10th International Pharmaceutical Conference
„Science and Practice 2019”

ABSTRACT BOOK

November 15th, 2019
Kaunas, Lithuania
The 10th International Pharmaceutical Conference „Science and Practice 2019” is organized by Lithuanian University of Health Sciences, Faculty of Pharmacy.

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Mindaugas Liaudanskas, PhD
Zivile Pranskuniene, PhD
Indre Sveikauskaite, PhD

Dear participants and guests of the conference,

On behalf of the organizing committee and the Lithuanian University of Health Sciences, it's my great pleasure to welcome you to the 10th International Pharmaceutical Conference „Science and Practice 2019” in the Lithuanian University of Health Sciences, Faculty of Pharmacy! The 10th International Pharmaceutical Conference is dedicated to the 200th Anniversary of the first Pharmacy Association in Lithuania. From today's point of view, the history of Pharmacy helps to explore the broad scope of the pharmaceutical field, it stimulates a professional esprit de corps.

Pharmacists are medicine experts and have deep and long-lasting learning behind their knowledge base. It begins at the University and continues during all life, conducting relevant scientific research and efficient practical training. The 10th International Pharmaceutical Conference will give the opportunity to meet experts of different Pharmacy fields and from different European countries to exchange ideas and experiences and most of all, to develop professionally. The 10th International Pharmaceutical Conference scientific program will foster discussions and hopes to inspire participants to initiate collaborations within and across disciplines for the advancement of Pharmacy field.

I welcome you to the Lithuanian University of Health Sciences!

On behalf of the organizing and scientific committee,
Prof. Ramune Morkuniene
Dean of the Faculty of Pharmacy
Lithuanian University of Health Sciences
DEDICATION

Conference dedicated to the 200th anniversary of the first pharmacy association in Lithuania

In 1819, Vilnius pharmacists founded the Department of Pharmacy of the Vilnius Medical Society (established in 1805). This community set specific goals: to provide the public with high-quality medications, to prevent the falsification of medical products, and to search for new medicinal substances. The priorities included scientific research and the dissemination of scientific knowledge. The members of this pharmaceutical organization published a periodical journal “Pamietnik Farmaceutyczny Wileński” (“Notes of Vilnius Pharmacy”) during 1820-1822. Practicing pharmacists performed experiments in their laboratories and presented their results to colleagues in reports that were published in the press. The community of pharmacists subscribed to newspapers of European and Tsarist Russian pharmacists’ associations and relevant publications were translated and published in the local press.

After the rebellion of 1830–1831, the Tsarist government closed Vilnius University. The Academy of Medical Surgery was reorganized from the University. It existed for ten years but, in 1842, it was closed as well. This gradually led to the loss of scientific knowledge and diminished social activities. Pharmacists began to limit themselves to pharmaceutical practice and business interests.
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## PROGRAMME

**Friday, November 15th, 2019**

### 8.00–9.00 Registration

### 9:00–11.00 Plenary section I

**Chairmen:** Prof. Ramune Morkuniene, Dr. Ramunas Kondratas

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<td>9.00–9.10</td>
<td>Opening and Welcome Speeches of University Representatives and Guests.</td>
<td>Ramunas Kondratas, PhD, Vilnius University and Assoc. Prof. Vilma Gudiene, LUHS (Lithuania)</td>
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<td>9.10–9.35</td>
<td>The First Pharmacy Association in Lithuania.</td>
<td>Ramunas Kondratas, PhD, Vilnius University and Assoc. Prof. Vilma Gudiene, LUHS (Lithuania)</td>
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<td>9.35–10.00</td>
<td>The Botanical Explorer’s Legacy: a Promising Bioprospecting Tool.</td>
<td>Prof. Axel Helmstädtler, Frankfurt University (Germany)</td>
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<td>10.00–10.25</td>
<td>Patient-centered Care Challenges in Geriatrics: Multimorbidity and Polypharmacy.</td>
<td>Prof. Vita Lesauskaite, The Head of LUHS Geriatrics Clinic (Lithuania)</td>
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<td>10.25–10.50</td>
<td>Electronic decision support to prevent adverse drug reactions – focus on drug interactions.</td>
<td>Kari Laine, PhD, University of Turku (Finland)</td>
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### 11.20–13.20 Section Activities

- **History of Pharmacy**
  - Moderator: Ramunas Kondratas, PhD
- **Scientific Section**
  - Moderators: Prof. Lina Raudone, Assoc. Prof. Giedre Kasparaviciene
- **Pharmacy Novelties** (Lithuanian language)
  - Moderators: Prof. Valdas Jakstas, Prof. Liudas Ivanauskas
- **International Student’s Forum**
  - Moderators: Domas Urniezius, Skirmantas Rastenis

### 11.20–11.45 Pharmaceutial Regulation: Current Situation and Future Steps.

*Andzelika Oraite, Department of Pharmacy, Ministry of Health (Lithuania)*

### 11.45–12.10 Medical Devices – What Does a Pharmacist Need to Know?

*Jurate Svarcaite, Association of the European Self-Medication Industry, Director General (Belgium)*

### 12.10–12.35 Clinical Academic Pathway in Pharmacy: XXI Century Challenges.

*Vilius Savickas, PhDc, University of Kent (United Kingdom)*

### 12.35–13.00 Economic Evaluation in Health Care.

*Prof. Natasa Bogavac-Stanojevic, University of Belgrade (Serbia)*

### 13.00–13.20 Phytotherapy Approaches in Stress-related Disorders.

*Oana Cioanca, PhD, University of Medicine and Pharmacy "Grigore T Popa" (Romania)*

### 13.20–14.20 Lunch Break

### 14.20–16.20 Section Activities II

- **History of Pharmacy**
  - Moderator: Assoc. Prof. Vilma Gudiene
- **Scientific section**
  - Moderators: Prof. Lina Raudone, Assoc. Prof. Giedre Kasparaviciene

### 16.20–16.40 Coffee Break

### 16.40–17.00 Conference Final Remarks

*Prof. Ramune Morkuniene, Dean of Pharmacy Faculty, LUHS*

### 17.30–18.30 Excursion to The Museum of History of Medicine and Pharmacy

*(Rotuses sq. 28, Kaunas)*

*Organised bus trip from Conference Hall, Sukileliu av. 13, Kaunas*

### 19.00–23.00 Gala dinner („Senieji Rusiai“ Vilniaus str. 34, Kaunas)
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<td>11:20–11:40</td>
<td>Ramunas Kondratas, President of Lithuanian Society for the History of Pharmacy and Axel Helmstätder, President of the International Society for the History of Pharmacy</td>
<td>Moderator: Ramunas Kondratas</td>
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<td>11:40–12:00</td>
<td>Egle Sakalauskaitė-Juodeikiene (Vilnius University)</td>
<td>Treatment of Nervous System Diseases in the First Half of the 19th Century in the Vilnius University Clinics</td>
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<td>12:00–12:20</td>
<td>Birute Railiene (Wroblewski Library of the Lithuanian Academy of Sciences)</td>
<td>Disseminating the Scholarly Heritage of Vilnius University Professor Jedrzej Śniadecki (1768–1838)</td>
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<td>12:20–12:40</td>
<td>Tatsiana Zablotskaya (National Institute for Higher Education; Minsk, Belarus) – Vilnius University Professor of Pharmacy Johann Friedrich Wolfgang (1775–1859)</td>
<td>– A Disciple of the Schuchin Confessors Piarists</td>
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<td>12:40–13:00</td>
<td>Zivile Pranckuniene (Lithuanian University of the Health Sciences)</td>
<td>Ethnopharmaceutical Knowledge in the Samogitian Region of Lithuania: Where Old Traditions Overlap with Modern Medicine</td>
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<td>Michael Pohar (Riga Stradins University)</td>
<td>Beyond the Nobel Prize – Excellence in Medicine in the Baltics 1900–1970</td>
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<td>14:20–14:40</td>
<td>Junona Almonaitiene (Lithuanian University of the Health Sciences)</td>
<td>Transdisciplinarity in the History of the Human Sciences: What can the Geographical Dimension Tell about Recent Trends?</td>
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<td>Ain Raal (University of Tartu, Estonia)</td>
<td>– Non-governmental Pharmacy Organizations in Estonia</td>
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<td>15:00–15:20</td>
<td>Dusanka Krajnovic (University of Belgrade, Serbia)</td>
<td>– A Historical Outline of the Development of the Faculty of Pharmacy in Belgrade</td>
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<td>15:20–15:40</td>
<td>Valentina Sosonkina (Association of Pharmacists &quot;Pharmabel&quot;; Minsk, Belarus)</td>
<td>– Depictions in contemporary Belarusian art of the 18th-century David Sheiba pharmacy in Minsk</td>
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<td>Aistis Zalnora (Vilnius University)</td>
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<tr>
<td>16:40 – 17:00</td>
<td><strong>Conference Final Remarks</strong></td>
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<td>Ramune Morkuniene, Dean of Pharmacy Faculty, LUHS</td>
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<td>17:30 – 18:30</td>
<td><strong>Tour to the Museum of the History of Lithuanian Medicine and Pharmacy.</strong></td>
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<td>19:00 – 23:00</td>
<td><strong>Gala dinner at the restaurant “Senieji Rusiai”, Vilniaus St. 34</strong></td>
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PLENARY SECTION
The First Pharmacy Association in Lithuania

Ramunas Kondratas¹, Vilma Gudiene²*

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The first professional pharmacy organizations were organized in Lithuania in the beginning of the 19th century. In 1819, Vilnius pharmacists founded the Pharmacy Section of the Vilnius Medical Society (established in 1805). This section set specific goals: to provide the public with high-quality medications, to prevent the falsification of medical products, and to search for new medicinal substances. Their priorities included scientific research and the dissemination of scientific knowledge. The members of this pharmaceutical organization published a periodical journal Pamiętnik Farmaceutyczny Wileński (Notes of Vilnius Pharmacy) during 1820–1822.

Pharmacists who belonged to this section would perform tests and experiments in their laboratories, and report their results in their journal. They subscribed to European and Tsarist Russian pharmacy association newspapers and journals. Relevant articles were translated into Polish and re-published in their journal. Due to this communication, the most recent innovations in pharmacy quickly reached Vilnius pharmacists, and they applied them in their laboratories.

Notes of Vilnius Pharmacy contained about 47% original publications, the rest were translations from European pharmaceutical journals. The works of the most prominent European pharmacists and chemists, such as Johann Bartholomew Trommsdorff (1770–1837), Louis Nicolas Vauquelin (1763–1829), and Johann Wolfgang Döbereiner (1780–1849) were published in the journal. Scientific news would reach the subscribers of the journal rather quickly.

However, a progressive dynamic development of pharmaceutical science was hindered by unfavorable political and economic factors. Vilnius pharmacists had to stop the publication of their journal due to a lack of funds. After the Polish-Lithuanian Uprising of 1830–1831, the tsarist government closed Vilnius University in 1832. The medical faculty was kept open and transformed into the Vilnius Imperial Medical-Surgical Academy, which after ten years was also closed. The university and academy were the major training grounds for chemists and pharmacists in the very large Vilnius governorate.

