oligomers, PRNP gene, neurotoxicity, treatment, protein misfolding.

## SYNTHESIS AND CHARACTERIZATION OF A NEW NITROIMIDAZOLE DERIVATIVE

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**INTRODUCTION:** Imidazole is a five-membered planar nitroheterocyclic derivative. It is a basic structure fragment in many compounds, possessing significant pharmacological activities, which are thoroughly documented, such as antifungal, antimicrobial, analgesic, anti-inflammatory, etc.

**AIM:** The aim of the present study is synthesis and characterization of a new amide nitroimidazole derivative.

**MATERIALS AND METHODS:** A literature review, review and evaluation of the screening methods for synthesis and analysis of amide derivatives applicable in practice have been made. All of the used organic reagents are suitable for research applications. The following equipment was used in the present scientific work: analytical balance MS304TS/00 (Mettler Toledo) was used for weighing operations—with Easy Direct Balance Software; during the synthesis a magnetic stirrer—liquid stirring instrument—magnetic stirrer MSH 300N was used; a T60 UV-visible spectrophotometers were used as well. Infrared spectra in the range 4000-500 cm<sup>-1</sup> were taken on a BRUKER FT-IR spectrometer.

**RESULTS AND CONCLUSION:** A two-step synthetic method for the preparation of amide derivative of nitroimidazole has been developed, with the aid of which one new amide derivative was obtained. The novel compound was structurally characterized and identified by IR spectroscopy and UV-VIS spectroscopy.

**Keywords:** *synthesis, imidazole, amide derivative, IR spectroscopy*

## TOXICOLOGICAL ANALYSIS OF ETHANOL IN BIOLOGICAL MEDIA

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**INTRODUCTION:** According to the pharmacotherapeutic activity, ethanol belongs to the group of antiseptics and disinfectants. Its main metabolic pathway is enzymatic, under the action of ALDH, alcohol dehydrogenase is metabolized to toxic acetaldehyde, which is metabolized by ADH (aldehyde dehydrogenase) to acetic acid, and the acid—to carbon dioxide and water. In the forensic practice of toxicological analysis of ethanol there are two groups of methods: screening—extraction and evidence (confirmatory)—instrumental methods (GC-FID).

**AIM:** The aim of the present study is to perform toxicochemical analysis of ethanol in biological environment—blood from dead individuals—by applying two screening methods: gas chromatographic analysis with flame ionization detection and Widmark's method.

**MATERIALS AND METHODS:** A literature review, review and evaluation of the screening methods for analysis of ethanol in biological media applicable in practice have been made. Indirect oxidimetric determination of ethanol by the Widmark method in model blood samples was performed. A procedure for validation and experimental staging of a gas chromatographic method with flame ionization detection (GC-FID) of biological blood samples from dead persons was performed.

**RESULTS AND CONCLUSION:** Data from the validation procedure applied by the Widmark method show that this method is inaccurate, non-reproducible and imprecise, and can lead to false positive or false negative results without forensic value. The performed procedure for validation of gas-chromatographic method with flame-ionization detection shows that the method is accurate, precise and reproducible and can be applied for forensic examinations in living and dead patients. The performed gas chromatographic analysis with flame ionization detection has been successfully applicable for real and accurate analyses in forensic practice, in compliance with the conditions for sampling and storage.

**Keywords:** *ethanol, Widmark, GC-FID*

## PHARMACEUTICAL ANALYSIS OF DEXAMETHASONE SODIUM PHOSPHATE IN DOSAGE FORM FOR THE EYES. PACKAGING STABILITY STUDY

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**INTRODUCTION:** Corticosteroids are all steroid compounds secreted by the adrenal cortex—these are glucocorticoids, mineralocorticoids, and sex hormones. Corticosteroids are involved in a wide range of physiological processes in the body—regulation of carbohydrate, lipid, protein and electrolyte metabolism, stress, immune response, and processes related to the reproductive system. According to the US Food and Drug Administration (FDA), dexamethasone sodium phosphate (DSP) is more commonly used in the form of injectable solutions, eye drops, eye ointments, aerosols, and topical creams.

**AIM:** The aim of the present study is to perform a pharmaceutical analysis of DSP in the form of eye drops and to investigate the effect of the package-closure system on the drug solution by a test for stability under stress conditions.

**MATERIALS AND METHODS:** A literature review, review and evaluation of the screening methods for analysis of DSP applicable in practice have been made. An HPLC analytical method was validated for the qualitative and quantitative determination of DSP in DSP formulation of 1 mg/mL eye drop solution in a 5 mL vial and the determination of DSP content and corresponding impurities in dosage form was performed. Tests for identity of the drug substance DSP were performed using HPLC, UV-VIS spectroscopy, IR spectroscopy, and a stress test of the dosage form was performed by HPLC analysis.

**RESULTS AND CONCLUSION:** An HPLC method for qualitative and quantitative identification of DSP substance and DSP in the form of eye drops has been successfully developed and validated. The maximum absorbance value of a DSP sample was determined by UV-VIS spectroscopy. The result obtained for Amah is identical to Amah in PhEur. The DSP identity test performed by IR spectroscopy showed a complete match with the spectrum of a standard DSP substance. The performed stress test of the packaging-closing system showed that it is not appropriate to use a cap-dropper closing system due to the increase the concentration of IMP A.

**Keywords:** *dexamethasone sodium phosphate, eye drops, instrumental analysis*

## ANALYSIS OF THE RUSSIAN RETAIL MARKET OF DIETARY SUPPLEMENTS CONTAINING VITAMIN D

Elena Krasilnikova<sup>1</sup>, Anastasia Suhova<sup>1</sup>, Elina Musina<sup>1</sup>, Ludmila Eliseeva<sup>1</sup>,  
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**INTRODUCTION:** The global pandemic caused by COVID-19 changed many economic patterns and retail businesses worldwide. The Russian retail market considered an opportunity to develop offline and online channels for sales of dietary supplements containing vitamin D. These actions were part of the company strategies for market growth, which were focused on the nutritional status of consumers, as an additional approach for prevention of COVID-19.

**AIM:** This study aimed to analyze market trends and strategies used by five leading Russian retailers for the market growth of dietary supplements containing vitamin D.

**MATERIALS AND METHODS:** This study used statistical data and financial statements. Assortment policy and market strategy of five leading Russian retailers (Perekrestok, Lenta, Magnit, Vkusvill, and Azbyka vkusa) based in Moscow were analyzed through previously developed methodology.

**RESULTS:** This study showed that despite the fact that all retailers used the COVID-19 pandemic situation to develop their own offline and online distribution channels, they had a different trade policy and operational strategy. They were not focused on vitamin D containing dietary supplements only, their focus was the concept of “nutritional status” as a marketing strategy for distribution of different dietary supplements and market growth.

**CONCLUSION:** Results from this study shed light on the fast and adaptive strategy of leading Russian retailers in a pandemic situation. For retailers, the pandemic situation is an opportunity to enter and expand their market share in the field of dietary supplements.

