


# Scripta Scientifica Pharmaceutica

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# Scripta Scientifica Pharmaceutica

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***Scientific and Practical Conference***
***"Challenges in the Education of Masters of Pharmacy"***
**Conference Hall of Hotel & SPA "Azalia", Varna, Bulgaria**
**November 1, 2014**

*The conference is organised with the financial support of European Social Fund within the Project BG051PO001-3.1.07-0046 "Updating and approbation of the curricula of the Faculty of Pharmacy, Medical University of Varna according to the needs of the pharmaceutical business and the requirements of the labor market"*

## PROGRAMME

09:00 – 09:30 Registration
09:30 – 09:50 **Opening ceremony**
09:50 – 16:40 *Oral presentations:*

**Session 1. State of pharmaceutical education in Bulgaria**

09:50 – 10:10 ***Todor Naydenov***, *Tsvetanka Decheva*
Challenges to the system of continuing medical education on the requirements of the labor market

10:10 – 10:30 ***Evgeni Grigorov***, *Valentina Belcheva*
The medical devices course in pharmacy education – an important tool for better professional realization

10:30 – 10:50 ***Michaela Jordanova***
Latin for Pharmaceutical Purposes. New Methodical Strategies

10:50 – 11:10 ***Stanitsvet Penev***
Culture and competence of pharmacists in the field of parapharmacy

11:10 – 11:30 *Hristianna Romanova*, ***Maria Panteleeva***
Position and significance of Disaster Medicine in the education of students at the Pharmacy Faculty

11:30 – 12:00 Coffee break

**Session 2. Contemporary research achievements of the pharmaceutical faculties in Bulgaria**

12:00 – 12:20 *Eleonora Ilieva, Nevena Petkova*, ***Rositca Nikolova***
Synthesis and applications of coumarin derivatives

12:20 – 12:40 ***Ognyan Petrov***, *Mariana Gerova*
New Efficient Synthesis of Combretastatin A-4 via Colvin Rearrangement

12:40 – 13:00 ***Danail Pavlov***, *Stefka Valcheva-Kuzmanova, Maria Tzaneva, Jan Garrard, Miroslav Novaković, Milka Nashar, Miroslav Eftimov, Kalin Kalchev, Svetlana Ignatova, Milka Jadranin, Ina Kobakova, Snežana Trifunović, Diana Ivanova*
In vivo antioxidant properties of Cotinus coggygria extracts

13:00 – 14:30 Lunch break

**Session 3. Varia**

14:30 – 14:50 ***Bisera Yustiniyanova***, *Marieta Georgieva, Blagovesta Nanova*
Immunofan – characterization and significance as immunomodulator in malignant diseases

14:50 – 15:10 ***Dimitar Kehayov***
Impact of drugs during the lactation period

15:10 – 15:30 ***Krasen Tonev***, *Stanila Stoeva, Bistra Galunska*
Recent analytical methods for measuring blood glutathione levels with focus on HPLC approach

15:30 – 15:50 *Nikolina Zarkova*, ***Viktoria Ivanova***, *Katya Nedeva*
High-fructose diet and health

15:50 – 16:10 ***Stanila Stoeva***, *Krasen Tonev, Svetlana Georgieva*
Dangerous food-drug interactions

16:10 – 16:40 Coffee break

16:40 – 17:30 **Poster session** (5 minutes for each poster with participation of students)

19:00 **Gala dinner and Student awards ceremony**

**List of posters**

1. ***Svetoslav Stoev****, Konstantin Kalaidjiev, Ilko Getov*
   Content analysis of teaching programs for pharmacovigilance in Bulgaria
2. ***Tsvetomil Voyslavov****, Stefan Tsakovski, Elisaveta Mladenova*
   Statistic challenges in pharmacy education
3. ***Djeni Cherneva****, Dobri Ivanov, Mariana Filipova-Marinova*
   Summer practices – an important element of Pharmaceutical Botany learning
4. ***Stela Dragomanova****, Marieta Georgieva, Rada Pehlivanova, Milka Mandova, Borislava Boeva, Hulia Toncheva*
   Problems with prescribing, reading and dispensing of drugs, and education of students of pharmacy, medicine and dentistry
5. *Milena Pasheva,* ***Milka Nashar****, Yoana Kiselova-Kaneva, Diana Ivanova, Bistra Galunska*
   Modernisation of the Biochemistry course for Pharmacy students at Medical University Varna
6. ***Milena Pasheva****, Milka Nashar, Oskan Tasinov, Diana Ivanova*
   Effects of mulberry heartwood extract on genes related to lipid metabolism

7. **Danail Pavlov**, *Miroslav Eftimov, Milka Nashar, Maria Tzaneva, Diana Ivanova, Stefka Valcheva-Kuzmanova*
Anti-inflammatory properties of aqueous infusion from Cotinus coggygria leaves in rats
8. ***Elisaveta Mladenova**, Tsvetomil Voyslavov, Sonja Arpadjan-Ganeva*
In vitro assessment of manganese bioavailability from Hibiscus sabdariffa (Karkade) tea
9. ***Tatyana Hristova**, Rumiana Cherkezova, Kolio Troev*
Polyphosphoesters Based - Paclitaxel Complexes. Synthesis and Characterization
10. ***Zdravko Nikolov**, Stela Dragomanova, Marieta Georgieva*
The role of pharmacists in the identification, treatment and prevention of depressive disorders and stress-related pathology
11. ***Marieta Georgieva**, Bisera Yustiniyanova, Nikolay Manolov*
Roles of Probiotics in Cancer Prevention: an update
12. ***Nikolay Gerassimov**, Miglena Doneva, Guenka Petrova*
Approaches at utilization of hernia meshes
13. ***Anna Todorova***
The Role of the Pharmacist in the Prevention and Treatment of Childhood Bronchial Asthma
14. *Anna Todorova, **Maya Radeva**, Ana-Mariya Velcheva, Kristina Decheva, Teodora Georgieva*
New inhalation therapies. The role of the pharmacist in educating patients in correct use of aerosol devices
15. ***Darina Naydenova**, Marina Atanasova, Rouzha Pancheva*
Can Folic Acid reduce the Risk of autism?
16. ***Staniela Porozhanova**, Rositsa Stancheva*
Royal jelly – a promising product for the pharmaceutical industry
17. *Lyuben Grigorov, **Svetlana Georgieva***
Bisphenol A – Diabetes Mellitus?
18. *Tanya Topalova, **Svetlana Georgieva**, Ivelina Borisova, Stanislava Stoycheva, Katya Nedeva*
Statins in polycystic ovary syndrome
19. *Tanya Topalova, **Svetlana Georgieva**, Iliya Jelev, Ivelina Borisova, Stanislava Stoycheva*
Natural preservatives vs. Artificial preservatives
20. ***Silvia Gancheva**, Maria Zhelyazkova-Savova, Bistra Galunska*
Vitamin K: The multiple faces of an old vitamin
21. ***Petya Georgieva**, Plamen Bekyarov, Bistra Galunska*
Vitamin D deficiency. How to test it?
22. ***Viliana Gugleva***
Current technological approaches in ocular drug delivery
23. ***Nadezhda Ivanova***
Microsponges – a new perspective in colon targeted drug delivery systems
24. *Toni Vekov, **Zhivko Kolev***
Study of the promotion, regulation and the drug advertising in the European Union
25. *Valentina Belcheva, **Evgeni Grigorov***
Study of background and main implications for medicinal products switch process
26. *Kader Dervisheva, **Stefka Valcheva-Kuzmanova***
Study of the use of products containing Ginkgo biloba extract in Bulgaria for the period 2011-2013