Even before the closings, persecutions of university lecturers, students and the Vilnius intelligentsia by tsarist government officials and loyal university officials deterred progressive professors, physicians, and pharmacists from coming to Vilnius. Having no center of science, the scientific and social activity of pharmacists gradually became more passive. Fewer research reports were prepared and presented at their meetings by members of the Pharmacy Section of the Vilnius Medical Society. Nevertheless, the Vilnius pharmacists cared for the collections in the pharmacology cabinet, discussed ways in which future pharmacists could be trained, organized meetings, and prepared reports.
The botanical explorer’s legacy: a promising bioprospecting tool

Axel Helmstaedter

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Introduction: In recent years researchers followed several approaches to investigate historical sources in order to reveal traditional plant uses as a starting point for phytopharmaceutical research. Those include historical pharmacopoeias, early modern herbals, or writings of Christian missionaries working in South-America or East Asia. Publications, notes, diaries, letters and reports of exploring botanists of the 19th and early 20th century are considered here as a hitherto neglected class of historical sources of relevance for uncovering traditional uses of medicinal plants.

Materials and methods: The botanists were mainly interested in the discovery and classification of new species but also recorded medicinal uses. Comparison of these records with current scientific knowledge reveals considerable gaps, so there are plant species which are enthusiastically been described as useful but were never seriously investigated. Therefore, the historical sources were screened in order to find new active agents or lead compounds of plant origin.

Results: Berthold Seemann (1825–1871), Melville William Hilton-Simpson (1881–1938), and René Nebesky-Wojkowitz (1923–1959) are presented as examples. Seemann worked in South America and Polynesia, Hilton-Simpson explored Northern Africa, while Nebesky-Wojkowitz was an expert for Tibetan culture. All these explorers left notes, diaries, letters and publications which could systematically be screened for ethnopharmacological information. It turned out that they described medicinal plants not at all or just roughly investigated by modern phytopharmacology. Against this background, some concrete proposals for further investigation will be made. In a survey covering the works of Seemann, Hilton-Simpson and the British explorer Arthur Francis George Kerr (1877–1942), 103 species could be identified along with their traditional indications. In 36 cases (35%), this information could be confirmed in experimental pharmacological studies. Forty-nine species (47.6%) were found to be potentially useful for other indications, six (5.8%) were investigated phytochemically, but not pharmacologically, whereas 12 (11.7%) have not been investigated at all.

Conclusions: The explorer’s writings should not be neglected while looking for starting points for plant screening; success seems more likely than with screening at random.

References
Electronic decision supports to prevent adverse drug reactions –
focus on drug interactions

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Introduction: Adverse drug reactions constitute a major health hazard in the Western
countries today (1). Most adverse drug reactions (ADRs) are preventable.

Materials and methods: Proper decision support to prevent drug-related harm requires
evidence-based databases on the most important preventable causes of ADRs. The scientific data
need to formulated to clinically usable warnings and recommendations with clear classification
system to help the clinician or pharmacist in detection of the potential problem and to find
appropriate alternative treatment or monitoring options. In addition, these scientific data need to
be localised to each country, i.e. translated to the local language and mapped to the local (national)
drug registry so that the system is usable with local trade names of drugs. Finally, a good technical
integration to electronic health record systems and pharmacy dispensing IT systems or e.g. national
e-prescription system is required.

Results: Drug interactions and dosage guiding in renal failure are the most important
sources preventable drug harm. Especially, correct dosage modification in reduced renal function
is all too often neglected and this causes compromised drug safety (2). With drug interactions, one
needs to be selective on what to warn on. Pharmacodynamic interactions have in our system been
moved to a separate database to reduce alert fatigue, which is the most important cause of
neglecting the real time warnings on drug interactions. Other clinical areas where decision support
can improve safe and effective use of drugs include pregnancy and lactation, hepatic impairment
and cross allergies.

Conclusions: With good and transparent evidence based data, well-prepared localisation
and technical integration, the decision support tools can significantly reduce mortality, morbidity
and healthcare spending.

References
1. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-
2. Blix HS, Viktil KK, Moger TA, Reikvam A. Use of renal risk drugs in hospitalized patients with impaired
Medical devices – what does a pharmacist need to know?

Jurate Svarcaite

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7 avenue de Tervuren, B-1040 Brussels
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Medical devices, like medicines and other health technologies, are essential for patient care. With innovation and the rapid advancement of technologies, medical devices are currently one of the fastest growing industries. As well as dealing with medicinal products pharmacists are also involved in the sale and provision of numerous medical devices for use either by themselves or by other healthcare professionals. In addition, with more patients wanting to diagnose and manage their own medical conditions, purchases of medical devices directly from pharmacies are also being undertaken. The types of medical devices pharmacists encounter are diverse, ranging from glucose monitors and walking sticks to substance based medical devices for example simethicone. It is important therefore as part of our role in ensuring the safe and effective use of medical devices that we are also aware of the medical devices regulation and numerous factors we need to consider when recommending, selling or purchasing a medical device.
Clinical Academic Pathway in Pharmacy: XXI Century Challenges

Vilius Savickas*

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The introduction of the UK National Institute for Health Research (NIHR) programmes for allied healthcare professionals have broadened the options available to pharmacists and pharmacy technicians aspiring to pursue a clinical academic career. This session will explore the benefits and challenges of a modern clinical academic career pathway for pharmacy professionals in either primary or secondary care settings. We will review different routes of career progression from a foundation level to specialist clinical academic posts while showcasing the opportunities to remain at the “cutting-edge” of clinical practice. I will share my experience of the NIHR Research Training Fellowship and engagement in several clinical research projects, for instance the multinational WELCOME (Wearable Sensing and Smart Cloud Computing for Integrated Care to COPD Patients with Co-morbidities) initiative and the Pharmacists Detecting Atrial Fibrillation (PDAF) study delivered in UK general practice surgeries and care homes. Last but not least, we will aim to forecast the future of this branch of pharmacy in light of technological and professional evolution.
Economic evaluations in health care

Natasa Bogavac-Stanojevic

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Aging, increasing of chronic diseases prevalence, growing in costly innovative health technology along to other demands for expanded care continue to increase health care costs. Global health care expenditures are expected to rise at an annual rate of 5.4% from 2017 to 2022 (1). In such surroundings it is challenging to develop sustainable base for affordable, accessible and high-quality health care.

Traditional cost-effectiveness analysis (CEA) is a part of health technology assessment and it focuses on improvements in patient quality of life and cost savings within healthcare. A novel approach, value based healthcare (VBHC), focuses on costs reduction, improvement of patient’s outcome and quality of life (2). Although, there are many similarities between the two analyses they differ regarding their perspective and the types of costs and outcomes they consider. CEA considers costs and benefits from health care sector perspectives, whereas VBHC includes patient perspective (3). It has become important for all involved in patients care to perform detail analysis of standard practice and to take steps building more cost-efficient healthcare environment.

Predictive and preventative healthcare requires real-life information, a personalized approach to patients and construction of algorithms capable to recognize critical health factors what will result in appropriate interventions at the right time (4). The increasing availability of health data has made possible successful applications of artificial intelligence (AI) in healthcare. High-income countries start to integrate AI into their healthcare systems. Use of AI could result in approximately $150 billion healthcare costs reduction annually by 2026 in the USA (5).

Accordingly, AI could be applied for public health in resource-poor countries. Utilizing data from the electronic medical records physicians can use existing resources to shorten length of stay in hospital, to improve medical diagnosis and consequently to reduce hospital costs.

All of this enables promptness of medical decision. Achievement of these goals could be possible through integration of new medical and biochemical data which altogether should enables decision making and consequently improvement of individual outcomes and cost-effectiveness of care. On this way healthcare systems should provide reasonably priced, high-quality health care solutions for all patients.

References
Phytotherapy approaches in stress-related disorders

Oana Cioanca, Monica Hancianu
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*Corresponding author e-mail: oana.cioanca@gmail.com

Following the long history of herbal medicines, aromatherapy is currently recognized as part of pain management and rehabilitation of patients. Usually, such therapy involves volatile or essential oils. The volatile oils are complex mixtures of various classes of terpenes either oxygenated or not, which share the property to evaporate completely over time without any trace.

The most claimed properties of volatile oils include antibacterial and antiviral activity, relaxation, anxiety and nervousness relief, promotion of sleep, immunomodulatory, mood and mental enhancing potential. However, the mechanism and efficacy data are still controversial and relatively few. The fact that aromatic plants generally contain small quantities of volatile oil is a cause for expensive preparations and leads to frequent adulteration. There are many variables due to the quality of the volatile oil and the route of administration. Moreover, the in vivo studies and clinical trials are yet to provide diverse concepts and perspectives about how volatiles affect health.

There are several theories in regards to the binding and systemic effects of volatile compounds, some of which are quite popular among aromatherapy practitioners. The understanding of the mechanisms behind the detection of odours and how the brain reconstructs these signals into an information (smell) has greatly advanced during the past 20 years. For a better understanding, we aim to present the link between different theories and research with an emphasis on chemical composition of commonly used aromatic plants, based on our own experience with animal models.
HISTORY OF PHARMACY SECTION
Treatment of Nervous System Diseases in the First Half on the 19th Century in Vilnius University Clinics

Egle Sakalauskaite – Juodeikiene*

Vilnius University, Faculty of Medicine, Institute of Health Sciences, Centre for Medical Ethics, Law and History, M. K. Ėturlionio g. 21/27; Vilnius University Hospital Santaros clinics, Vilnius, Lithuania
*Corresponding author e-mail: egle.sakalauskaite-juodeikiene2@santa.lt

Introduction: The Faculty of Medicine in Vilnius University (VU) was founded in 1781, and special attention was paid to the promotion of natural sciences. By the early 19th century, VU had become the largest such institution in the Russian Empire, based on student numbers and university departments. The aim of the study is to reveal how nervous system (NS) diseases were treated in the first half of the 19th century in Vilnius clinics.

Materials and methods: We analysed 25 doctoral dissertations written in Latin on the subject of NS diseases and defended at VU. A historical–medical analysis and synthesis of primary sources, comparative analysis, analogy, and descriptive methods were used.

Results: Bloodletting, the use of purgatives, leeches, cupping therapy, and diet adjustments were frequently employed as treatment options for patients with apoplexy, myelitis, St. Vitus’ dance, epilepsy, encephalitis, tetanus, hydrophobia, and other NS diseases. Opium tincture was used as an analgesic and hypnotic; strict diet and liquids were recommended. Calomel (mercury chloride) was used as an anti–inflammatory drug. Peruvian bark (source of quinine) was prescribed as an anti–inflammatory drug for treating NS diseases and various fevers. In the cases of traumatic tetany and traumatic arachnoiditis, surgical wound treatment was recommended in order to stop the spreading of the inflammation. The use of acidum borussicum (hydrocyanic acid) in patients with hydrophobia represents an example of a desperate, ‘heroic’ medicine while treating a fatal illness. Sleep hygiene and lifestyle recommendations (e.g., maintaining a safe environment for sleep, avoiding long periods of sitting and sleeping during the daytime) were suggested for patients with sleep disorders.