**Keywords:** *retail market, vitamin D, Russia, dietary supplements*

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## CHALLENGES FACING THE ACTIVITIES OF A HOSPITAL PHARMACY DURING THE COVID CRISIS

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**INTRODUCTION:** The last year and a half has been extremely difficult for the healthcare sector, and the socioeconomic life of the country and the world. The pandemic situation was extreme, dynamic and required precise and rapid actions regarding infection control, treatment and medication.

**AIM:** The aim of the study was to analyze the organization of hospital services and the activities of a hospital pharmacy, which put to the test in all directions the managers of various hierarchical levels and the possibilities of solving problems by making a number of managerial, often fateful decisions.

**MATERIALS AND METHODS:** Various regulatory documents and internal regulatory documents related to the organization of the activities of a hospital pharmacy were used.

**RESULTS:** The organization of the hospital pharmacy at SHOGAT, Varna is carried out in accordance with a number of regulatory legal and subordinate documents, but in the unprecedented situation, the supply of medicines and consumables was complicated due to difficult logistics and distribution of leading suppliers in the market with whom the structure has contractual relations. The increased demand for consumables and medicines has increased their prices in the context of an unprecedented health crisis. A number of medicines and personal protective equipment disappeared from the pharmaceutical chain, and their supply to hospitals was difficult.

**CONCLUSION:** Last year, 2020, revealed gaps in the distribution of medicines and consumables and pointed to methods of dealing with crises in relation to the implementation of a stable policy.

**Keywords:** *hospital pharmacy, regulatory action, organization*

## MONITORING THE TREATMENT EFFECT OF CONFIRMED CASES OF TOXOCARIASIS IN CHILDREN AND ADULTS

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**INTRODUCTION:** Toxocariasis is a widespread zoonosis caused by the roundworms *Toxocara canis* and *Toxocara cati* affecting children and adults. The clinical spectrum of the disease comprises four syndromes—visceral larva migrans, ocular toxocariasis, neurotoxocariasis, and the more recently recognized „common“ (in adults) and „covert“ (in children) forms.

**AIM:** The aim of the study is to observe the changes of several laboratory markers in confirmed cases of toxocariasis during and after the anthelmintic treatment.

**MATERIALS AND METHODS:** The study includes 34 children and 38 adults seropositive for *Toxocara* IgG antibodies detected by enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blot. Aetiological therapy with albendazole 10 mg/kg/day BID was combined with antihistamines to avoid larva lysis syndrome. The clinical symptoms and changes in specific laboratory markers (complete blood count, blood eosinophil count, and total IgE) were established before, during, and on the first and sixth month after the treatment.

**RESULTS:** The therapy regime with albendazole for seven days for common form in adults and ten days for all the other patients reduced the clinical symptoms and improved laboratory parameters on the first month of the follow-up period. On the 6th month, full recovery was observed in most patients with a considerable decrease in serum anti-parasite antibody concentration in ELISA.

**CONCLUSION:** The therapy of toxocariasis should comprise both aetiological and antiallergic treatment, and the course should be tailored individually according to the specific clinical form of each patient.

**Keywords:** *albendazole, anthelmintic treatment, ELISA, toxocariasis, Western blot*

## SYNTHESIS OF $^{18}\text{F}$ -LABELED RADIOPHARMACEUTICALS AND POSSIBLE PROSPECTS

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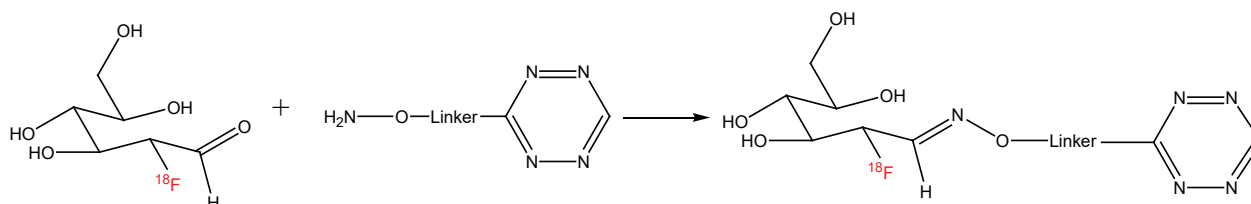
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The radionuclide  $^{18}\text{F}$  is a positron emitter and is most commonly produced in the cyclotron by proton bombardment of  $^{18}\text{O}$ -enriched water by the next nuclear reaction  $^{18}\text{O}(p, n)^{18}\text{F}$ . It is used in the production of  $^{18}\text{F}$ -labeled radiopharmaceuticals used in positron emission tomography (PET-CT) imaging techniques. PET radiopharmaceuticals consist of two components—a basic structural molecule—a ligand and a radionuclide—a positron emitter.

There are various chemical methods for introducing  $^{18}\text{F}$  into the desired molecule. The main synthetic strategies fall into two main categories: direct radiofluorination, i.e.  $^{18}\text{F}$  is directly attached to the molecule to be labeled and indirect fluorination, where in  $^{18}\text{F}$  is introduced in the form of  $^{18}\text{F}$  containing a prosthetic group.

At the Clinic of Nuclear Medicine at St. Marina University Hospital, the radiopharmaceutical  $^{18}\text{F}$ -fluorodeoxy-glucose ( $^{18}\text{F}$ -FDG) is synthesized for routine clinical purposes by nucleophilic radiofluorination.  $^{18}\text{F}$ -FDG is the most widely used PET radiopharmaceutical.  $^{18}\text{F}$ -FDG, as a glucose analog, can be used to assess the metabolism in the brain and heart, and also to study malignancies. Apart from being unselective universal PET-radiopharmaceutical,  $^{18}\text{F}$ -fluorodeoxy-glucose has been used in recent years as a prosthetic group for indirect radiofluorination of sensitive macromolecules. The development is a method for modifying  $^{18}\text{F}$ -FDG synthesized in the clinic by forming an oxime chemical bond with a bifunctional compound.

**Keywords:**  $^{18}\text{F}$ -FDG, radiopharmaceuticals, PET-CT, radiolabeling, oxime formation



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POSTERS



## PERSPECTIVES IN THE PREPARATION OF RADIOPHARMACEUTICAL MEDICINES IN BULGARIA

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**INTRODUCTION:** At present in Bulgaria, radiopharmaceuticals (RPhs) are prepared mainly by means of industrially produced kits. The development of nuclear medicine in our country poses challenges to the methods of preparation of the RPhs. The extemporaneous preparation of RPhs represents an opportunity to meet the specific needs of an individual patient, thus increasing the range of tools available to the specialist in nuclear medicine in terms of diagnosis and treatment.

**AIM:** The purpose of this study is to present the current global trends in the production of the RPhs, which would find application in the centers of nuclear medicine in Bulgaria and to indicate the features and requirements for the implementation of extemporaneous preparation of the RPhs.

**MATERIALS AND METHODS:** Methods for synthesis and analysis of extracted data and interpretation of documents regulating the order, the manner and the organization of the work with radioactive materials and in particular radiopharmaceutical medicinal products (RPhMP) were applied. The peer review method was also applied to summarize some key factors in the preparation of RPhMP.