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# CHALLENGES TO THE SYSTEM OF CONTINUING MEDICAL EDUCATION ON THE REQUIREMENTS OF THE LABOR MARKET

**Todor Naydenov, Tsvetanka Decheva**

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**The role of the pharmacist has evolved in recent years from a specialist responsible for the preparation of medicines through distributor of finished pharmaceutical products to a provider of pharmaceutical care. Increasingly, health systems in many countries are based on the knowledge and skills of pharmacists to meet the increased expectations of society and to cope with rising deficits in healthcare. This change in focus of the pharmaceutical profession is even more significant in Bulgaria as a result of changes in the socio-political and economic life of the country. Along with the opening of new career prospects, the requirements of the pharmaceutical business and the labor market for what kind of knowledge and competences Masters of Pharmacy should possess have been significantly increased and changed. Through the system of continuing medical education Masters of Pharmacy could meet these requirements by being aware of the innovations in the field of Medicine and Pharmacy and by acquiring knowledge and skills that are applicable in their daily practice.**

**The system of continuing education established by Bulgarian Pharmaceutical Union combines models and best practices proven to be effective and professional experience of a number of specialists from universities and pharmaceutical business and practice. At the same time constantly changing business environment in terms of financial and economic uncertainty, creates new needs and the need for new models of collaboration between stakeholders. Their main function is to ensure the sustainability of the process of acquiring knowledge, in addition, to help decrease costs and increase the quality and accessibility of continuing education.**

# THE MEDICAL DEVICES COURSE IN PHARMACY EDUCATION – AN IMPORTANT TOOL FOR BETTER PROFESSIONAL REALIZATION

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**Introduction: Pharmacists are the most accessible healthcare professionals. They are educated to consult patients for various problems and give them advices for a large number of products.**

**The aim of the work is to analyze the curriculums of the Medical devices course, performed in master degree study programs in "Pharmacy", among the different universities in Bulgaria. We supposed that, this subject is underestimated in the students' education. The objectives of the work are: to critically assess the information which is supposed to be learned, to classify and evaluate the topics covered in curriculum and to make recommendations to improve the studying process. According to the Unified State requirements (USR) for master of pharmacy educational programs the medical devices course is not mandatory.**

**Materials and Methods: Qualitative analysis was performed to enhance understanding of specific dimensions of the "Medical devices" course. We find the curriculums of master degree education in "Pharmacy" from the universities in Bulgaria, preparing the future pharmacists.**

**Results: In 3 of them the "Medical devices" course is mandatory discipline, held in 5th semester and in the rest does not exist at all. The average study horarium is 30 hours for semester. The ECTS vary in the different universities.**

**Conclusion: The knowledge for this group of products is very important for the students graduating "Pharmacy". This field is getting larger and more and more different medical devices are launched on the market every day. Pharmacist must be prepared to dispense them and give the appropriate consultation. General study result is to amend the USR with medical devices subject.**

**Keywords:** *pharmacists, education, pharmacy, medical devices, Bulgaria*

# LATIN FOR PHARMACEUTICAL PURPOSES. NEW METHODICAL STRATEGIES

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**The presentation is based on a newly edited text-book in Pharmaceutical Latin. The text-book is based on communicative language teaching methods aiming at the presentation of basic Latin grammar and vocabulary as well as its practice and production. As concentrated on practical aspects, the text-book is not aimed at presenting the whole Latin grammar.**

**While compiling the material, is paying special attention to the terms and expressions that are dominant in pharmaceutical practice. However, due to the characteristic features of this specialist language, there is not focus on oral communication but mainly on the practice and correct production of the special vocabulary and grammar.**

**During grammar instruction, lecture should provide meaningful input through context and provide an opportunity to put grammar to use, and relate grammar instruction to real life/practice situations.**

**Although grammar instruction has recently been associated with contextual teaching is needed to go beyond this movement to bring grammar instruction fully to practical aspects and to make it purposeful and communicative. The presentation based on realia is followed by less and less controlled practice making students able to freely produce the language of Pharmacy as well as read prescriptions and formulate preparations as prescribed.**

# CULTURE AND COMPETENCE OF PHARMACISTS IN THE FIELD OF PARAPHARMACY

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**Pharmacies and other outlets of the professional development of pharmacists are a venue for presentation skills, selling, innovations and produce goods which, although not drugs, are important for the health of the population. It implies masters of pharmacy of the circle of knowledge and competencies that are outside or between the narrow fields of pharmacy.**

**Such goods may be: nutritional supplements, including vitamins, herbal teas, dietary and other special purpose foods, functional foods, medical devices, cosmetic products, other products.**

**Pharmacists need to be aware and possess a minimum of professional competence in terms of status, the difference of the medicinal products, General and specific features and properties of parapharmaceutical products, field of application, action, etc.**

**For this purpose, it is necessary the curricula of the faculties of Pharmacy to provide more training courses of one or more curricular subjects affecting various aspects of parapharmaceutical topics.**

# POSITION AND SIGNIFICANCE OF DISASTER MEDICINE IN THE EDUCATION OF STUDENTS AT THE PHARMACY FACULTY

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**An overview was made of the necessity the discipline Disaster Medicine to be included in the program of Pharmacy specialty as it is in the compulsory curriculum of specialties medicine, dental medicine, nurse, midwife, assistant pharmacist, radiology technician, management of health care medical cosmetic and more.**

**Education in Medical University - Varna and Medical College - Varna is on an extremely high level and contemporary worldwide trends paying great attention to training, organization and dealing with disasters and accidents should not be neglected due to the increased frequency at a global scale.**

**As a result of disasters, accidents or terrorist attacks, pharmacists may be either injured, or in the role of first aid responders at the site of the accident.**

**Ever since the establishment of the Faculty of Pharmacy in Medical University – Varna the members of Disaster Medicine Subdepartment believe that it is essential in the education of the students of pharmacy dur-**

ing the second summer semester course, the Disaster Medicine discipline to be included in the compulsory curriculum as 45 hours course (30 hours practicals, 15 hours lectures). This will help to increase their preparedness to deal with natural and anthropogenic disasters and catastrophes in real situations.

**Keywords:** *disaster medicine, disasters, accidents, catastrophes, terrorism.*

## SYNTHESIS AND APPLICATIONS OF COUMARIN DERIVATIVES

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**During the last few decades the interest in the synthesis and investigation of different coumarin derivatives and analogues has vastly increased mostly due to their multidisciplinary application in organic synthesis, agrochemistry, medicine, laser technologies, and etc. The object of our investigations is concerned on the chemical behaviors of these compounds because they are good acceptors in reactions with nucleophillic reagents, they can be used as dienophiles in Diels–Alder reaction, 1,3-bipolar cycloaddition reactions etc. The combination of coumarin structure and phosphono moiety assumes a biological activity, which can be a result of each of both units as well as a blend of both. It is clear that coumarins can be used as ligands in complexes with variety metal ions. Another aspect about coumarins which is of great interest for us is the possible photochemical properties of these compounds.**

**Here we report reactions of cycloaddition and new rearrangement reaction resulting in potential biologically active derivatives.**

## NEW EFFICIENT SYNTHESIS OF COMBRETASTATIN A-4 VIA COLVIN REARRANGEMENT

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**Combretastatin A-4 (CA-4), the natural cis-stilbene, is a potent anticancer agent originally isolated from the bark of the South African Combretum caffrum tree. The compound strongly inhibits the polymerization of tubulin by binding to the colchicine site and induces selective vascular dysfunction in tumors by reducing the blood supply to them. This ability distinguishes CA-4 from other anticancer drugs, angiogenesis inhib-**

**itors for example, and defines it as a first member of new class of therapeutic compounds known as vascular disrupting agents.**