Conclusions: Humoralism was the most popular system of medicine in the 19th-century Vilnius, therefore antiphlogistic treatment methods were widely used at the VU clinics.

References
Disseminating a scholarly heritage of Jedrzej Śniadecki (1768–1838),
a professor of Vilnius University

Dr. Birute Railiene*

Wroblewski Library of the Lithuanian Academy of Sciences
*Corresponding author e-mail: b.railiene@gmail.com

The paper will present a short history of initiatives to preserve and disseminate information about prof. Jedrzej Śniadecki (1678–1838), professor of chemistry and pharmacy at the old Vilnius University:

- Establishing an annual seminar *Lectiones Andreae Sniadecki*. First event was organised in 2012 by the representatives of the Lithuanian Association of History and Philosophy of Science and the Wroblewski Library of the Lithuanian Academy of Sciences; the event was organised in historical places, connected to the heritage of Jedrzej Śniadecki;
- Translating and publishing famous works by Jedrzej Śniadecki;
- Translating the most important work *Theory of Organic Beings* to Lithuanian (translated by Irena Katiliene) English (translated by Krzysztof Mazurek) languages was an attempt to present Jedrzej Śniadecki and his ideas of chemical processes in a living body to contemporary international scientific community, thus initiating the revision of chronology of ideas in life and environmental sciences in Europe;
- Establishing *Annual Fellowship of Jedrzej Śniadecki* (with a generosity of a company *Thermo Fisher Scientific Baltic*) to encourage the outstanding students of life sciences at the Vilnius University;
- Joining forces of specialists of life sciences of 19th ct. for a collective monograph on Jedrzej Śniadecki;
- Joining initiatives of neighbour countries (Belarus and Poland) to organise international conferences and studies of Jedrzej Śniadecki scholarly and literature heritage;
- Creating a Jedrzej Śniadecki website with a generosity of Ruta Baranauskiene and Rimvydas Baranauskas: https://andrewsniadecki.org/
The well-known professor of pharmacy at Vilnius university Jan Frideric Wolfgang – a disciple of the Schuchin confessors piarists

Tatsiana Zablotskaya*

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The monastery of the catholic order of piarists in the town of Schuchin in Lida district appeared in 1718. The confessors piarists started educational and enlightenment activities immediately after their arrival. The collegium of piarists in Schuchin was known for its rich library, botanical garden and pharmacy.

The monastery pharmacy was founded with its own expenses by the monk Ludwik Brennet (Ludwik Brennet 1738–1808). It can be noted for sure, that the pharmacy building was built in the third quarter of the 18th century. Some graduates of the piarists collegium became an assistant pharmacist and got a pharmaceutical education.

Jan Frideric Wolfgang (1776–1859) was the son of a doctor of medicine Jan Wolfgang from the Netherlands. The future scientist got his primary education at home, and later continued it at the educational institution of the order of piarists in the town of Schuchin in Lida district.

Wolfgang showed himself as a very diligent and hardworking student during his pharmaceutical practice. Therefore, having passed it, Brennet sent his pupil to the Main Vilnius School for a course in medical and natural sciences.

After having completed his studies on June 9, 1801, Wolfgang got the title of master of pharmacy and returned to Schuchin, where he began to manage the pharmacy of the piarists monastery. This work did not give him the full opportunity to show his skills. A year later, he accepted the offer to take the management of the pharmacy for minors Wagner and returned to Vilna.

He was appointed to the position of pharmacy manager at Vilnius University in 1804. Thus, he had the opportunity to engage not only in the preparation of medicines, but also to test his scientific assumptions. Wolfgang managed to show himself as a man with a deep knowledge of his field and with outstanding organizational skills. He became one of the co-founders of the Vilnius medical society of doctors in December 1805, which began to publish scientific works of the members of this society.

Wolfgang began to teach pharmacy as an auxiliary subject after receiving a doctorate in philosophy in 1807. But after the creation of the department of pharmacy and pharmacology in 1810, Wolfgang took its leadership as a professor. He remained in this position until the closing of the university in 1832.

From youth the instilled industriousness and interest in pharmacy in the Schuchin collegium helped J. F. Wolfgang to become an outstanding scientist in the field of pharmacy and pharmacology.
Ethnopharmaceutical knowledge in Samogitia region of Lithuania: where old traditions overlap with modern medicine

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Introduction: Modern ethnopharmaceutical studies are still quite unusual in Northern Europe. Data regarding the medicinal use of plants, animals, and fungi and also of spiritual rituals of healing is obtained mostly from ethnographic and folkloric sources in Lithuania [1,2]. We hypothesized that despite positive changes in modern medical assistance during last years, and despite increased accessibility to commercially produced remedies that can be purchased at pharmacies or recommended by qualified physicians, local inhabitants in villages still actively use traditional medicine.

Materials and methods: The study was performed in the central part of the Samogitia region located in the western part of the country, Telsiai County. Ethnopharmaceutical information was collected using semi-structured and structured interviews. The study sample was selected using a snowball technique. We tried to obtain as much information as possible by recording local names of plants, their preparation techniques, parts used, modes of administration and application for therapeutic purposes, use of single or mixture of plants for remedy preparation, dose requirement, and usable duration regarding each medicine. Information concerning other traditional remedies used in local folk medical practices was also collected. Materials of animal, mineral, and other origin were considered.

Results: The most popular plant preparations for use were tea and extract with alcohol. The most popular material of animal origin was Bufo bufo, and the most commonly used fungus was Phallus impudicus. The most popular mineral material in Samogitia traditional medicine was sand. Medicinal plants were the most frequently used for treatment of digestive tract disorders and disorders of respiratory tract. The Asteraceae family had the highest number of references. It was stated the most commonly used medicinal plants.

Conclusions: As modern medical assistance is quite expensive, self-medication with homemade medicines is still popular here. It shows how important it is to collect and systematize this information as soon as possible, to save this information as traditional Lithuanian heritage and also use it for scientific investigations.

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An ongoing research project at the Institute of History, Theory and Ethics of Medicine at the Heinrich Heine University Düsseldorf in Germany, led by Prof. Dr. Nils Hansson, analyzes the history of Nobel Prize nominees in medicine from several countries including the United States, Canada, Switzerland, Austria, and Germany. Together with the Latvian professors Prof. Dr. Juris Salaks and Prof. Dr. Ieva Libiete of Riga Stradins University in Latvia, Institute of the History of Medicine, the doctoral student Michael Pohar is going to analyze excellence in medicine in the Baltic Sea region. The prime focus is on the Baltic States and Germany during the first half of the 20th century. In that period German-Balt professors were very active at the University of Dorpat (now University of Tartu, Estonia). It includes Nobel Prize nominees, nominees of local medical awards and their winners, and it screens and critically discusses the process of enacting excellence in medicine at that time. Also, it emphasizes trends for nomination in the Baltics and evaluates the prizes for excellence in medicine from the distance of time.

As a part of the research, the history of modern pharmacology is analyzed. Therefore, its history is refurbished and all Nobel Prize Nominations in the category Physiology or Medicine for pharmacologists are evaluated. Likewise, single researchers like professor Oswald Schmiedeberg (1838-1921) from the Baltics, who implemented the “modern pharmacology” as a permanent subject area in medical studies are highlighted. At the same time, the spread of modern pharmacology, as well as its current influence, are emphasized.
Transdisciplinarity in the history of human sciences:
What the geographical dimension can tell about recent trends?

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Interdisciplinarity seems to be encouraged in many fields, including health care and human sciences, as a methodology and as a practice. On the other hand, many of those working interdisciplinarily complain about lack of understanding in institutions, difficulties in accessing funding, etc. Transdisciplinarity – integration of the natural, social and health sciences in a humanities context, may be even more inspiring, yet, even more “risky”. It seems reasonable to start depicting the situation from various perspectives, relying on credible data. Aiming this, participation of academics in the conferences of the European Society for the History of Human Sciences (ESHHS) during past 5 years was analysed focusing on physical geography (institutions) and intellectual geography (main themes). The purpose of the ESHHS is “to promote international, multidisciplinary cooperation in scholarly activity and research in the history of the human sciences”, and transdisciplinarity is characteristic to its conferences. The research problem of the paper presented here was defined as participation in the conferences of academics from the Baltic States and neighbouring countries, and the themes of their presentations. The materials – books of abstracts of the annual conferences of the Society – were assessed quantitatively and qualitatively. The results showed infrequent and scarce participation of the target subjects, representing Lithuania and psychology in most cases, which invites to further discussions.

References:
Non-governmental pharmacy organisations in Estonia

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The oldest pharmacy organisation in Estonia was the Society of Pharmacy Students of Dorpat (*Verein Studierender Pharmazeuten zu Dorpat*, 1872), established by German students. The students from Latvia and Poland organised their societies soon after that (*Lettgallia* in 1899 and *Lehicija* in 1908), Estonian students registered their academic organisation (*korp! Fratenitas Liviensis*) in 1918.

The Estonian Pharmacists’ Association (*Eesti Apteekrite Selts*) and Union of Estonian Pharmacists (*Eesti Farmatsöitide Ühisus*) were established after declaration of independence of the Republic of Estonia in 1918, the first one was the organisation of owners and second for employees of retail pharmacies, both had their professional journals (*Pharmacia* (1921-1940) and *Eesti Rohuteadlane* (Estonian Pharmacist, 1926-1940, 1990…), respectively.

The oldest umbrella organisation with the greatest number of members is the Society of Estonian Pharmacists (*Eesti Farmaatsia Selts*, 1950) founded in the Stalinist period and was first called a scientific society.

During the privatisation of pharmacies in the beginning of the 1990s, the Estonian Pharmacists’ Association uniting owners and/or managers of pharmacies was founded (*Eesti Apteekide Liit*, 1993). The relatively younger pharmacists have joined the Chamber of Estonian Pharmacists (*Eesti Proviisorite Koda*, 1997). Pharmacists working in hospital pharmacies are pursuing their aims through the Estonian Society of Hospital Pharmacists (*Eesti Haiglaapteekrite Selts*, 1995). Assistant pharmacists with a special secondary education have formed the Association of Estonian Assistants of Pharmacists (*Eesti Farmatseutide Liit*, 1999). Retired pharmacists are organised into the Senior Pharmacists’ Assembly (*Vanemate Rohuteadlaste Kogu*, 1997). The Tartu University Society of Pharmacy (*Tartu Ülikooli Rohuteaduse Selts*, 1990) joins the students of pharmacy and some of the teaching staff, and the Estonian Academic Society of Pharmacy (*Eesti Akadeemiline Farmaatsia Selts*, 2006) joins mainly the academic staff of the Institute of Pharmacy at the University of Tartu.

There are also six business-related pharmacy organisations in Estonia.
A historical outline of the development of the faculty of pharmacy in Belgrade

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Eighty years of historical development of the Faculty of Pharmacy at the University of Belgrade will be presented with the aim to analyze (I) the circumstances that influenced the establishment of the Faculty and its departments and (II) the development of the scientific disciplines and curricula.

