The 6th International Pharmaceutical Conference

Science and practice 2015

November 5-6, 2015
Kaunas, Lithuania

BOOK OF ABSTRACTS

The 6th International Pharmaceutical Conference

"SCIENCE AND PRACTICE 2015"

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The International Pharmaceutical Conference "Science and Practice 2015" is organized by Faculty of Pharmacy of Lithuanian university of Health Sciences in collaboration with LSMU FF Alumni Association, Lithuanian Pharmaceutical Association and Lithuanian Pharmacists' Society.

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CONFERENCE PROGRAMME

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10.45-11.15	*Valuing of new medicines with HTA. Lithuanian experience*	**Gintautas Barcys** *Head of State Medicine Control Agency*
11.15-11.35	*The modern management of pharmaceutical care*	**prof. A.B. Zimenkovsky** *Danylo Halytsky Lviv National Medical University*
11.35-11.55	*Role and impact of medical technology related services in primary health care in the Nordic and Baltic countries*	**Assoc. prof. PhD Daisy Volmer** *University of Tartu, Estonia*
11.55-12.15	*Muscle-derived stem cells for regenerative medicine*	**Assoc. prof. PhD Arvydas Ūsas** *Lithuanian University of Health Sciences*
12.15-12.35	*Quality control of compounding preparation in Ukraine*	**Prof. Victoriya Georgiyants** *National University of Pharmacy, Kharkov, Ukraine*
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16.30-17.00 **Mykolas Aniūnas** *Lietuvos sveikatos mokslų universitetas* Vaistinės monitoriaus įtaka, teikiant farmacinę paslaugą		**16.20-16.40** **PhD Rūta Mickienė** *Vytautas Magnus University* In vitro evidence of synergistic-antagonistic effect for *Monarda Didyma* L. secondary metabolites
		16.40-17.00 **Indrė Šulskytė** *Vytautas Magnus University* Multidrug resistance reason of MX – 1 cell culture
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WELCOME SPEECH

Dear participants and guests of the conference,

Welcome you to the 6th International conference of pharmacy and allied sciences, organized by Faculty of Pharmacy of Lithuanian University of Health Sciences, Alumni organization of Faculty of Pharmacy, Lithuanian Pharmaceutical Society and Lithuanian Pharmacists' Union. The conference is becoming an important pharmacy science's event in Lithuania, and it attracts a number of high level researchers and speakers from different European institutions. The 6th conference is dedicated to link pharmacy professionals who are motivated and responsive to new challenges and remain open to new ideas. Modern pharmacy is confronting multifaceted challenges and undergoing significant changes on the national and global scale. The world of pharmacy is an exciting area to work, and we'll continue to meet and bring inspired people together in international forums like this.

I'd like to give you an idea of what you can expect and what we hope to achieve over the next few days. It is obvious that pharmacy is integrating with cognate areas of biomedical, technological and social research. This process requires knowledge, presents challenges to research, manufacturing, development, safety and efficacy of products, though opens new opportunities for the scientists. You will have the opportunity to meet professionals in the areas of pharmaceutical and analytical chemistry, pharmacognosy, clinical aspects of pharmacy, history of pharmacy, pharmaceutical technology, biopharmaceuticals and social pharmacy. Hence all the participant of the conference are invited for productive networking and cooperation in developing new and actual scientific ideas, to discuss opportunities and risks.

You are welcomed to enjoy invited lectures, oral presentations and poster sessions. Also you are invited to take closer look to the Center of Advanced Pharmaceutical and Health Technologies at "Santaka" valley and to establish new contacts, to develop new research projects. We strongly believe the results of the conference will serve for the advancement in pharmacy science, practice, and will have positive impetus on human health and welfare.

Let me wish you all the best for the most successful conference.

My personal respect and thanks goes out to all of you!

On behalf of the organizing committee

Chair Prof. Vitalis Briedis

Dean of the Faculty of Pharmacy

Lithuanian University of Health Sciences

Monitoring of the pharmaceutical care as a tool of pharmacotherapy quality

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Introduction. There are many interpretations of the term pharmaceutical care today, they differ significantly from each other very often; pharmaceutical care can be individualized and collective; the vector of its provision is directed at a doctor, nurse, patient, pharmacist; there are features of the pharmaceutical care providing in a hospital, ambulatory health care institution, pharmacy etc. Therefore, the concept of pharmaceutical care includes a number of components and different approaches to its implementation, although they are united by the fact that the pharmaceutical care is a tool of quality, in particular, clinical pharmacy specialist's activity. The study of the quality as a whole, and the quality of pharmaceutical care in particular, is to be carried out in dynamics, that is, it needs the monitoring of changes. Conducting such monitoring is possible by means of the indicators usage, on the choice of which there depends the objectivity of the results and, therefore, the possibility of improving the quality.

Aim of the research: determination of the study methods and the pharmaceutical care quality improvement by means of the use of indicators.

Methods: system approach, bibliographic, analytical, modeling methods.

Results. To our concern, the primary task here is to assess the conditions for pharmaceutical care implementation, which is possible through the choice and use of the structure indicators. We believe that the availability of pharmaceutical care standard, implementation of programs for patients with chronic diseases, conduction of pharmaceutical care documenting etc. may serve as such indicators for the pharmaceutical care. However, in order to have comparable results, the choice of indicators, their measurement and interpretation, need unification.

Taking into account that the patient is the main beneficiary of pharmaceutical care, important criteria of its quality assessment are changes in health state indicators, patient's satisfaction, the number of repeated requests to obtain pharmaceutical care, however, disadvantages of these indicators are their non-specificity, subjectivity and ambiguity of the interpretation which restricts their practical significance. Instead, among the number of applied to pharmaceutical care indicators the quantity of revealed drug related problems is considered to be classic. Since this indicator does not characterize the results of pharmaceutical care, but only points to issues which require control or modifications, to our belief, it is considered to be an indicator of the pharmaceutical care process. In our opinion, the outcome indicators should include clinical-pharmaceutical interventions, which in their turn also require classification and standardization: agreed with a doctor medicines cancellation or prescription, drugs substitution etc.

Conclusion. Since pharmaceutical care is the quality tool, its provision requires continuous monitoring of changes to improve results. It is possible through the choice and application of measurable, specific, standardized indicators in practice, on the choice of which the objective monitoring depends, and among which the most representative is considered to be the determination of drug related problems and clinical-pharmaceutical interventions quantity.

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Role and impact of medical technology related services in primary health care in the Nordic and Baltic countries

Daisy Volmer

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Medical Technology (MT) encompasses a wide range of health care products, and is used to diagnose, monitor or treat every disease or condition that affects humans (1). MT covers pharmaceuticals, medical devices, procedures and organizational systems used in health care.

With aging of population, increase of ambulatory care and multiple-use of medicines, different technology tools have been used to contribute to the safe and effective use of medicines and decrease health care costs on medicines.

Today, little is known on the role and impact of MT and technology assisted services in the health care and society. Community pharmacies and MT are closely linked. In the Nordic and Baltic countries, community pharmacies are an important source for counseling and dispensing of MT. Increasingly, people prefer to buy MT from pharmacies as they are considered to be closely related preparations to medicinal products (2).

In 2014, the network of Nordic and Baltic countries was established to evaluate the current status in education and practice of MT in pharmacy.

The aim oral presentation is to present and discuss the results of the Nordic-Baltic joint research on MT education and to map the future activities in education, practice and research of MT related services in pharmacy.

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Muscle-derived stem cells for regenerative medicine

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Various adult organs and tissues harbor stem and progenitor cells that could potentially be used to regenerate and repair a variety of different tissues following injury or destructive diseases. Skeletal muscle is readily available and plentiful source of somatic stem cells. It contains several distinct populations of myogenic stem cells including satellite cells that are responsible for muscle growth and regeneration, and multipotent muscle-derived stem cells (MDSCs). Although both cell populations share some phenotypic similarities, MDSCs isolated by a modified preplate technique exhibit long-term proliferation, high self-renewal, and multipotent differentiation capabilities in vitro, and are capable of regenerating various tissues in vivo [1]. Remarkably, when genetically modified ex vivo to express specific growth factors, these cells can differentiate into osteogenic and chondrogenic lineages and have been shown to promote the repair of bone and cartilage. MDSCs not only participate in the regeneration process by differentiating into tissue-specific cell types, but also promote endogenous tissue repair by secreting a multitude of trophic

factors, mobilizing the host's progenitor cells and attracting them to the injury site.

A human counterpart to MDSCs has been isolated from human skeletal muscle using fluorescence-activated cell sorting (FACS) to select cells coexpressing myogenic and endothelial markers. These cells can retain the expression of surface markers and capacity of myogenic differentiation during long-term culture and exhibit multilineage developmental potential in vitro and in vivo at the clonal level [2, 3]. Most recent scientific data indicate that muscle-derived stem/progenitor cells (MDSPCs) isolated from adult human skeletal muscle can adopt neuronal and glial phenotypes in vitro and promote functional peripheral nerve regeneration in a murine model [4].

Muscle-derived stem cell-based therapy and tissue engineering is promising approach in regenerative medicine. The relative ease of muscle stem cell isolation and purification, the cells' tolerance for ex vivo manipulation, and cellular behaviors make them very attractive for future medical therapies.

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Search for new antitrypanosomal agents among 4-thiazolidinones

Kaminskyy D.[1], Kryshchyshyn A.[1], Havrylyuk D.[1], Zelisko N.[1], Khyluk D.[1], Zimenkovsky B.[1], Grellier P.[2], Lesyk R.[1*]

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Creation of new drugs for the treatment of neglected diseases is one of the problem areas of modern pharmacy/medicine. Trypanosomiasis (sleeping sickness & Chagas disease) is among the most serious regional neglected tropical diseases which have now spread to other continents and require new effective and non-toxic drugs. Despite the advances in understanding the biology of protozoa, global intensification of the antitrypanosomal agents creation (e.g. within Special Programme for Research and Training in Tropical Diseases) no new drugs were marketed since eflornithine was approved in 90[s]. Currently the main directions in the new antitrypanosomal agents' discovery are design of new high affinity ligands and search for new indications of existing drugs. Limitations of highly active ligands application are due to low effectiveness *in vivo* or toxicity. Following the current trends, pentamidine analogues; benzofuran derivatives; thiosemicarbazone and thiazoles; and metal complexes are of special interest. 4-Thiazolidinones as examples of privileged scaffolds and mimics of thioureas/thiosemicarbazones can be treated as attractive tool for new antitrypanosomals design mainly within structure-based design. The presented project is an extension of our ongoing efforts towards search for new 4-thiazolidinone-based antiparasitic agents.

The design of the project involved: primary screening of antitrypanosomal activity (*T. brucei*, *T. cruzi*) of the diversity in house thiazolidinones library; SAR analysis, design and synthesis of

focused sub-libraries within combinatorial and privileged-substructure-based diversity oriented synthesis strategies and molecular hybridization; sub-libraries screening, hits and leads identification; (Q)SAR(P) analysis and formation of the direction for structure optimization; in depths study of mode of action, toxicity evaluation. Additionaly the row of thiazolidinone-based compounds with anticancer activity was involved into the study following the new findings about the simultaneous anticancer and antitrypanosomal activities.

Screening results led to the formation of focused 4-thiazolidinone based compounds sub-libraries and identification of hit- and lead-compounds. Project outcomes allow us to summarize some findings: 2-amino(imino)substituted-4-thiazolidinones subtype is the most prominent one; anticancer thiazolidinones are the good sources for antitrypanosomal agents gesign; thiopyrano[2,3-*d*]thiazole core is perspective scaffold for further optimization; and molecular hybridization realization give the best results. Further structure optimization allowed to identify the most efficient trypanocidals (*in vitro*). The latter were found to be active against *T.brucei brucei* and *T.brucei gambience* with IC_{50} 0.01–0.10 μg/mL and possessed low toxicity against mammalian cell lines.

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Search for new anticancer agents; 4-thiazolidinone motif

Lesyk R*., Zimenkovsky B., Kaminskyy D., Kryshchyshyn A., Havrylyuk D., Zelisko N., Devinyak O., Khyluk D., A. Lozynskyi, M. Lelukh

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The search for new anticancer agents among small molecules is one of the most investigated areas in the modern medicinal chemistry. The exploitation of 4-thiazolidinone cores as privileged scaffolds in the design of new lead-compounds is the subject of interest of small research groups as well as large projects. Nowadays, the advances in anticancer 4-thiazolidinones field are associated both with screening programs' findings and discovering of new high affinity ligands to numbers of validated anticancer targets (JSP-1, TNFα, Bcl-X_L-BH3, integrin $\alpha_v\beta_3$, SHP-2 etc.). Despite the chemical diversity of thiazolidinones (2,4-thiazolidinones, rhodanines, 2-amino(imino) thiazolidinones-4 etc.) 5-ylidene derivatives are of special interest. The majority of the drug-like compounds belong to mentioned 4-thiazolidinones subtype. Moreover, the latter are often treated as Michael acceptors – a tool for new entities creation. This had reflected into the thesis about the crucial role of the presence/nature of the C5-substituent for the biological activity realization. Among discovered antitumor molecular mechanisms of 4-thiazolidinones the most investigated (except PPARs-dependent) are Bcl-2/Bcl-X_L function inhibition; proteasomal degradation of target proteins; transcriptional repression of AR through Sp1 degradation; caspase-dependent pathways; and mitochondria-mediated apoptosis. These findings do not reflect the whole range of the experimental data and are not sufficient for the design of new high-active agents. The aim of presented project is the search for new anticancer agents based on 4-thiazolidinone core.

Based on 5-ylidene-4-thiazolidinone fragment and chemical diversity of 4-thiazolidinones the in-house library of new heterocycles have been designed and synthesized. Synthetic routs involved the modification of C2, N3, C4 and C5 positions, as well as *b* and *d* edges of main core via various reactions (Knoevenagel condensation, [2+3]-cyclocondensation, N-alkylation, acylation, thionation, heterodiene synthesis, "domino"-reactions etc.). The screening of anticancer activity within US NCI DTP protocol (> 1500 assays) as the first stage was carried out. The screening results (SAR-database and lead-compound structures) led to the formation of structure optimization

directions: creation of the hybrid molecules (hybridization with isatin, pyrazoline, oleanane etc.); complications of C5 fragment and/or functionalization of N3; fixation of 5-ylidene-4-thiazolidinone residue in fused heterocycles via annulation (thiopyrano[2,3-*d*][1,3]thiazoles were found as cyclic isosteric mimetics of 5-arylidene-4-thiazolidinones); and use of the structures of the lead-compounds with another type of activity (e.g. antitrypanosomal). Following the above mentioned a number of focused sub-libraries were designed and synthesized. The analysis of the selectivity and cyto-toxicity paterns of the compounds led to identification of the leukemia panel to be the most sensitive among all cancer types. Following the *in silico* data and pharmacological data to explore the anticancer effect associated with the thiazolidinone framework the arguments in favor of the apoptotic related and mild prooxidant actions for the active compounds have been found.

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Validation of the compounding solution preparation technological process

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The main objective of any preparation manufacturer is to ensure its quality. In Ukraine compounding preparations quality is regulated by the "Compounding preparations" monograph of the State Pharmacopoeia of Ukraine and The Order № 812 of the Ministry of Health of Ukraine. According to the requirements of the Order № 812 a business entity that operates compounding drugs preparation has to ensure functioning of drugs quality system. This system, among other things, includes quality control requirements for premises and equipment, active substances and excipients, and technology process. Besides individual preparation of compounding drugs various forms are prepared serially. According to the requirements of the Order № 812 compounding forms series preparation, compounding provision and compounding preparations in store are carried out according to the technological instructions. The main problem of the technological instructions drafting is accounting of all possible deviations during drug preparation due to using of specific equipment, which is achieved through a validation of technological process.

Thus, the aim of the study was validation of technological process preparation of some liquid form for external use with serially preparation for its technological instruction development:
Rp.: Sulfuris praec. 3,0
Spir. Camphorati 10 %-3 ml
Sol. Ac. borici 2 %-25 ml
Spir. aethylici 96 %- 25 ml
M. D. S.
During validation of technological process all equipment used and the stages of the dosage form preparation process (balances for weighing of boric acid and sulfuris; measuring cylinders for measuring of water, ethanoli and spiriti camphorati; for formulation and packaging of solution to vials) have been taken into account. Result of the theoretical calculation of the dosage form preparation uncertainty was 2,79 %.

In addition to the theoretical calculations for validation of the technological process it was necessary to determinate assay of active ingredients. The alkalimetric method in the presence of mannitol according to the requirements of the SPhU has been used for the boric acid dosing accuracy determination. To prove the possibility of using this method for the analysis of this particular solution validation of method has been conducted. It has showed the possibility of its use for the determination of boric acid in this compounding solution. The results of the experiment indicate conformity of boric acid quantity to the regulatory framework (Z = 99,55%; relative standard deviation 0.34; systematic error – 0.45).