**We report here a new four-step approach for the preparation of natural combretastatin A-4. The method includes the Colvin rearrangement of the benzophenone derivative phenstatin to the key diarylalkyne followed by stereoselective semi-reduction to CA-4 in good overall yield. Currently, we are investigating the applicability of this method for the preparation of new heterocyclic analogues of combretastatin A-4.**

## *IN VIVO* ANTIOXIDANT PROPERTIES OF *COTINUS COGGYGRIA* EXTRACTS

**Danail Pavlov[1], Stefka Valcheva-Kuzmanova[2], Maria Tzaneva[3,6], Jan Garrard[4], Miroslav Novaković[5], Milka Nashar[1], Miroslav Eftimov[2], Kalin Kalchev[6], Svetlana Ignatova[4], Milka Jadranin[5], Ina Kobakova[6], Snežana Trifunović[7], Diana Ivanova[1]**

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**The Smoke tree (*Cotinus coggygria* Scop.), well known as poisonous plant, is used mainly externally by the Balkan folk medicine for its antiseptic and anti-inflammatory properties. The aim of our study was to explore the effect of aqueous infusion from *C. coggygria* leaves (AICCL) and ethanol infusion of *C. coggygria* heartwood (EICCW) in two experimental models of oxidative stress: Paracetamol (P)-induced liver toxicity (PILT) and Indomethacin (IN)-induced gastric ulcerogenesis (INIGU). Additional aim was to identify and extract the major phytochemical components of both infusions by Ultrahigh-Performance Liquid Chromatography coupled with Time-of-Flight mass spectrometry analyzer (ToF/MS) with an Electro Spray Ionization (ESI) source (UPLC-ESI/ToF/MS), as well as by High-Performance Counter-Current Chromatography (HPCCC). Eight groups of Male Wistar rats (n = 64; 200-250 g) were used in the PILT model: Water control (C), P, 1/100 AICCL+P, 2/100 AICCL+P, 4/100 AICCL+P, Ethanol control (Et), Et+P, 1/1000 EICCW+P. Similar eight groups were used in the INIGU model (IN instead of P). Rats were orally pretreated with AICCL or EICCW (10 ml/kg) by intragastric gavage. Groups C and P/IN received distilled water. Groups Et and Et+P/IN received 20% Ethanol. The pretreatment in the PILT model lasted 7 days before a single intraperitoneal injection of P (1 g/kg) and two days afterwards. The duration of pretreatment in the INIGU model was 3 days, followed by a single intragastric treatment with IN (100 mg/kg). The effects were evaluated by biochemical, morphometrical and histopathological methods. The blood serum levels of aspartate aminotransferase were significantly lower in the group 1/100 AICCL+P, compared to group P. The hepatic parenchyma of group 1/100 AICCL+P was with preserved architectonics without necrosis. Morphometrical examinations of stomachs showed that the 2/100 AICCL significantly decrease the ulcer number and area. EICCW induced a reduction of the depth and severity of indomethacin-induced mucosal lesions. Our results demonstrated the hepatoprotective ef-**

**fect of 1/100 AICCL, and gastroprotective effect of 2/100 AICCL and EICCW in support of the scarce reports about internal usage of decoctions from *C. coggygria*. The most probable mechanism of these beneficial effects is the significant decrease of lipid peroxidation, due to the antioxidant properties of the plant investigated. Phytochemical analyses showed that the major components of the AICCL are gallotannins and gallic acid. Fustin and sulfuretin were the major bioflavonoid constituents of the EICCW.**

# IMMUNOFAN – CHARACTERIZATION AND SIGNIFICANCE AS IMMUNOMODULATOR IN MALIGNANT DISEASES

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**Immunofan is a modern effective immunomodulator as a product of the newest tendency in world medicine – the molecular nanotechnology. The author and discoverer of the unique patent medicine is Prof. Dr. Vasilii Lebedev. The product is manifectured in three forms: sterile ampullae, spray doses and suppositories in Scientific-manufacture complex "Bionox" in Moscow. Pharmaceutical effect of Immunofan is manifested in three basic directions:**

- **Restoration the balance of the oxidation and restoration processes in the organism;**
- **Correct the immune system in cases, when the immune system is destroyed in appearance of malignant formation, disease respectively;**
- **Remove the possibility for multiple drug resistance (MDR), and by this way the effect of the treatment with other drugs is increased in patients with malignant disease.**

**For the first time in the world a new medicine is created that give the chance to be used to abolish the multiple drug resistance. In the treatment of malignant diseases it is concerned that during the period of chemotherapy should not be taken immunomodulators, because they increase cellular mitotic activity. Just the opposite is the idea that Immunofan should be taken exactly during the time of chemotherapy, because the multiple drug resistance is avoided, returning the cellular sensitiveness to therapeutic effect of chemotherapy. Overcoming multiple drug resistance, the most powerful effect of medicines is achieved in treatment. The effect of Immunofan is developed and keeps for 2-3 hours (rapid phase) and is continued to 4 months (moderate and prolonged phases). In patients with cancer two ways of therapy is recommended. First: by inclusion in general scheme of multipurpose treatment (chemotherapy and operation), and at that moment start the application of Iimmunofan just before chemotherapy or operation, and second followed by continuing of application the medicine during the whole therapeutic period. It is accepted that Immunofan is a patent medicine that has no analogue among immunomodulators manufactured to this moment in different countries in the world. In patients with cancer Immunofan is with proved effectiveness and is received permission and license for application in medicine. Immunofan is recommended not only for cancer prevention, but for appropriate therapeutic patent medicine with proved effectiveness in secondary and tertiary prevention of cancer. That gives the possibility for prolongation and improvement of life property of patients with cancer.**

**Keywords:** *immunofan, immunomodulator, malignant diseases, prevention, therapy*

# IMPACT OF DRUGS DURING THE LACTATION PERIOD

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**Classification of drugs used during lactation is a poorly explored field in present day pharmacology. The purpose of this study is to provide practicing health care specialists with a stable and broad qualifications system as the base for making the right choice when administering drugs to breast-feeding patients.**

**The development of the present qualification scheme is based on logical and statistical methodological approaches keeping in mind the purpose of this study - to classify drugs registered in Bulgaria.**

**Initially obtained results lead to interesting conclusions, which should be used for further therapy refinement in patients of this high-risk therapeutic group.**

**Drugs are divided into 4 categories:**

1. **Considered safe for the infant.**
2. **Relatively safe for the infant.**
3. **Safe for the infant after the elimination of the drug out of the mother`s body.**
4. **Considered safe for the mother, but toxic for the infant.**

**Keywords:** *Toxicology, drugs, lactation, pharmacotherapy*

# RECENT ANALYTICAL METHODS FOR MEASURING BLOOD GLUTATHIONE LEVELS WITH FOCUS ON HPLC APPROACH

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**Introduction: Glutathione, a tripeptide normally found in nearly all mammalian cells, is the major intracellular non-protein thiol compound. Its metabolism in the body is described by the γ-glutamyl cycle. Glutathione has various important functions, including detoxification of xenobiotics and hydrogen peroxide and its role as an endogenous antioxidant. It can exist in reduced (GSH) and oxidized state (GSSG). The ratio of these two forms of glutathione determines the cell redox potential and is used as an indicator for oxidative stress. Determining blood and plasma concentrations of total (tGSH), reduced (GSH) and oxidized (GSSG) glutathione provides information on the oxidative status of the human organism.**

**Aim: To overview the recent analytical methods for quantitative analysis of blood glutathione concentration and to analyze their strengths and limitations.**

**Materials and methods:** **Systematic review of web databases (PubMed, ScienceDirect and Google Scholar) on the problem.**