**RESULTS:** In the clinical practice, short-lived radionuclides (RNs) are mainly used for the preparation of RPhs, which requires the introduction of the concept of “hospital radiopharmacy”—a structure that prepares RPhs, performs quality control and manages all related activities until RPhs reach their clinical application. In these structures, RPhs prepared by kit-based synthesis or by fully automated synthesis are prepared and released. No structure in Bulgaria practices extemporaneous compounding of RPhs, i.e. RPhs that are not available or there are no registered equivalents on the territory of the country, there are no significant deviations in individual dose/radioactivity from the indications of the manufacturer of the kit.

**CONCLUSION:** It is necessary to draw the attention of the regulatory authorities in the country to the benefits of the ability of specialists in nuclear medicine to provide new or already established RPhs. In this way it will be possible to direct the specialty towards personalized therapeutic and diagnostic approaches tailored to the specific needs of Bulgarian patients who deserve the best medicines, radiopharmaceuticals or not.

**Keywords:** radiopharmacy, radiopharmaceuticals, medicine

## MAIN EXCIPIENTS USED IN THE FORMULATION OF DOSAGE FORMS FOR PEDIATRIC USE

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**INTRODUCTION:** The development of dosage forms targeted to the pediatric population is a significant challenge for pharmacists today, despite serious advances in pharmaceutical technology, as this particular patient population requires specific needs. This is mainly due to differences in swallowing abilities, taste preferences, and dosage requirements for medicinal products administered in childhood.

**MATERIALS AND METHODS:** This review aims to look at the main excipients used in pediatric medicines, as well as to present the various additives included in the pediatric medicines available on the pharmaceutical market. For this purpose, commonly used medicines for children, including food supplements and over-the-counter medicines (OTCs), were considered. The most commonly used in practice dosage forms for children are solutions, syrups, powders, capsules, and tablets.

**RESULTS:** Over 35 pediatric drugs from each dosage form for oral use were randomly selected (OTC, food supplements, and prescription drugs). The most commonly used pediatric forms are syrups, powders, and lozenges. Their composition and used excipients indicate that in syrups the most often used (over 50% from the drugs) are sorbitol, sucrose, fructose; in powders—saccharin sodium, sucralose; in chewable tablets—glucose, sucrose.

**CONCLUSION:** The most commonly used excipients in these forms are sweeteners. They improve the taste, thus improving the medication compliance.

**Keywords:** *dosage forms for pediatric use, excipients*

## VONOPRAZAN—INNOVATIVE TREATMENT OF GERD AND PEPTIC ULCER DISEASE

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**INTRODUCTION:** Many acid-related disorders may be treated with medications that affect the proton pump in the stomach and reduce the acid secretion. Vonoprazan is a novel potassium-competitive acid blocker that shows high efficiency by inhibition of the H<sup>+</sup>/K<sup>+</sup> – ATPase.

**AIM:** The aim of the article is to investigate the efficacy and safety of vonoprazan for the treatment of GERD (gastroesophageal reflux disease) and peptic ulcer disease. Furthermore, we intend to compare vonoprazan with other well-known medications for acid-related diseases (ARDs) such as PPIs (proton-pump inhibitors).

**MATERIALS AND METHODS:** The acid-suppression effect of vonoprazan is both *in vitro* and *in vivo* tested: in isolated porcine stomachs vonoprazan shows 400 times more powerful inhibitory effect than lansoprazole—a type of PPI. Another experiment with anesthetized rats proves that vonoprazan can increase the gastric pH to a higher value, compared to lansoprazole, and that effect is continued for a longer period of time. Clinical studies have similar outcomes. In regard to safety of the medication, it has been proven to be clinically safe, because all of the adverse effects are considered mild to moderate.

**RESULTS AND CONCLUSION:** The mentioned drug is an innovative alternative to the recently used PPIs. More comprehensive studies with larger sample sizes are needed.

**Keywords:** *vonoprazan, potassium-competitive acid blocker, ARDs, peptic ulcer disease, GERD*

## THE BACTERIAL SOS SYSTEM FOR DNA REPAIR AS A NOVEL TARGET FOR ANTIMICROBIAL THERAPY

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**INTRODUCTION:** The SOS response is one of the main mechanisms of DNA repair in bacteria, which ensures their survival under DNA-damaging factors such as some antibiotics, UV radiation, etc. Beyond that, it has also been shown to be a driving force behind the acquisition of mutations responsible for resistance towards antibiotics. Thus, the inhibition of the SOS response can increase the effectiveness of some antibiotics and prevent the spread of drug resistance genes.

**MATERIALS AND METHODS:** We have reviewed publications since 2001 year concerning the SOS system, with reference to its two main regulatory proteins—RecA and LexA, as well as LexA/RecA-repressor molecules and their use as antimicrobial agents in combination with a number of different antibiotics.

**RESULTS:** A number of studies show that both LexA and RecA can substantially increase the effectiveness of different antibiotics, most notably—antibiotics that induce DNA damage. Those include the fluoroquinolones, which inhibit the bacterial topoisomerase and DNA gyrase, and nitrofurantoin, a bactericidal antibiotic that causes direct damage to the bacterial DNA. We have deduced that the combination of a LexA/RecA repressor and an antibiotic that damages DNA can be used in much the same way as the beta-lactam/beta-lactamase inhibitor combinations and can aid us in the treatment of multidrug resistant microorganisms.

**CONCLUSION:** LexA/RecA repressors show great promise as future antimicrobial agents in combination with a number of antibiotics and can aid us in tackling the ever-growing problem of bacterial resistance to antibiotics.

**Keywords:** *SOS response, bacteria, DNA repair, LexA/RecA suppressors, antibiotics, resistance*

## **ANALYTICAL METHODS FOR IDENTIFYING VALERIAN'S ACTIVE COMPONENTS AND THEIR DEGRADATION PRODUCTS IN DIETARY SUPPLEMENTS**

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**INTRODUCTION:** The use of food supplements is becoming increasingly popular in modern society. Valerian is a very popular dietary supplement used to treat conditions such as nervousness, anxiety, insomnia and other stress-related conditions. Efficacy data for valerian is conflicting, with some studies showing that valerian is a good sedative, and others showing that the effect of valerian is comparable to placebo. The composition of valerian includes monoterpenes, sesquiterpenes, valepotriates, caffeic acid derivatives, flavonoids, lignans, and amino acids.

**AIM:** The aim of our study is to conduct a literature review and to establish some analytical methods easily and effectively identifying the active components of valerian, as well as their decomposition products in various pharmaceutical products, as some of them pose a risk of toxicity.

**MATERIALS AND METHODS:** References were made in the scientific databases PubMed, Google Scholar and ResearchGate.

**RESULTS:** Our review established the existence of many different methods for analysis of valerian's active components in pharmaceutical products such as HPLC, gas chromatography/mass spectrometry, and absorption spectrometry. In this article we will discuss some of the most appropriate analytical methods for valerian analysis based on their analytical characteristics.

**CONCLUSION:** Poor regulation of food supplements on the market, the widespread use of products containing valerian, as well as the possibility of the presence of degradation products with mutagenic and carcinogenic effects during storage of valerian supplements requires the use of an accurate and effective analytical method that can easily identify the active and degrading components of valerian in products from the Bulgarian market in order to ensure patient safety.