Obtained results allow developing displayed solution's technological instruction preparation by using specific type of equipment for use in any pharmaceutical establishment. In future these results can be used for maximum storage period determination of this dosage form.

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Skeletal muscle-derived stem/progenitor cells: a potential strategy for the treatment of acute kidney injury

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Introduction. The skeletal muscle-derived stem/progenitor cells (MDSPCs) are mesenchymal multipotent stem cells, demonstrating high self-renewal, long-term proliferation and promoting endogenous tissue repair.[1,2] MDSPCs have been thoroughly investigated in preclinical studies.[2,3] However, the therapeutic potential of MDSPCs for acute kidney injury (AKI) has not been evaluated. We aimed to compare rat MDSPCs with bone marrow mesenchymal stem cells (BM-MSCs) in vitro and evaluate the feasibility of MDSPCs therapy for AKI in a pilot study in rats.

Methods. We isolated and characterized rat MDSPCs and BM-MSCs. We also assessed feasibility of MDSPCs in a pilot study in vivo. The characteristics of rat BM-MSCs and MDSPCs were assessed by the population doubling time, flow cytometry, immunohistochemistry, multipotent differentiation capacity and RT-PCR. A gentamicin-induced AKI model in rat was used to examine therapeutic effect of MDSPCs. AKI was induced by gentamicin (80 mg/kg/day; i.p.) for 7 consecutive days. Physiological and histological kidney parameters were determined.

Results. The MDSPCs exhibited similar immunophenotype, gene expression and multilineage differentiation as BM-MSCs, but demonstrated higher proliferation rate. A single MDSPCs injection ($1X10^6$ cells; i.v.) accelerated functional kidney recovery and regeneration, as reflected by significantly lower serum creatinine levels, higher urinary creatinine and glomerular filtration rate levels ($p<0.05$). MDSPCs significantly attenuated renal tubular damage, as shown by the kidney histology and significantly lower renal injury score 17.5±14.5% ($p<0.05$) in GM+MDSPCs group, compared with the injury score of 41.1±18.3% in the GM group 2 weeks after injection. PKH-26-labeled MDSPCs were identified within the renal cortex 2 weeks after the administration of MDSPCs, indicating the capacity of MDSPCs' to migrate and populate the renal tissue.

Conclusion. In conclusion, MDSPCs are capable of mediating functional and histological kidney recovery and can be considered as a potential strategy for the treatment of AKI.

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In vitro evidence of synergistic-antagonistic effect for *Monarda Didyma L.* secondary metabolites

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Synergistic interactions are of vital importance in phytomedicines, to explain difficulties in always isolating a single active ingredient, and explain the efficacy of apparently low doses of active constituents in a herbal product (1). *Monarda Didyma L.* is a wild plant in North America and is cultivated also in Europe. In our study *Monarda Didyma L.* originated from the sector of medicinal plants botanical garden of Vytautas Magnus University Lithuania. The aim of this study was to verify the existence of synergistic antibacterial effect between essential oils and phenols compounds. In this experiment evaluated the interactions between the essential oils (*d*-limonene, myrcene, *p*-cymene, α, γ–terpinene, thymol, germacrene-*d*, carvacrol) and phenols compounds (rutin, hyperoside, quercitrin, luteolin, quercetin, gallic acid, chlorogenic acid).

We investigated the effectiveness *in vitro* of the association of essential oil/phenol compounds against different strains microorganisms: *Escherichia coli*, *Proteus vulgaris* and *Staphylococcus aureus* with and without antibiotic resistances originating from livestock. The antibacterial effects of these phytochemicals combinations were evaluated by using the series microdilution method. Strong synergistic interaction was observed against *Staphylococcus aureus* with and without antibiotic resistances 0.5 % v/v. The antimicrobial activities of extracts were described by determination of the minimal inhibitory concentration. The total amounts of phenolic compounds and total amounts of flavonoids were tested in the methanolic extracts of the plants. Identification of the phenolic compounds and evaluation of the radical scavenging activity of the compounds were performed by means of high performance liquid chromatography coupled with on-line 2.2-diphenyl-1-picrylhydrazyl radical scavenging reaction detection (HPLC-DPPH) analysis. The essential oils were analyzed by gas chromatography – mass spectrometry (GC-MS). The observed synergistic interactions clearly indicate that different complex secondary metabolites collectively contribute to the enhanced antimicrobial effect.

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Multidrug resistance reason of MX – 1 cell culture

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Background. Multidrug resistance in chemotherapy using drug is a major reason to failure treatment of cancer. The most exploring multi-drug resistance are related with drugs effluxion from cells in the presence of ATP-binding cassette (ABC) transporters The major MDR transporters is P – glycoprotein (P – gp/ ABCB1), multi-drug resistance protein 1 (MRP1/ ABCC1) and breast cancer resistance protein (ABCG2) (Giacomini ir kt., 2010). Molecular research with cancer cells can help to prevent and improve efficiency of this disease treatment.

The aim. To investigate multi-drug resistance pattern, P-glycoprotein (P-gp) expression, P-glycoprotein and other MDR pumps function in wild-type and lipophilic agents-induced human breast carcinoma MX-1 cell lines.

Methods. The multi-drug resistant cell sublines were developed exposing the parental cells to stepwise increasing concentrations of tetraphenylphosphonium (TPP^+). The levels of resistance DOX and EtBr were assessed in terms of IC_{50} values using the MTT valiability assay. Functioning of P-gp and other MDR pumps was evaluated by fluorimetric assay using a fluorescent dyes – ethidium bromide. The cells ATP synthesis was inhibited using antiglycolytic reagent – DG and alkylating agent 3 – BP. APT level was measured using liuciferin dye.

Results. Two MX-1 cell sublines were cultivated with hight concentracion of TPP^+. MX-1/ TPP^+ subline revealed a 7-fold increase of resistance to ethidium bromide, compared to the parental cell line. Resistance to DOX of MX-1/ TPP^+ cell subline was very hight though to established IC_{50} in this cells was impossible, because in this research DOX concentration was to low. DG has been show as reduced ATP level more low than did 3 – BP.

Conclusion. MX-1/TPP^+ cell sublines was more resistant to doxorubicin and ethidium, moreover ATP depletion is suitable method for inhibition of MDR pumps.

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The assessment of pharmacy monitor influence on providing qualified pharmaceutical service

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Background and objective: Many studies have investigated consumers' needs and demands for pharmaceutical service, specifically: both verbal and written information: information on warnings, side effects, explanations of usage directions, storage directions and possibilities of poisoning. But visual information about the prices, surcharges, pharmacy discounts and manufacturers of prescription medicines with the same generic name are necessary for nowadays pharmacy patients too. The information on the pharmacy monitor screen will give more freedom to make a choice and purchase cheaper prescription medicine or prescription medicine of appropriate manufacturer. It will promote the accessibility of prescribed medicines and competition for pharmaceutical manufacturers, it will also reduce the financial interest of doctors. Pharmaceutical information can be seen as an extra service with the purpose to involve the pharmacy patient in the decision-making.

The aim of our study was to evaluate the pharmacy monitor influence on providing visual information about prices, surcharges and manufacturers of prescribed medicine choices.

Design: The questionnaire method study was made in March – April, 2014. 100 pharmacy patients took part in this research. The people were selected to sample size at random method. Their ages ranged from 20 to 64 years.

Setting: Lithuanian community pharmacy.

Main Outcome Measurement: Patients' assessment of provided visual information on the pharmacy monitor screen for choosing the suitable and needed prescription medicine.

Results: The pharmacist advice had the biggest influence on choosing the suitable medicine manufacturer for 41 pharmacy patient, physician advice – for 29 patients, the price of prescribed medicine – for 22 patients and 8 patients preferred another influencing factors. 87% of respondents asked for pharmacist's advice on choosing the suitable medicine manufacturer in the community pharmacy and only 9% based their choice on the monitor information. 4% of patient asked for both - pharmacist advice and were based on the monitor information or were consulted somewhere else, if that was possible.

Before this research, 61% of patients knew about the monitor that informs pharmacy patients in the community pharmacy. Only 46 respondents knew about the pharmacy monitor functions until filling this questionnaire. 66 respondents will look at the pharmacy monitor, the displayed information after this assessment. 34 patients will not take a look at the pharmacy monitor on purchasing prescription medicine in the future. The opinion there was no useful information on pharmacy's monitor screen was expressed by 70 respondents.

The 16 respondents evaluates the clarity of monitor provided information as bad. 45 patients – as satisfactory. 29% of respondents think that the pharmacy monitor is not adapted for people with visual impairments. 27% think that is only adapted partially. 61% of respondents agreed or partially agreed that pharmacist can orally provide all information about prescription medicines of the same generic name. 15% of respondents disagreed with this idea.

Conclusions: The information provided by monitors is not clear and comprehensible, especially for people with visual impairments. Pharmacists provide all necessary information about prescription medicines of the same generic name produced by different manufacturers. The patients trust pharmacy specialists. Sometimes the pharmacy patients prefer the prescription medicines they already used and they don't need any information. Only a small portion of people use the pharmacy monitor. The pharmacy monitor is insignificant in choosing the prescription medicines.

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Time-of-Flight Secondary Ion Mass Spectrometry bio-imaging analysis of soybean oil fatty acids skin penetration

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The topical use of natural oils has been increasing each year and their effects on human health are being debated as controversial. Changes in skin barrier permeability profiles after application of fatty acids found in natural oils have been demonstrated. Current study is a continuum of previous research, when the effect of fatty acids to enhance tolnaftate dermal penetration has been evaluated, and a biological imaging Time-of-Flight Secondary Ion Mass Spectrometry (TOF-SIMS) technique has been applied (1,2)linoleic, lauric and capric acids into human skin was studied by time-of-flight secondary ion mass spectrometry (TOF-SIMS. The same technique was applied to study penetration of palmitoleic, palmitic, linoleic, oleic, and stearic fatty acids into the skin alone and from soybean oil – which is now being used for various health promoting effects.

Excessive human skin was used in the penetration studies. Linoleic, oleic, palmitoleic, palmitic and stearic fatty acids 10% (w/w) solutions in PEG 400 and pure soybean oil were applied on the skin. The experiments were performed using Bronaugh-type flow-through diffusion cells for 6 h. A commercial TOF-SIMS IV mass spectrometer was used for sample analysis (1)linoleic, lauric and capric acids into human skin was studied by time-of-flight secondary ion mass spectrometry (TOF-SIMS.

Measurements of intensity of linoleic, oleic, palmitoleic, palmitic and stearic fatty acids in skin samples demonstrated changes of their quantitative distribution. Most significant changes were determined in the intensity of linoleic acid which has unsaturated structure and C18 alkyl chain, and this is related with better penetration ability (3). After separate application of linoleic, stearic and palmitic acids, the intensity changes for linoleic acid were +97.3 %, +111.3 %, and +135.9 %, respectively. When palmitoleic, and oleic acids were applied, the change in linoleic acid intensity was +43.8 % and +28.7 %, respectively. Analysis of fatty acid quantities in epidermis and derma, revealed higher accumulation of applied on the skin fatty acid in epidermis, except for linoleic acid which was determined in similar intensities in both layers, and palmitic acid which did not demonstrate a significant change in any layer. It may be presumed that changes of fatty acid contents partially were caused by migration of fatty acids from stratum corneum of the skin.

Application of soybean oil resulted in the increased intensities of all tested fatty acids: palmitic +31.9 %, palmitoleic +10.9 %, linoleic +99.7 %, oleic +16.9 %, and stearic +34.6 %. It was noted that linoleic acid and oleic acid changes appeared greater in epidermis +179,73 % and +24,96 % compared to +86,97 % and +15,86 % in dermis respectively. Palmitic and palmitoleic acids changes were higher in dermis +32,77 % and +14,86 % compared to +23,60 % and -13,77 % in epidermis respectively. Such results shows that soybean oil application to the skin changes the lipids composition, but it could have been foreseen due to composition of fatty acids in soybean oil. It is worth to highlight limited possibilities to predict penetration changes of individual fatty acids when their mixture is applied on the skin and each analogous case should be evaluated individually. For this type of evaluation bio-imaging techniques like TOF-SIMS becomes the most convenient approach.

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International approaches to the quality control and standardization of herbs

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Abstract's main body. Herbs and herbal remedies are of interest to modern medical and pharmaceutical sciences. The use of herbs as medicine is the oldest form of healthcare, and herbs have been used in all cultures throughout history. It is well-known that all medicines, without reference to their origin, first of all should fulfill the basic requirements of being safe and effective [1].

Therefore, nowadays standardization of herbs and improvement of their quality control is one of important questions of pharmacy. Standardization of herbal medicines is necessary process of

prescribing a set of standards or characteristics, parameters, definitive qualitative and quantitative values for giving an assurance of their quality, efficacy, safety and reproducibility. According to WHO definition, standardization and quality control of herbs is the process of physicochemical evaluation of covering aspects of herbs, such as selection and handling, safety, efficiency and stability assessment of finished product, documentation of safety and risk based on experience, provision of product information to consumer and product promotion [2].

Different Pharmacopoeial conventions worldwide are engaged in the process of development and implementation of normative documents to herbs and herbal remedies. For example, Ukraine's full membership of European Pharmacopoeia gives Ukrainian scientists opportunity to be guided by its monographs during elaboration of quality control methods of herbs. In 2012 through participation in the USP scientific program National University of Pharmacy's employees managed to take part in the development of quality control methods using portable equipment for quality control of herbs in the USA. During the scientific program members of *Lamiaceae* family were examined considering the main problems of standardization of herbs: chemically and naturally variability of herbal material, source and quality variability of the raw material, influence of harvesting, drying, storage, transportation, and processing methods on herbal quality, possibility to combine qualitative and quantitative evaluation in method of analysis, etc. Different types of portable equipment for NIR spectroscopy, FTIR, GCMS, XRF, NIR-microscopy, Raman spectroscopy have been used during analysis. It should be noted that only dried and powdered herbs have been used during the experimental study without any extraction procedures. It has been found that portable GCMS equipment allows recognizing species of powdered herbs, e.g. species of *Ocimum basilcum* (Magical Michael, Genovese Gigante, Dark Opal, etc.). XRF equipment has occurred to be promising in heavy metals content definition. The worth results have been shown after Raman spectroscopy equipment research. It has been found that analysis of unprocessed herbal material was pointless.

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Influence of cyclosporine dose on the main mycophenolate motefil pharmacokinetic parameters

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Cyclosporine (CsA) and mycophenolate mofetil (MMF) pharmacokinetic interaction is clinically important, because the combination of CsA and MMF is one of the most often prescribed combinations in kidney transplantation. Moreover, MMF has become an integral component of toxicity-sparing regimens that seek to minimize exposure to the nephrotoxic calcineurin inhibitors (CNI). Arguments on standard or concentration-controlled MMF dosing regimen makes it more complicated. The objective of the present study was to assess the effect of a CsA dose on the main MMF pharmacokinetic parameters.

Methods. 12 hour total serum concentration-time profiles of mycophenolic acid (MPA) and 12 hour total blood concentration-time profiles of CsA were obtained after an oral administration.

MPA concentration was determined by a validated HPLC method and CsA - by using a LC-MS method. The total 12 hour area under the concentration tome curve ($AUC_{(0-12)}$) was calculated using a Bayesian estimator and a 3-point limited sampling strategy.

Results. A significant positive correlation between the main MPA pharmacokinetic parameters ($AUC_{(0-12)}$ and C_{max}) was noticed. The patients taking higher CsA doses displayed higher MPA $AUC_{(0-12)}$ exposure than those who were taking lower CsA doses: 43.07±6.83 h mg/L versus 28.85±11.08 h mg/L, (r_s) = 0.429 ($p < 0.01$). A positive correlation was also observed between the CsA dose and MPA C_{max}, (r_s) = 0.390 ($p < 0.01$). The patients taking higher CsA doses had an increased Cmax compared with the patients taking lower CsA doses, whose peak concentration (C_{max}) was lower: 22.67±9.77 mg/L versus 13.00±6.82 mg/L. Linear regression analysis showed that $AUC_{(0-12)}$ of MMF was CsA dose dependent (R^2=0.376) and explained 14.1% of cases.

Conclusion. The study results show that CsA has influence on the main MPA pharmacokinetic parameters in the CsA dose-related manner. It should be noted that the intake of low cyclosporine doses (less than 160 mg/d) in coadministration with MMF reduces MPA AUC. Coadministration of high CsA (> 300 mg/d) doses is related to higher MPA C_{max} compared with coadministration of low CsA doses. Particular attention should be paid to the implementation of CNI minimization strategies related to a decrease in MMF $AUC_{(0-12)}$ and an increased risk of ineffective treatment.