**Results:** **Identification of the strengths and limitations of three analytical approaches based on Ellman's reaction, enzymatic and high performance liquid chromatography (HPLC), recently used for analysis of both reduced and oxidized glutathione in blood plasma. A critical analysis evaluates the HPLC methods as one of the most accurate and robust.**

**Conclusions:** **The HPLC is evaluated as one of the methods of choice for routine determination of low blood glutathione concentrations due to its excellent analytical performance.**

**Keywords:** *glutathione, HPLC method, analytical performance*

# HIGH-FRUCTOSE DIET AND HEALTH

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**Introduction:** **In recent decades fructose has largely replaced sucrose as a sweetener in prepared foods and in carbonated soft drinks. Scientific researches reveal that high fructose diet may contribute to metabolic disturbances such as hyperlipidemia, metabolic syndrome and obesity.**

**Aims:** **To investigate what part of the Bulgarian population use products, which contain fructose; to make an overview of the latest scientific data on the fructose effects on human health.**

**Methods:** **An inquiry among students of Medical university of Varna was conducted and the data was processed; after a survey of various websites for biomedical literature, certain publications in recent years were selected and summarized.**

**Results:** **Scientific studies from recent years expand our knowledge of the negative effects of high-fructose diet on human health. Fructose, consumed with mixed meals, results in altered levels of circulating insulin and leptin and to attenuated postprandial suppression of ghrelin. A big part of the population is not acquainted with the harmful effects of products with fructose.**

**Conclusion:** **Excessive consumption of fructose may be one of the causes of health problems such as metabolic disturbances and obesity in the Bulgarian population.**

**Keywords:** *fructose, diet, metabolic diseases*

# DANGEROUS FOOD-DRUG INTERACTIONS

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**Aim:** **To increase patients' awareness of the health risks of certain drug-food interactions and to present their competence in the problem.**

**Materials and methods:** **Systematic approach of available scientific literature on the problem and specially designed questionnaire.**

**Results:** **Interactions between food and drugs may affect treatment results and be the reason of undesirable side effects. The clinical significance of this type of cooperation is varied. Some foods may sensitively influence the rate and extent of absorption of the active substance. That in turn could cause serious side effects, toxicity or treatment failure. In other cases, the food-drug interaction could have a favorable aftereffect by increasing the drug efficacy or reducing the side effects. Our dynamic present offers increasingly wide range of medicines. This requires the study of precisely these two types of interactions with food before the release of a drug on the market**

**Conclusions:** **The results of the survey should reflect on patients' general health culture and their awareness of proper drug intake**

**Keywords:** *food-drug interactions, health risks, health culture*

# CONTENT ANALYSIS OF TEACHING PROGRAMS FOR PHARMACOVIGILANCE IN BULGARIA

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**Modern fast pace of development of pharmaceutical and medical knowledge, drug regulation, pharmacotherapy and innovative approaches to control and treat diseases caused an acute need for a modern system for detection, assessment and prevention of adverse effects of medicinal products or pharmacovigilance.**

**In this context and to response growing shortage of competent professionals in the field of post-marketing surveillance puts the need of wider implementation of pharmacovigilance and pharmacoepidemiology educational qualification requirements, skills and programs of higher medical schools curricula.**

**The aim of this study was to establish to what extent the training of pharmacists in Bulgaria meets the current requirements of pharmacoepidemiology and pharmacovigilance, and what are the short and medium term challenges. By the systematic literature review and comparative analysis of regulatory documents and**

**training programs were established the following results: tendency of adequate synchronization between the Bulgarian educational training programs and postgraduate courses and the modern European practices for training of professionals in the field of pharmacovigilance. There are introduced subjects and modules for practical training in pharmacoepidemiology and pharmacovigilance, lectures and classes for risk management, free elective subjects in the field of pharmacovigilance, etc. However, there is still the challenge to strengthen the focus on practical training in the methods of pharmacovigilance. The degree of training is insufficient in the new branches of science for vigilance, namely monitoring the safety of medical devices (materiovigilance), drug information (infovigilance), cosmetics (cosmeticovigilance).**

**There is no separation of pharmacoepidemiology as an independent discipline and still there is no specific postgraduate training.**

# STATISTIC CHALLENGES IN PHARMACY EDUCATION

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**The graduate programs in pharmacy education are designed to prepare students for teaching and research careers in academia, for pharmaceutical industry, for drugs controlling agencies and research institutes. The aim of this presentation is to discuss the necessity of including basic knowledge on statistic techniques in education of students from pharmaceutical faculties. Some practical examples of using statistics in quality control, particularly in validation of analytical procedures, will demonstrate the application of statistics in pharmaceutical analysis. The debate stays open concerning the optimal range of statistical methods, included in education programs. It is intended that the pharmacists after graduation will be capable to apply regulatory guidance documents, to develop statistical thinking within the pharmaceutical industry, to validate analytical procedures. Students are expected to use statistics in all pharmaceutical disciplines including medicinal chemistry, pharmacology, toxicology and pharmaceutics.**

**Keywords:** *statistic techniques, pharmacy education, basic knowledge*

# SUMMER PRACTICES – AN IMPORTANT ELEMENT OF PHARMACEUTICAL BOTANY LEARNING

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**Identification of medicinal plants and distinguishing them from similar species that do not have the same medicinal properties is an important prerequisite to ensure quality material for the production of pharmaceuticals. For the rational use of natural plant resources serious practical knowledge of botany is needed, the acquisition of which is achievable only by conducting field work in natural habitats followed by preparation of herbarium.**

**Conducting summer practice in pharmaceutical botany is of great value for the professional realization of master of pharmacy. It enables students to get acquainted with exclusive variety of species of medicinal plants in different habitat, to acquire skills for collecting plants during the spring and summer expeditions and to acquire laboratory skills to work with diagnostic keys.**

**The natural conditions on Bulgarian Black Sea coast allow educational practice of Pharmaceutical Botany to be held in extremely diverse habitats, namely forest formations, primary steppes of coastal Southern Dobrogea, aquatic ecosystems and sand communities. The combination of various floral elements is the reason for the great variety of species of medicinal plants, the identification of which is the primary aim of the fieldwork.**

**Visits to the Natural History Museum - Varna and Botanic Garden - Balchik in order to conduct field work in labeled plant collections further enrich the knowledge of future pharmacists.**

**Keywords:** *summer practice, Pharmaceutical Botany*

# PROBLEMS WITH PRESCRIBING, READING AND DISPENSING OF DRUGS, AND EDUCATION OF STUDENTS OF PHARMACY, MEDICINE AND DENTISTRY

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**Medical services and care for patients today are increasingly liberalized and relying on awareness and active participation of the patient. But problems with the spelling and the correct allocation of prescription drugs remain. Many countries have introduced electronic prescriptions, which reduces the possibility of error to a minimum. In Bulgaria such a project is currently in progress.**

**Will focus primarily on the problems at discharge and dispensing of medicines prescribed on regular ("white") form - Ordinance № 4, Official Gazette No. 3, year LV, Annex 2 to Article 6, paragraph 1.**

**The recipe is an official document with medical, legal and financial burden. We put emphasis on the responsibility that the pharmacist is often forced to take, performing incorrectly or illegibly written forms for humane reasons and not for financial reasons, as suspected.**

**Training of medical professionals about the rules of prescription and dispensing of prescription drugs is subject to improvement. In this regard, the project "Updating the curricula of the Faculty of Pharmacy at the Medical University Varna in accordance with the needs of the pharmaceutical business and the requirements of the labor market" is absolutely necessary.**

**Paying attention to this aspect of the work will improve the performance of pharmaceutical care in pharmacies and reduce the possibility of the occurrence of errors.**