**Keywords:** *valerian, analysis, HPLC*

## A REVIEW OF THE POTENTIAL HERB-DRUG INTERACTIONS OF GREEN TEA EXTRACT

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**INTRODUCTION:** Green tea beverages are very popular and consumed daily all over the world. Green tea contains a variety of biologically active compounds such as polyphenols, alkaloids, polysaccharides, amino acids and saponins. The main polyphenols in green tea are catechins (epigallocatechin-3-gallate, epigallocatechin, epicatechin gallate, and epicatechin), while the most abundant alkaloid is caffeine. Many studies have reported that green tea catechins, as well as epigallocatechin-3-gallate alone may modulate the activity of CYP450 enzymes. In addition, modulation of some transporters is also reported. Caffeine is known for its ability to modulate CYP1A2 activity.

**AIM:** The purpose of the present study was to review the available data about the potential herb-drug interactions of green tea extract, as well as its main constituents.

**MATERIALS AND METHODS:** A literature review in databases such as PubMed, Scopus, Web of science and Google Scholar was conducted.

**RESULTS:** A number of in vitro and in vivo studies about the influence of green tea extract on the activity of different enzymes and transporters were found in the researched literature. The results showed that green tea extracts may affect the pharmacokinetics of some tyrosine kinase inhibitors (imatinib, erlotinib, lapatinib), statins (atorvastatin, simvastatin), calcium channel blockers (verapamil, diltiazem) and others, leading to an increased risk of adverse reactions or therapy failure.

**CONCLUSION:** The present study showed that green tea extracts may influence the metabolism and transmembrane transport of various drugs if taken together. Therefore, it is necessary to avoid daily green tea consumption with certain medications, especially anticancer agents.

**Keywords:** herb-drug interactions, green tea, catechins, methylxanthines

## THE PHARMACISTS' POINT OF VIEW ON THE PAYMENT FOR SPECIALIZED PHARMACEUTICAL CONSULTATION WHEN PERFORMING A WHITE PRESCRIPTION FORM

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**INTRODUCTION:** Master pharmacists are the most available medical specialists, professionally engaged in providing health information and pharmaceutical care for the society. The specialized consultation, focused on specific patient, adds extra value of pharmaceutical service and participates in the maintenance and improving public health.

In the pharmacy, as health facility, consultations related to rational use of drugs, health care and prevention of diseases, are daily conducted. There is also a promotion of a healthy lifestyle and so many other activities, all of which are free for the patients.

At this point, the legislation does not give the opportunity to pay for this specialized pharmaceutical consultation and care while giving the prescribed drugs on a white recipe.

The payment of skilled labor is common practice in most European countries. In Bulgaria, that kind of activity is paid only for the patients, receiving drugs by the order of the law for health insurance. Pharmaceutical care for the others prescription forms is not paid to the specialist.

**MATERIALS AND METHODS:** A survey was conducted on the territory of Varna with the participation of 56 Masters of Pharmacy. The survey tracks the opinions and attitudes of the specialists on the payment for their individual work with the patients, which provides pharmaceutical care and rational use of drugs.

**Results:** The results of the survey show that 74.10% of the pharmacists who took part think that additional payment, while consulting the patients for rational use of drugs and providing pharmaceutical care, is needed.

Also, the survey tracked the opinions of the pharmacists for the value of the specialized service, and the results show that 57% of the specialists indicate the amount of 2–3 BGN. Between 3–10 BGN must be the payment according to 30% of the pharmacists. Percentage of the final amount of the prescription is the most appropriate option according to 13% of the pharmacists who took part in the survey. The amounts are equal for the pharmaceutical care and consulting while dispensing the drugs from the prescription.

**CONCLUSION:** The survey shows that the pharmacists want to assign value to their knowledge, labor and care. In the center of the modern health care system is the patient and the pharmacists have direct responsibility for the successful treatment and the rational use of drugs. The introduction of a fee for specialized care and consultation while dispensing drugs from a white prescription will stimulate the professional development of the pharmacists, increasing the number of health professionals involved.

**Keywords:** *white prescription form, master of pharmacy, payment, pharmaceutical care*

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## CHANGES IN THE AMOUNT OF VALUE ADDED TAX IN A PHARMACY RELATED TO THE COVID-19 PANDEMIC

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**INTRODUCTION:** Due to the epidemic health situation in 2020, a number of changes took place worldwide and specifically in Bulgaria, requiring a rapid response from the government of each country. One of the important steps at a national level is to change the percentage rate of value added tax (VAT) for some products dispensed in a pharmacy.

**MATERIALS AND METHODS:** A documentary method—the normative requirements and changes in the VAT Act concerning the work and management of the pharmacies when servicing the population, has been used. A comparison is made with the reduced tax rates in Bulgaria compared to several European Union countries.

**RESULTS:** The study presents the main changes made in the VAT Act, directly related to the work of pharmacists. The first change concerns the reduction of VAT from 20 to 9 percent for products such as food suitable for babies or young children, baby diapers and similar baby hygiene items. These changes have a definite term, come into force on 01.07.2020 and are valid until 31.12.2021.

The next change coming into force on 01.01.2021. and valid until 31.12.2022 is the abolition of the tax rate of 20 to 0 percent for products used for diagnosis or vaccines for COVID-19. This measure is aimed at timely diagnosis of sick people and stimulating the prevention of citizens.

Compared VAT data from the beginning of 2021 in a number of EU countries show that countries such as Sweden, Malta and Ireland have a 0% minimum rate for certain pharmaceutical products or medical services. They are followed by France (2.1%), Luxembourg (3%), and Spain (4%) with their respective minimum tax.

The study shows changes in VAT rates related to COVID-19 in many European countries in terms of hospital care or pharmaceutical services. Examples are Austria—rate reduced to 5%, Germany—to 7%, and Ireland—9%. Like these countries, Bulgaria has also made changes to its legislation.

The data show the progress and timeliness of legal changes as part of the country's measures to address the economic consequences of COVID-19.

**CONCLUSION:** The changes in VAT concerning pharmacies, made in the period July 2020–March 2021, aim to favor the work of business and strengthen the purchasing power of citizens through a temporary measure. A comparison with other EU countries shows progress in legislation at national level.

**Keywords:** *change, rate, value added tax, pharmacy, Covid-19, pandemic*

## ADVERSE CARDIOVASCULAR EFFECTS OF ANTI-COVID-19 DRUGS

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**INTRODUCTION:** To this date, more than 230 million individuals suffered a COVID-19 infection, with more than 4.5 million having lost their lives. With the devastating health and socioeconomic impacts of the disease, numerous off-label and investigational drugs have gained popularity because of the relatively positive pre-clinical trials. However, practice shows that several medications can exhibit significant adverse effects on cardiac function.

**MATERIALS AND METHODS:** The study features a literature review on research surrounding the current anti-COVID-19 drugs. We conducted a retrospective analysis of the relevant articles and evaluated and compared their findings. We used PubMed as our primary database and the FDA website to observe the current treatment protocols and guidelines.

**RESULTS:** Chloroquine and hydroxychloroquine can induce severe cardiac toxicity even at therapeutic doses, namely, QT prolongation and the risk of torsade de pointes. Remdesivir, the only FDA-approved COVID-19 drug, is associated with bradycardia, hypotension, and prolonged QT interval. Azithromycin and moxifloxacin may also prolong the QT interval. Ritonavir/lopinavir show QT and PR interval prolongation, along with rare cases of atrioventricular blocks. Drug-drug interactions may also lead to myocardial injury. Monoclonal antibodies, such as tocilizumab and sarilumab, do not show cardiotoxicity.