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The effects of nickel and zinc ion exposure on the concentrations of reduced glutathione and malondialdehyde in mice liver

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Nickel (Ni) naturally occurs in the earth's crust and reflecting its characteristics, is widely used in industry and manufacture. According to the form and route of exposure, Ni is known to cause toxicity, carcinogenicity and dermal sensitization. One of the possible mechanism by which Ni triggers its hazardous effects may involve generation of reactive oxygen species [1]. Zinc (Zn) is essential trace element to all living organisms. It's required for the activity of plenty of enzymes, and has ability to retard oxidative processes within the body [3]

The present study was devoted to evaluate the capability of Zn to protect the liver of the mice from oxidative damage, induced by Ni.

Determination of reduced glutathione (GSH) concentration was carried out according to Moron [2]. Malondialdehyde (MDA) formed after reaction with thiobarbituric acid. Experiments were done on 4-6 weeks old outbreed mice. For acute single intoxication (24 h) mice were once intraperitoneally injected with metal salts, dissolved in saline. For repeated intoxication mice were continuously injected for 14 days (once in a day) with metal salts solutions. Mice received injections of $NiCl_2$ solution in deionized water (5.625 mg Ni^{2+} per kg of body weight) for acute and (1.125 mg Ni^{2+} per kg of body weight) for repeated intoxication; $ZnSO_4$ solution at a dose level 1.56 mg Zn^{2+} per kg of body weight.

The obtained results showed that single as well as repeated exposure to Ni^{2+} decreased liver GSH content by 18 % and 24 %, however injections of $ZnSO_4$ solution had no effect on liver GSH content at neither time point. Single Zn^{2+} injection before Ni^{2+} didn't provide any protective effect on content of GSH, however repeated Zn pre-treatment provided protective effect against Ni in-

duced GSH oxidation and raised GSH concentration by 8 %, compared to Ni treated mice group.

Single and repeated doses of $NiCl_2$ increased liver MDA content by 277 % and 45 % respectively, as compared to the control. Neither single, nor repeated exposure to $ZnSO_4$ didn't affect lipid peroxidation, while Zn pre-treatment not only didn't protect lipids from peroxidation, but even raised liver MDA contents by 524 % and 24 % after single and repeated exposure respectively, comparing to the control group of mice.

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The evaluation of collaboration between physicians and pharmacy specialists from public pharmacies

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The interprofessional cooperation between pharmacists and physicians is becoming of crucial importance in ensuring safe and appropriate healthcare services. A solid amount of evidences suggests that this collaboration is beneficial for all participants and provide benefits for patient. However, this collaboration is facing challenges and obstacles for applying it in wide practice. Nation and international surveys suggest that both physicians and pharmacists do not avail themselves of cooperation opportunities. The **aim** of the study was to evaluate pharmacists experience and attitude towards collaboration between physicians and pharmacy professionals working in community pharmacies.

The qualitative method with mixed data collection strategy has been used. It has focused on collaboration between pharmacists (with work experience of 15 years and more) and physicians. The focus group discussion has been carried out with four pharmacy professionals constantly cooperating with physicians. The vignette survey was performed with 21 pharmacy professionals. The data collection was performed from December 2014 to September 2015.

Our findings suggest that pharmacists are involved in communication with physicians quite often. However, these interactions are sufficiently short and usually limited to a phone call dealing with a wrong prescription or medication dosage prescribed to the patient. It means that the collaboration is still not so efficient and effective teamwork. Physicians communicate with pharmacists for getting information regarding different aspects of medicines, i.e. dosage, international name, manufacturer, etc. It should be noted, that only a small number of pharmacists maintain regular contacts with physicians and regularly discuss developments, legislative changes, medicines and their benefits to the patient. The respondents believe, that effective cooperation between physicians and pharmacists is hampered by professional prejudices, lack of a common goal, underestimation of the pharmacist knowledge and skills, etc.

In summary, the results suggest that current interprofessional collaboration between physicians

and pharmacist is not based on the efficient and effective teamwork. However, the majority of interviewed pharmaceutical professionals identified the benefits of cooperation. Moreover, it was mentioned, that the given field requires changes, new approaches and initiatives in order to ensure an efficient and effective service delivery to patients.

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Electrospun nanofiber mats containing propolis extract and silver nanoparticles – manufacturing and characterization

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Antibacterial, antiviral, antifungal, antioxidant, anti-inflammatory, and anticancer activity of propolis and its ability to stimulate the immune system and promote wound healing make it attractive component of products for topical application. Silver nanoparticles are recognized to demonstrate strong antiseptic and antimicrobial activity, thus it also could be considered in the development of products for topical use. Combination of propolis extracts and silver can result in new properties that could be of interest designing products for wound healing and care.

The target of the study was to produce electrospun mats containing ethanolic propolis extract and silver nanoparticles, and to characterize the product. Electrospun mats were produc using roller rotating electrospinning equipment Nanospider™.

Produced nanofiber mats were evaluated studying their structure, dissolution rate, release of propolis phenolic compounds and silver nanoparticles. The structure of electrospun mats was confirmed by scanning electron microscopy equipped with energy dispersive X-ray spectrometer for investigation of composition of electrospun mats. Additionally FT-IR was applied for evaluation of solid phase structure in nanofibers. Biopharmaceutical characterization of nanofiber mats was performed by evaluating the release of phenolic acids (coumaric, ferulic, caffeic, and vanillic acids) and vanillin that were characteristic for propolis extracts, and by release studies of silver nanoparticles.

The results of present study confirmed possibility to incorporate biologically active compounds of propolis ethanolic exacts into nanofiber mats produced by electrospinning. Nanofiber mats exhibited efficient release of propolis phenolic marker compounds. Inclusion of propolis ethanolic extract into electrospun solution demonstrated no significant influence on the structure of produced nanofiber mats. Additional inclusion of colloidal silver nanoparticles resulted in formation of more uniform and thinner nanofibers. The above results indicate potencial possibilities of electrospinning technique and its suitability in developing propolis extract and silver nanoparticles containing products for stimulating wound healing.

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POSTER SESSION

Variation of qualitative and quantitative composition of phenolic compounds of the apple cultivars grown in Lithuania

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Apples are a significant source of phenolic compounds which have a number of disease preventive effects [1].
The aim: Evaluation of phenolic composition of six apple cultivars grown in Lithuania.
Materials and methods: The following apple cultivars were included in the study: 'Aldas', 'Auksis', 'Connel Red', 'Ligol', 'Lodel', 'Rajka'. Analysis of lyophilised apple extracts was performed according to the previously validated and described high-performance liquid chromatography (HPLC) method [2].
Results. The predominant component in the apple samples of 'Aldas', 'Auksis', 'Connel Red', 'Ligol' and 'Lodel' cultivars was chlorogenic acid. Procyanidin B2 was the predominant component in the cultivar 'Rajka' apple samples. The total amount of phenolic compounds determined in the sample extracts of the apple cultivars varied from 2.21 mg/g (cultivar 'Connel Red') to 5.82 mg/g (cultivar 'Aldas'). The highest total amount of identified quercetin glycosides (0.73±0.02 mg/g) was determined in the cultivar 'Aldas' apple samples. It was 1.92 times higher than the lowest total amount of quercetin glycosides (0.38±0.01 mg/g) determined in the cultivar 'Auksis' apple samples. The highest amount of (−)-epicatechin (0.93±0.02 mg/g) was determined in the cultivar 'Lodel' apple samples, the lowest − in the cultivar 'Connel Red' and cultivar 'Ligol' apple samples (0.32±0.01 mg/g and 0.31±0.01 mg/g respectively). The highest amount of (+)-catechin (0.12±0.01 mg/g) was determined in the cultivar 'Rajka' apple samples. The highest amount of procyanidin B2 (1.28±0.02 mg/g) was determined in the cultivar 'Lodel' apple samples. It was 2.66 times higher than the amount of this compound (0.48±0.01 mg/g) determined in the cultivar 'Connel Red' apple samples. The determined amounts of procyanidin B1 were lower. They varied from 0.04±0.001 mg/g (cultivar 'Connel Red') to 0.16±0.003 mg/g (cultivar 'Aldas'). The highest amount of chlorogenic acid (3.07±0.07 mg/g) was determined in the cultivar 'Aldas' apple samples. It was 4.99 times higher than the lowest amount of this acid (0.62±0.01 mg/g) determined in the cultivar 'Rajka' apple samples. The highest amount of phloridzin (0.27±0.02 mg/g) was determined in cultivar 'Aldas', the lowest amount (0.11±0.007 mg/g) – in cultivar 'Rajka' apple samples.
Conclusions: The results obtained during the research enriched the scientific knowledge about the composition of phenolic compounds of apples grown in Lithuania. The highest total amount of the identified phenolic compounds was accumulated in the samples of 'Aldas' apples, therefore this cultivar is perspective for growing in Lithuania's orchards. **Acknowledgment.** This work was supported by the Foundation of the Lithuanian University of Health Sciences.

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Extraction conditions of proteins from *Echinacea purpurea* L . (Moench) roots and leaves

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The purple coneflower (*Echinacea purpurea* L. (Moench)) has been known and used in traditional medicine for decades, but the interest of this plant pharmacological properties isn't decreasing. Previous studies [1] showed hemagglutinating activity of ethanolic extracts from purple coneflower roots and leaves. Nevertheless, information about purple coneflower proteins and their hemagglutinating properties are still not defined.

Aim of experiment: To determine the best extraction conditions with highest protein yield and highest hemagglutinating activity.

Experiment tasks: 1. Extraction of proteins from coneflower roots and leaves. **2.** Determination of extraction conditions for the highest protein yield; **3.** Determination of extraction conditions for the highest hemagglutinating activity.

Materials and methods: 1. Proteins were extracted out of coneflower leaves (ratio of herb material and extraction buffer - 1:10) and roots (ratio of herb material and extraction buffer -1:6) in different conditions: *A*. At 20±2°C for 2 hours in 3 buffers with different pH (Written below); *B*. At 4±1°C temperature for 2 hours with 5% of protease inhibitor cocktail (Halt™, Thermo Scientific). *C:* At 4±1°C for 2 hours with 1 % of polivynyl polypirolidone, 0.5 % of dithiotrethiol and 0.5 % of ethylenediaminetetraacetic acid. After extraction proteins were precipitated with 13.3 % trichloracetic acid in acetone and 0.2 % of β-mercaptoethanol. **2.** Protein amount was measured by Bradford assay [2]. **3.** Determination of hemagglutinating activity: protein fractions were poured on suspension with 2% trypsin treated rabbit erythrocytes and incubated for 30 min at 20±2°C temperature. *Buffers used for extraction*: Acetic buffer pH=5.0, Phosphate buffered saline (PBS) pH=7.4, Tris-HCl buffer pH=8.0.

Results: 1. The highest protein yield from roots (29,123±1,716 mg/mL) and leaves (82,594±1,695 mg/mL) was determined followed by extraction in PBS buffer (pH=7,4) with 1 % of polivynyl polypirolidone, 0.5 % of dithiotrethiol and 0.5 % of ethylenediaminetetraacetic acid at 4°±1°C temperature for 2 hours. **2.** The highest hemagglutination titer of proteins in roots was 1:1000 and leaves - 1:10000 after extraction in PBS (pH=7,4) at 20±2°C temperature for 2 hours.

Conclusions: 1. Different yield (from 9,622±1,831 mg/mL to 82,594±1,695 mg/mL of proteins extracted from purple coneflower roots and leaves in all extraction conditions; 2. The highest yield of proteins in the roots (29,123±1,716 mg/mL) and leaves (82,594±1,695 mg/mL) was determined using extraction conditions "C", when pH of extraction buffer was 7,4; 3. The highest hemagglutinating activity of leaves protein extract (1:10000) and root protein extract (1:1000) was determined using extraction conditions "A", when pH of a buffer was 7,4.

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POSTER SESSION

Original standardization of pharmacologically valuable compounds in phytopharmaceuticals: separation of variation of carvacrol amount in two different raw materials of large thyme (*Thymus pulegioides* L.)

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Introduction. The standardization of quantity of biologically active and pharmacologically valuable compounds in herbal drugs istopical in modern phytopharmacy. However, the intra-specific chemical polymorphism (variation), characteristic of many species of medicinal plants, can exacerbate the selection of chemically homogeneous herbal raw material in natural habitats. Therefore, the cultivation of chemically valuable clones can vouchsafe the chemically homogeneous herbal raw material and stand the original stage of standardisation of pharmacologically valuable compounds in phytopharmaceuticals. The high infra-specific chemical variation is also characteristic of large thyme (*Thymus pulegioides* L.): the plants of this essential oil bearing species growing wild in Lithuania can accumulate several biologically active compounds (Mockutė and Bernotienė, 2001; Ložienė et al., 2003), where of the monoterpenic phenols thymol and carvacrol are most pharmacologically valuable in all species of genus *Thymus* (European Pharmacopoeia, 2008).

The aim of these studies was to evaluate the variation of amount of carvacrol in raw material of *T. pulegioides* collected from natural habitats and raw material growing up in culture.

Materials and methods. The first raw material of *T. pulegioides* was collected separately from 45 natural habitats located in east and southeast Lithuania. The one individual plant of carvacrol chemotype was moved from natural habitat into field collection of the Nature Research Centre (Vilnius, Lithuania),vegetative propagated and grown in open ground under the same environmental conditions in 2008–2013. The aerial parts of this carvacrol chemotype (the second ram material) was annually collected at the full flowering stage and dried at room temperature. The essential oils from either raw material were isolated by hydrodistillation, analysis of carvacrol carried out by GC-FID and GC-MS.

Results. It was showed that the carvacrol varied from 4.73% to 48.00% (CV=52.91%) across investigated 45 natural habitats of *T. pulegioides*. Mean while the carvacrol amounted 24.43±4.30% in essential oil of raw mater of cultured carvacrol chemotype and varied from 16.88% to 29.29% (CV=18%) during investigated period (2008–2013).

Conclusions. Carvacrol varied less in essential oil of *Thymus pulegioides* L. from cultured than from natural habitats.

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Interaction of efflux pumps inhibitors in suspension *Salmonella enterica* cells

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Background. Multidrug resistance efflux pumps are active transporters responsible for the extrusion of toxic substances and antibiotic out of the cells. Efflux pumps inhibitors are the compounds that interfere with the activities of pumps and therefore are potentially useful for strengthening the actions of antibiotics by allowing them to reach threshold concentrations required for their bacteriostatic or bactericidal activities (Bhardwaj, Mohanty, 2012). Inhibition of efflux pumps has several advantages as it can increase the efficacy of antimicrobials by reversing the acquired resistance and decrease the frequency of emergence of antimicrobial resistance among bacteria due to mutations and associated structural changes in the efflux pumps (Lomovskaya *et. al*., 2001).

The aim. To determine effects of the efflux inhibitors on accumulation of indicatory tetraphenylphosphonium (TPP^+) ions in *S. enterica* ser. Typhimurium cells.

Materials and methods. Potentiometric analysis was used to assay TPP^+ concentration in the incubation medium. The most effective inhibitor of RND-type efflux pumps is Phe-Arg-β-naphthylamide (PAbN) but it cannot completely suppress TPP^+ efflux from the cells. Moreover, the exact mechanism of PAbN action is still not clarified. For this reason in our experiments we used also other efflux inhibitors, such as chlorpromazine (CPZ), 1-(1-naphthylmethyl)piperazine (NMP) and reserpine (RES).

Results. Our experiments revealed that interaction between PAβN and CPZ is competitive but RES and NMP do not affect the activity of PAβN. Our results indicated that NMP has two operating targets and one of them is common with CPZ. Therefore, CPZ does not operate added after NMP, but NMP is effective added after CPZ. RES and NMP compete for the interaction with TPP^+- extruding pumps, but CPZ and RES have different targets in *S. enetrica* cells.

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The quantification of hydroxycinnamic acids in the grass of black horehound

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Black horehound has a long history of herbal use, though is not widely employed in modern herbalism because of its unpleasant flavour. Nonetheless, it does have a range of medicinal virtues, being especially effective in its action as an antiemetic. In the past it was often used for treating problems connected with the respiratory system, convulsions, low spirits and the menopause, but present-day authorities differ over whether it was effective in these applications [2, 3].

The plant is harvested as it comes into flower and is dried for later use. It should not be stored for longer than a year. The fresh herb is sometimes used to make a syrup.

The main active ingredient of Black horehound are phenolic compounds such as derivatives of hydroxycinnamic acid, hydroxycoumarins, flavonoids and their quantitative, aglycons of flavonoids (luteolin, kaempferol, quercetin, apigenin) etc [2, 4].