At the beginning of the 1830s, pharmaceutical staff in Serbia consisted of graduate pharmacists from outside, such as Serbs from Vojvodina, Croats, Checks, Slovaecs and others. Later came domestic stuff educated in Vienna, Budapest, Prague, Gratz, Zagreb. The official proposal regarding the establishment of the Pharmaceutical Department at the Great School in Belgrade gave the Apothecary Society as early as 1896, but this effort was in vain, as preceded the activities in 1904, 1920, 1930 and 1937. The Pharmaceutical Department of the Faculty of Medicine in Belgrade was established in October 24th, 1939. Afterwards, the Pharmaceutical Department outgrew into the Faculty of Pharmacy in October 19th, 1945. In the last eight decades, the key roll in teaching and scientific activities at the Faculty of Pharmacy had the institutes that were later reorganised into departments. Many social changes when the Faculty worked on developing its teaching stuff also produced significant organisational reforms. Also, there were very important reorganisations of regime and study as well as those referred to the professional titles of graduate pharmacy students. Since the Faculty’s foundation until today the master diploma acquired 13440 students, while the academic and health specializations completed more than 2700 candidates. At the Faculty were defended 423 doctoral theses and 295 master of science theses. Scientific and research activities within the projects supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia were strengthened in the last decade of the Faculty development through bilateral and other international projects with foreign institutions and researchers. The Faculty of Pharmacy in Belgrade outshines with a few international projects carried out by itself. These projects are very significant for the development of integrated and postgraduate education of pharmacists in Serbia.
The image of pharmacy of David Sheiba in Minsk (XVIII c.) in Belarusian art works

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The 1st pharmacy in Minsk was created in 1748. The opening of the 1st pharmacy was permitted by the Privilege of The Polish-Lithuanian Commonwealth King Sigismund III Augustus (November, 28th, 1748). The king allowed the pharmacist and the member of Magistrate Yan David Sheiba to open it. It catered for clergymen and men of the world, and also people who arrived at the Tribunal in Minsk. The pharmacy was exempt from taxes and the opening of other pharmacies in town was prohibited.

In Belarussian archives there are very few documents about the work of Sheiba’s pharmacy. But the remaining information rouse not only historians’ interest, but also figures from the world of the arts.

Famous Belarussian writer Lyudmila Rublevskaya in her works of fiction described the history of Old pharmacy in Minsk: «Жених панны Дануси» (Minsk, 2012), and «Ночы на плябанскiх млынах» (Minsk, 2013). The protagonist is a pharmacist Joseph, a clever and common herbalist, studied in Prague and Sorbonne, who made miraculous medicines even for the King Sigismund III Augustus. It’s about Joseph’s hidden love for Yugasya, the great beauty of Minsk and the town councilor of Magistrate’s daughter. Unhappy love and excellent skills led to the tragic fate - life imprisonment in a town prison. According the order of Zavish, Minsk Magistrate, who was also in love with Yugasya, he made the medicine for immortality instead of medicine for rejuvenation. The medicine for immortality took away the youth, but gave an eternal life.

A Minsk artist, a member of Belarusian union of designers Lydia Lozovskaya depicted a pharmacist Joseph on one of her paintings. While painting she used Lyudmila Rublevskaya’s books and the information from the Internet about European pharmacies of that time. In the public pharmacy in Minsk (Trinity Suburb) visitors can buy souvenirs with the image of Joseph.

On 29th November, 2018 in Mikhail Savitskiy art gallery (Minsk) the presentation of cultural educational project “The history of pharmacy practice in Minsk”, in commemoration of the opening of the 1st pharmacy of Sheiba was held. The event was attended by pharmacists, historians, writers, poets and artists.
The occupational poisoning issues in the works of Vilnius Stephen Bathory University doctors and hygienists

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Introduction: The research on the occupational health issues that were carried by Vilnius Stephen Bathory University scientists were one of the most innovative of that time in Vilnius region and Poland. One of the fields of interest of the hygienist Kazimierz Karaffa-Korbutt (1878-1935) as well as a doctor, pathologist and toxicologist Sergiusz Leopold Schilling-Siengalewicz (1886-1951) was occupational poisoning.

Materials and methods: Our research is based on a primary and secondary historical sources which are being preserved in Vilnius university library as well as Lithuanian Central State Archives.

Results: Our research revealed the definition, causes and mechanisms of the occupational poisoning which were discussed in a scientific discourse of the interwar practitioners and hygienists.

Conclusions: The mechanisms and interpretations of the occupational poisoning which have been debated by the Stephen Bathory University’s scientists are relevant as a monument of the interwar toxicology as well as occupational hygiene.

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Large inspections of pharmacies in Belgrade and the newly liberated parts of Serbia since the late 19th century

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Introduction: After the liberation and annexation of four counties with a population of 300,000 to the Principality of Serbia, in 1878 a cultural, economic and social upheaval took place in the country. A fundamental transformation of health policy was also under way. This paper is purposed to show the impact of the inspection of the quality of work in pharmacies on health policy development in Serbia at the end of the 19th century.

Materials and methods: The paper is based on the historical method and the documentary analysis of primary and secondary data sources.

Results: In 1881, a new Law on Health Care and Public Health Protection came into force, due to public pharmacies were under the supreme control of the minister of internal affairs (1,2). Ten years after the annexation of the newly liberated regions of Serbia, in March 1888, the first quality control reviewed six existing pharmacies in Belgrade. The inspection included as follows: the facility where the pharmacy was located, the pharmacy premises, the equipment and medicines whose quality had to comply with the regulations of the current pharmacopoeia. All expired drugs and illicit raw materials were immediately discarded. In 1889, ten pharmacies were inspected in eight cities that included newly liberated parts of Serbia. In 1892, nine pharmacies in five cities were inspected, while in 1894, thirteen pharmacies were inspected in ten cities. The inspection of pharmacies included the control of premises, equipment and apothecary work and services. The largest number of pharmacies fully met the requirements in terms of staff, equipment and space. A small number of irregularities were noted by pharmacists who had to correct them immediately or within a short time limit.

Conclusions: The results of the research indicate that the founders of the first pharmacies in all corners of Serbia operated in pharmaceutical care highly professionally in accordance with the legal regulations of that time and endeavoured to contribute to public health enhancement and strengthening medical profession.

References

Acknowledgment: The work of DK is carried out under the Project funded by the Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant Number 41004.
Lithuanian delegation at the third pharmaceutical congress (1899-1900)

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Due to the development of the pharmaceutical industry, a pharmaceutical class was formed in Russia, which sought to consolidate itself on a professional basis. In 1803, a Chemical and Pharmaceutical Society was founded in Riga, in 1818 the St. Petersburg Pharmaceutical Society and in 1819 Vilnius Society of Pharmacists were founded, and later in Moscow, Kiev, Warsaw, Odessa and other major cities. The St. Petersburg and Moscow Societies initiated a series of pharmaceutical congresses. One of them, the Third All-Russian Pharmaceutical Congress, opened on December 30, 1899 in the assembly hall of Moscow University. The Congress lasted 7 days.

The geography of the “pharmaceutical family” that came together for the convention was very extensive. Transferred to the modern world map, there were delegates from Russia (245), Ukraine (58), Belarus (11), Lithuania (11), Latvia (11), Poland (9), Georgia (7), Estonia (6), etc. An Album of the delegates from the congress, which lists the names of at least 370 participants, is kept in the Russian Medical Museum of the National Research Institute of Public Health named after N.I. Semashko (Moscow).

The program of the congress included the following current issues: scientific reports on pharmacy and pharmacognosy, raising the prestige of the pharmaceutical profession, improving pharmaceutical education, and improving organization of pharmacy in the country.

The peculiarity of this congress was the participation in congress (for the first time) of two warring parties: pharmacy owners and employees. The meetings on class questions about improving the life of employees, reducing working hours, destroying pensions in pharmacies, and expanding the rights of pharmacists were especially lively.

At the congress there was also a report by the Vilna pharmaceutical employees on the theme “The decline of pharmacy: the reasons that caused it, and the measures that could be taken to eliminate it”.

The following pharmacists represented the Lithuanian delegation: I.V. Broyt, T.G. Kinkulkkin, E.I. Maruhes, E.Yu. Tromshchinsky (Vilno); M.I. Wolf, G.W. Segal, S.G. Eliashevich; M.A. (Kovno); Gurvich (Shavli) and A.L. Lipshitz (Kurshany of Shavlensky district); BY. Bulavski (Verzhbolovo); Magister of Pharmacy V.V. Grüning (Palangen).
PhD STUDENTS SECTION
The study of biologically active substances and standardization of thick extract of the feverfew herb

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Introduction: The search of the new plant sources of biologically active substances is an actual issue of the pharmaceutical science. Herbal medicines occupy approximately 30% of the global pharmaceutical market and their part will increase in the future. Plants with significant raw material base and successful experience in folk medicine are interesting for science. [1]. Feverfew (Tanacetum parthenium (L.) Schultz Bip.) is one of the representatives. We have established the chemical content and technological characteristics of the feverfew herb before. As a result of the study it was identified that phenolic compounds, such as hydroxycinnamic acids and flavonoids are contained in large quantities in the raw material. So the aim of this research was creating of the thick extract of the feverfew herb, the study of its chemical content and standardization

Materials and methods: The object of the study was herb maize grass. The extract was obtained by percolation with a following evaporation using a vacuum-evaporating apparatus. The qualitative composition and quantitative content of phenolic compounds were investigated by thin layer chromatography (TLC) and spectroscopy using unified methods of the State Pharmacopoeia of Ukraine (SPhU). The general articles of SPhU to determine the dry residue, weight loss on drying, heavy metals content were used [2].

Results: A thick extract of the feverfew herb using 70 % ethanol was obtained. As a result of the extract chromatographic profile analysis the zones at the level of chlorogenic and chicoric acids, luteolin, luteolin-7-glycoside and santine in comparison with the zones of standards were identified. The content of hydroxycinnamic acids was 12.75 %, flavonoids – 5.16 %, respectively. The obtained extract is a thick, viscous mass of a dark brown color with a characteristic specific odor. The extract was well soluble in water, ethanol, slightly soluble in methanol, practically insoluble in chloroform. The dry residue was 93.4 %, weight loss on drying – 8.4 %.

Conclusions: As a result of the study, a standardized thick extract of the feverfew herb was obtained. Analysis of the qualitative composition of the biologically active substances of the extract showed the presence of phenolic compounds. The content of hydroxycinnamic acids was 12.75%, flavonoids – 5.16%. The thick extract meets the requirements of the State Pharmacopoeia of Ukraine on indicators such as solubility, dry residue, weight loss on drying and heavy metals content, which makes it prospective in further pharmacological studies.