**Keywords:** *recipe, prescribing, reading and dispensing of drugs, improving curricula*

# MODERNISATION OF THE BIOCHEMISTRY COURSE FOR PHARMACY STUDENTS AT MEDICAL UNIVERSITY VARNA

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**Research results on students' content regarding the basic biochemistry course of the "Pharmacy" programme at Medical University Varna are presented based on a three year survey (from 2011/2012 up to 2013/2014 academic year). The respondents comprised 80% of all pharmacy students. The questionnaire involved evaluation of course content, appropriateness of available study materials, assessment of students' knowledge during the semester, as well as the final exam. The students evaluated the course content as being up-to-date (90% of the respondents) and a prerequisite for their future specialized training in pharmaceutical sciences (70%). Based on the student opinion from the survey a book with specialized study materials (a collection of theoretical and practical tasks and tests) was prepared and published. Furthermore, beginning from the current 2014/2015 academic year all lecture notes were uploaded online using the new MUV e-learning platform Blackboard. Continuous assessment approach was adopted in addition to the final exam, as required by most of the students involved in the survey. In conclusion, the biochemistry teaching was optimized and adjusted to the specific requirements of the pharmacy students, thus contributing to a better education quality of the future professionals.**

**Keywords**: *pharmacy students, biochemistry teaching, three year survey*

# EFFECTS OF MULBERRY HEARTWOOD EXTRACT ON GENES RELATED TO LIPID METABOLISM

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**Scientific evidences exist that extracts from different parts of Morus nigra (mulberry tree), mainly fruits, leaves and root bark, exhibit various beneficial effects such as antiviral, antihyperglycemic, antiatherogenic and hypotensive activity. Although it is known that the heartwood has a specific phytochemical composition the biological effects of this part of the plant are not yet clarified. This study examined the effect of 40% ethanol infusion from the heartwood of mulberry on two genes related to lipid metabolism: adipogenic transcriptional factors peroxisome proliferator-activated receptor gamma (PPARγ) and fatty acid-binding protein gene (aP2) in adipocytes. Results obtained present that treatment with two concentrations of mulberry ethanol extract decreased expression of aP2 messenger RNA compared to controls.**

**Based on these results we concluded that heartwood mulberry extract has beneficial effects on lipid metabolism and could be a potential source for search of active compounds for treatment of metabolic disorders related to adipose tissue metabolism.**

**Keywords:** *Morus nigra, heartwood extract, adipocytes, gene expression, lipid metabolism*

# ANTI-INFLAMMATORY PROPERTIES OF AQUEOUS INFUSION FROM *COTINUS COGGYGRIA* LEAVES IN RATS

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**Introduction:** **Decoctions from the Eurasian Smoke tree (*Cotinus coggygria* Scop.) are used by the Balkan folk medicine for their antiseptic and anti-inflammatory properties. Although infusions from *C. coggygria* have been applied mainly topically because of traditionally reported toxicity, there are scarce reports on the internal administration of infusions from its leaves to treat gastric ulcer and diabetes mellitus. Despite the well documented *in vitro* antioxidant properties of *C. coggygria* extracts, the plant has been somewhat ignored by pharmacological studies.**

**Aims:** **The aim of this study was to explore the anti-inflammatory effect of aqueous infusion from *Cotinus coggygria* leaves (AICCL) in an acute experimental model of Carrageenan (Carr)-induced rat paw oedema (CIRPO).**

**Materials and Methods:** **Five groups of Male Wistar rats (n = 40; 200-250 g) were used in the CIRPO model: negative control (C), Carr, 1/100 AICCL+Carr, 2/100 AICCL+Carr, 4/100 AICCL+Carr. Rats were pretreated by stomach intubation with AICCL (10 ml/kg) by orogastric cannula. Groups C and Carr received distilled water. The pretreatment lasted 15 days before a single sub-plantar injection into the left hind paw of 1 mg λ-Carrageenan as 100 µL freshly prepared 1% w/v solution in 0.9% saline. The group C was injected with a vehicle (0.9% saline). The effect was evaluated by Digital plethysmometer LE7500 (Panlab, Barcelona). Average paw volume was measured 1/2, 1, 2, 3, 4, and 5h after the injections and Percentage values of Paw oedema (PO) and Inhibition of paw oedema (IPO) were calculated. The CIRPO model was verified by histopathological analysis (Hematoxylin and eosin staining; Light microscopy).**

**Results:** **The average PO volume in group 2/100 AICCL+Carr was significantly lower ($P<0.05$) compared to the group Carr, 5 hours after injection. AICCL caused IPO, that was highest half an hour and lowest 5 hours after the injection. Percentage values of IPO were moderate to low. Histopathological verification showed that Carrageenan caused acute inflammation in the dermis and skeletal muscle, severe oedema, clusters of neutrophil leukocytes and formation of phlegmons.**

**Conclusion:** **Our study demonstrated the protective effect of aqueous infusion from *Cotinus coggygria* leaves (AICCL) against acute carrageenan-induced inflammation. Most probably, this effect is due to the antioxidant properties of the infusion.**

# *IN VITRO* ASSESSMENT OF MANGANESE BIOAVAILABILITY FROM *HIBISCUS SABDARIFFA* (KARKADE) TEA

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**Karkade tea may be a rich dietary source of Mn, since the dried hibiscus calyces contain 300–950 mg/kg of this essential element. The soluble elemental content was between 55% and 85% in dependence on the plant origin and on the tea preparation procedure (temperature, leaching duration). The potential bioavailability of dissolved Mn was studied using chemical fractionation including ion exchange, liquid phase extraction and selective precipitation. Flame atomic absorption spectrometry was applied for element determination in all fractions. The main part of Mn (>90%) presents in fresh prepared tea as positively charged species with low molecular weight (free cation or labile complexes) considered as potentially bioassimilable.** *In vitro* **assessment of manganese bioaccessibility was performed using sequential enzymatic simulation of gastro-intestinal digestion in combination with operational fractionation. Under simulated intestinal conditions the bioaccessible fraction of Mn was approximative 40% from its total content. Daily drinking of 200 ml karkade tea will contribute around 9 % of RDA/RDI of this element in a potentially bioaccessible form.**

**The bioavailability of Mn from hibiscus infusions was compared with that of other major and trace essential elements. The percentages of low molecular weight and potentially more bioabsorbable forms of elements following simulated gastro-intestinal digestion were around 35% (Ca), 83% (Cu), 44% (Fe), 55% (Mg), 90% (K), 85% (Zn) from their total dissolved content.**

**Keywords:** *karkade, manganese, bioavailability, fractionation*

# POLYPHOSPHOESTERS BASED - PACLITAXEL COMPLEXES. SYNTHESIS AND CHARACTERIZATION

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**Paclitaxel, a natural occurring diterpene alkaloid, is a relatively new antineoplastic agent for clinical treatment of breast, lung, ovarian, head and neck cancers. Anti-cancer agents in the cancer therapy cause a large number of toxic side effects which require a reduced dosage of chemotherapeutic agents or occasionally interruption of the therapy itself. Thus, invention of new effective agents preventing tumor cell growth without causing non-specific side effects is clinically important. Here below, we demonstrate a strategy for the preparation of new types of biodegradable, water-soluble polyphosphoester-based paclitaxel complexes.**

**Object: Presentation of a new type of covalently bonded or physically immobilized paclitaxel.**

**Materials: Used substances: Poly(ethylene glycol) with number-average molecular weight 600 g/mol (PEG 600); Paclitaxel (99%): distilled Dimethyl H-phosphonate.**