We have determined the content of hydroxycinnamic acids in the grass of Black horehound, growing in Ukraine. Extracts, stock solutions and test solutions were prepared according to the method of European Pharmacopeia 8.0 [1].

Measure immediately the absorbance *(2.2.25)* of the test solution at 525 nm, by comparison with the compensation liquid.

Calculate the percentage content of total *ortho*-dihydroxycinnamic acid derivatives, expressed as chlorogenic acid, taking the specific absorbance of chlorogenic acid to be 188.

Thus, the 5 series grass of Black horehound was determined the content of hydroxycinnamic acids. Determination was carried out by spectrophotometric method presented in the monograph of the European Pharmacopeia «Black Horehound». The content of total *ortho*-dihydroxycinnamic acid derivatives in the Black horehound's grass, expressed as chlorogenic acid varied between 1.1 % and 0.75 %. According to the requirements of this monograph hydroxycinnamic acid content should be minimum 1.5 per cent of total *ortho*-dihydroxycinnanic acid derivatives, expressed as acteoside ($C_{29}H_{36}O_{15}$; Mr=625) (dried drug).

Therefore, the standardization of grass of Black horehound, growing in Ukraine, and the development of regulatory documents, it is necessary to carry out valuation of the content of hydroxycinnamic acids, given the results obtained.

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Analysis of essential oil of leaves of *Iris germanica* L.

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Introdaction. *I. germanica* are native of Italy and Morocco and is also cultivated as an ornamental plant [2]. An essential oil of iris rhizomes known as "Orris butter," consisting of myristic acid, with irone, ionone, methyl myristate. Isoflavonoids include irisolidone, irigenin and iridin. In volatile oil, chief constituents are cis-α and cis-γ-irones. Rhizomes also gave xanthones [3]. Rhizomes have anti-inflammatory [1], anticancer [5] action. Volatile components of iris leaf not studied. The **objective**: determination of component composition of essential oil of leaves of *Iris germanica* L. by chromatography-mass spectrometry method.

Materials and study methods. Leaves of the *I. germanica* had been collected in spring of 2012

in Botanical Garden's territory of V.M. Karazin, Kharkiv National University. Essential oil was produced by steam distillation. Its constituent composition was studied by GC-MS on an Agilent Technologies 5973/6890N. The analysis conditions were published [4]. Constituents were identified using NIST05 and Wiley 2007 mass-spectra libraries in combination with AMDIS and NIST programs for identification.

Results and discussion. We found that the air-dried leaves contained 0.06±0.01% essential oil. A total of 28 compounds were found in essential oil from leaves of *I. germanica*. The constituent contents varied from 0.03 to 17%. The essential oil included terpenoids, their oxygenated derivatives (alcohols, ketones, aldehydes, esters), aromatic compounds, and triterpenoids. The analysis established the principal constituents of *I. germanica* essential oil as the monoterpene ketone – irone in minor amounts as 0.03±0.00% in leaves. Norterpenoids and their derivatives were observed for the first time, e.g. β-damascenone (0.50±0.01%), β-ionone-5,6-epoxide (1.41±0.02%) and β-ionone (1.19±0.02%). The dominant terpenes in essential oil of leaves were squalene (17.01±0.01%), hexahydrofarnesylacetone (9.10±0.02%), farnesylacetone (1.95±0.03%), phenylacetaldehyde (7.48±0.01%) and geranilasetone (3.86±0.01%). Amount of aromatic compounds was 19.97±0.02%. Aromatherapy recommends [3] the use of iris oil for bronchial inflammation, coughing, as well as in mixtures for the care of the skin. Essential oil of iris normalize function of the brain, has a detoxifying, diuretic, expectorant, strengthens the immune system.

Conclusions. Qualitative and quantitative analysis of essential oil of leaves of *Iris germanica* by method of GC-MS was conducted for the first time. Phytochemical studies conducted show perspective of the further study of Iris also as a source of bioactive substances.

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Possibility of developing original drugs using the seeds of wild carrot

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Presently it is difficult to find a branch of medicine, which would not have used herbal medicine. Modern herbalists use stems, roots, flowers, leaves and fruits of plants. Herbal preparations are becoming more popular, because they have minimal risk of side effects and addiction. Herbal medicine is used in the national health care systems in most countries of the European Union, which view it not only as a part of the folk medicine, also of traditional. Ukrainian plant`s world is a valuable source for fitomedicine therapy. On the territory of Ukraine in the fields and open spaces as a weed grows herb of the kind of Celeries (Apiaceae) – wild carrot (Daucus carota). Its name was formed from several languages (Greek daukos – different celeries, Latin daio - burn, heat, Latin carota - disintegration Greek karota – carrot). The most useful medicine are the seeds of wild carrot, which are used as a carminative, antispasmodic, diuretic, choleretic and anthelmintic remedy. It is also known as a folk medicine. In folk-fi toterapii dermatological use the essential oil of wild carrot seeds, as it stimulates

the renewal of skin cells, the sweat and sebaceous glands, slowing the aging process, a skin and smoothes wrinkles. Essential oil of wild carrot seeds is used in the cosmetics industry for the preparation of creams and ointments with softening, moisturizing and restorative actions. Grass wild carrot is included in the British Pharmacopoeia, and the seeds are officinal raw materials in China and the Russian Federation (ФС 42–2817-91) [1, 2].

On this basis, we have investigated the range of medicines, which contain the seeds of wild carrot in the Ukrainian pharmaceutical market. For the study used conventional methods of information retrieval, statistical and marketing analysis. The subject of our work was the information about registered in Ukraine drugs, which include wild carrot seeds.

Results of the study the range of drugs with the seeds of wild carrot showed that the Ukrainian pharmaceutical market registered only two drugs “Urolesan” (Production Plant - industry “Kiïvmedpreparat”, Kiev and industry “Halychpharm”, Lviv) and “Uroholum” (producer – industry “Farmatsevtichna fabrica”, Zhitomir). There are also commercially available carrot wild product`s extract (industry “Halichfarm”, Lviv). The investigated drugs produced only in three dosage forms: oral drops, extracts and syrups. Conclusions: Thus, the seeds of wild carrot are a promising material for developement of new drugs to treat a wide range of diseases.

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Winter savory (*Satureja montana* L.) essential oil extraction, chemical analysis and determination of antioxidant activity using 2,2´-diphenyl-1-picrylhydrazyl free radical scavenging method

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The problem: medicinal and aromatic plants (MAPs) are widely used for prophylaxis and treatment of diseases. Essential oils of MAPs are perspective group of antioxidants because of its extended spreading and transport possibilities due to the volatility.

Research object: essential oil of medicinal plant winter savory (*Satureja montana* L.).

The aim: perform extraction of essential oil from medicinal plant *S. montana* L. raw material using different extraction methods, evaluate and compare chemical composition and antioxidant activity between the essential oil extracts.

Methods: extraction of the essential oil was carried out using aqueous 75 % methanol solution, supercritical CO_2 fluid extraction (SFE) and hydro distillation (HD). Qualitative and semi-quantitative analysis of the extracts was performed using gas chromatography (GC). Moreover, concentration of total phenolic compounds, total flavonoids and antioxidant activity was determined using spectrophotometric methods.

Results: results of the investigation have shown that highest extraction recovery (mass units of essential oil per 1 g of dry plant raw material) of the *S. montana* L. essential oil was obtained

in 75 % methanol extract - 6.84 ± 0.12 mg/g. The recoveries resulted from SFE and HD were 3.32 ± 0.42 mg/g and 5.69 ± 0.69 mg/g respectively. According to GC analysis results the main compound of the obtained essential oil in the extracts was volatile antioxidant carvacrol which belongs to oxygenated monoterpenes and comprised more than 65 % of total essential oil. Highest concentration (equivalent mass units of standard phenolic antioxidant rutin per 1 g of dry raw plant material) of total phenolic compounds and total flavonoids were determined in *S. montana* L. 75 % methanol extract, i.e. 62.52 ± 3.79 mgRE/g and 8.27 ± 0.43 mgRE/g respectively. Nevertheless, most of the total phenolic compound concentration and all of the total flavonoid concentration in aqueous methanol extract was represented by non-volatile phenolic compounds. Volatile phenolic compounds, namely carvacrol and thymol, which are subjected to the essential oil of the extract, represented 6.66 ± 0.12 mgRE/g and was higher than in SFE and HD essential oil extracts. No flavonoids were identified in the SFE and HD extracts because of selectivity of these methods, suitable to extract a pure essential oil, which contains only volatile compounds. Maximum antioxidant activity was determined in 75 % methanol extract - 3336.45 ± 368.29 mgRE/g. Interestingly, essential oil in this extract presented 37.90 ± 0.67 mgRE/g of the antioxidant activity and was exceeding that determined for SFE and HD essential oil extracts calculated per 1 g of dry raw material. Moreover, it was estimated that antioxidant activity of the *S. montana* L. essential oil extracts positively, strongly and significantly correlates with extraction recovery and concentration of volatile phenolic compounds ($r>0.90$; $p<0.001$).

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Superoxide dismutase activity in mice brain: The effects of selenium and aliuminium ions

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Introduction. Superoxide dismutases (SOD) are enzymes that alternately catalyze the dismutation (or partitioning) of the superoxide radical into either ordinary molecular oxygen or hydrogen peroxide. Superoxide is produced as a by-product of oxygen metabolism and, if not regulated, causes many types of cell damage. Hydrogen peroxide is also damaging, but less so, and is degraded by other enzymes such as catalase. Within a cell, the SOD constitute the first line of defense against reactive oxygen species (ROS). Thus, SOD is an important antioxidant defense in nearly all living cells exposed to oxygen.

The aim of this sudy. The present study was conducted to evaluate the effects of selenium and/ or aliuminium ions on the SOD activity in brain cells of laboratory mice.

Materials and methods. Experiments were done on 4-6 weeks old outbreed mice weighing 20-25 g according to the Republic of Lithuania Law on the Care, Keeping and Use of animals. SOD activity was determined in brain of laboratory mice after a single (24 h) and 14 days duration of Al^{3+}, SeO_3^{2-} and (Al^{3+}+SeO_3^{2-}) solution injections in the abdominal cavity. Control mice were i.p. injected with the same volume of saline. SOD activity was determined spectrofotometrically by the inhibition of nitroblue tetrazolium recovery rate in the nonenzymatic system phenazine methosulfate and NADH. Changes in absorbance were recorded after 5 min reaction at 540 nm

light wavelength. The concentration of protein in the brain homogenates was measured by using the Warburg-Christian method. Results were expressed as the mean ± SEM.

Results. It was evaluated the effect of Al^{3+} on SOD activity in mouse brain after a single i.p. injection of Al^{3+} (0.5 LD_{50}) solution. The results showed that enzyme activity was the same value in control and experimental groups. A single dose of SeO_3^{2-} reached 0.25 LD_{50}. The experiment showed that in this case SOD activity decreased by 28.6% if compared to the control group. Subsequently, were evaluated changes in mouse brain SOD activity following a single injection of a combination of SeO_3^{2-} and Al^{3+} solutions. The doses of both metals were analogous to those used before. However, the mice first received SeO_3^{2-} solution, and after 20 min – Al^{3+} solution. In this case was also observed a statistically significant decrease in SOD activity by 17.8%. In further experiments, there was evaluated the effects of Al^{3+} (0.1 LD_{50}) and/or SeO_3^{2-} (0.025 LD_{50}) on SOD activity in mouse brain after 14 days of i.p. daily injections. The results showed that 14 day-long injections of these metals salt solutions alone did not cause changes of brain SOD activity at this time-period of mice intoxication and was remained at the control level. The data of the effect of both metals showed certain differences, compared to the control group. Thus, after the injections of Al^{3+} solution (following the previous injections of SeO_3^{2-} solution), SOD activity statistically significant decreased by 41.5%, compared to that in the control mice.

Conclusions. Our studies revealed that the SeO_3^{2-} and Al^{3+} total antihypertensive effect in the brain reduce the enzymatic activity of SOD after single 24 h and after 14 days repeated exposure. This may be caused by one of metal's (possibly Se) competitive interaction with the metals, which are located in the enzyme's (SOD) active center.

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Terminology aspects of pharmaceutical care

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As a result of detailed study of the 44 sources of scientific literature 49 interpretations of the term "pharmaceutical care" (PC) were revealed. All sources were found in Google Scholar with search term "PC" in English, Ukrainian, Polish and Russian. During studying their essence it was found that the PC provider is specified in 29 (59.2%) of them. Particularly pharmacist as PC provider is mentioned in 18 (36.7%) cases. In 5 (10.2%) or terms a practician is defined as FD provider. practicing. In other (40.8%) definitions PC provider is not specified.

As for the recipient of PC, the 35 (71.4%) definitions are concerning to the patient (patient); 4 interpretations (8.2%) – a sick man, 2 (4.1%) - of people and individuals, and on 1 (2.0%) – the patient and society or pharmacy visitor. In 7 (14.3%) cases recipients of PC were not defined.

Subjects of PC are considered as:
– Medicines – 18 definitions (36.7%);
– Medicines and medical devices – 2 (4.1%);
– Pharmacotherapy – 17 (34.7%);
– Drug-related problems – 1 (2.0%)
– Communication process – 5 (10, 2%);
– Professional care – 3 (6.1%)
– All activity of pharmacist – 1 (2.0%);
– Responsibility – 1 (2.0%);
– Procedures – 1 (2.0%).

As a result of PC authors saw:
– Quality of life – 14 (28.6%);
– Pharmacotherapy Optimizing of – 6 (12.2%);
– Prevention and management of drug-related problems – 2 (4.1%).

More than half of interpretations (22 or 55.1%) did not contain the expected results of PC. Thus, in the literature there are many different interpretations of PC, which differ significantly from one to another with ambiguity and multiplicity of reading and content invested into them. To a large extent this leads to the 9

No single view of determining the essence of PC, enabled own interpretation of this concept.

In our opinion, PC is a philosophy of pharmaceutical practice, which consists of pharmacist's (in collaboration with a physician) taking care over the parties (patients, family members and closed to persons) during the whole period of individualized pharmacotherapy for in advance prepared plan in order to prevent and manage drug-related problems and maintain or improve the quality of life.

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The role and place of medium level specialists in pharmacy

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Pharmaceutical education systems in the world are different in many ways. Training programs have varying duration, and different types of qualification are assigned. Staff resources parameters analysis is necessary for understanding of requirements unification for pharmaceutical education in order to improve its quality and international acceptance of education results. Medium level specialists are of particular interest. It's a sufficiently powerful system of staffing in pharmacy in many countries. The main and classical components of the pharmaceutical industry are municipal or social pharmacies. In many countries pharmacist is considered to be a specialist with complete higher education (provisor in Ukraine). Pharmacy assistant and pharmacy technician are medium employees in pharmacies (pharmacists in Ukraine). According to the FIP data, the amount of medium level specialists as a part of pharmaceutical employees is 28% in American countries (of both continents), and 68% in South Asia countries. In European countries this index averages 43%: Romania 90%, Netherlands 85%, Sweden 83%, Denmark 77%, Poland 48%, Ukraine 50%, Great Britain 40%, France and Lithuania 39%, Germany 17,5% [1].

In most countries pharmacy assistant performs auxiliary functions, such as: realization of OTC drugs, healthcare products, compounding preparation, registration and storage, logistics, management in the pharmacy by IT systems, etc. In developed countries, they work under the

supervision of pharmacist. In less developed countries, they work independently.

In Ukraine since the 90s of the past century, technical schools and colleges were included in the system of higher education. It should be noted that the current system of education in Ukraine is characterized by rapid changes, motivated by both the integration into the European educational space, and focus on the Ukrainian market requirements market to the specialists training level. Accordingly, mid-level specialists (pharmacists) training has been reformed according to the pharmaceutical market needs and higher education requirements. Educational standards of The Bologna Process, Europeanization, GPP requirements, and National framework classifications globally contribute to the progressive development of pharmaceutical education [2].

The comparative staff resources analysis has shown that basic needs were common to all countries. It is well known that in a modern market relations employers prefer to receive competent specialists, capable not only to perform their direct professional responsibilities and aspiring to development, professional self-education and constant knowledge renewal, and ready to learn new technologies and features of their professional activity. At the same time necessary for pharmacists competencies in many ways are universally recognized. Thus, competent pharmaceutical professionals can independently find the necessary information, analyze production problems as well as find ways of solving them, and are able to adapt their professional skills to solve new practical questions.

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Extraction of phenolic compounds from *Melissa officinalis* L. leaves usingultrasound

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Classical methods of extraction are popular and widely used, but it is time-consuming and needs more equipment, while ultrasound extraction is short and more effective. Phenolic compounds are active antioxidant substances; therefore the best extraction conditions using ultrasound were determined.