References
Development bases of suppositories for treatment anorectal diseases

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Introduction: The presence of inflammatory processes in the rectum lead to changes in biopharmaceutical parameters due to the destruction of capillaries of the mucous membrane. One of the steps in the pharmaceutical development of rectal dosage forms is the selection of a base, which is a significant factor in creating the required pharmacological effect at the site of the drug. It was established that suppository bases of diphilic type provide better release of active substances, have the necessary technological parameters (homogeneity, time of full deformation, solubility) and better bioavailability. According to previous studies, we have selected a complex of bioflavonoids as active substances [1].

Materials and methods: We used samples of suppositories as the objects of study, which consists the following substances: Witepsol (№1-3), Witepsol with the addition of HPMC (№4-6), Witepsol with the addition of sodium alginate (№7-9) in various ratio, emulsifier Lanette SX, the content of the water phase ranged from 20% (№ 1,4,7) to 40% (№ 3,6,9).

Results: According to the results of the study, it was found that the minimum hardness is observed in samples №4-6, maximum - in samples №1, №7-9. The results of pharmaco-technological studies, depending on the content of the water phase showed that it is rational to add the water phase in the amount of 30%. The microscopic method was found that the best distribution of the complex of bioflavonoids observed in the samples with sodium alginate.

Conclusions: The conducted researches show expediency of addition of sodium alginate in the composition of suppositories with the amount of water phase of 30%, which will contribute to the formation of a stable system with the necessary technological parameters.

Reference
Necessity of the control methods development for the starting raw materials of Amizone synthesis in the working zone and atmospheric air

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Introduction: Pharmaceutical manufacturing is characterized by usage of different types of chemical raw materials, the variety of intermediate products of the synthesis of medicines, the multi-stage and intermittent nature of technological processes, the imperfection in some cases of technological schemes, which can lead to significant emissions of harmful substances into the air of the working area and atmosphere. Therefore, hygienic standards and methods for the analytical determination of the content of harmful substances in the air of the working area and environmental objects should be developed at the pharmaceutical enterprises, taking into account hygienic criteria to justify the development of methods for monitoring the maximum permissible concentrations (MPC) of harmful substances.

Materials and methods: Existing methods and approaches to measuring the MPC of harmful substances, as well as approaches to normalization of their content in the working area air of pharmaceutical enterprises and atmospheric air were studied by analyzing literature and Internet sources.

Results: Analysis of literary sources showed that a large number of different analysis methods are used to measure the MPC of harmful substances in the working area and atmospheric air. However, today there is no single approach to standardization and measurement of MPC in the air, each country and manufacturer are forced to develop their own approaches.

For Ukraine, the development of modern methods of determining the MPC of harmful substances in the working area and atmospheric air it is highly relevant due to the constant increase in production technologies and the need for harmonization of the national approaches with the European requirements.

Amizone relates to the preparation of large-scale production and consumption in Ukraine. Benzylamine and iodomethane, which belong to hazard class 2, are the starting raw materials for the Amizone synthesis. The toxicity of the above substances requires the development of control methods in the working area and atmospheric air. The problems of controlling pollutants cannot be considered within one particular country, since pollutants are spread everywhere due to air circulation.

Conclusions: Based on the analysis of literary sources, the development of methods for measuring the MPC of harmful substances in the air of the working area of pharmaceutical enterprises and atmosphere is very relevant.

References
Carbonic anhydrase IX/XII inhibitors enhance doxorubicin delivery into 2D breast cancer cell cultures at acidic pH

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Introduction: Carbonic anhydrase (CA) is a transmembrane enzyme complex which catalyses the reversible hydration of carbon dioxide to bicarbonate, thus increasing extracellular acidity [1]. Two of the isoforms – CA IX and CA XII – gene expression is highly increased in many types of tumors. Increased extracellular acidity of tumor causes basic drugs ionization, therefore, the penetration of these compounds declines and their therapeutic efficacy decreases [2]. It is hypothesized that the inhibition of CA IX and XII reduces extracellular acidity, thus preventing weakly basic drugs from ionisation and enhancing their delivery into tumor [3]. The aim of our study was to evaluate the influence of two CA IX and XII inhibitors methazolamide and U-104 on doxorubicin (DOX) delivery into monolayer-cultured cancer cells at pH 6.0 and 7.4.

Materials and methods: Experiments were performed on 4T1 murine breast cancer cell line. The effect of CA inhibitors on cell viability was evaluated by MTT assay. DOX penetration into cancer cells was assessed using fluorescence microscopy. All the experiments were done in at least triplicate independent measurements. Student’s t-test was used, and p-values were calculated. A value of p<0.05 was considered as the level of significance.

Results: Both tested compounds did not decrease the viability of 4T1 cells at 100 μM and lower concentrations, therefore in further experiments 100 μM CA inhibitors were used. At physiological pH both methazolamide and U-104 did not enhance DOX (5 μM) delivery in cells. In acidic conditions methazolamide increased DOX delivery into cell nucleus by approximately 1.4-1.7-fold after 2 and 4 hours of incubation. U-104 increased DOX delivery into cell nucleus by approximately 1.3-1.7-fold at the time period from 30 min to 4 hours.

Conclusions: Both methazolamide and U-104 increase DOX penetration into monolayer-cultured cells at acidic pH and are worth further studies as transport modulators of weakly basic drugs.

Acknowledgement: The research was supported by Science Foundation of Lithuanian University of Health Sciences project "Application of carbonic anhydrase IX and sodium–proton exchanger inhibitors to improve doxorubicin and its pegylated formulation delivery in 2D and 3D cell cultures", 2019.

References
Qualitative and quantitative analysis of phenolic compounds in lingonberry leaves within cultivars and lower taxa

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Introduction: The wide spectrum of various biological properties of lingonberry (Vaccinium vitis-idaea L.) leaves is related to their phenolic constituents [1,2]. Genetic background of plants determines production of phenolic compounds, therefore genetic diversity may cause wide variations even within a single species [3]. The identification of phenolic profile among cultivated lingonberries is important in chemotaxonomical aspect and for determination of most promising cultivars. This study was carried out to determine phenolic composition of cultivated lingonberry leaves.

Materials and methods: We have chosen to analyze ten different cultivars (‘Sussi’, ‘Sanna’, ‘Erntekrone’, ‘Erntesegen’, ‘Erntedank’, ‘Masovia’, ‘Koralle’, ‘Kostromskaja rozovaja’, ‘Rubin’, ‘Kostromička’), one subspecies (V. vitis-idaea subsp. minus) and one variety (V. vitis-idaea var. leucocarpum) of lingonberries. Phenolic composition of lingonberry leaves were determined by HPLC-PDA method, using ACE C18 reversed phase column in the solvent system with 0.1% trifluoracetic acid and acetonitrile under gradient elution.

Results: Eleven phenolics, belonging to subgroups of simple phenols, flavonols, flavanols, proanthocyanidins and hydroxycinnamic acids were detected in cultivated lingonberries. Arbutin was the most abundant phenolic compound and contributed approximately 41–78% of the total phenolics in different cultivars and lower taxa of lingonberries. Furthermore, considerable amounts of flavonol glycosides and procyanidins C1 and A2 were found. Cultivars ‘Rubin’, ‘Kostromskaja rozovaja’ and Vaccinium vitis-idaea var. leucocarpum surpassed all others cultivated lingonberries by contents of phenolic compounds. The cluster analysis has separated investigated lingonberry cultivars and lower taxa into three statistically significant clusters. The predominant phenolic markers in German cultivars (‘Erntekrone’, ‘Erntesegen’, ‘Erntedank’) were hyperoside and quercitrin, while in the Russian cultivars (‘Rubin’, ‘Kostromička’)—procyanidins C1 and A2.

Conclusions: Lingonberry leaves could be a promising source of phenolic compounds. There is a wide genetic diversity for phenolic composition of lingonberry leaves and phenolic profile is related to the countries of origin of cultivars and lower taxa.

References
Introduction of *Artemisia pontica* L. and phytochemical analysis of volatile compounds in Lithuania

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**Introduction:** The introduction of medicinal, spice (aromatic) plants and the study of the biological and chemical properties of introduced plants increase the diversity of plant species with pharmacological action [3]. There are scarce literature data about the composition of *Artemisia pontica* L. essential oils. It has been determined that *A. pontica* growing in different continents is dominated mostly by the monoterpene fraction [2,4]. The aim of this study was to investigate qualitative composition of essential oils of *Artemisia pontica* L. At present, there no data on the essential oil composition of *A. pontica* in Lithuania.

**Materials and methods:** The object of investigation was *Artemisia pontica* L. a perennial medicinal, aromatic plant of *Asteraceae* (Bercht. & J. Presl) family. Raw material of *A. pontica* was collected in Medicinal plants collection *ex situ* of Botanical Garden at Vytautas Magnus University in 2018.

The essential oils have been extracted by hydrodistillation method and analysed by the chromatographic techniques in the gas phase and chromatography in gas phase coupled with mass spectrometry (GC/MS) so as to determine their chemical composition and identify their chemotype. The percentage composition of the essential oils was computed from GC peak areas without correction factors. Qualitative analysis was based on a comparison of retention times, indexes and mass spectra with the corresponding data in the literature [1] and computer mass spectra libraries.

**Results:** In the composition of the essential oil of *Artemisia pontica* L. 33 substances were identified. Principal compounds were found to be 1,4-cineole (37.92%), camphor (29.41%), endo-borneol (8.21%), 4-thujanol (5.24%), isogermacrene D (2.71%), β-phellandrene (2.14%), aromandendrene (0.91%).

**Conclusions:** The data showed that the amounts of compounds with the content of major constituents varied significantly. Most of these constituents dominated in *Artemisia pontica* L. essential oils in other countries, however, there no data in the literature on the prevalence of 4-thujanol, isogermacrene D, β-phellandrene, aromandendrene in *A. pontica* essential oils.

**References**

Estimation of Phenolic Compounds Amounts from *Elsholtzia ciliata* Ethanolic Extracts obtained from Various Plant Parts

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**Introduction:** Polyphenols of medicinal plants, have become an emerging field of interest in nutrition, prevention, and treatment in recent decades. *Elsholtzia ciliata* – an annual plant belonging to *Lamiaceae* family is widely distributed throughout China, Korea, and Europe and used for prevention and treatment. The aim of our study was to analyze and compare phenolic compounds amounts obtained from different *E. ciliata* plant parts.

**Materials and methods:** Ethanolic extracts obtained from dried *E. ciliata* herb. Powdered material of dried *E. ciliata* plant parts (each for 1 g) were extracted with 20 mL of 70% (v/v) (1:20) ethanol in a round bottom flask by using ultrasound-assisted extraction at 25 °C for 30 min. The samples were centrifuged and filtered before HPLC analysis.

The spectrophotometric measurements were carried out with a UV/VIS 1800 Shimadzu spectrophotometer (Shimadzu, Japan). The total phenolic contents (TPC) in *E. ciliata* extracts were determined using the Folin-Ciocalteu method. The colorimetric aluminum chloride method with some modifications was used for quantification of the total flavonoid content (TFC) of the ethanolic extracts.