**Methods: 1) Synthesis of poly(oxyethylene H-phosphonate); 2) Synthesis of poly(hydroxyoxyethylene phosphate); 3) Synthesis of Polyphosphoestes-Paclitaxel Conjugate; 4) Physical immobilization (hydrogen bonding) of paclitaxel onto of poly(hydroxyoxyethylene phosphate).**

**Results: After the synthesis of the polyphosphoesters, their structure was proved by 1H, 13C{H} and 31 P NMR spectroscopy. Paclitaxel was immobilized onto poly(oxyethyle H-phosphonate)s with Mn = 5117 Da and Mn = 8822 Da via covalent bond using Atherton-Todd reaction conditions. Different types of complexes were synthesized as a result of the physical immobilization of paclitaxel onto polyphosphoesters.**

**Conclusion: We have developed new water-soluble paclitaxel-polyphosphoesters complexes. The synthesis of covalently bonded paclitaxel onto poly (oxyethylene H-phosphonate) was conducted at room temperature. Paclitaxel was physically**

# THE ROLE OF PHARMACISTS IN THE IDENTIFICATION, TREATMENT AND PREVENTION OF DEPRESSIVE DISORDERS AND STRESS-RELATED PATHOLOGY

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**Bulgaria is a country with high rates of suicide attempts and realized suicides, morbidity from unipolar depression, neurotic and eating disorders. Social instability, low income, and bullying at school and home create a high-stress medium. Chronic stress leads to intellectual and behavioral deficiencies which significantly worsen quality of life and productivity. The exact morbidity and prevalence are unknown because of persistent fear of stigmatization and misunderstanding. Attempts for self-medication with tobacco, alcohol and marijuana worsen the condition and create bigger problems with alcoholism and addictions.**

**As the most accessible healthcare professionals, pharmacists can play an important role in the treatment and prevention of such disorders. A significant part of the patients prefer visiting the pharmacy for advice or recommendation before a visit to their GP, if such follows.**

**Review of the tolerability, cost/effectiveness and risk/benefits ratios of the second generation of antidepressants, and especially SSRI`s class, shows that they have favorable profile and some meta-analysis show significant decline in suicide rates in countries with traditionally high baseline suicide rates.**

**Giving pharmacy professionals prescription capabilities for the safest drugs can reduce the burden of the national healthcare and social systems, primarily by preventing serious healthcare issues by an early onset of proper treatment for mild cases and by more efficiently directing moderate-to-severe cases for psychiatric consultation.**

**Keywords:** *Depression, SSRI`s, Prevention, Health benefits, Pharmacists*

# ROLES OF PROBIOTICS IN CANCER PREVENTION: AN UPDATE

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**Cancer is a serious global public health problem and incidence and mortality have been steadily rising throughout the past century in most places of the world.**

**There are several epidemiological evidences that support a protective role of probiotics against cancer. Probiotics are live bacteria that could exert health beneficial effects upon consumption. At least one-half of all cancers are suggested to have a dietary component. Therefore many of the dietary agents and natural health products have attracted the attention of scientists. In addition to regulation of intestinal epithelial homeostasis and immune responses, certain probiotics have been reported to activate anticancer mechanisms.**

**In-vivo and molecular studies have demonstrated encouraging outcomes, mainly attributed to its antimicrobial effects against carcinogen-producing microorganisms, antimutagenic properties, and alteration of the tumor differentiation processes.**

**The use of probiotics to prevent colon cancer has gained much attention due to positive outcomes. The increased interest in these areas demonstrated the need for further evaluation to better understand the exact mechanisms involved, and to generate uncontroversial experimental evidence.**

**Keywords**: *probiotic, dietary component, cancer prevetion, mechanisms, antimutagenic properties.*

# APPROACHES AT UTILIZATION OF HERNIA MESHES

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**Aim: The purpose of the present research is to investigate what Hernia Meshes ("HM") are used within Varna region during hernia surgery and to make estimation of the factors that influences the choice of HM.**

**Materials and methods: During the survey has been collected information on the number and the type of hernias that have underwent surgery in Multiprofile Hospital For Active Treatment – Dobrich, Multiprofile Hospital For Active Treatment – Silistra and Multiprofile Hospital For Active Treatment "St. Marina" – Varna within the period 2012 – June, 2014, as well as on the mesh amount being used in hospitals for active treatment in Sofia, Dobrich, Silistra, Razgrad and Varna. The said survey has involved 55 surgeons from main clinical centers. On the basis of the questions in the survey card there have been clarified with what HM brands the surgeon operate with, which factors influence on the decision to be put a mesh. There has**

**been also investigated which are the three most important technical characteristics of the HM pursuant to the specialists involved in the survey. The statistical differences are explored with the "Statistica" program.**

**Results: The executed research shows that it was used over 20 types HM with manufacturers Microval, (Microval France), Serag Weissner, Ethicon, Sentinel Italy, Covidien, Bbraun, Angiologica. The prices of the meshes vary from BGN 98 to BGN 1600. There are used mainly meshes 7/15 from costs reasons in Multiprofile Hospital For Active Treatment – Dobritch and Multiprofile Hospital For Active Treatment – Silstra, as in Varna (Multiprofile Hospital For Active Treatment "Sveta Marina") the costs amount to be lower. The main mechanical characteristics of the used meshes (weight, thickness, pores' amount, fibre's diameter) are very variable. It is operated with knitted, monofilament, polypropylene meshes having pores' amount 0,6 - 4 mm, thickness 0,45 – 0,6 mm and weight from 11 to 130 g per $m^2$. The meshes are prevailing heavy. It is rare to be used semi- absorbable meshes.**

**Conclusion: Cheaper HM are preferred which may be followed by the worsening of the post-surgery results because they are with worse technical characteristics.**

# THE ROLE OF THE PHARMACIST IN THE PREVENTION AND TREATMENT OF CHILDHOOD BRONCHIAL ASTHMA

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**Pharmacists are the medical professionals that are most frequently visited and most accessible to the public. When the medical condition of patients with chronic diseases necessitates a drug therapy, the role of the pharmacist is to assist the follow-up of patients' condition and the proper use of medications, as well as to facilitate the collaboration between patients and physicians in order to ensure the optimal medical treatment. Considering the social significance of the disease and the increased bronchial asthma morbidity in children, we have developed a behavioral algorithm that stipulates the conduct of pharmacists in counseling the parents of children suffering from bronchial asthma.**

**At present, there is no such written work in Bulgarian language developed or available for the needs of pharmacy practitioners. This approach is intended to facilitate sustained disease control in pediatric patients. It comprises all consecutive steps of pharmaceutical care for the purposes of pharmacy practice in the country.**

**Keywords:** *pharmacists, consultation, algorithm, asthma, children*

# NEW INHALATION THERAPIES. THE ROLE OF THE PHARMACIST IN EDUCATING PATIENTS IN CORRECT USE OF AEROSOL DEVICES

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**The delivery of aerosolized medication directly to the airways is a mainstay in the emergency treatment and long-term management of chronic obstructive pulmonary disease (COPD), asthma, and other chronic lung diseases in both the adult and pediatric populations. Medication delivery by inhaled aerosols has significant advantages over systemic drug delivery.**

**Drug deposition within the lung is influenced by several factors including particle size, properties of medication to be delivered, type of aerosol generator used, disease state and ventilatory patterns; as well as patient technique, preference and acceptance of the aerosol delivery device.**

**Three common types of aerosol generators are used for inhaled drug delivery: the small-volume nebulizer (SVN), the pressurized metered-dose inhaler (pMDI), and the dry-powder inhaler (DPI).**

**Meta-analysis reports indicate that when used correctly, the amount of actual drug delivered to the airways is comparable with all 3 types of devices. However, both the pMDI and the DPI, while more convenient, are more difficult to use since they both require that specific steps be followed, in precise order, to achieve optimal airway deposition and the desired therapeutic effect.**