**CONCLUSION:** Several anti-COVID-19 medications exhibit a broad spectrum of adverse cardiovascular effects, including worsening preexistent cardiovascular disorders, irreversible cardiomyopathy, atrioventricular blocks, QT interval prolongation, and risk of torsades de pointes. These findings urge a careful evaluation and continuous monitoring for cardiovascular complications of all patients undergoing treatment with the presented anti-COVID-19 drugs.

**Keywords:** *COVID-19, anti-COVID-19 therapy, cardiotoxicity*

## COMPARISON BETWEEN ZOTAROLIMUS AND SIROLIMUS DRUG-ELUTING STENTS IN PATIENTS WITH CORONARY ARTERY DISEASE

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**INTRODUCTION:** Coronary stents are used in percutaneous coronary intervention (PCI) in narrowed coronary arteries causing ischemia. Drug-eluting stents (DES) have proved to be superior to bare-metal stents (BMS) in regard to major adverse coronary events (MACE). The first DES approved for clinical use was coated with sirolimus, a potent antiproliferative agent, blocking the cell cycle mainly of smooth-muscle cells. The second generation DES deliver zotarolimus, a synthetic analogue of sirolimus. Zotarolimus-eluting stents (ZES) have demonstrated good results in comparison to BMS, however, their safety and efficacy compared to sirolimus-eluting stents (SES) are yet to be established.

**AIM:** The aim of the study is to compare zotarolimus to sirolimus DES for PCI in patients with coronary artery disease (CAD).

**MATERIALS AND METHODS:** Randomized trials comparing SES and ZES in patients with CAD were collected using the PubMed and Cochrane Central Register of Controlled Trials database. The following outcomes of interest were assessed: MACE, mortality, myocardial infarction, target vessel revascularization (TVR), stent thrombosis, and in-stent restenosis.

**RESULTS:** We included 6 randomized trials in our study. No significant differences in mortality rates, myocardial infarction and stent thrombosis between ZES and SES at up to 1-year follow-up were observed. The group treated with ZES had considerably higher odds of TVR compared to SES. ZES were associated with higher rates of in-stent restenosis at up to 1-year follow-up. A greater number of MACE was detected in the ZES group at up to 1-year follow-up. Nonetheless, MACE rates were similar between both groups at a 5-year follow-up.

**CONCLUSION:** ZES appear to be inferior to SES in terms of MACE and in-stent restenosis at 1-year follow-up. However, the superiority of SES is lost after 5 years.

**Keywords:** *sirolimus, zotarolimus, drug-eluting stent*

## A HPLC-UV ANALYSIS OF DIFFERENT BANCHA GREEN TEA EXTRACTS

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**INTRODUCTION:** Green tea is one of the most consumed beverages in the world. Different types of green tea are available depending on the time of harvest and post-storage conditions. For instance, bancha is one of the most popular green teas in Japan. It is produced by the third or fourth harvest of the tea leaves (*Camellia sinensis*, L.).

**AIM:** The aim of the present study was to determine the quantity of caffeine, epigallocatechin gallate (EGCG) and (+)-catechin in bancha green tea extracts.

**MATERIALS AND METHODS:** A total plant extract and a methylxanthine fraction were isolated from bancha green tea leaves. A HPLC-UV method was used for qualitative and quantitative analysis of caffeine, EGCG and (+)-catechin in the obtained extracts.

**RESULTS:** The amount of caffeine and EGCG in the total extract was  $4.19\% \pm 0.14$  and  $4.12\% \pm 0.44$ , respectively. (+)-catechin ( $0.26\% \pm 0.28$ ) was also found in the extract. A high amount of caffeine ( $81.03\% \pm 0.72$ ) was determined in the methylxanthine fraction, while catechins were not detected. It was calculated that the total bancha green tea extract contains 6.86 mg caffeine and 6.74 mg EGCG, while the methylxanthine fraction contains 7.70 mg caffeine per 1.0 g of dried tea leaves.

**CONCLUSION:** The present study showed that bancha green tea contains less quantity of caffeine and catechins compared to other types of green tea. However, bancha green tea is widely consumed and its health benefits, as well as possible herb-drug interactions, need further investigation.

**Keywords:** HPLC-UV, bancha, green tea, methylxanthines

## CURRENT REGULATION OF THE ELECTRONIC PRESCRIPTION OF MEDICINAL PRODUCTS IN BULGARIA

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**INTRODUCTION:** Historical records show that in 1983 the world's first electronic transfer of a prescription from a doctor's office to a community pharmacy located next door took place. Electronic prescribing, according to the US Institute of Medicine, can reduce mistakes and significantly impact health outcomes. At the beginning of August 2011, the National Health Insurance Fund (NHIF) announced the launch of the Electronic Prescription Project with the aim of building a centralized online system in Bulgaria, which covers the activities of prescribing and dispensing medicines. Unfortunately, at that time the project remained only at the level of pilot application for the territory of the town of Slivnitsa. Almost 10 years later, the functionality of the National Health Information System (NHIS) was rewarded and at the end of 2020, the actual prescribing and fulfilling of electronic prescriptions in Bulgaria became a fact.

**AIM:** The aim of this article is to explore and analyse all options for e-prescribing of medicinal products in Bulgaria by September 2021.

**MATERIALS AND METHODS:** Review of the legislation in the field of prescribing of medicinal products in Bulgaria and SWOT analysis of the implementation of this option over the country have been conducted.

**RESULTS:** The normative documents show that in Bulgaria prescribing by electronic prescription of medicinal products is regulated on a regular prescription form with white colour and medicinal products paid fully or partially by the NHIF, where the use of the electronic prescription is even obligatory. At present, September 2021, there is no possibility to prescribe medicines containing narcotic substances on a special prescription form via an electronic prescription. Among the benefits of the introduction of e-prescriptions is, on the one hand, the reduction of mistakes caused by misinterpretation of the handwriting on the prescriptions and, on the other hand, the reduction of waiting time in pharmacies, as well as the reduction of errors in reporting by pharmacies to the NHIF, reduction of time for administrative activities and automation of the filling process, etc.

**CONCLUSION:** There is a need for improvement of the medical software used for issuing electronic prescription, as well as a change in the current regulatory framework concerning the prescription of drugs containing narcotic substances, in order to enable their application in Bulgaria for all medicinal products.

**Keywords:** *medicinal products, electronic prescriptions, prescribing*

## ATR-FTIR SPECTROSCOPY IN THE GERANIUM MACRORRHIZUM ESSENTIAL OIL AUTHENTICITY ANALYSIS

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**INTRODUCTION:** Geranium macrorrhizum L. is an endemic plant species. Over the years, many phyto-preparations have been developed from that plant. From a medical point of view, the most valuable of these are the ones that include Geranium macrorrhizum essential oil. Too often, however, Geranium macrorrhizum oil is adulterated with its much cheaper imitator—the Pelargonium graveolens stem leaf oil. Doubtless, the two oils possess radically different compositions and properties. To distinguish the authenticity of the two essential oils, we decided to apply the analytical potential of the attenuated total reflectance-fourier transform infrared spectroscopy (ATR-FTIR) technique.