In this study phenolic compounds were extracted from *Melissa officinalis* L. leaves using ultrasound and the impact of the extraction duration and the ratio of materials was evaluated according the quantities of total phenolic compounds (expressed Rosemary acid equivalents) and antioxidant activity using the 2,2-difenil-1-picrylhydrazyl (DPPH) free radical inactivation test. The solvent was distilled water. Extraction time 5, 10, 15 and 30 min, raw material and solvent ratio was 1:10, 1:20 and 1:30. Statistical analysis was performed using Microsoft Excel program.

Total quantity of phenolic compounds ranged between 13 – 56 mg/mL RAE. The highest amount was extracted after 30 minutes at 1:10 ratio (56,11 ± 0,812 mg/mL RAE). Antioxidant activity ranged between 38 % and 85 % inactivated DPPH radicals, the highest activity was achieved at 1:30 ratio after 15 minutes of extraction (85,29 ± 0,84 %). Results of our study coincide with the results, obtained by Middle East Technical University scientists, when the highest amount of phenolic compounds from lemon-balm leaves was extracted after 20 minutes at the ratio of 1:30 [1].

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The kinetics of dissolution of metronidazole tablets in the medium with addition of metal salts

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Along with the efficacy and safety of drugs, the interaction of drugs with each other and with other accompanying substances is important too. The guidelines for medical application comprise common recommendations for use such as separate intake of medicines with metal salts with other drugs because of the possibility of insoluble complexes formation. However, patients do not always follow the common rules of taking drugs, referring to the need of immediate elimination of symptoms of heartburn and pain in the stomach [2].

There are no data about the interaction or influence of antacids and other drugs with polyvalent cations on the metronidazole bioavailability. The purpose of this research was to study the metronidazole release kinetics from the tablets in an environment that simulates stomach conditions with the addition of metal salts, which are part of widespread drugs. The research was carried out to assess the impact of possible interactions between the active substance and polyvalent metal cations on their bioavailability and efficacy.

The object of study was "Metronidazole-Zdorovya" (S.: 40415) metronidazole tablets. 0.1 M HCl solution with addition of metal salts was chosen as the medium dissolution. The metal salts were of analytical purity grade. The "PharmaTest-DT70" Device with a basket, the "Evolution 60S" Spectrophotometer, the "AB 204 S/A METTLER TOLEDO" analytical balances as well as the class A measuring vessel and reagents, that conform to the State Pharmacopoeia of Ukraine, were used in the study.

Dissolution profiles are very similar to each other, deviation within the allowed norms, nature of charts are not significantly different between themselves and with the control experiment. Similarity factors of dissolution (f_2) profiles of metronidazole tablets in various mediums are ≥90%, in the case study of solubility in the medium with Fe^{2+} salt, the figure is 84% (dissolution profiles are considered similar if the similarity factor is $f_2 \geq 50\%$ [1]). The value of relative standard deviation also conforms with the given criteria and is no more than 2% for each of the samples.

As we can see, the chemical interactions between the chosen medicines are not observed in the "in vitro" experiment. Thus, separate intake of metronidazole with other drugs, containing metal cations, is important for further research in the "in vivo" experiment.

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POSTER SESSION

Evaluation of phenolic compounds and their antioxidant activities in ethanolic herb extracts from intensively and organically farmed six cultivars of *Fagopyrum esculentum* Moench

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The interest of polyphenolics as therapeutic agents against diseases involving radical damage is constantly growing [1]. Buckwheat herb as the natural flavonoids-rich material seems to be an attractive choice for these requirements [3]. Most common phenolic compounds in buckwheat herb are flavonoids (rutin, quercitrin, quercetin and others) and phenolic acids (chlorogenic acid, neochlorogenic acid and others) [2, 3]. Phenolic compounds demonstrate antioxidative, antihypertensive, anti-inflammatory, antidiabetic, antihaemorrhagic effects, normalise the increased vascular permeability etc. [1, 2]. The aim of this research was to quantitate content of phenolic compounds and evaluate antioxidant activity of six intensively and organically cultivated buckwheat varieties' herb using HPLC method. Methods: buckwheat herb was extracted using ultrasonic sound assisted extraction. 60% ethanol was used as extracting agent. Extraction time was set at 15 min at 45°C. Extraction was repeated two more times to extract full content of phenolics. HPLC analysis was carried out on a Waters Alliance 2695 separation module system equipped with Waters 996 PDA detector. ACE C18 (150 mm x 4.6 mm, 5 µm) analytical column was used. Mobile phase was eluted at the flow rate – 1.0 ml/min with injection volume of 10 µl. Mobile phase for gradient elution system consisted of 2% acetic acid and acetonitrile. After chromatographic separation antioxidant activity was measured by reduction of absorption using ABTS radical. ABTS radical (flow rate – 0.5 ml/min) was mixed with mobile phase and absorption was measured using Waters UV/VIS 2487 detector at 650 nm. Results: five phenolics (rutin, quercitrin, quercetin, chlorogenic and neochlorogenic acids) were quantitate and their antioxidant activity was estimated in buckwheat herb samples. Highest amount of rutin (34994.0441 ± 692.14 µg/g DW) was found in 'Žniajarka' cultivar (organic farming). Highest amount of quercitrin (2545.1834 ± 75.00 µg/g DW) and chlorogenic acid (1183.5142 ± 23.17 µg/g DW) was found in 'Žaleika' cultivar (organic farming). Highest amount of quercetin (225.2430 ± 20.31 µg/g DW) and neochlorogenic acid (1082.6002 ± 92.07 µg/g DW) was found in 'Žniajarka' cultivar (intensive farming). Highest radical scavenging activity of identified phenolic compounds was observed in 'Žniajarka' (33.0546 ± 1.99 µmol TE/g DW) cultivar (organic farming). Acknowledgment: this work was supported by a grant (No. SVE-02/2014) from the Research Council of Lithuania.

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Knowledge, attitudes and usage of apitherapy for disease prevention and treatment among undergraduate pharmacy students in Lithuania

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Background: Traditional medicine therapies are historically used worldwide for disease prevention and treatment purposes. Complementary medicine practices which incorporate use of some traditional herbal, mineral or animal kind substances very often are discussed with pharmacy professionals because these products are often sold in pharmacies as dietary supplements. This study is aimed to determine the attitude, knowledge and practices of apitherapy among under graduated pharmacy students (Master of Pharmacy) who has already a pharmacy technician diploma and from 1 to 20 years practice working at community pharmacy as pharmacy assistants.

Methods: Data were collected by cross-sectional survey. A method of questionnaire was chosen. The questionnaires were distributed during the 2014-2015 academic year at Lithuanian University of Health Sciences to the intensive 3years MPharm course students. The questions about attitudes, experience, knowledge and practices for disease prevention and treatment of different bee products, their safety and informational sources were included. The return rate of the questionnaire was more than 90%.

Results: Respondents shared opinion that use of bee product is part of traditional medicine. All 72 (100%) of the respondents indicated that they use and aware at least one of bee products. Honey was the most popular choice for all indicators. More than half (62%) convinced usage of bee products by themself and almost one third (34 %) reported about recommendation to pharmacy patients. The most popular choice for "disease prevention" purposes was "honey" for family members (28%) and propolis (16%) or "royal jelly" (13%) for pharmacy patients. The main indication of apitherapy products were for enhancing of immune system and prevention/treatment of respiratory tract infections. "The main sources of information on apitherapy were internet (62,2%), journals (59.7%) and formal lectures of continuing education(52.8%). Participants of the study indicated that apitherapy products have less contraindications than other remedies. The most known indicated side effect is allergy (97.2 %) and according to respondents bee product use should be recommended with warnings to allergic patients (90.3%), pregnant woman (61.1%) and children under 3 years (62.5%).

Conclusions: Pharmacy students in Lithuania showed interest towards bee product use for diseases prevention and treatment purposes. They self reported use and awareness of apitherapy products. Enhancing immune system, prevention and treating the respiratory tract infections according to respondents were the main areas of bee product use.

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Phenolic compounds quantitative research in *Solidago* L. using Thin-layer chromatography and High performance liquid chromatography

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Introduction. Phenolic compounds are the subject of increasing scientific interest because of their multiple biological effects, including antioxidative activity that is associated with the prevention of various degenerative diseases [1]. The aim of our study – to compare phenolic compounds quantities, obtained by thin-layer chromatography (TLC) and high performance liquid chromatography (HPLC).

Materials and methods. Leaves of *Solidago canadensis* L. and *Solidago gigantea* L. were collected in 2012 in different places of Lithuania and dried at 25 °C for chemical analysis.

Extraction. 0.1 g of air-dried *S. canadensis* and *S. gigantea* leaves were extracted with 10 mL of methanol water mixture (70:30 v/v) by ultra-sonication at 25 °C for 50 min. The prepared extracts were passed through a 0.22 μm filter [1].

Thin-layer chromatography. TLC was performed on silica gel 60 UV_{254} glass plates. Samples were applicated using CAMAG Linomat 5. 20.0 μL of every sample were sprayed over 10.0 mm band length. As solvent systems were used anhydrous formic acid R, glacial acetic acid R, water R, ethyl acetate R (7.5:7.5:17.5:67.5 V/V/V/V). Detection of the phenolic compounds was carried out by spraying with a 10 g/L solution of diphenylboric acid aminoethyl ester R in methanol R and then with a 50 g/L solution of macrogol 400 R in methanol R and observed using CAMAG TLC. Then dried and visualized under ultraviolet light (366 nm).

High performance liquid chromatography. Waters 996 PDA diode-array detector (DAD) was used for HPLC analysis. The data were analysed using the Empower Software chromatographic manager system. The separation of the compounds was carried out on a YMC-Pack ODS-A column (3.0 μm, 150 mm × 4.6 mm i.d.). The mobile phase consisted of eluent A (0.05% trifluoroacetic acid in water) and eluent B (100% acetonitrile). The elution programme was fixed as follows: 5% B at 0–5 min, 12% B at 5–50 min, 30% B at 50–51 min, 90% B at 51–56 min, and 5% B at 56–57 min. The flow rate was 1.0 mL/min, injected volume was 10 μL. Detection was monitored at a wavelength range of 210–550 nm.

Results. Using TLC method, there were found 1.097 times less rutin, 1.091 times more chlorogenic acid, 1.009 times more isoquercitrin in *S. gigantea* and 3.216 times less rutin, 1.7 times more chlorogenic acid, 1.428 times more isoquercitrin in *S. canadensis* than using HPLC method.

Conclusion. Quantity of Phenolic compounds (determined by TLC and HPLC) were not statistically different, but TLC is faster and cheaper. TLC is less sensitive than the HPLC method.

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TLC-screening in diagnostics of acute intoxication by mushrooms

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Poisoning by mushrooms still constitute a significant proportion of the total number of food poisoning both in Ukraine and Lithuania. TLC-screening widely uses in practice of analytical toxicology [2]. We tried to apply this analytical method for laboratory testing mushroom poisoning. We investigated cases of food poisoning with strong psychotomimetic syndrome [3, 4]. This type of intoxication is characteristic for poisoning by some mushrooms of species Amanita, Inocybe, and Clitocybe. Toxins of these fungi are substances – isoxazole derivatives: muscarine, ibotenic acid, tricholomic acid, muscazone, and muscimol [1].

The objects of our investigation were fruiting bodies of fungi that cause mentioned poisoning, and biological fluids (blood, urine) of poisoned persons. Samples of body fluids (50 ml of urine or 10 ml of serum) were acidified by 10% solution of sulphate acid to pH 2 and infused for 1 hour. Investigated substances were extracted by 5 ml of chloroform. Chloroform extracts from biological fluids were dried and reconditioned in ethanol. Ethanolic extracts from biological material and ethanolic solutions of standards were applied on the chromatographic plates "Silufol UV-254".

Standard solutions of muscarine, ibotenic acid, and muscimol were prepared from stock substances in ethanol with different concentrations (from 10.0 to 100.0 µg/ml). As mobile phase for chromatographic separation was used mixture of solvents ethyl acetate: methanol: ammonia – 85: 10: 5. Zones (spots) of investigated substances were visualized by UV-radiation and sprayed various reagents: Dragendorff's reagent, Mandelin's reagent, and solution of hydrogen iodoplatinate in dilute chloride acid. Were established R_f and detection limits of investigated samples.

The proposed method TLC-screening allows to quickly and reliably identifying fungal toxins-derivatives of isoxazole in fruiting bodies of fungi and in biological liquids. This method allows determining muscarine, ibotenic acid, and muscimol semi quantitatively in investigated objects.

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POSTER SESSION

Reological properties of hydroalcoholic ciclopirox gels

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Introduction. Reological properties of semi- solid formulations are very important and may indicate their stability. Excipients like menthol, thymol, rosemary oil, juniper oil, cinnamon oil can alter rheology and drug delivery characteristics of topical gels. The objective of this study is to perform detailed and extensive rheological characterization of hydroxypropyl cellulose gel formulated using different excipients.

Methods. Hydroalcoholic gels with different excipients were prepared by dissolving hydroxypropyl cellulose and ciclopirox in co- solvent. Menthol, thymol, rosemary oil, juniper oil, cinnamon oil were aded to different formulations. Steady and transient shear measurements were performed to measure viscoelastic properties, temperature dependency, yield strength of pharmaceutical gels. Flow curves were constructed for the range of temperature. Flow curves were made after reological measurements and it were described using mathematical model- power law slope. Flow index and consistency coefficient were calculated for all formulations at 3 temperatures: 25, 32 and 37 C.

Results. Gels with rosemary oil and thymol show lower consistency coefficients and higher flow index compared to gel without oils. Menthol, juniper oil, cinnamon oil have marginal influence for viscosity. Structural recovery after stress were observed. All formulations are stable when shear rate is changing and structure returns to its original state after the cessation of stress. Changes of temperature can destroy structure and gel do not recover. Gels with menthol and rosemary oil are not resistant to torsional effects.

Conclusions. The topical pharmaceutical gels exhibit remarkable shear stability and most of the tested gel are stable at temperature fluctuations. Flow curves obtained at different temperatures indicate gels show pseudoplastic behavior. Insignificant yield strenght is required to break the gel network of the topical gel.

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Stability of chloramphenicol in electrospun antimicrobial nanofibrous mats

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Electrospinning is an effective continuous method to fabricate polymeric nanofibers for a wide range of applications including various pharmaceutical and biomedical systems. Nanofibers have very large surface area to volume ratio and flexibility in surface functionalities, which makes them ideal preparations for the use as topical wound dressings [1]. To increase the attachment time and to avoid too fast dissolution of wound dressings, photocrosslinking with ultraviolet (UV) radiation can be used [2]. The aim of the present study was to evaluate the chemical and physical solid-state stability of an antimicrobial agent, chloramphenicol (CAM), in photocross-linked electrospun nanofibers intended for wound treatment.

CAM (Sigma-Aldrich) was used as a primary antimicrobial agent. Suberin fatty acids (SUB FA) (VTT, Technical Research Centre of Finland, Espoo, Finland) isolated from outer birch bark by depolymerization was included in a formulation as a secondary antimicrobial agent. PVP (Kollidon K90, BASF, Germany) and ethanol (96% w/V) were used as a carrier polymer and solvent for electrospinning (ES), respectively. Nanofibers were prepared using an ESR200RD robotized ES system (NanoNC, Korea) and subsequently photocrosslinked using UV light (254 nm) for 5, 10, 30 and 60 min (UV lamp Heraeus model TNN 15/35, Germany). X-ray powder diffraction (XRPD) and Raman spectroscopy were used for the physical solid-state analysis. The surface topography of nanofibrous mats was analyzed by scanning electron microscopy (SEM). High-performance liquid chromatography (HPLC) was used to determine the chemical stability of CAM. The nanofibers were analyzed immediately after fabrication (0 day) and after a 6-month storage at room and low temperatures (0% RH).

The results suggest that CAM incorporated in nanofibrous mats was physically stable during the storage of 6 months and did not show any crystallinity. Exposure to the UV radiation, however, led to a decrease in the CAM content in the nanofibrous mats studied, although, the CAM remained still in amorphous state. Incorporation of antimicrobial drug (CAM) and a biomaterial (SUB FA) into nanofibers enables to develop novel multifunctional wound dressings.

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Influence of urine pH on efficacy of olanzapine isolation on H-klinoptilolite columns

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Olanzapine is derivative of benzodiazepines. It is widely administered in psychiatric practice for treatment of schizophrenia. This preparation has high affinity to serotonin and dopamine receptors. However, sometimes this medication is used for suicide. In the overdosage are observed pronounced toxic effects, sometimes with lethal consequences [1, 2].

Aim of investigation was to assess the efficacy of olanzapine isolation from urine on columns with H-klinoptilolite compared with other isolation techniques: liquid-liquid extraction and flash chromatography, applied in toxicological laboratory practice [3].