**It's known that poor inhaler technique can markedly reduce the proportion of drug that reaches the lung. Many patients do not use the correct technique when using their inhalers, either because they have never been taught or because they have modified the technique following instruction. Pharmacists can offer advice and education to help improve inhaler technique in various settings and to achieve better therapeutic effect.**

**Keywords:** **asthma, aerosol devices, pharmacists, education**

# CAN FOLIC ACID REDUCE THE RISK OF AUTISM?

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**Introduction:** **Under the collective name Generalized Violation Of the Autism Spectrum (Autism Spectrum Disorders, ASD) are included several different forms of abnormal neurological development, the most common of which is autism. Over the past 20 years, diagnosed with ASD cases worldwide have increased by 600%. Evidence is accumulated for the etiology of autism.**

**Objective:** **The aim of this work is to summarize the data from the on-line scholastic publications which analyze the non-genetic factors in the etiology of autism.**

**Results:** **In addition to the genetic factor, whose role is proven, also are important a great number of non-genetic factors acting in the perinatal period. They can affect the development of the nervous system of the fetus. Among this group of factors most convincing links are established with the environmental pollution (particulate matter and toxic elements in the air), the prepregnancy overweight of the mother, unhealthy nutritional habits and lack of some essential nutrients at the start of pregnancy. The results show that the periconceptional folic acid intake reduces the risk of having a child with autism by 40%. There is evidence that the lack of n-3 fatty acids affect the onset of symptoms in children with autism.**

**Conclusion:** **Intervention programs at the periconceptional period, associated whit folate supplementation would be effective strategies for reducing the risk of having a child with autism.**

**Keywords:** *autism, folate, non-genetic factors, micronutrient deficiencies*

# ROYAL JELLY – A PROMISING PRODUCT FOR THE PHARMACEUTICAL INDUSTRY

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**Royal jelly is a bee product, unique in its composition and biological activity. Its proven biochemical properties attract the attention of researchers in recent years. Bee products including royal jelly are valuable components of the modern pharmaceutical industry. Either used as food or food supplements, they promote health and longevity, increasing the chances for adaptation.**

**Objective of this review is to focus on the biological activity of royal jelly and its role in human health.**

**The review is made referring to publications found in Science Direct and BioMed Central.**

**Keywords:** *royal jelly; biological activity; human health*

# BISPHENOL A – DIABETES MELLITUS?

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**Aim: Presentation of existing data on the possible relationship between exposure to BPA and the development of diabetes mellitus.**

**Materials and methods: Systematic approach of the available scientific literature on the problem.**

**Results: Bisphenol A is a chemical used in the manufacture of polycarbonate plastics. It has estrogenic activity and belongs to the group of endocrine disrupting chemicals.**

**Studies conducted in animals have shown that BPA may lead to impaired insulin and glucose tolerance, hyperinsulinemia, abnormal β cell function and reduced insulin sensitivity. In addition, in cultured human adipocytes has been found that BPA decrease the release of adiponectin, involved in the regulation of blood sugar levels.**

**Analyzing the data from human studies, which are mainly cross-sectional, researchers make different and contradictory conclusions regarding the possible correlation between the amount of BPA in the urine (a measure of exposure to BPA) and the development of diabetes.**

**Inappropriate extrapolation of data from animal studies, and the possibility a number of factors to influence the conduct and interpretation of epidemiological studies hinder the identification and understand the relationship bisphenol A - diabetes.**

**Conclusions: It's necessary to introduce of precise and clear principles in conducting epidemiological studies of BPA and in the interpretation of results from animal studies. Despite existing controversy on the subject, it's requiring active research to determine the full extent BPA effects on human health, given the ever-increasing exposure to BPA.**

**Keywords:** *bisphenol A, endocrine disrupting chemical, diabetes, studies, controversy*

# STATINS IN POLYCYSTIC OVARY SYNDROME

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**Aim:** **Review of the present data from investigations on the role of statins in the treatment of PCOS.**

**Materials and methods:** **Systematic approach of the available scientific literature on the problem.**

**Results:** **Polycystic ovary syndrome (PCOS) is common endocrine disorder in women in reproductive age. It is associated with menstrual disorder and disturbance of reproductive and metabolic functions in severe form.Often the syndrome is connected with insulin resistance,systemic inflammation and oxidative stress which lead to endothelial dysfunction and dyslipidemia. Statins are inhibitors of 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase with intrinsic antioxidant properties. By blocking an early step of the mevalonate pathway, statins inhibit proliferation of several cell types, improve the lipid and hormone profile of women with PCOS. This article reviews the present data from investigations with statins and their role in PCOS.**

**Conclusions:** **The recent investigations suggest that statins have potential in the treatment of PCOS.**

**Keywords:** *statins, polycystic ovary syndrome, antioxidant properties*

# NATURAL PRESERVATIVES VS. ARTIFICIAL PRESERVATIVES

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**Aim:** **To increase the awareness towards the health risks of the usage of artificial preservatives and to inform about the advantages of natural preservatives.**

**Materials and methods:** **Systematic approach of the available scientific literature on the problem.**

**Results:** **Preservatives prolong the shelf-life of food, cosmetics and pharmaceuticals by preventing their spoilage caused by microbial growth and unwanted chemical reactions. Nowadays the artificial preservatives - nitrites, nitrates and benzoats (parabens) that possess antimicrobial activity, are widely used. They destroy or inhibit the growth of bacteria, molds and yeasts in the products. Some of them are toxic; some even have life-threatening effects. The recent investigations show that big part of the artificial preservatives**

**such as nitrates, benzoates, sulphates,p arabens etc. can cause serious health hazards - from headaches and diarrhea to hypersensitivity reactions, asthma attacks, neurological disorders and cancer. Therefore people are looking towards the nature in search of natural preservatives.**

**Conclusions: The recent investigations recommend the use of natural preservatives as safer to human health.**

**Keywords:** *preservatives, human health, health risks*

# VITAMIN K: THE MULTIPLE FACES OF AN OLD VITAMIN

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**Introduction and aim: Recently vitamin K has received much attention because of his newly recognized effects unrelated to haemostasis. It was the aim of the present review to make a survey of the literature during the last decade, concerning the emerging role of vitamin K in regulation of variety of physiological processes.**

**Materials and methods: We performed a search of PubMed database using the following key words: vitamin K, menaquinone, phylloquinone, osteocalcin, matrix gla-protein, vascular calcification, bone metabolism, diabetes, neurodegenerative diseases, cancer.**

**Results: Most of the effects of interest are mediated through vitaminK-dependent proteins, such as osteocalcin (OC), matrix-gla protein (MGP), Gas6, protein S. However, in the brain, it is involved in the regulation of the sphingolipid metabolism also by directly affecting the activity of different enzymes.**

**In cardiovascular research, MGP appears to be one of the major inhibitors of vascular calcification. At the same time, OC has long been considered a protein specific to osteolblasts and important for their functions. Subclinical deficiency of vitamin K is relatively common, especially in elderly, possibly contributing to bone demineralization and vascular calcification. Thus, the "calcium paradox" of older age may turn out to be manageable by adequate substitution with this vitamin.**

**An exciting research, indirectly linked to vitamin K itself, is related to OC as a key factor in the suggested regulatory loop between the bone and the pancreas. Experimental evidence shows that osteoblasts-derived OC acts as a hormone to induce insulin secretion, improve insulin sensitivity and enhance glucose uptake.**