**AIM:** The principal objective of this work is to develop a rapid and reliable spectral method of determining the Geranium macrorrhizum essential oil authenticity.

**MATERIALS AND METHODS:** Geranium essential oil was purchased from a commercial source. It was obtained by hydrodistillation, using a specially designed extraction apparatus. All FTIR spectra were recorded on a Tensor II FTIR spectrophotometer in the attenuated total reflection (ATR) mode, at a resolution of 4.0 cm<sup>-1</sup>.

**RESULTS AND CONCLUSION:** In our series of measurements, the potential of the ATR-FTIR spectroscopy in question for analyzing the authenticity of the title aetheroleum was successfully proved. At first sight, the resulting spectra are quite different (highly specific) from each other. As a whole, the spectral features of the major constituent of Geranium macrorrhizum essential oil, germacrone, contour the spectrum of the examined oil. On this ground, we conclude that the present method has a special place in the Geranium macrorrhizum essential oil authenticity analysis.

**Keywords:** *ATR-FTIR spectroscopy, Geranium macrorrhizum essential oil, geranium essential oil, aetheroleum, Geranium macrorrhizum L.*

## INFLUENCES WHEN DECIDING TO STUDY PHARMACY: A SURVEY AMONGST PHARMACISTS AND PHARMACY STUDENTS

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**INTRODUCTION:** There are various reasons why individuals choose a particular career path. Awareness of motivational factors could enhance student recruitment strategies as well as help them to focus on specializations/elective disciplines while studying.

**AIM:** The objective was to investigate what factors influenced students to study pharmacy. Comparisons were conducted to ascertain whether gender, age, year of study and city where students received their education affected responses.

**MATERIALS AND METHODS:** Data were collected in September using a Google-based questionnaire developed with reference to the published literature. Responses were coded and entered into SPSS for statistical analysis.

**RESULTS:** Responses were received from 284 pharmacists and pharmacy students. A total of 70.4% of the participants were female; 31.7% were last year students and 16.5%—first-year students. A total of 87% responded that the desire to work in the health sector was very important/important for their decision to choose pharmacy. Only 8.1% answered that the orientation from career consultation centers was important for their choice of pharmacy study.

**CONCLUSION:** Students' and pharmacists' reasons for choosing pharmacy focused mainly on the desire to work in the health sector, the possibility to improve people's health, the variety of opportunities for professional realization (pharmacies, manufacturing, clinical trials, labs, pharmaceutical marketing, etc.), job security, high recognition and status of the pharmacy profession in the society. Shortage of pharmacists and flexible working hours have less importance on the choice to study pharmacy. Advice from classmates, friends and family members and positive personal experience as a patient from pharmacies/pharmacists have the least influence.

**Keywords:** *pharmacy, education, university, students, career, choice*

## THE PHARMACIST AND HIS KEY ROLE IN THE PROCESS OF PROVIDING PHARMACEUTICAL CARE IN THE CONTEXT OF A COVID-19 PANDEMIC

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**INTRODUCTION:** From ancient times to the present day, mankind has experienced many pandemics that have claimed the lives of many people. Vaccines are a powerful and proven effective tool for controlling infections.

**MATERIALS AND METHODS:** The comparative historical method, analysis of documents, as well as the methods of analysis and synthesis of the studied problems are applied.

**RESULTS:** Historical information is given about the worst pandemics experienced by mankind and about the vaccines developed from the end of the 18th century until now. The role of the global and European pharmaceutical industry in the development of medicines and vaccines to deal with the Covid-19 pandemic has been analyzed. Emphasis is placed on the key role of pharmacists as the most accessible health professionals to limit the spread of the pandemic by complying with the measures in place, providing the necessary medicines to treat the infected and providing sufficient effective vaccines to vaccinate the population and achieve collective immunity.

**CONCLUSION:** Good pharmaceutical practice requires the modern pharmacist to continuously improve his/her professional competence in order to monitor the therapeutic results of the patients and improve their quality of life.

**Keywords:** *pharmacist, role, Covid-19 pandemic*

## BETA ANTAGONISTS. CHARACTERISTICS AND PHARMACOLOGICAL EFFECTS

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This research summarizes the pharmacological functions of beta-adrenergic (AR) inhibiting agents, a wide group of which are beta blockers. Their main function is to antagonize the effects of epinephrine and nor-epinephrine. These catecholamine neurotransmitters affect the cardiovascular system by binding to beta-AR receptors in the membrane of the myocytes, through which a complex mechanism is induced. As a result of the activation, the neurotransmitter indirectly influences the opening and closing of Ca<sup>2+</sup> channels and respectively increases the intracellular concentration of Ca<sup>2+</sup> ions. The ion influx enhances the inotropy (myocyte contractility) and chronotropy (heart rate) of the heart. In conclusion, the beta-AR stimulation of neurotransmitters increases heart rate and blood pumping. In case of rhythm and heart disorders, beta blockers are prescribed. They serve as concurrent inhibitors of beta-AR, which explains their opposite effects—they exert negative inotropy, chronotropy, dromotropy (electrical conduction), and lusitropy (relaxation), which affirms their use in treating hypertension, angina, myocardial infarction, arrhythmias, heart failure, etc.

The research serves as an informative generalization of the different effects that beta blockers cause in explanation of their wide-range medical applications. It presents the types of beta-adrenergic receptors and analyzes the mechanics of their activation in cardiac and vascular myocytes, as well as their general effects on the cardiovascular system. Consistently the research classifies different types of beta blockers and characterizes their pharmacodynamics and pharmacokinetics. It gives information about their medical uses and drug interactions. At the same time, it gives caution on adverse side effects. In conclusion, it summarizes the necessity of beta blockers in medical practice.

**Keywords:** *beta antagonists; beta-adrenergic receptors, catecholamines, Ca<sup>2+</sup> ions; Ca<sup>2+</sup> channels*

## NEUROAXIAL APPLICATION OF MORPHINE

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**INTRODUCTION:** Morphine is one of the world's oldest medicinal remedies. Its analgesic properties as well as its side effects (euphoria, somnolence, nausea and vomiting, addiction, respiratory depression, etc.) have been known for thousands of years. It was isolated at the beginning of 19th century like the active ingredient of opium. Morphine's application can be achieved in an oral, i.m., i.v., s.c., and a neuroaxial way. Its action is based on binding to specific receptors ( $\mu_{1,2}, \kappa, \delta, \sigma$ ) located throughout the central nervous system and other tissues. Intrathecal or epidural administration of morphine selectevly modifies the pain transmission impulses at dorsal horn level in the spinal cord.

**AIM:** The aim of this article is to analyze the benefits of the neuroaxial application of medicinal products containing morphine.

**MATERIALS AND METHODS:** Different full-text publications and scientific articles concerning morphine application were analyzed. Literature was accessed through PubMed and Google Scholar.