Materials and methods. Olanzapine was extracted from blood with chloroform at pH 10-11, and protein fraction was precipitated by 20 % solution of sulfosalicylic acid. Flash chromatography was provided on the GraceResolv Silica 5g/25ml columns; olanzapine was eluted by 0.5 % ammonia solution in ethanol.

Natural aluminosilicate klinopltilolite was used for ion-exchange chromatography. Natural sorbent was transformed to H-form by M HCl treatment. Handmade column for olanzapine isolation contains 0.6 g of H-klinoptilolite (0.22-0.31 mm particles). Before the use the sorbent was conditioned by 1 ml of 1 M HCl solution in 96 % ethanol and 2 ml of distilled water.

Urine samples (artificially spiked by olanzapine) were treated on H-klinoptilolite columns at different pH from 3.0 to 10.0. A urine acid in every probe was previously precipitated by 20 % $CaCl_2$ solution. Olanzapin was eluted by 0.2 M solution of NH_4OH in 96 % ethanol. Eluate was dried; and dry residue was dissolved in methanol.

Olanzapin was detected and quantified on Agilent GC-MS System with HP-1 (30 m × 0.25 mm i.d. × 0.25 μm) column. Limit of olanzapine quantitative determination is 25 ng/ml.

Results and discussion. Liquid-liquid extraction (chloroform) allows isolating 59.9 – 65.9 % of olanzapine. On the GraceResolv Silica columns it is possible to isolate 74.9 – 82.8 % of this preparation. Columns with H-klinoptilolite are the most suitable to isolate 90.1 – 93.0 % of olanzapine from urine at pH 10.

Conclusions. Conditions of purification and concentration of olanzapine isolated from urine on H-klinoptilolite columns were elaborated. Influence of biological liquid pH on efficacy of olanzapine isolation from urine was studied. Isolated olanzapine can be quantified by GC-MS.

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Application of Chezasorb AW-HMDS as sorbent for solid phase extraction of sertindole from biological liquids

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Population research indicates that up to 50% of patients with schizophrenia have substance abuse syndromes and the risk of committing suicide among them is 10% [3]. Reported sertindole overdose [2, 4] was a reason to work out a method of solid-phase extraction (SPE), which would be suitable for its simultaneous isolation, cleaning, and concentration from biological fluids.

Methods. The procedure of extraction using special cartridges filled with solid sorbents allows preparing complex sample analysis on the content of toxic substances [1]. For this purpose, we had used a plastic column with an internal diameter of 9 mm filled with a layer of dry sorbent and restricted on entering and leaving the column by paper filters. We have considered the possibility of using CHEZASORBAW-HMDS with 15% apiezone, (fr. 0.200-0.360 mm) as a filler, the amount of sorbent per sample was 200 mg. Sample flow rate was 1 ml/min. Volume of loaded samples was 4 ml (for model solutions) and 2 ml (for plasma). After elution the cartridge was dried and washed with 2 ml of water and 1 ml of 96 % ethanol.

Results. Sertindole solution (12 μg/ml) was loaded onto handmade SPE cartridges which had been preconditioned by rinsing with 1 ml of 96 % ethanol, 2 ml of water. Thereafter, the sorbents were washed twice with 2 ml of water. A better recovery was obtained using 96% ethanol, acidified with 0.1 M HCl solution to pH 4 rather than 96% ethanol in the elution step. The quantification of sertindole was conducted by measuring the absorbance of the eluate on the spectrophotometer Ulab 101 at 258nm.

For the above conditions 44% of sertindole has been allocated from aqueous solutions. It was found that air-conditioning in rounds 1 ml of ethanol, 2 ml of water and 1 ml of 10% ammonia and transmission of alkalined to pH 10 samples, increase the content of sertindole in eluate to 77%. The developed technique was used for the isolation, purification and research of drugs from human plasma. By the proposed method 57% of sertindole were isolated from reduced biological fluid.

Discussion and conclusions. The first time we have demonstrated the possibility of using modified sorbent CHEZASORB AW-HMDS as a solid phase for extraction of sertindole from biological agents. The chosen SPE sorbent has strong powers of absorption, particularly for other hydrocarbon molecules due to its complex carbohydrate structure and very high molecular weight. Good extraction performance in terms of plasma purity, recoveries and repeatability were hence obtained. Moreover, it reduces solvent consumption, thereby saving cost and offering environmental benefits.

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Influence of reagent-precipitant on quantitative determination of sildenafil in blood

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Introduction. Sildenafil citrate is inhibitors of phosphodiesterase type 5 (IFDE 5) [1]. Inhibitors of FDE 5 are effective and safe for erectile dysfunction treatment, but their application is contraindicated with organic nitrates, because simultaneous administration of these preparations can cause hypotensive effect until severe and deaths [2, 3, 4]. Therefore, chemical-toxicological research of this preparation is an actual task.

Work objective: To study the dependence of the results of quantization of the content of sildenafil in the blood after purification by solid phase extraction method from deproteinizator nature.

Methods. To study the influence of the nature of deproteinizator on the degree of isolation of sildenafil was used a mixture models containing 1 ml of blood with different content sildenafil (0.1 to 0.5 mg). For deproteinization acetonitrile, 96% ethanol, aqueous solutions of zinc sulfate 10% and 20% sulfosalicylic acid, saturated solution of oxalic acid, phosphotungstic acid, and ammonium sulfate crystal were applied.

Cleaning the blood samples after precipitation of protein components was performed by solid-phase extraction method on cartridges such as Oasis HLB (30 mg Waters, USA). The optimal eluent is 96% ethanol. Quantitative determimation of the selected sildenafil was performed by GC-MS method in the capillary column HP-1 (methyl siloxane).

Results. Up to 10-20% of sildenafil is isolated from the blood using deproteinizator of 20% solution of sulfosalicylic acid or acetonitrile saturated solution of phosphotungstic acid. Adding a saturated solution of oxalic acid in the presence of ammonium sulfate crystal up to 41% of sildenafil was received. The best reagents to precipitate the proteins in isolation from the blood of sildenafil are 10% solution of zinc sulfate and 96% ethanol. Using these deproteinizators can isolate up to 60% of the preparation from the blood. The relative error of detection in blood by GC-MS method is 5 ng / mL, and the limit of quantification is 7 ng / ml. Quantify the relative error is ± 1,11% on the day of trial production, and ± 1,17% at 24 hours after its preparation.

Discussion and conclusions. The influence of nature deproteinizators on the isolation degree from blood sildenafil when using solid-phase extraction was studied. The optimal reagent for deproteyinization in isolation sildenafil from the blood by solid-phase extraction is a 10% solution of $ZnSO_4$, which is isolated to 60,2% of the preparation.

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GC-MS determination of Sertraline and Desmethylsertraline in blood

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Sertraline is an oral antidepressant drug of the selective serotonin reuptake type [1]. Its metabolite – desmethylsertraline – eliminated slowly and contribute limited pharmacological activity [2]. The aim of this research was the development of rapid and sensitive methods of determination sertraline and its metabolite in whole blood by GC-MS, which can be applied for routine chemical-toxicological analysis. Our studies were focused on natural zeolites sorption ability evaluation and particularly on clinoptilolite originated from the Transcarpatian deposits.

Methodology: Samples of citrated human whole blood was obtained from Lviv station of blood transfusion and verified drug free. The samples of blood were kept frozen at -20 °C. 2 ml human blood was spiked with sertraline and desmethylsertraline at five concentrations: 0.01; 0.10; 0.50; 0.80 and 1.0 μg/ml each compounds. In all samples of blood were added the internal standard (100 μl aqueous solution of bupropione hydrochloride 1 μg/ml) and 2 ml of phosphate buffer (pH 7.4). Then the samples were vortex mixed for 5 min and sonicated for 15 min at 20 °C. The whole liquid was transferred on column for SPE (with 0.6 g of H-clinoptilolite, fraction 0.20-0.22 mm). SPE columns were conditioned with 1 ml of 0.1 M solution of HCl in methanol and 1 ml of water. After samples pass the columns were washed with 4 ml phosphate buffer (pH 7.4), 3 ml of water and methanol-water mixture (1:1, v/v). The sorbent was dried in nitrogen flow. The compounds were eluted with 2.5 ml 0.1 M solution of NH_4OH in methanol. Elutes were dried, dissolved in 200 μl of methanol and analysed by GC/MS technique (Agilent 6890N gas chromatograph equipped mass-selective detector 5978MSD, HP-1 capillary column 30 m × 0.25 mm). Initial temperature of the column – 60 °C (2 min), racing with 20°C/min to 280°C, finally – 2 min at 280 °C. Carrier – helium (1 ml/min).

Results. Both compounds were detected according to their retention time (13.511±0,032 min for sertraline and 12.019±0.052 min for desmethylsertraline). Calibration curve was linear in the concentration rang of 0.01-1.0 μg/ml for each compounds. H-form of clinoptilolite sorbs 76.9–78.6 % of sertraline and desmethylsertraline from blood. The LOQ for sertraline and desmethylsertraline in blood is 10 ng/ml with 1 μl injection.

Conclusions. H-clinoptilolite was assayed as the efficient sorbent for SPE of sertraline and desmethylsertraline from blood and their GH-MS detection.

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Evaluation of phenolic compounds, total flavonoids and radical scavenging activity in *Lepidium sativum* Linn., *Lepidium latifolium* L. herb collected in different vegetation phases

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Lepidium sativum Linn. and *Lepidium latifolium* L. are reported to have high antioxidative activity. [1].

The aim of this study – to determine the quantity of total phenolic compounds, to establish the quantity of flavonoids and to measure radical scavenging activity in herb of *Lepidium sativum* Linn. and *Lepidium latifolium* L. collected at different vegetation phases. Tasks- 1. to determine the quantity of total phenolic compounds; 2. to estimate the total flavonoid content and DPPH radical scavenging activity by spectrophotometry; 3. to compare the distribution of these active compounds in different vegetation phases; 4. to compare the quantity of active compounds and DPPH radical scavenging activity in *Lepidium sativum* Linn. and *Lepidium latifolium* L.

Materials and methods. Herb of analyzed plants (*Lepidium sativum* Linn.; *Lepidium latifolium* L.) was collected at Kaunas Botanical Garden of Vytautas Magnus University at different vegetation phases (intensive growing, bud, early flowering, peak flowering, late flowering). Extraction was performed using methanol/water (75/25 v/v %). Total phenolic content was determined using Folin-Ciocalteau assay, total flavonoids - using aluminium chloride calorimetric assay. Concentration of phenolic compounds and total flavonoids was calculated using standart curve of rutin (0,01-0,75mg; R^2=0,998). The results were expressed as mg rutin equivalent (mg RE) in 100 g dry weight of herb. DPPH radical scavenging activity was expressed as the % of inhibition. Results were calculated using Microsoft Excel for Mac 2011.

Results. The highest amount of total phenolics, flavonoids, and radical scavenging activity was observed during the early flowering phase for *Lepidium sativum* Linn. herb – respectively - 291,55±0,01 mg RE/100g, 176,42±0,02 mg RE/100g and 48,66±0,1%. In *Lepidium latifolium* L. herb the highest concentrations of these compounds were observed in the bud phase – phenolics - 284,80±0,02 mg RE/100g, total flavonoids -208,79±0,02 mg RE/100g, DPPH radical scavenging activity - 48,31±0,2%.

Conclusions. Herb of *Lepidium sativum* Linn. accumulated more phenolic compounds, but *Lepidium latifolium* L. had more flavonoids and showed a stronger antioxidative activity by inhibiting DPPH. In both plants the total amount of phenols and flavonoids appeared to correlate with radical scavenging properties.

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An explorative survey of pharmacy students` and practicing pharmacists` perception towards medical technology education in the Nordic and Baltic countries

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Community and hospital pharmacists provide important counselling to patients using medical devices (MDs) and drug-delivery products (DDPs). The aim of this study was to assess the current medical technology education of MDs and DDPs for pharmacy students and pharmacists in Estonia, Finland, Iceland, Latvia, Lithuania and Norway.

A qualitative explorative survey with focus group approach was undertaken among academic staff members, BSc or MSc Pharm students and representatives of community and hospital pharmacists from May to October 2014 using an internet based questionnaire.

Total 50 responses were collected: 34 from academia and 16 from professional organizations. Two third of the respondents considered professional knowledge about MDs as important for pharmacists. Of practicing pharmacists, more than half reported to never participated in any continuing education courses about MDs and DDPs. At universities, the knowledge on MDs and DDPs was in most cases obtained in the courses of medicine and pharmaceutical technology. Specialists of MDs or medical technology industry were more involved in the courses for practicing pharmacists than for pharmacy students. More than the representatives of academia, the practicing pharmacists underlined the need for increasing the education about MDs for pharmacy students and importance of international courses about MDs.

There is an increasing need for professional knowledge about MDs and DDPs among pharmacy students and practicing pharmacists in the Nordic and Baltic countries. Networking for the effective exchange of existing knowledge on medical technology would foster to improve the competency of pharmacists in the field of MDs and DDPs in the future.

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POSTER SESSION

Evaluation of medication adherence among primary care patients using statins: a pilot study in Tartu, Estonia

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Treatment of atherosclerosis aims to prevent the condition from escalating to a serious cardiovascular disease by employing statins. Compliance among patients receiving statin treatment, however, has been relatively low. The objectives of this study are to monitor medication adherence of ambulatory patients who have started statin therapy and evaluate factors influencing the treatment compliance.

Ambulatory patients (n=29) started statin therapy (atorvastatin, rosuvastatin, simvastatin) in primary care setting in Tartu, Estonia, were recruited to participate in the study between September 2014-2015. Of the study patients, 75% were using polypharmacotherapy. Multi-method approach was used for evaluation of medication adherence: pre-structured interview (to provide information about general perceptions towards the use of medicines and medication adherence), calculation of pill count adherence and electronic prescription claims data adherence (all 1, 3, 6 months); taking blood samples for blood cholesterol and creatine kinase (both at 0 and 6 months). Approval from the Ethics Committee of the University of Tartu was granted.

Interview results demonstrated that negative general perception towards the use of medicines and medication adherence, asymptomatic disease and experienced malaise considered as possible side effect of statins has strong influence to the treatment compliance. More frequently described side effects were pain in legs and hands, itching skin, tiredness, sleep problems, leg cramps and dry mouth. Among the study patients two (8,3%) withdrew from the study after first contact. 18.5% (n=5) of the study patients stopped taking statins after 6 months. Among patients claimed regular use of statins (n=22), the pill count adherence varied from 55 – 100% at month 1, 45,5 – 100% at month 3 and 45 – 93% at month 6 and electronic prescription claims data adherence varied from 57-100% at month 1, 54-100% at month 3 and 51-100% at month 6. Of the concomitantly used prescription medicines warfarin was identified as well-known medicine interacting with statins and may lead to the clinically relevant side effects.

Negative beliefs about medicines and experience of potential side effects are some of the reasons for low adherence to statin therapy. About 1/3 of the study patients would benefit from the regular communication with healthcare specialists to understand better the need for compliance in statin therapy.

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The production of a framework of competences for pharmacy practice in the European Union: the PHAR-QA project

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The goal of the PHAR-QA (Quality assurance in European pharmacy education and training) project is the production of a European framework of competences for pharmacy practice. This PHAR-QA framework (www.phar-qa.eu) will be European and consultative i.e. it will be used for harmonization—but will not to replace existing national QA systems.

Using the proposals for competences produced by the previousPHARMINE(Pharmacy education in Europe; www.pharmine.eu) project, together with those of other sources, the authors produced a list of 68 personal and patient care competencies. Using internet survey tools the stakeholders—European pharmacy community (university department staff and students, community, hospital and industrial pharmacists, as well as pharmacists working in clinical biology and other branches, together with representatives of chambers and associations)—were invited to rank the proposals and add comments.

Pharmacology and pharmacotherapy together with competences such as ''supply of appropriate medicines taking into account dose, correct formulation, concentration, administration route and timing'' ranked high. Other topics such as ''current knowledge of design, synthesis, isolation, characterisation and biological evaluation of active substances'' ranked lower. In the short term, it is anticipated that this survey will stimulate a productive discussion on pharmacy education and practice by the various stakeholders. In the long term, this framework could serve as a European model framework of competences for pharmacy practice.

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POSTER SESSION

Effects of aluminium and selenite ions to oxidative stress in mice brain and blood

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Introduction: Aluminium (Al) is considered as pro-oxidant and it can potentiate oxidative and inflammatory events by activating ROS generation that eventually leads to tissue damage and neurodegenerative disorders [1]. Several experiments have shown that Al can reduce glutathione (GSH) level. GSH level depends on selenium (Se) which can increase the antioxidant capacity of several intracellular systems and the level of GSH [2].

The present study was carried out in order to examine a possible protective effect of selenite ions (SeO_3^{2-}) on the redox status in mice blood and brain under short-term (24 hours) exposure to aluminium ions (Al^{3+}).