# VITAMIN D DEFICIENCY. HOW TO TEST IT?

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**Introduction:** **Traditionally, vitamin D has been considered almost exclusively related to calcium homeostasis. The era of the pleiotropic effects of vitamin D starts with the discovery of vitamin D receptor in tissues not involved in calcium homeostasis (e.g., skin, placenta, pancreas, breast, prostate and colon cancer cells, activated T-cells). Animal and clinical studies indicate that vitamin D deficiency could be linked to several chronic diseases, including cardiovascular, autoimmune disease and cancer. Recently it is estimated that vitamin D deficiency is a global health problem. Over a billion people worldwide and 66% in Bulgaria are vitamin D deficient or insufficient. A reliable evaluation of vitamin D status by measuring the circulating 25-hydroxy vitamin D levels (25OHD) is needed for making decision for vitamin D supplementation.**

**Aim:** **To study the literature in web databases regarding the analytical methods for accurate and robust determination of circulating vitamin D serum levels.**

**Results:** **Immunoassays and protein binding assays can only report the total concentration of 25OHD (D2 and D3) in blood plasma. They can be used for routine screening of circulating vitamin D levels.**

**Chemical assays (HPLC-UV, LC-MS/MS, GC-MS) are the most accurate, selective and specific for both 25OHD2 and 25OHD3. LC-MS/MS is considered as reference method for measuring 25OHD2/D3 levels.**

**Conclusion: There is no standardized 25OHD assay to arbitrarily establish the "deficient" threshold of 75 nmol/L and to provide clinicians with accurate tool to diagnose vitamin D hypovitaminosis and to make decision for supplementation.**

**Keywords:** *vitamin D deficiency, 25-hydroxy vitamin D assay*

# CURRENT TECHNOLOGICAL APPROACHES IN OCULAR DRUG DELIVERY

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**Efficient ocular drug delivery remains a challenge for pharmaceutical scientists, due to anatomical and physiological barriers of the eye and its protective mechanisms. Most commonly available ophthalmic preparations are in form of eye drops and ointments. These conventional dosage forms suffer from different disadvantages like poor ocular bioavailability, impermeability of corneal epithelium, short residence time, need of frequent instillations. In order to overcome these limitations are developed different nanoscale drug delivery systems. This review highlights the current technological approaches and applications of nanoparticulate systems like liposomes, niosomes, microemulsions, nanosuspensions, nanoparticles, dendrimers, cyclodextrins. Advantages and disadvantages of various drug delivery systems are compared and briefly described their formulation approaches, physicochemical properties and therapeutic significances. They can provide sustained and controlled drug delivery, resolve solubility and stability issues and enhance the number of drugs available for formulations and development. Nanoparticulate systems in the field of ocular drug delivery promise a significant improvement in the therapy of ocular diseases managing better bioavailability and drug efficacy.**

**Keywords:** *eye, drug delivery systems, nanotechnology*

# MICROSPONGES – A NEW PERSPECTIVE IN COLON TARGETED DRUG DELIVERY SYSTEMS

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**Colon specific drug delivery is a preferable route of administration for drugs used in the treatment of local diseases associated with the colon, drugs with significant gastro-intestinal side effects, pH-sensitive or sensitive to enzymatic degradation molecules or drugs which therapeutic activity requires the use of delayed-release dosage forms. Colon as a specific site of drug delivery provides reduced digestive enzymatic activity, pH values near neutral and much longer transit time compared to the stomach and small intestine. Several approaches are developed to achieve colon targeted drug delivery based on pH-sensitivity, time-dependency, prodrug formulation, microbial degradation, osmotic pressure and ect. Use of multiparticulate formulations, such as microsponges, in colon site-specific drug delivery systems (CDDS) achieves uniform distribu-**

**tion at the target region, higher bioavailability and lower risk of dose-dumping and local irritation. Microsponges are microporous polymeric microspheres which have the flexibility to entrap a wide range of therapeutic agents within a non-collapsible structure. The sponge-like microspheres serve as a reservoir which releases the drug in controlled manner through the pores and allows extended action up to 12 hours. Moreover, microsponges can potentially enhance the stability and solubilization of poorly soluble drugs, achieve efficacy at the minimum dose, reduce side effects and improve therapy results. These and other advantages of microsponges arouse interest in their application as drug carriers in CDDS.**

**Keywords:** *Colon specific drug delivery, Microsponges, Porous microspheres*

# STUDY OF THE PROMOTION, REGULATION AND THE DRUG ADVERTISING IN THE EUROPEAN UNION

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**The focus of our study is about the comparative analysis of the normative requirements for marketing, promotion and advertising of the drugs in European Union. The aim is to evaluate the regulatory normative mechanisms in Bulgaria. Having in mind the increase of the expenditures for medicines and the chronic deficit of public financial resources for reimbursement it is necessary the good European practices to be implemented. Thus the modulation of the prescription model will be possible.**

**Keywords:** *drugs, marketing, promotion, commercials, normative requirements, European Union*

# STUDY OF BACKGROUND AND MAIN IMPLICATIONS FOR MEDICINAL PRODUCTS SWITCH PROCESS

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**Introduction:** **Nowadays self-medication becomes more and more popular among the patients. One of the main prerequisites for this is the presence of an increasing number of medicinal products that people can buy without a prescription. This group of drugs is the focus of the pharmaceutical companies around the world, due to the increased sales in this segment and the variety of opportunities for promotion and advertising.**

**The aim of this study is to present the factors that result in change of regime in prescribing of a medicinal product and to analyze the competences of pharmacists in managing the process of self-medication of the patients.**

**Methods:** **Assessment of the main premises leading to the change of status of prescribing of medicines was performed. We described and classified the main implications and trends in the conducting of this process. Addition task of the study was to identify the learning objectives of the students in pharmacy, during their education in pharmaceutical marketing.**

**Results and Discussion:** **In recent decades it is observed an enhanced tendency to increase the number of drugs with a change in the regime of prescribing. With the accumulation of more data on safety, regulatory agencies allow pharmaceutical companies to apply for change of status of some of their medicines. Thus patients are facilitated in accessing treatment for their symptoms and can perform the self-medication, without the need to visit the doctor. However, globally some strict criteria have been developed which a medicinal product must fulfill, for authorizing its sale as a medicine without a prescription (OTC status). Students in pharmacy needed some additional knowledge to achieve during their education in pharmaceutical marketing.**

**Keywords:** *change, status, prescribing, medicinal product*

# STUDY OF THE USE OF PRODUCTS CONTAINING *GINKGO BILOBA* EXTRACT IN BULGARIA FOR THE PERIOD 2011-2013

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**On the Bulgarian market, the products containing *Ginkgo biloba* extract are three categories – medicinal products (MP) and food supplements (FS), which are mono-products and combined products. The purpose of this study was to analyze the use of products containing *Ginkgo biloba* extract in Bulgaria for the period 2011-2013 and by a questionnaire method to study the practice of doctors to prescribe such products. The market research is done according to data from IMS Health and by interviews with doctors from the regions of Varna and Dobrich. The results from the study showed that in the years 2011-2013 there was an increase in the sale of products containing *Ginkgo biloba* extract, both in number of packs sold and in terms of value at a relatively unchanging average package price. In the study period, the greatest was the increase in the use of MP. The greatest was the market share of the combined FS. The predominant share of combined FS cuold be explained by the greater variety and number of these products. The four products with the greatest market share were combined FS. The survey showed that almost all physicians prescribe products containing *Ginkgo biloba* extract. The most prescribed and recommended are the combined FS. Most often *Ginkgo biloba* containing products are prescribed for disturbances in blood flow and memory in patients above the age of 60. Decisive in the choice of a product is the combination of efficacy, quality and price.**

**Keywords:** *Ginkgo biloba, medicinal products, food supplements, use, Bulgaria*

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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

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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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