**Results:** The TPC in extracts obtained from dried plant parts ranged from 61.25±1.91 to 94.67±1.91 mg GAE/g DW. The amount of phenolics is statistically significantly higher in the whole herb (94.67±1.91 mg GAE/g DW), leaves (89.55±3.91 mg GAE/g DW) and flowers (77.39±0.94 mg GAE/g DW) extracts than stems (61.25±1.91 mg GAE/g DW) extract (p < 0.05). The TFC was ranged from 5.06±0.08 to 15.43±1.86 mg RE/g DW. The highest flavonoid levels have been obtained in whole herb (15.43±1.86 mg RE/g DW), flowers (14.22±0.67 mg RE/g DW) and leaves (14.16±0.65 mg RE/g DW) extracts.

**Conclusions:** Our study shows that there are differences between *E. ciliata* plant parts according to TPC and TFC amounts. *E. ciliata* herb is a rich source of biologically active substances – polyphenols.
Determination of amino acids profile in leaves of *Hedera helix* L. collected from different European countries using gas chromatography-mass-spectrometry (GC-MS)

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Introduction: Amino acids are vital components and play an important role in biochemical process of human body such as building protein or synthesis of hormones *Hedera Helix* L. (common ivy) is a well-known plant, which grows in different European countries as well as in some parts of North America and Asia. Thus, different regions have various environmental factors may affect to profile of amino acids. The aim of this study was to determine main compositions of amino acids are inherent to ivy leaf.

Materials and methods: Ivy leaves were collected from different regions of Europe. The powdered herbal material (0.5 g) was weighed into a 10.0 ml volumetric flask with methanol and sonicated for 15 minutes on the ultrasonic bath. 1.0 ml of solution was evaporated to dryness under a stream of nitrogen. After evaporation, 100.0 μl of acetonitrile and 100.0 μl of MBTFS derivatization reagent were added and then heated 2.5 h at 120°C in glycerol bath. Derivatized product was carried out with SHIMADZU GC-MS-QP2010 Ultra chromatography system with RXI-5ms (Restek Corporation) capillary column (30 m long, with 0.25 mm outer diameter and 0.25 μm liquid-stationary phase thickness) with a liquid stationary phase (5% diphenyl and 95% polysiloxane), as carrier gas of chromatography we used helium. The column temperature was set by 75°C. Column flow rate 1.5 ml/min. The initial temperature was set at 75°C held for 5 min, ramp 10°C/min to 290°C held for 5 min, then finally ramp 20°C/min to 320°C held for 5 min. The analysis was repeated 3 times. Amino acids were determined by comparison with database mass spectra of compounds, analyzing ions characteristic of mass spectra, and retention times of standards.

Results: For all samples the most general was valine, also other amino acids were determined and quantified, such as leucine, isoleucine, 4-aminobutanoic acid, proline, and serine. Three of them are essential for humans and cannot be produced by the body.

Conclusion: Amino acids were determined and quantified in ivy leaves by GC-MS. The main substance for all samples was found and according to obtained results, the presence of 7 amino acids has been discovered, also valine was in all ivy leaves collected from different European countries.
The influence of magnesium aluminometasilicate on chemical composition of essential oil made from *Myristica fragrans* seeds

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**Introduction:** Magnesium aluminometasilicate (MAMS) is an excipient. It was used in solid drugs forms such as tablets [1]. However, in this experiment we have decided to test it by using hydrodistillation. MAMS is a white amorphous powder with high surface area, practically insoluble in water. It has the ability to absorb materials, which is characterized by liquid absorption capacity [2,3]. The aim of this work was to compare chemical composition in pure nutmeg essential oil and essential oil which was obtained using 1-2% of MAMS.

**Materials and methods:** The dried seeds of *Myristica fragrans* were from Grenada (brown-beige color, had a characteristic odor, and strong, bitter, and spicy flavor). Magnesium aluminometasilicate (Neusilin\(^®\) US2, Fuji Chemical Industries Co., Ltd., Toyoma, Japan) was used as an excipient. Distilled water was used throughout the experiment. Hydrodistillation was continued for 4 hours (Clevenger type apparatus). The chemical composition was analyzed by using gas chromatography-mass spectrometry GCMS-QP2010 system and data library.

**Results:** Four samples of essential oil were produced using hydrodistillation (magnesium aluminometasilicate’s concentration was: 0%, 0.5%, 1% and 2%). 24 chemical compounds were determined in the pure nutmeg essential oil (0% MAMS). In the other three samples, 21 chemical compounds were determined. The excipient significantly increased the quantity of α-pinene, sabinene, and limonene although it decreased the quantity of β-pinene. In pure essential oil 8.27%, 6.53%, 0%, and 26.61% of these chemical compounds were obtained. The essential oil with 1% MAMS has 15.02%, 61.42%, 4.2%, and 4.32% of these compounds’ quantity.

**Conclusion:** The magnesium aluminometasilicate has influence on chemical compounds’ quantity in essential oil. MAMS increased some of the chemical compounds’ quantity (sabinene, limonene, α-pinene). The highest influence was in essential oil when 1% excipient was used. The sabinene quantity was increased about 10 times more than in pure essential oil.

**References**
Seasonal variation of the qualitative and quantitative composition of triterpenic compounds in apple samples of cultivars grown in Lithuania

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Introduction. Apples are an important source of different groups of biological active compounds. Triterpenic compounds detected in apples, have antibacterial, antidiabetic, anti–inflammatory, antiviral, cholesterol lowering and hypolipidemic effects [1].

The purpose of the study – to determine qualitative and quantitative composition variability of triterpenic compounds in apple samples of cultivars grown in Lithuania during the vegetation period.

Materials and methods. We studied the apple sample of the 'Ligol' apple cultivar during the vegetation period. The samples of apples were lyophilized, extracted with 100% (v/v) acetone in ultrasonic bath for 10 min at room temperature. Triterpenic compounds analysis was performed by HPLC method.

Results. Analysis of the composition of triterpenic compounds in apple samples grown in Lithuanian during the vegetation period were performed. Betulinic, corosolic, oleanolic and ursolic acids were determined. The highest total amount of triterpenic compounds (2.63 ± 0.26 mg/g DW) was detected at the beginning of vegetation period (the 168th day of the year), the lowest amount (1.72 ± 0.28 mg/g DW) was determined at the end of the vegetative period (the 308th day of the year). The amount of ursolic acid detected during the vegetative period was the highest of all the identified triterpenic compounds, the amount of betulinic acid – was the lowest amount. The highest amount of ursolic acid (2.13 ± 0.17 mg/g DW) was detected at the beginning of vegetation period (the 168th day of the year), the lowest amount of this compound (1.32 ± 0.24 mg/g DW) was determined at the end of the vegetative period (the 308th day of the year).

Conclusions: four triterpenic compounds were identified and quantitated in researched 'Ligol' apple cultivar during the vegetation period samples: betulinic, corosolic, oleanolic and ursolic acids. The highest total amount of triterpenic compounds was detected at the beginning of vegetation period (the 168th day of the year), the lowest amount was determined at the end of the vegetative period (the 308th day of the year).

References:
Tools to improve reporting of adverse drug reactions – a systematic review

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Introduction: Spontaneous adverse drug reactions (ADRs) are a significant cause of morbidity and mortality. Every report of a suspected ADR by patient or healthcare professional has a significant impact on signal detection of new, rare, or serious ADRs [1]. The number of reports received by EudraVigilance, the European database for ADRs is growing yearly, however, it does not correspond to the amount of used medicines. Under-reporting remains a major issue undermining the effectiveness of spontaneous reports [2]. Our work presents a systematic review on the use of different tools for the promotion of ADR reporting [3, 4, 5, 6, 7, 8, 9].

Materials and methods: A systematic review was performed of studies describing or evaluating the use of different tools to promote ADR reporting. Studies with data related to the number of ADRs reported before and after each intervention were included in the analysis. Data sources were PubMed (MEDLINE) and ScienceDirect for searches on ADR reporting (2015 to 2019) using keywords: “adverse drug reaction”, “adverse drug reactions”, “promoting”, “training”, “perception”, “education”, “awareness”.

Results: From a total of 3984 articles, 7 articles were included in the analysis; 1496 subjects were included in these articles described projects. Six studies performed passive promotion of ADR reporting by organizing workshops and lectures which targeted healthcare professionals. One study performed promotion by including regular phone calls to the patients and was oriented to patient ADR reporting only. All used promotion tools showed positive results: enrolled healthcare professionals were able to transfer their skills to the care of authentic patients by enhancing skills and changing behaviours. The highest increase in ADR reporting reaches 273% [8]. The active toll increased patient reporting up to 8.1% [3].

Conclusions: Participants gained knowledge, which tended to increase the reporting of ADRs. Both types of methods for ADR reporting can improve efficiency and accuracy for detecting ADRs. Methods with educational intervention appear to be effective, however, the long-term effects need to be assessed.

References
Determination of the quantitative content of aromatic acids in the herb of Astragalus dasyanthus

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Introduction: The search for new perspective sources of medicinal plant raw materials and the development of new medicines based on them is extremely relevant [1]. Astragalus dasyanthus is a perennial herbaceous medicinal plant of the family leguminous (Fabaceae). Astragalus dasyanthus belongs to the endangered plants and is listed in the Red Book of Ukraine. This plant is cultivated as an ornamental. Medicines from this plant have antihypertensive, cardiotonic and sedative effects. In medical practice, infusion of Astragalus dasyanthus is used for treatment of hypertension of the 1st and 2nd stages, of angina, heart defects and anomalies of the cardiovascular system [2]. However, the chemical composition of this medicinal plant has not been sufficiently studied.

Materials and methods: The herb of Astragalus dasyanthus was harvested in Kharkiv region in 2018. Quantitative determination of aromatic acids content was carried out by liquid chromatography method on liquid chromatograph Agilent Technologies 1200 (USA). The mobile phase was methanol and 0.1% solution of formic acid in water. Elution was performed in gradient mode. The chromatographic column was Zorbax SB-Aq (4.6 mm ± 150 mm, 3.5 μm). Detection was performed on a diode-array detector with signal registration at 250 and 275 nm.

Results: In the course of the experiment, we obtained the following results: mostly the herb of Astragalus dasyanthus contains chlorogenic acid in the amount of 615.17 ± 0.05 μg / g; the content of trans-ferulic acid is 268.34 ± 0.03 μg / g, caffeic acid – 190.72 ± 0.05 μg / g, p-coumaric acid – 144.76 ± 0.04 μg / g, trans-cinnamic acid – 78.49 ± 0.03 μg / g and syringic acid – 61.24 ± 0.03 μg / g.

Conclusions: The determination of the quantitative content of aromatic acids in the herb of Astragalus dasyanthus will be used in further pharmacognostic investigations.

References
The prospect for phytochemical and pharmacological research of *Epilobium hirsutum* L

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Introduction: *Epilobium* L. is the largest genus of family Onagraceae, comprising approximately 170 species. One of widespread in Eurasia, North America and Africa species is *Epilobium hirsutum* L. (villous willow herb) [2, 3]. Extracts from its aerial part has been used for the treatment of benign prostate hyperplasia and other inflammatory diseases [1, 2]. The aim of this abstract is to give a brief review on the chemical composition, reported pharmacological activities of *E. hirsutum* and potential for developing medicines from its raw materials.