**RESULTS:** A lot of research works and meta-analysis on the neuroaxial use of morphine were conducted. It was the first opioid drug to receive the USA Food and Drug Administration approval for intrathecal and epidural use. Neuroaxial application of morphine produces long-acting analgesia with minimal incidence of opioid systemic side effects. The medicament can be used solely for pain relief or as adjuvant to local anesthetic (LA) agents for spinal or peridural anesthesia. Thus, a better analgesic effect is achieved with reduced LA doses i. e. decreased LA toxicity. Neuroaxial use of preservative-free morphine is conceivable across all age groups. It finds its place in a lot of surgeries (traumatology, urology, obstetrics and gynecology, etc.), as well as in the treatment of different pain syndromes (cancer pain, rheumatic diseases, chronic pain syndroms etc.).

**CONCLUSION:** Morphine use is considered to be the gold standard in the neuroaxial administration of opioids.

**Keywords:** *morphine, pain, neuroaxial application*

## COGNITIVE ENHANCERS AND ALTERNATIVES

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**INTRODUCTION:** Cognitive enhancers are more often related to medicals and supplements, which enhance brain function and better memory and ability for concentration. As a positive side effect, they may increase the level of motivation and energy. In general, most of them are better known as nootropics, but we can find them as study pills, smart pills, brain boosters, memory boosters, etc. These drugs were originally developed as cognitive enhancers for the treatment of neurodegenerative diseases and mental disorders, including Alzheimer's disease, attention deficit hyperactivity disorder, and schizophrenia. The increasing use of cognitive enhancers by healthy individuals raises many safety concerns and opens questions of cognitive enhancement alternatives. Considering that nootropics improve the connection and communication between one neuron and another, boosting some of the neurotransmitters like dopamine, serotonin, epinephrine, norepinephrine and others, the aim is for natural alternatives increasing the function of the same neurotransmitters to be found.

**AIM:** The aim of this article is to analyze the natural alternatives of cognitive enhancers.

**MATERIALS AND METHODS:** Researches related to neurotransmitters, cognitive enhancers, and flow were analyzed and compared with personal observation from IT specialists, sales persons and sportsmen.

**RESULTS:** Improving performance through an improved function of cognitive perception is increasingly desirable, given the increasing competition in each sector. Drugs to improve the cognitive function have a positive effect, but they also have highly undesirable and dangerous side effects. There is an increasing study of natural supplements that can simulate a similar effect, as well as the natural state of optimal experience, or flow, which can largely be an alternative.

**CONCLUSION:** The search for alternatives for improving cognitive abilities is becoming a leading topic for researchers seeking to improve human performance, happiness and longevity.

**Keywords:** *nootropic, drugs, flow, cognitive enhancer*

## **MOLECULAR MECHANISMS OF ACTION OF A NOVEL NUTRITIONAL SUPPLEMENT: NEW KNOWLEDGE IN SUPPORT OF ANTIOXIDANT AND NEUROPROTECTIVE EFFECTS**

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**A novel nutritional supplement containing citicoline (CDP-choline) and three plant extracts rich in vitamin C and polyphenols will be the focus on a multidisciplinary project. The beneficial effects of each of the ingredients of this newly developed product are well known.**

**CDP-choline is the natural intermediate in the biosynthesis of phosphatidylcholine, which is the major phospholipid in cell membranes. Many studies have presented scientific evidences in support of the neuroprotective properties of citicoline such as improving the stability of the cell and mitochondria membranes, and alleviation of lipid peroxidation, apoptosis and other mechanisms involved in neuronal damage.**

**The other ingredients in the supplement are vitamin C from extracted from rosehip (*Rosa canina*), and extracts from black chokeberry (*Aronia melanocarpa*) and green tea (*Camellia sinensis*). These dietary plant extracts are rich in polyphenols, which together with vitamin C are known to be powerful antioxidants with contribution in maintaining the redox balance and in protecting cells, including neurons from oxidative damage.**

**Although the beneficial effects of all active ingredients have been well studied individually, for the first time their synergistic action will be explored in a human intervention study.**

**We expect to obtain new data revealing the molecular mechanisms behind neuroprotective and antioxidant effects of a novel nutritional supplement with implication in human health.**

**Keywords:** *citicoline, plant extracts, polyphenols, antioxidants, neuroprotective effects, human health*

## THEORETICAL APPROACH FOR ESTIMATION OF POTENTIAL EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS (PAHS) BY INTAKE OF FOOD SUPPLEMENTS WITH HERBAL INGREDIENTS

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**INTRODUCTION:** Medicinal plants may be contaminated with polycyclic aromatic hydrocarbons (PAHs), particularly if they grow near industrial areas and urban regions. Benzo[a]anthracene, chrysene, benzo[b]fluoranthene, and benzo[a]pyrene are the four priority pollutants pointed out by European Food Safety Authority.

**AIM:** The aim of the study was to assess the potential exposure to PAHs for five medicinal plants mostly used as ingredients in food supplements.

**MATERIALS AND METHODS:** The potential exposure to PAHs was assessed as theoretical evaluation of daily intake (DI), hazard quotient (HQ) and margin of exposure (MOE) for carcinogenic and genotoxic chemicals. The PAHs concentrations were determined in the plant species: *Matricaria chamomilla* L., *Thymus serpyllum* L., *Tilia tomentosa* Moench, *Sambucus nigra* L., and *Achillea millefolium* L. The levels of 13 PAHs in the samples were measured by gas chromatography using mass spectrometry detection. The MOE was calculated for evaluation of potential cancer risk as dividing benchmark dose lower confidence limit (BMDL10) by the DI for the sum of 4 PAHs.

**RESULTS AND DISCUSSION:** The highest sum of the 4 PAHs was found in *Tilia tomentosa* Moench (4.13 µg/kg dry weight) and was below the permissible limit of 50 µg/kg set by EU legislation. The most toxic compound benzo[a]pyrene was not found in the plant species investigated. The maximum value of HQ was evaluated for fluorene 0.00015 (for food supplement with *Tilia tomentosa* Moench) and was much lower than 1, suggesting that intake of supplements would not pose any non-cancer risk. The MOE values were in the range from 3 129 520 to 29 824 561 (for food supplements with *Achillea millefolium* L. and *Matricaria chamomilla* L., respectively).

**CONCLUSION:** The theoretical safety assessment of medicinal plants has shown that the intake of supplements would not pose any health risk.

**Keywords:** polycyclic aromatic hydrocarbons (PAHs), food supplements, risk assessment, margin of exposure (MOE)

## PHARMACEUTICAL CARE ISSUES DURING THE COVID-19 PANDEMIC FROM A PATIENT'S PERSPECTIVE

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**INTRODUCTION:** In the last year and a half, pharmacists have faced a new challenge—the Covid-19 pandemic. This set new requirements for the organization of work in pharmacies and required changes in patient care.

**MATERIALS AND METHODS:** A documentary method and an anonymous survey among pharmacy visitors are used. The survey aims to identify the main problem areas in pharmaceutical services, in the context of the Covid-19 pandemic from the patient's point of view.