Materials and methods: Experiments were done on 4-6 weeks old Balb C mice once intraperitoneally injected with $AlCl_3$ (0.5 LD_{50}) and/or Na_2SeO_3 (0.25 LD_{50}) solution/s. The exposure-time to metals was 24 hours. Control mice were injected with the same volume of saline solution. (License of State Veterinary Service for Working with Laboratory Animals No. 0221). Reduced glutathione (GSH) was determined by reaction with 5,5'-dithiobis (2-nitrobenzoic acid), absorbtion was measured at 412 nm. Lipid peroxides were estimated by measuring thiobarbituric-acid-reactive substances and were expressed as malondialdehyde (MDA).

Results: Our results indicated, that the treatment with Al^{3+} and/or SeO_3^{2-} did not cause any significant changes in the concentration of GSH in the brain. However, the treatment with Al^{3+} as well as treatment with both effectors (Al^{3+}+SeO_3^{2-}), induced statistically significant decrease (by 14%) of GSH concentration in blood. Whereas, treatment with SeO_3^{2-} reduced GSH concentration in the blood just 10% ($p>0.05$), as compared to the control.

The single injection/s with Al^{3+} or Al^{3+}+SeO_3^{2-}, did not cause any significant changes in brain MDA concentration. Even though SeO_3^{2-} increased MDA concentration in the brain by 18% as compared to control, this change was not statistically significant. After $AlCl_3$ injections, MDA concentration in the blood of laboratory mice increased by 28% and was non-statistically significant. However, the treatment with both effectors (Al^{3+}+SeO_3^{2-}) induced statistically significant increase in blood MDA concentration by 33%. Therefore SeO_3^{2-} together with Al^{3+} brought even higher lipid peroxidation than Al^{3+} itself. Thus, the pre-treatment with Na_2SeO_3 20 min. before $AlCl_3$ injection could not reduce Al-induced brain lipid peroxidation.

Conclusions: The single injection/s with Al^{3+} or/and SeO_3^{2-} do not cause any changes either to GSH or to MDA concentration in mice brain. Increase in blood MDA concentration after coexposure to SeO_3^{2-} and Al^{3+} may be due to GSH depletion.

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Optimization of *Rhaponticum carthamoides* DC. Iljin extraction using spectrophotometric method for total amount of phenolic compounds

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Introduction: Since ancient times people were using various herbs to heal illnesses, regain strength and improve health. One of many valuable herbs is Rhaponticum carthamoides (*Rhaponticum carthamoides* DC. *Iljin*) also known as Maral root, Leuzea carthamoides, Cnicus carthamoides [2]. Rhaponticum is poorly examined, however researches which were made had shown that plant has lots of beneficial qualities. It is known that Rhaponticum has phenolic compounds. Phenols determine plant colors, smell, affect growth [1,3].

Aim: To investigate which solvent is the best for *Rhaponticum carthamoides* DC. Iljin extraction of phenolic compounds.

Materials and method: Rhaponticum (rootstock, blossom and leafs) was collected and prepared in Vytautas Magnus University Botanic Garden. There were analysed 5 phases: intensive growth, budding, blossoming, massive blossoming, ending of blossoming and fructification. For extract preparation we used three different solvents: methanol (75%), ethanol (70%) and 1-propanol (99.5%).Total amount of phenolic compounds was determined by spectrophotometric method. Extracts samples were mixed with Folin – Ciocalteu reagent and sodium carbonate solution. Sample was measured at 760nm. We used standard calibration curve of rutin to quantify the amount of total phenolic compounds. The data were processed using Microsoft Excel.

Results: The results showed that the biggest amount of phenolic compounds was found in extracts with ethanol solvent (11.4mg/mL-21.3mg/mL ($p<0.05$)), less was found in extracts with methanol solvent (6.2mg/mL-8.3mg/mL ($p<0.05$)). The extracts with solvent 1-Propanol is very poor in phenolic compounds (0.54mg/mL-0.7mg/mL ($p<0.05$)). The biggest amount of phenolic compounds was found in massive blossoming phase.

Conclusions: The best solvent for *Rhaponticum carthamoides* DC. Iljin extraction determination of total amount of phenolic compounds is ethanol (70%). The results show that massive blossoming phase has the biggest amount of phenolic compounds.

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Spectrophotometric phenolic compounds and flavonoids investigation of black currant *(Ribes nigrum* L*)* leaves

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The problem - the contribution WHO to improve people's state of health promoting the prevention of medicinal plants.

Research object – black currant *(Ribes nigrum* L.*) –Grossuariaceae* family of multi-bush, the accumulation of phenolic compounds, which mainly consist of flavonoids, as well as essential oils, vitamins. Leaves recently recognized as medicinal plant raw material and was included in the European Pharmacopoeia (Ph. Eur. 07/2013:2528)[1]. Flavonoids have anti-oxidative, anti-inflammatory, antiviral effects [3]. Leaves have been used as a traditional remedy for rheumatic diseases, arthritis in the Europe [2].

The aim – to determine the total phenolic compounds, flavonoids of black currant *(Ribes nigrum* L.*)* leaves, collected at different fruit ripening time, and to compare the distribution of these compounds in flowers, shoots and buds.

Methods. Total phenolic compounds: total phenolic compounds, expressed as rutin equivalent is determined by the Folin-Ciocalteu method. For analysis was taken 3000 ml of 20% sodium carbonate solution, added 100 ml of medicinal plant raw material extract, mixed and added 100 ml of Folin-Ciocalteu (2N) reagent. The absorption was measured after 30min at 760 nm wavelength. Total flavonoid content, expressed as rutin equivalent, determined AlCl3 colorimetry. For analysis was taken: 1920 ml a reagent (60 ml of 100% methanol, 3 ml of 33% acetic acid, 12 ml of 5% hexamine, 9 ml of 10% aluminum chloride, 60 ml bidistilated water), 80 ml of medicinal plant raw material extract. The absorption was measured at 407 nm wavelength.

Results: The obtained data were evaluated by rutin calibration graph of the linear regression equation. The highest total phenolic compounds was identified in leaves, when the berries are still green -60,02 RE mg/g, at least – during fruit ripening – 53,69 RE mg/g. Compared buds, shoots and flowers – the smallest amount of phenolic compounds was found in flowers (respectively 54,98; 53; 33,56 RE mg/g).

Black currant leaves have the highest amount of flavonoids when berries are overripe, even wrinkled – 27,79 RE mg/g. The minimum amount of flavonoids in leaves is during flowering – 12,9 RE mg/g. Compared buds, shoots and flowers at least flavonoids have flowers (respectively 19,73; 20,26; 8,73 RE mg/g).

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Risk evaluation of pediatric pharmaceutical poisoning: Parents' of preschool children attitude towards home medication cabinet safety

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Background: Home accidents are the main cause of death and morbidity in early childhood. The type and influence of factors associated with poisoning may wary between countries. This variation may be due to differences in environmental conditions, cultural or lifestyle factors as well as availability agents.[1-3] The parents of preschools children attitude towards safe keeping of home medication cabinet can be good indicator of risk of pediatric pharmaceutical poisoning.

Aim: To evaluate the parents of preschool children attitude towards home medication cabinet safety..

Methods: Data were collected by cross-sectional survey. A method of questionnaire was chosen. The questionnaires were distributed during the January- June 2015 at random selected preschool children education institution. The parents of preschool children were asked to fulfill the questionnaire. The questions about home medication cabinet, attitude towards medication storage, experience with pediatric pharmaceutical poisoning and family health habits.

Results and discussion. Majority of the respondents (98%) agree that parents of preschool children are responsible for their health issues and safe use of medication. Most of them also agreed with a statement that home medication cabinet should be not achievable to the preschool children and this would help to reduce the risk of pediatric pharmaceutical poisoning. Even 87 % think that home medicine cabinet should be locked, 90% expressed opinion that temperature changes and high humidity can be dangerous for the active pharmaceutical substances. Only few of the respondents 37% do keep medication in place higher than 140 cm, 36% could not answer this question and admitted to having practice of keeping medication in several places where some of the medication may be reachable for the children. 37 % keep medication in bathroom (risk of high humidity) or near window (risk of high temperature). 17 % do not turn light when give medication to the children, 58% use medication by themselves in front of the children, and calls medication prescribed by physician – "candies" ("saldainiukai"/ "salduciai"/"skanestai")

Conclusions: Although most of the preschool children's parents declare being responsible for their children health and safe use of medications, but in some families the hazardous medication use and keeping habits were detected. Pharmacists, as most easy accessible health care providers and medication experts, have an important opportunity to assist in preventing pediatric pharmaceutical poisoning by instructing parents how enhance safety of home medication content and limit children's access to medications.

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POSTER SESSION

The effect of pharmaceutical compounds on common carp spermatozoa

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Carmoisine is the synthetic food azo dye, used in the manufacturing of some medicals, food and cosmetic products. Series of experiments were carried out and proved, that the carmoisine can form ion associates with medicinal substance as chlorpheniramine maleate - an antihistamine medicine. Physical and chemical properties of formed ion associate differ from the original dye; in particular, it is soluble in organic solvents (chloroform, butanol, ethyl acetate etc.). This fact suggests, that the formation of ion associate between chlorpheniramine maleate and carmoisine may affect the bioavailability of components.

The aim of the work was to study the effects of carmoisine, chlorpheniramine maleate and their mixture on live cells *in vitro.* Fish spermatozoa were chosen as a model due to their availability and susceptibility toward different groups of chemicals [2]. We analyzed common carp (*Cyprinus carpio* L.) spermatozoa motility, velocity, the level of oxidative stress and changes in protein phosphorylation after incubating spermatozoa in solutions of test compounds.

Incubation of sperm in solutions containing different concentrations of the dye had a little effect on the spermatozoa motility and velocity. We observed different percentage of motile cells at the same concentration of chlorpheniramine maleate in pure solution and in mixture with the dye. Specifically, addition of the dye reduced the effect of chlorpheniramine maleate on spermatozoa more than twice. Oxidative stress in spermatozoa incubated in test solutions was studied by calculating the value of CP (carbonyl proteins) and TBARS (the products of lipid peroxidation). The obtained results showed that the substances had no effect on lipid peroxidation and oxidations of proteins in spermatozoa. Effect on intracellular signaling was studied by means of western blotting with polyclonal antibodies to phospho-(Ser/Thr) protein kinase A (PKA) substrate. The obtained results showed that tested compounds, except carmoisine, influenced intracellular signaling by changing phosphorylation state of PKA substrate.

We showed that the test substances affect biological functions of sperm cells *in vitro* by changing sperm motility, velocity and intracellular signaling. It has been shown that interaction occurs between substances after mixing and alters their activity.

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Quality of life and regular use of medications among the elderly in Kaunas, Lithuania

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The use of medicines by elderly people is a growing concern in social pharmacy and beyond. There have been several attempts to measure the size of this problem in Lithuania and beyond. However, generally we still are lacking data on associations between use of medications and other health related factors, like quality of life. In this presentation, we investigate association between regular use of medications and quality of life.

Data for this study was collected during the European project "Elder abuse: a multinational prevalence study – ABUEL". Participants in this study consisted of randomly selected women and men from the general population living in Kaunas. Data was collected through face-to-face interviews in April to July, 2009. The total number of returned survey questionnaires was 624 (response rate 48.9%). Use of medications was measured following the respondents answers to the question about how often they used medications. They could choose one of the following answers: "No", "At need", "Regularly", and "Daily". Quality of life was measured with the WHOQOL-OLD [1], consisting of 24 items (graded 1-5). The total score amounts to 100 and items may be divided into 6 subscales, i.e. sensory abilities, autonomy, past, present and future activities, social participation, death and dying and intimacy. High scores correspond to high QOL (total/sub-scales). The statistical significance of difference between two groups was assed using a two-tailed Student (t) test for continuous variables. Differences in results at the $p<0.05$ level were considered statistically significant. The Lithuanian State Data Protection Inspectorate and the Kaunas Regional Bioethics Committee granted permission to perform this study

Our findings suggest that more than half (50.8%) of respondents used at least one drug daily. 18.3% responded that they use medications regularly but not on a day-by-day basis. One quarter (25.6%) used medication only on an "at need" basis. The mean WHOQOL-OLD for total score for all respondents was 61.09±13.00 (max 100). No statistically significant differences haven't been estimated in different groups of respondents by the usage of medications. However, we have identified some statistical differences in sub-scales autonomy and intimacy scales. Higher autonomy rates were among regular uses of medications. Meanwhile intimacy scale scores were higher among "at need" and non-users group.

These finding suggest that quality of life has a little correlations with use of medication among older people in Kaunas, Lithuania.

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The research of four antihypertensive drugs mixture using thin layer chromatography

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Hypertension, also known as elevated blood pressure is a chronic medical condition in which the blood pressure in the arteries is elevated. In Lithuania the death rate of cardiovascular diseases is 53% [2]. The combination of calcium channel blockers with beta blockers can help treat hypertension, but it can also trigger side effects like bradycardia, hypotension or atrioventricular block [2].

Objective of this research: To develop a thin layer chromatographic method suitable to separate the components of a mixture of antihypertensive drugs (nifedipine, verapamil, diltiazem and propranolol) and identify them.

Methods: DC-Fertigfolien alugram chromatographic plates coated with silica gel were used. Based on data found in literature, in order to identify chromatographic spots, iodine chamber and UV light 254 nm were used [1]. Methanolic standard solutions were prepared of 0.5 mg/ml nifedipine, verapamil, diltiazem and propranolol. Six solvent systems were developed that were suitable for nifedipine, verapamil, diltiazem and propranolol mixture for distribution and components identification: MP-1 ethyl acetate : methanol : glacial acetic acid (38:57:5); MP-2 acetone : ethanol: 25% ammonium hydroxide (47:47:6); MP-3 methyl ethyl ketone : methanol : glacial acetic acid (85:10:5); MP-4 acetone : methanol : glacial acetic acid (18:77:5); MP-5 acetone : methanol : ethyl acetate : glacial acetic acid (30:32:32:6); MP-6 acetonitrile : methanol: 25% ammonium hydroxide (85:10:5).

Results: The most appropriate methodology for mixture separation and identification of its components was produced using the solvent system of ethyl acetate : methanol : glacial acetic acid (38:57:5) R_f values (n=5) of MP-1 were 0.83, 0.48, 0.29 and 0.61 for nifedipine, verapamil, diltiazem and propranolol respectively.

Conclusion: This thin layer chromatographic method is suitable for the separation and identification of antihypertensive drugs in the mixture. Final objective of this research is to develop method suitable for identification and quantification of antihypertensive drugs from human plasma in the future.

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Naphthoquinones exert cytotoxic and anti-proliferative effects on *Glioblastoma multiforme* C6 culture cells

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Glioblastoma multiforme tumor (GMB) is the highest grade glial tumor and most common in the astrocytic line, causing approximately 50% of all glial tumors [1]. GMB could be treated by surgery, radiation or chemotherapy, but median survival is 9 to 14 months with a 5-year survival rate approximately 3% [5]. Bioactive compounds could be used to increase cancer cell sensitivity to chemotherapy. Naphthoquinones are compounds extensively used in studies due to their role in plants as chemicals for defense. Studies have shown that naphthoquinones such as menadione, plumbagin and lawsone have anti-cancer effects on GMB [2,3,4]. The aim of this study is to investigate and compare the results between different concentrations of plumbagin, menadione and lawsone effectiveness on rat glioblastoma cell culture C6 viability, and to assess their impact to the GBM cell proliferation. Methods: Cell viability was assessed by measuring their ability to metabolize MTT. Cell staining with Hoechst 33258 and Propidium iodide was used to investigate anti-proliferative effect. Results: Our results have shown that investigated naphthoquinones induced a dose-dependent reduction in viability of C6 cells. The EC_{50} values after 24 h were approximately 7.7 ± 0.28μM of plumbagin, 8.6 ± 0.75 μM of menadione and 1368 ± 280 μM of lawsone. Furthermore, incubation of cells with 3-4 μM of plumbagin and 4-6 μM of menadione after 48-72 hours reduced cell proliferation by 30,8-65,5%. Incubation of cells with 500–750 μM of lawsone reduced cell proliferation 50,1 – 95,7%. In conclusion, plumbagin and menadione showed similar anti-proliferative and cytotoxic effect on GMB C6 cells, effect of lawsone is approximately 15-fold lesser compared with other investigated naphthoquinones.

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POSTER SESSION

Social Pharmacy in Ukraine: problems and prospects

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According to the Basic Law – the Constitution of Ukraine, our country is a socially-oriented state where life, health and safety of citizens considered the main value. That is why the issues of social protection of the population, the creation of effective systems of the medical and pharmaceutical care are given permanent attention by public authorities and national science and education.