Materials and methods: For this abstract information was collected in scientific bases: NCBI-PubMed, Web of Knowledge, Science Direct and Wiley Online Library.

Results: *E. hirsutum* produces diverse phenolic compounds. The herb of this species contains a relatively high amount of tannins. Oenothein B is main ellagitannin in *E. hirsutum* as in other *Epilobium* spp. Also this species produces a wide variety of flavonoids. Quercetin glycosides are predominant among them. Extracts of *E. hirsutum* exhibit anti-oxidant, anti-tumour and anti-inflammatory activity due to high content of polyphenols [1, 2].

Conclusions: *E. hirsutum* is common in Europe, has significant phytomass and its extracts are promising in treatment of chronic inflammatory diseases and cancer. Therefore development of medicines and food supplements from its raw material is perspective in the Europe.

References
Composition of phenol compounds and antimicrobial properties of Japanese quince fruit and leaves extracts

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Introduction: The phenolic compounds may act as a new type of antimicrobial agent and possibly overcome the problem of antibiotic resistance [1]. The fruit and leaves of the Japanese quince (Chaenomeles japonica) accumulate a large amount of phenolic compounds with strong antioxidant properties [2, 3].

Materials and methods: The phenolic compounds in quince fruit and leaves extracts were identified using High-Performance Liquid Chromatography (HPLC) method. The antimicrobial properties of different extracts concentrations were assessed by the agar well diffusion method. The effects of each extracts was tested against Bacillus subtilis (ATCC 6633), Enterococcus faecalis (ATCC 29212), Staphylococcus aureus (ATCC 25923), Escherichia coli, Pseudomonas aeruginosa, Salmonella and Candida albicans. The correlation coefficient between the inhibition zone size and each phenol amount was calculated.

Results: The strongest antibacterial effect and the highest amount of rutin were found in the 'Rasa' cultivar fruit. A strong correlation was reported between the inhibition zone size and amount of rutin in quince fruit, r = 0.93, 0.98, 0.92 and 0.95 for Bacillus subtilis, Staphylococcus aureus, Enterococcus faecalis, and Escherichia coli, respectively. A high correlation was also found between inhibition zone size and the amount of procyanidin B2 in the leaves for Salmonella, and Staphylococcus aureus, r = 0.99 for both strains. Although quince leaves accumulate more phenolic compounds, fruit extracts have a stronger inhibitory effect, this may be related to each phenol content and pathways of action. It might be also due to the synergetic effect of the phenol compounds with organic acids, as fruits have a high content of organic acids.

Conclusions: Extracts of Japanese quince leaves and fruits have an inhibitory effect on various microorganisms and could be used as a natural antibacterial ingredient in natural products.

References
Development and validation of glycine standardization technique in the new combination drug with the antialcohol effect

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Introduction: The alcoholic intoxication treatment and the alcohol withdrawal syndrome (AWS) is not specific, aimed at a detoxification. In the AWS pathogenesis a very important role is given to the alcohol metabolism products, especially acetaldehyde. In the alcohol dependency (AD) therapy, glycine medicinal products (MP) act as endogenous regulator. Glycine MP reduce acetaldehyde, offer moderate sedative effect and can be used at all the stages of treatment for alcohol [1].

Materials and methods: The object of the research was the new MP (by the ATC code: N07B B – drugs used in AD) in the form of effervescent powder for the preparation of an oral solution. The MP consists of two sachets: sachet №1 (glutamic acid, acetylsalicylic acid, ascorbic acid and anhydrous citric acid) and sachet №2 (glycine and sodium bicarbonate). Glycine content is rationed within the limits of 300 mg ± 7.5 %. For glycine quantification a spectrophotometric technique, based on the ability of the products of the interaction of amino acids with ninhydrin to absorb in the visible spectrum region, was developed and validated [2].

Results: The research results have shown that the introduction of a reducing agent into the reaction mixture (ascorbic acid) does not change the spectrum, but increases the reaction product absorption intensity. The maximum optical density is reached with the pH value of 6.8 in the pH interval from 6.4 to 7.2. Spectrum are characterized by the distinct maximum at a wavelength of 568 ± 2 nm, the position of which does not depend on the pH of the buffer solution. The assessment results of validation parameters for quantitative determination of glycine are given in Tab. 1.

Table 1. The assessment results of validation parameters

<table>
<thead>
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<th>Criterion satisfaction</th>
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<td>&lt; 0,77</td>
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<td>$</td>
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<td>$\Delta intra$</td>
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<td>Satisfied</td>
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</table>

Conclusions: Validation of the quantification technique of glycine in the new medicine, used in alcohol dependency, was carried out. The validation characteristics meet the acceptance criteria.

References
Chemical compositions of the essential oil of Irises hybrid rhizomes

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Introduction: Essential oil of iris rhizome is used not only in the folk medicine, but also in the perfume industry due to its aromatic qualities [1]. The chemical composition of iris oil is represented by different compounds (terpene derivatives, alkanes, alcohols, aldehydes, fatty acids, etc.). Cyclohexene ketones such as ionones and pseudoionones are most valuable in terms of the essential oils aromatic qualities as these compounds are quite rare in plants materials [2]. The aim of our work was the establishment the component composition of the essential oil of two varieties of hybrid irises.

Materials and methods: The objects of study were rhizomes of Standart Bearded Iris varieties: I. hybrida `Little Dream`and I. hybrida `Mini Dynamo` harvested in the vegetation phase in 2017 in the National Botanical Gardens named. N.N. Grishko NAS (Kiev, Ukraine). Essential oil of hybrid irises rhizomes was obtained by the steam distillation. The chemical composition of the essential oil was determined using gas chromatography-mass spectrometry (Agilent Technologies 6890) [3].

Results: Iris rhizome essential oil has 42 common components, there are also compounds identified in only one variety. The yield of essential oil was 6659.47 mg/kg (I. hybrida `Mini Dynamo`) and 3562.49 mg/kg (I. hybrida `Little Dream`). According to the results, the essential oil of irises rhizome has a similar content of ketones (6.81-7.02%) and aldehydes (2.32%), among the main components are α-ionon (1.08 - 1.29%), trans-2,6-γ-ionon (2.18-3.42%), β-ionon (0.19-0.52). The essential oil of I. hybrida `Little Dream` rhizome contains more terpenes – 16.7% (squalene – 10.83%), alkanes – 23.19% (hexacosan – 8.05%, heptacosan- 9.34%) and aromatic compounds – 3.14%. The essential oil of I. hybrida `Mini Dynamo` rhizome has a higher content of carboxylic acids – 76.81% (lauric acid – 27.13%, myristic acid – 12.73%).

Conclusions: The yield of I. hybrida `Little Dream` rhizome essential oil is lower, but the component composition of such groups as terpenes and alkanes is much higher. The main components - ketones - are in the average values in the both varieties. Analysis of the component composition of rhizomes essential oil confirms the promise of using varietal irises as essential oil raw materials.

References
Development of new approaches for studying the dissolution profiles of herbal preparations according to the requirements of the biopharmaceutical classification system

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Introduction: Nowadays, the important issue is the study of the bioavailability of herbal preparations in pharmaceutical industries as a part of the development and qualitative analysis of medicines.

Based on this, the main goal of our work was to study the release of active substances from the herbal preparation Canephron® by high performance liquid chromatography with mass detection (HPLC-MS) in buffer systems with different pH values.

Materials and methods: The development was performed by using HPLC method with mass spectrometer detection. We used the Agilent 6530 Q-TOF mass-selective detector as the detection system in conjunction with the Agilent 1290 liquid chromatograph. As an object of study, we used Canephron® drops. Also, the rosmarinic acid EP standard was used in the work. For sample preparation, laboratory scales, laboratory glassware, and reagents were used.

Results: In the course of the study, the criteria for choosing a marker substance were substantiated. Based on this, a choice was made of a substance that promoted studying of the release of active substances according to the requirements of the Biopharmaceutical classification system. An analytical method that has been developed allows you to determine rosmarinic acid with a given accuracy and correctness for the studied concentrations. The dissolution profiles of the studied preparation in three buffer systems with pH = 6.8; 4.5; 1.2 were studied.

The foundations of a method for studying the release of active substances from plant preparations with low solubility in aqueous media have been developed. The developed analytical methodology was validated.

Conclusions: According to the results of the tests, the solubility limit was determined and the stability of rosmarinic acid in three buffer systems was studied (6.8; 4.5; 1.2).

Based on the obtained data, it can be concluded that it is possible to use the developed analytical methodology for determining the release of active substances that are poorly soluble in aqueous systems for studying dissolution profiles, according to the requirements of the Biopharmaceutical classification system.

References
STUDENTS SECTION
The content of total phenolics, total flavonoids and essential oil composition of *Calendula officinalis* L. flowers collected in different homesteads

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**Introduction:** *Calendula officinalis* common pot marigold is an annual herb, belongs to *Asteraceae* family. Pot marigold is one of the most commonly used medicinal plants; also as a dye for foods, fabrics and cosmetics. The flowers contain carotenoids, triterpenoids esters, flavonol glycosides, essential oils, phenolic compounds and others biologically active components, which are responsible for anti-bacterial, anti-fungal, anti-oxidant, antiseptic, anti-cancer, anti-inflammatory, anti-viral, carminative activities, and other pharmacological properties. Herbal preparations of *C. officinalis* are widely used for the treatments of wounds, scratches, burns, ulcers, hips and other skin lesions; also, for inflammatory digestive problems, gingivitis and even oncological diseases.

**Materials and methods:** Flowers were collected from three different homesteads in Marijampolė, Alytus and Vilnius districts. Total phenolics (TPC) were measured with Folin-Ciocalteau reagent. The essential oil (EO) was isolated from dried herb in a Clevenger-type apparatus during 3 hrs. The composition of calendula EO was analysed by GC-MS method on Shimadzu GC-2010 gas chromatograph with Shimadzu GCMS-QP2010 mass detector with RTX-5MS capillary column.

**Results:** The highest contents of total phenolics and flavonoids were determined in *C. officinalis*, collected in Kalveliai (Vilnius district) and dried at 35 °C temperature in the dryer compared to that of dried at room temperature. The yield of calendula EO was 0.22±0.02 ml/100 g. More than 30 volatile compounds were identified in the *C. officinalis* EO by GC-MS. The major components were α-cadinol, ep-α-cadinol, δ-cadinene, γ-cadinene, α-Thuje, α-muurolene; they depend to oxygenated sesquiterpenes and sequiterpene hydrocarbons. Bicyclic monoterpenes α-thujene and α-pinene were also of higher percentages. Similar chemical composition of calendula EO was also reported in other study [1].

**Conclusions:** It could be suggested that well selected drying method can influence the higher levels of biologically active compounds. Phenolics, flavonoids and EO volatiles may be an important group of pharmacologically active components that might be responsible for the activity and applications of marigold (*C. officinalis* L.).