**RESULTS:** The introduced measures for keeping a physical distance increased the number of people waiting for pharmaceutical services outside the pharmacy. Large queues are also mentioned as a major problem in accessing pharmaceutical care as per the subjects' point of view. Patients are not satisfied with the lack of time for consultations by health professionals. Other problems reported by pharmacy visitors are the lack of masks and personal protective equipment during the first wave of the pandemic. Lack of medicinal products is also a problem noticed by patients that affects the pharmaceutical services offered. During the Covid-19 pandemic, an infodemic also spreads among the population. Healthcare professionals aim to introduce awareness and educate patients struggling with mass panic. Nearly a third of the subjects cite pharmacists as the main source of reliable information.

**CONCLUSION:** During the Covid-19 pandemic, the importance of the role of pharmacists in the consultation process is clear. The large number of patients seeking help from pharmacists form queues and healthcare professionals are not able to meet all patients' needs for protective equipment, medicines and consultations. Changes are needed in the organization of work in a pharmacy in order to adapt to the new working environment.

**Keywords:** *pharmaceutical care, Covid-19 pandemic, pharmaceutical care issues*

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## EFFECT OF POLYPHENOL-RICH *ARONIA MELANOCARPA* FRUIT JUICE ON ANTIOXIDANT DEFENSE SYSTEM IN RATS WITH DIET-INDUCED METABOLIC SYNDROME

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**INTRODUCTION:** The role of oxidative stress in the development of metabolic syndrome (MS) has been well established. *Aronia melanocarpa* fruits are very rich in polyphenols, which possess an antioxidant effect.

**AIM:** The aim of this article is to evaluate the effect of *Aronia melanocarpa* fruit juice (AMFJ) on the antioxidant defense system in rats with diet-induced MS.

**MATERIALS AND METHODS:** Fifty male Wistar rats were allocated into 5 groups: control, MS, MS + AMFJ2.5, MS + AMFJ5 and MS + AMFJ10. For 10 weeks, the control group received regular diet and the other groups—high-fat high-fructose diet (HFHF). During this period, the control group and MS group were treated daily orally with 10 mL/kg distilled water and the other groups—with increasing volume (2.5 mL/kg, 5 mL/kg, and 10 mL/kg) of AMFJ. Superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities were measured in the serum using commercial kits for enzyme-linked immunosorbent assay (ELISA).

**RESULTS:** A significantly higher SOD level was observed in MS group ( $0.0069 \pm 0.0007$  U/mL) compared to the control group ( $0.0051 \pm 0.0003$  U/mL) ( $p < 0.01$ ). AMFJ treatment returned the level of SOD to the control values, with the effect being most significant in MS + AMFJ2.5 ( $0.0053 \pm 0.0003$  U/mL) and MS + AMFJ5 ( $0.0053 \pm 0.0003$  U/mL) groups ( $p < 0.05$  vs. MS). No significant difference was detected in the activity of GPx in all groups.

**CONCLUSION:** HFHF diet-induced MS might be associated with compensatory activation of SOD. AMFJ counteracted the MS-induced elevation of SOD level in the treated groups and had no effect on GPx activity.

**Keywords:** *Aronia melanocarpa*, metabolic syndrome, rats, antioxidant enzymes

# IR AND UV-VIS SPECTROSCOPIC ANALYSIS OF A NEW COMPOUND—N-[1-(4-HYDROXYPHENYL) AMINOETHILYDEN]-4-[1-(3,5,5,8,8-PENTAMETHYL- 6,7-DIHYDRONAPHTALEN-2-YL)-ETHENYL] PHENYLCARBOHYDRAZIDE

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**INTRODUCTION:** Bexarotene is commonly classified as a retinoid due to its selective activity at retinoid X receptors (RXRs). It can be used systemically in patients with cutaneous T-cell lymphoma, specifically when patients have extensive plaques and tumors. It can also be given topically in patients with less severe and localized diseases. Paracetamol has a pronounced analgesic and antipyretic effect. It is used to treat mild to moderate pain in headaches, migraines, toothaches, rheumatic and muscular pains, menstrual cramps, sore throats, as well as to relieve malaise and colds. In the present study, we describe methods for identification of a product, a hydrazone of bexarotene and paracetamol, synthesized by us.

**AIM:** The main stage after obtaining a chemical molecule is its qualitative characterization. This article discusses IR and UV-VIS methods for the analysis of N-[1-(4-hydroxyphenyl) aminoethilyden]-4-[1-(3,5,5,8,8-pentamethyl-6,7-dihydronaphtalen-2-yl) ethenyl]phenylcarbohydrazide. It is a product of the interaction between the hydrazone of the antineoplastic drug bexarotene and paracetamol.

**MATERIALS AND METHODS:** For the purpose of our work, IR and UV-VIS spectroscopy were used. Infrared spectrophotometry allows determination of the molecule structures of various organic (and inorganic) substances based on the absorption spectra of emission.

UV-VIS spectroscopy is a type of electromagnetic spectroscopy that examines the interaction between light and matter. Historically, this branch of science arose when light from the visible spectrum was used to study the structure of matter, but later the ultraviolet and infrared ranges of the electromagnetic spectrum began to be applied. This allows obtaining a significant amount of information about the structure of substances at an atomic and molecular level.

**RESULTS:** Due to the close structural similarity, the IR spectra of the newly synthesized compound shows similar bands with bexarotene and paracetamol. However, there are specific bands that are not observed in the bexarotene and paracetamol spectra.

**CONCLUSION:** Both infrared and UV-VIS spectroscopy are basic approaches to the analysis and identification of newly obtained molecules. Based on the data obtained during the analysis, we believe that the newly obtained compound needs further purification and re-analysis by appropriate methods.

**Keywords:** *hydrazone, bexarotene, paracetamol, IR spectroscopy, UV-VIS spectroscopy*



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References should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals: Sample References ([www.nlm.nih.gov/bsd/uniform\\_requirements.html](http://www.nlm.nih.gov/bsd/uniform_requirements.html)) webpage and detailed in the NLM's Citing Medicine, 2<sup>nd</sup> edition ([www.ncbi.nlm.nih.gov/books/NBK7256/](http://www.ncbi.nlm.nih.gov/books/NBK7256/)). These resources are regularly updated as new media develops, and currently include guidance for print documents (journal articles, books or other monographs); unpublished material; audio and visual media; material on CD-ROM, DVD, or disk; and material on the Internet (url, DOI, database).

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Iwamoto Y, Koide H, Ogita K, Nishizuka Y. The protein kinase C family for the regulation of cellular functions. *Biomed Rev.* 1992;1:1-6.

### Journal article with more than 6 authors

Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. *Brain Res.* 2002;935(1-2):40-6.

### Book

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. *Medical microbiology.* 4<sup>th</sup> ed. St. Louis: Mosby; 2002.

### Book chapter

Thornton T. On the interface problem in philosophy of psychiatry. In: Broome MR, Bortolotti L, editors. *Psychiatry as Cognitive Neuroscience: Philosophical Perspectives.* Oxford: Oxford University Press; 2009. p. 121-137.

### URL

American Medical Association [Internet]. Chicago: The Association; c1995-2002 [updated 2001 Aug 23; cited 2002 Aug 12]. AMA Office of Group Practice Liaison; [about 2 screens]. Available from: <http://www.ama-assn.org/ama/pub/category/1736.html>

## DOI, PMID

Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. *BMJ*. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752. PubMed PMID: 19129307; PubMed Central PMCID: PMC2615549

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