Evolutionary development of social thought today generates new social directions of development of science, including pharmacy, which implies the construction of a new terminological apparatus. If such terms as medicine, pharmacy, pharmacist, prescription, pharmacotherapy are known to virtually every educated person, the term «Social Pharmacy» raises questions not only from the ordinary person, but also from individual professionals who are not always clearly aware of its theoretical and practical importance. However, the term «Social Pharmacy» integrates all modern and perspective aspects of pharmaceuticals science and practice, their interaction with the living conditions and the environment, with a complex of social, psychological, ecological factors, because it defines the science of public health, its dependence on above factors and the complex of scientific based measures that can minimize the negative impact of unfavorable factors. Thus, Social Pharmacy concerns each and everyone in the health care system – doctors, pharmacists and patients.

As is well known pharmaceutical practice is viewed in close conjunction with the pharmaceutical education and science. Pharmaceutical education provides the necessary knowledge and skills, a request of which is put forward by practical pharmacy. Based on this, in the National Pharmaceutical University – a higher educational institution, which has more than 200-years history and occupies leading positions in the domestic and foreign pharmaceutical education and science – the first Department of Social Pharmacy in Ukraine was created in 2011. The main purpose of research in the Social Pharmacy is to study the issues of pharmaceutical practice and the various aspects of drugs' using with the actualization of its social component. In fact, Social Pharmacy is a hybrid sphere of research that applies the theories and methods from different social sciences, humanitarian disciplines to study all aspects of pharmaceutical practice. At present, question «How to build an effective system of health care and pharmaceutical provision?» remains open. A significant part of the answers we can get by using the directions that are considered by Social Pharmacy. The main ones include: the impact of legislation on the development of new drugs; the impact of new drugs on public health and the national economy in general; the effect of the level of training and availability of pharmacy specialists on public health; definition of the role of the pharmaceutical worker in society; patient compliance; the organization and the process of pharmaceutical care.

Taking into account the dynamic development of the national pharmacy in recent decades, we believe that the future of Social Pharmacy, its development, multidisciplinary and multisectoral nature are closely linked to the reform process in the socio-economic, political, cultural and educational life of Ukraine.

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Reimbursement the cost of medicines: Ukrainian experience

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Today, most European countries are characterized by an effective system of reimbursement the cost of medicines, as a mechanism to ensure the availability of pharmaceutical care and the rational use of budget resources and insurance. The term "reimbursement" was introduced by scientists of NUPh in the national scientific and practical terminology (2008), and is considered as a socio-economic system, aimed at ensuring the availability of medicines and pharmaceutical care in general. The reimbursement system is secreted subject - authorized state bodies carrying out compensation payments from certain sources of funding (state and local budgets), the object - certain groups of the population and group of patients who receive compensation for the purchase of medicines, and the mechanism for reimbursement.

Today in Ukraine is used compensation (benefit) cost of pharmaceutical care to certain categories of the population, namely free pharmaceutical care to inpatients; ambulatory preferential medicines ensuring to socially vulnerable groups, as well as patients socially dangerous and hard-occurring diseases, Pilot Projects. However, unfortunately, in the national health care system did not implement a unified system of reimbursement and drug pricing, the basic principles are been developed and recommended by the WHO and approved in European countries. For example, in 2012 the Pilot Project was launched to create a system of reimbursement of antihypertensive medicines, which included 10 international nonproprietary names of medicines and assumed level of compensation to 90%. At the same time these names were not correlated with an already existing system preferential drug provision, which has not led to significant changes in the availability of high-quality pharmaceutical care to the population.

However, based on its analysis introduction of the Pilot Project are defined as positive results and problem aspects. Positive results are the growth of motivation of patients to purchase precisely those medicines whose cost is compensated for by the state, reducing the retail prices of these medicines, increase their sales. The problematic issues, among which are: the need for the introduction of compulsory health insurance system, as the guarantor of an additional source of funding; introduction of the mechanism of differentiation compensation the cost of medicines to the population, depending on the criteria of reimbursement; improvement of mechanisms for reimbursement of the cost of medicines pharmacy institutions; the actual suspension of the Pilot Project in 2014 for an indefinite period.

Thus, taking into account the first experience of implementation reimbursement the cost of medicines in Ukraine on the example of the Pilot Project for the treatment of patients with hypertension, the major achievements of this project is, in our view, approbation of new legal organizational, financial and economic mechanisms, that directed at improving the efficiency and accessibility of medical and pharmaceutical care to the population during the transitional period of national health systems to medical insurance that will ensure the social protection of the interests of all citizens of Ukraine.

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POSTER SESSION

Content and composition of essential oil in oregano (*Origanum vulgare*) growing in Estonia

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Origanum vulgare ssp. *vulgare* (oregano, wild marjoram, Lamiaceae) as well-known medicinal and spice plant is the most commonly found oregano subspecies in Europe. Several chemotypes of oregano were found by lot of authors studied *O. vulgare* samples from different countries, three of them from Estonia (1).

The aim of the present paper was to analyze the content and composition of essential oil of *O. vulgare* samples (aerial parts without stems) growing or cultivated is Estonia, to study dynamics of principal compounds of essential oil during vegetation period and to find different chemotypes of oregano from Estonia.

Four samples of oregano were gathered from the same place in different vegetation period stages: leaf formation; leaves and buds; leaves and blooms; leaves and withered blooms. Five samples of oregano were collected from different areas in Estonia during full blooming and one sample was purchased from a retail pharmacy. The essential oil was isolated from dry aerial parts of oregano (n=10) by the hydrodistillation method described in the European Pharmacopoeia. GC analysis was carried out using a Chrom 5 chromatograph with FID on two fused silica capillary columns with bonded stationary phases (1).

The oil yield from oregano collected during full blooming was 0.26-0.79% on a dried weight basis. Regarding vegetation period of oregano, the minimum yield of oil (0.10%) was found in the sample of during leaf formation and maximum (0.51%) during full brooming, after flowering the content of essential oil decreased in some extent (0.47%).

GC analyses resulted to the identification of a total of 80 compounds, comprising 87-95% of the oils. In contrast, Estonian oregano contains plenty of sesquiterpenes and has caryophyllene oxide (4.3-20.7%), sabinene (3.5-14.7%), (Z)-β-ocimene (1.5-12.7%), and (E)-β-caryophyllene (2.7-11.8) chemotypes. Also β-myrcene (0.4-9.3%) and 1.8-cineole (1.2-7.4%) were present as principal constituents in some samples of oregano. The content of sabinene, 1.8-cineole, p-cymene, (Z)-β-ocimene, (E)-β-ocimene, (E)-β-caryophyllene, and increased during vegetation period from leaf formation to full blooming and decreased after flowering.

The Estonian oregano contains a very small amount of essential oil, as well as sum of thymol and carvacrol (0.25-2.75%), which is why none of the samples respond to the requirements of the European Pharmacopoeia (not less than 2.5% of oil and 60% of sum of thymol and carvacrol).

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Dragendorff's reagent from Tartu: background and using

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One of the characteristics of the University of Tartu (founded in 1632) is that here pharmacy became an independent discipline relatively early. It was separated from chemistry, and an independent professorship and Institute of Pharmacy were created on October 19, 1842. At that time a number of other Russian universities were still lacking such institution.

The development of pharmacy in Tartu was supported by several outstanding specialists of the field. The pharmacognostical collection of the University of Tartu was probably the largest in Europe in the end of the 19th century. A long-time professor G. Dragendorff (1864-1894) focused solely on pharmacy, pharmacognosy and forensic chemistry. Dragendorff's handbook-like works were published in several editions and in different languages. The best known textbook (1) written by Dragendorff was published in 1868-1895 in four volumes and described most important analyses in forensic chemistry, especially used in case of intoxication with alkaloids. 90 master's and 87 doctoral theses in pharmacy were defended in Tartu during the professorship of G. Dragendorff. It was quite usual that research and the writing of doctoral dissertations on fields bordering on pharmacy, predominantly in forensic chemistry. The key to the successful studies performed by Dragendorff and his students was the investigation and implementation of qualitative and quantitative analyze methods for alkaloids, glycosides as well as others biologically active substances.

The reagent developed and put into use by Dragendorff is well-known and widely used. Dragendorff`s reagent is a color reagent to detect alkaloids in a test sample. Alkaloids, if present in the solution of the sample, will react with Dragendorff`s reagent and produce an orange or orange red precipitate. Dragendorff`s reagent is a solution of potassium bismuth iodide prepared from basic bismuth nitrate (Bi(No3)3), tartaric acid, and potassium iodide (KI) of Dragendorff`s reagent was described for the first time in 1865-1866. Thus we can talk about a 150-year history practice of use (2,3).

Today Dragendorff's reagent utilization has expanded. For example, it is now also in use for processing of surfactants, where non-ionic surfactant is precipitated in agueous solution with modified Dragendorff`s reagent (KBiI4+BaCl2+glacial acetic acid). Dragendorrf's reagent has been modified in many ways. Some of these modifications are in use for the quantitative determination of certain chemical substances.

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Pharmacogenomics of warfarin: impact of clinical and genetic factors on warfarin dosage after heart valve surgery

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Introduction: Warfarin is one of the most widely used oral anticoagulants worldwide. It is prescribed after heart valve surgery to prevent thromboembolic complications. The dosage of this drug is non rarely complicated due to its narrow therapeutic window. The aim of this study was to show the impact of clinical and genetic factors on warfarin dosage during induction and long-term treatment.

Materials and methods: This study involved 91 patient who reached stable warfarin dosage (the therapeutic range of INR (from 2 to 3.5) was achieved and maintained for two days of treatment) during discharge from the hospital. Totally 72 patients, who used warfarin for at least 3 months, were included into the further study. Study involved 38 (52.8 %) men and 34 (47.2 %) women. DNA extraction, DNA quality assessment and real-time polymerase chain reaction (RT-PCR) were performed at the laboratory of Molecular Cardiology of LUHS.

Statistical analysis: Prevalence of genotypes is presented in % (percent). Warfarin dosage is presented as mean ±SD. A p value<0.05 was considered as significant.

Results: Men (60.7±12.8) were younger than women (67.2±9.2, p=0.01). Amiodarone non-users (87.5%) required lower warfarin dosages during long-term treatment (LTT) – (5.2±1.9 mg) than during discharge from the hospital - (6.1±2.8 mg, p=0.05). During hospitalization, 26 patients (36.1%) received amiodarone therapy. During LTT it was used by only 9 patients (12.5%). No significant effect on warfarin dosage was determined in carriers of CYP2C9*2, CYP2C9*3 and VKORC1 C1173T genotypes. The tendency in decrease of warfarin dosage was observed in patients, carrying CYP4F2 rs1558139 G/G genotype (from 6.3±2.9 mg to 4.9±2.0 mg, p=0,07). No other factors were identified to have an impact on daily warfarin dosage during induction and during LTT.

Conclusion: Data from this study revealed that daily warfarin dosage during LTT was significantly affected in amiodarone non-users. Novel polymorphism in gene CYP4F2 rs1558139 might determine stable warfarin dosage during LTT.

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Anticancer activity of 2,5-substituted thiazolidinone derivatives

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Thiazolidinones are five-membered ring heterocyclic compounds having sulphur atom at position 1 and nitrogen atom at position 3, meanwhile the carbonyl group can occupy positions 2, 4 or 5. Adding substituents to the structure affects the compounds properties and their biological activity [1,2,3]. Thiazolidinone derivatives have a broad spectrum of biological and pharmacological effects, including anticancer activity [4,5]. 4-thiazolidinone derivatives substituted with pyrazoline and benzothiazole at 2 position show high levels of anticancer activity [6].

The aim of our research was to evaluate anticancer activity, pharmacokinetic properties and toxicity of novel thiazolidinone derivatives substituted at positions 2 and 5. Structure of these compounds was confirmed by elemental analysis, ^{1}H NMR, IR and MS/MS. Purity was determined by HPLC/MS and was in the range of 93-99%. The cell growth inhibitory effects of compounds were tested using MTT assay on human lung carcinoma (A549), glioblastoma (U87) and melanoma (IGR39) cells. Apoptotic and necrotic effects were tested using Hoechst 33342 and Propidium iodide double staining. The toxicity and pharmacokinetic properties of the compounds were evaluated *in silico* using ACD/I-Lab software.

The results of *in vitro* screening showed that the compound with 4-nitro-1-naphthylamine had the highest anticancer activity ($GI_{50} < 10$ $\boldsymbol{\mu M}$). It was also found that compounds induced apoptosis in A549, U87 and IGR39 cells. Majority of compounds are expected to have medium or better oral bioavailability. The compounds are also presumed to possess low toxicity (LD_{50} in the range of 500–5000 mg/kg).

In conclusion, the study suggests that 2,5-substituted thiazolidinones could be developed as potential anticancer compounds.

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Anticancer activity of Filipendula ulmaria herbal liquid extracts

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According to the World Health Organization, cancer is one of the leading causes of death worldwide [1]. Usually chemotherapeutic drugs used to treat cancer are toxic both for cancer and normal cells, so it is very important to seek for more natural treatments, such as treatment with herbal preparations [2].

Meadowsweet (Lat. *Filipendula ulmaria*) is common plant growing wild in the north-eastern part of Europe. Its raw material contains has high amount of elagotannins, whose main ingredients are rugosin A and D, and telimagrandin I and II. Many studies demonstrate antitumor efficacy of tannins, as they may protect the cell wall from the adverse effects of environmental conditions [3]. Meadowsweet herb also contains flavonoids such as rutin, hyperoside, quercetin and spireoside. They show antithrombotic, antiviral, antibacterial, anticancer activity [4].

The aim of our research was to evaluate the anticancer activity Meadowsweet herbal liquid extracts. The object of research was Meadosweet herbal ethanolic extracts (1:10), made using ultrasonic extraction. Samples were collected from different Lithuanian regions. Cell growth inhibition was tested in vitro by tetrazolium/formazan assay on three selected human cancer cell lines: lung adenocarcinoma (A549), melanoma (IGR39) and glioblastoma (U87). Apoptotic and necrotic activity were tested using Hoechst 33342 and Propidium iodide double staining.

Nine out of ten tested Meadowsweet ethanolic extracts inhibited the growth of at least one cancer cell line at concentration lower than 10 mg/ml. Extracts possessed the highest activity against A549 cell line, and they did not affect the viability of U87 cells in tested concentrations. It was also found that majority of extracts induced apoptosis in A549, U87 and IGR39 cells, only two extracts induced necrosis.

This study suggests, that Meadowsweat ethanolic extracts possess anticancer activity and could be tested more thoroughly to determine the main constituents and their proportions required for such activity.

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Development and characterization of 1% naftifine hydrochloride medical nail lacquers

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Onychomycosis is a fungal infection of nails that causes thickening, discoloration and separation from the nail bed [1]. Nail lacquers are designed to enable extended release and create a reservoir of active substance in the infected nail plate [2].

The aim of the study: to investigate the quality (drying time, water resistance, permeability for

moisture and stability) of formulated medical nail lacquers, containing 1% naftifine hydrochloride.

Materials and methods. Twelve formulations of nail lacquer containing 1% (w/v) naftifine hydrochloride, Eudragit RL 100 and triacetin were developed. The formulations contain 96% ethanol, butyl acetate and ethyl acetate as solvents system. The time taken to dry was measured obtaining dry-to-touch condition. Water resistance of formed film had been evaluated for 7 days: glass slides with nail lacquer films were soaked into a water and visual film changes were considered every day. Structural changes of films were visualized by means of inverted microscope Olympus IX71 combined with LCAchN40xPH lens. Permeability for moisture was determined by storing formed film on the water bath at a fixed 37°C temperature for 24 hours. A ratio of evolved and adsorbed heat of developed formulations was determined by microcalorimetry. Mean values and standard deviations of the results were calculated using Microsoft Office Excel 2007 software.

Results. The drying time for the formulations with 0,5% plasticizer content was less than 60 seconds, and for those with 2% plasticizer content was 3-4 minutes. All developed formulations produced homogenous, smooth, glossy and transparent films. The most stable and resistant to water was formulation containing 13,6 % Eudragit RL and 2 % triacetin – film color changed just on 5th day of an experiment. Film containing 15,6% Eudragit RL and 2,1 % triacetin washed out after 1st day of an experiment, this result was apparent in structural changes – visible non-homogeneity was visualized. All lacquer films were permeable to water and formulations with lower plasticizer content were able to release humidity back to primary weight. Formulation containing 15,3% Eudragit RL and 0,5% triacetin content was the most stable to microcalorimetric heat changes.

Conclusions. The obtained results comply with the standarts for this type of dosage forms with regard to the drying time, water resistance, as well as film appearance. A ratio of film former and plasticizer impacts drying time, water resistance and permeability for moisture.

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