**References**

Evaluation of essential oils composition of *Ruta chalepensis* L. and *Ruta corsica* DC. using GC-MS

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Introduction: *Ruta chalepensis* L. (Rue) and *Ruta corsica* DC. are aromatic herbs that belong to the family of Rutaceae [1]. Environmental factors strongly influence the *Ruta* species chemical compositions because of the variability of the plant subspecies and the existence of different chemotypes which change from each region, depending on the soil nature and the climate [2]. The aim of this study is to evaluate essential oils composition of two Rutaceae plants raw materials using GC-MS method.

Materials and Methods: Plant material. The plants were collected in the butonization phase (on June 2019). Distillation. 30 g of raw material were weighed into a 1 L round-bottomed flask, 500 mL of distilled water was added and the mixture was stirred. The thermostatic bath with glycerol was used for extraction, maintaining a constant temperature of 120°C. The prepared test samples were kept in a thermostatic bath for 3 hours until the essential oil layer was separated. 1 mL of hexane was added to the collected distillate. Gas chromatography-mass spectrometry. Analysis of essential oils was performed by GC-QP2010 (Shimadzu, Japan) with a mass spectrometer (RTX-5 MS column, 30 m × 0.25 mm × 0.25 μm; Perkin Elmer, USA). Analytical conditions: injector temperature 240°C, column temperature 60 °C, injectable sample volume - 1 μL. The temperature in the gas chromatograph was programmed step by step from 60°C (0 min) to 150°C raise 2°C /min. speed and from 150°C to 285°C raise 10°C /min. speed.

Results: According to peak reports 24 essential oil components were identified in *Ruta corsica* DC. and 24 components in *Ruta chalepensis* L. Most of the components were the same, except, 2-dodecanon (0.25%), (Z,E)-α-Fornesol (1.60%), 3-octen-2-one (0.76%) and 2-nonanol acetate (27.04%) were identified only in *Ruta corsica* DC. Also, 2-nonen-4-one (0.37%) and 2-undecanol acetate (0.22%) were determined only in *Ruta chalepensis* L. The main components of essential oil in different amounts were 2-nonanol acetate and 2-nonanone (52.67% and 12.85% respectively in *Ruta corsica* DC. and 62.38% and 7.70% respectively in *Ruta chalepensis* L).

Conclusion: According to the results, composition and quantity of essential oils components in *Ruta chalepensis* L. and *Ruta corsica* DC. are similar (87.5%).

References
Technology development and evaluation of medicinal syrups with liquid extracts of *Tilia cordata* mill and *Rubus idaeus* l.

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**Introduction:** Herbs are important sources of compounds, that can work as antioxidant or antimicrobial agents, so herbal extracts are being used in many medicinal syrups. *Tilia cordata* Mill alcoholic extracts is known in folk medicine and used in treatment of cold-related coughs. These extracts chemical composition consists of many derivatives such as hydrocarbons, esters, terpenoids, quercetin, kampferol, phenolic compounds, condensed tannins and scopoletin [1]. *Rubus idaeus* L. have been well recognized of its nutritive value and known for strong antioxidant capability because of the high levels of anthocyanins and other phenolic compounds. Alcohol extracts from *R. idaeus* leaves have been used for centuries to treat common cold, fever and flu-like infections [2]. The aim of this study is to produce a syrup with the best properties, which contains of ethanolic liquid extracts of *Tilia cordata* Mill and *Rubus idaeus*.

**Material and methods:** Syrup was made and tested in the laboratory scale with three different ethanol extracts of *Tilia cordata* flos and *Rubus idaeus* leaves (with 40%, 55% and 70% of ethanol solutions). Tested objects 6 liquid extracts were analyzed by gravimetric dry residue method. The total phenol content was determined by the Folin-Ciocalteau colorimetric method. Antioxidant activity was determined spectrophotometrically by DPPH radical scavenging method. Dynamic viscosity and stability studies of prepared syrups were conducted. The results were analyzed using Microsoft Office Excel 2016.

**Results:** The dry residue content of lime flowers and raspberry leaves liquid extracts have shown that 40% of ethanol’s extract has the highest results. Lime flowers liquid extract with 40% ethanol solution has a total phenolic compound content of 6.65±0.3 mg/ml and the same concentration ethanolic raspberry leaves liquid extract has a total phenolic content of 7.65±0.4 mg/ml. The antioxidant activity value of the most appropriate lime flowers extract tested is 74.88% and in raspberry leaves liquid extract is 89.17 %. The lowest results were obtained in a 70% concentration of liquid lime flowers and raspberry leaves extracts.

**Conclusion:** Appropriate concentration of ethanol for lime flowers and raspberry leaves liquid extracts production is 40%. These extracts had the highest amount of dry residue and the maximum total amount of phenolic compounds and antioxidant activity.

**References:**
Assessment of the provision of the content of counseling in public pharmacies to patients with cold symptoms

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Introduction: A large number of people with symptoms of fever come first in a community pharmacy looking to purchase over the counter (OTC) medicines for self-medication and seeking for pharmacists' advice. Pharmacists play a key role in counselling patients on their medication in order to monitor the use of non-prescription medicines, to ensure that patients use medicines safely, appropriately and effectively. The aim of this study was to analyze the content and quality of the encounter when customers buy non-prescription medicines fever.

Methods: A “Mystery shopper” research methodology was used. 82 community pharmacies in Klaipeda were visited. The adult with fever scenario was chosen. The data was analyzed by organizational, situation and consultation dimensions by using SPSS. The descriptive statistics as frequencies, averages and percentages were calculated.

Results: During the consultation, pharmacists often comment on the effectiveness and frequency of their use of cold medications, and on how long they should last. Less frequently, pharmacists discuss side effects and contraindications, and no one discuss risk factors for self-medication. The most common questions asked by pharmacists are: 'what does the patient complains about', 'how long the patient is ill', less frequent questions are: 'what is allergic to' and 'what medication is being used'. Also during the consultation open-ended questions is being asked: "what is the most common symptom" and "what does the patient want a pill or tea". The average duration of the consultation is 1 min 20 s. Pharmacists usually sell powder for oral solution containing paracetamol 500 mg., less frequently they sell paracetamol 1000 mg. Additionally they issue 200 mg of ibuprofen and ascorbic acid. Teas containing thorns, elderflowers, raspberries, rose flowers, Melissa leaves, linden flowers, sweet fennel fruits and strawberry leaves were the rarest issued.

Conclusion: This study showed that patients received counselling mostly about drug administration and dosage, while many other aspects were ignored.
The sale of antibiotics without prescription
at community pharmacies in Israel

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Background: Antibiotic consumption has an important effect on microbial resistance. Nationwide data on the comparative use of antibiotics in outpatient settings in Israel have only been partially collected and published [1]. Moreover, the pharmacists play an important role in providing consultations and advices to patients. According to CDTM (Collaborative Drug Therapy Management), one of the pharmacist’s activities is initiating, modifying, and monitoring a patient’s drug therapy and educating patients about their medications which might reduce the microbial resistance development [2].

The aim of this study was to analyze the sale of antibiotics without prescription in Israel.

Methodology: A simulated client methodology was used. Two cases of urinary tract infection were presented at pharmacies. Three levels of demand were used to convince the pharmacist to sell an antibiotic. The actor was a tourist from Russia and visited a sample of pharmacies among few community and private pharmacies existing in Israel. Overall all 32 pharmacies of Holon region were visited.

Results: The antibiotics were not sold in any of 32 visited pharmacies. Even after three levels of demand which were used. A number of reasons with explanations were given by consulting pharmacists and what are other options of treatment without antibiotics were presented. The pharmacists referred to the prohibition of selling an antibiotic without an official prescription, they also added that violation of pharmacy laws or regulations will lead to the revocation of pharmacist’s license. Furthermore, the pharmacists offered any alternative instead of the antibiotic. For instance: a preparation with cranberries for treatment. Most the pharmacists also recommended to see a doctor and the overall duration of consultation was 10-15 minutes.

Conclusion: This research has shown that overall it is difficult to get antibiotic treatment without prescription in Israel, Holon region. The sample of demonstrated high compliance with pharmaceutical regulation rules. The main justification given was administrative reason. The further research is needed.

References
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Standardization of *Paeonia anomala* L. with the aim of developing the national requirements for incoming verification of a raw material quality control

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**Introduction:** *Paeonia anomala* L. (*P. anomala*) is a valuable medicinal herbal raw material (MRM). However, the imported MRM is commonly used in Ukraine for manufacturing the finished medicinal products (FMP) on *P. anomala* basis. The regulatory documentation (RD) has been given only in foreign pharmacopeias, but in the State Pharmacopoeia of Ukraine (SPhU) there are only manuscripts on the other peony species. That is why developing the national requirements for incoming verification of a MRM quality control is immediate interest.

**Materials and methods:** 7 batches of *P. anomala* rhizomes and roots, which were harvested throughout 2018-2019 in the Altai Territory (the Russian Federation) and which have been offered by the domestic suppliers of MRM, have been chosen as the subject of the research. The manuscripts on *P. anomala* MRM and also certified pharmacopoeial descriptions on other peony species (*P. alba* L., *P. rubra* L.) have been used as the RD.

**Results:** In the result of the carried out experimental research *P. anomala* MRM properties (smell and taste) have been defined and morphological-diagnostic features of the MRM by macro- and microscopy methods have been studied. For the identification and quantification of *P. anomala* by thin-layer, high-performance thin-layer and liquid chromatography methods, monoterpene glycoside paeoniflorin was chosen as an active marker, as it determines the main pharmacological effects [1]. The desirable chromatographic conditions for conducting the research were experimentally chosen and some validation characteristics were studied. MRM quality indicators under the section "Tests" were defined and the requirements for standards were set: by weight loss upon drying – ≤ 13 %, for the common ashes – ≤ 10 %, for the ashes, insoluble in hydrochloric acid – ≤ 1 %, by the content of extraneous impurities (rhizomes with remains of stems up to 3 cm long) – ≤ 10 %, organic impurities – ≤ 0.5 %, mineral impurities – ≤ 1 %.

**Conclusions:** As a result of the conducted standardization of *P. anomala* MRM the criteria and their normalization have been proposed with the aim of developing the national requirements for incoming verification of MRM quality control.

**References**

Chromatographic profiles comparison of vegetative and generative black poplar buds according to the flavonoids content

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Introduction: In the existing literature sources different species of black poplar buds have been described as medicinal herbal raw material – vegetative (Industry standard 4286) or a mixture of vegetative and generative buds (British herbal pharmacopoeia). With the aim of developing the national regulatory documentation (RD), the main task is to choose pharmacologically active buds species. A thin-layer chromatography method (TLC) is a method, thanks to which it is possible to get a primary assessment of the component content.

Materials and methods: The black poplar buds, which had been collected in Ukraine (spring, 2018) and pre-separated by macro- and microscopy methods into vegetative and generative, were chosen as the object of the research. The analysis was carried out with the help of a TLC method for the flavonoids class, as they show signified anti-inflammatory effect of the black poplar buds raw material. That is why coffee and chlorogenic acids, quercetin, rutin and hyperoside were chosen as marker substances. The research was conducted in mobile phases as the mostly described for the flavonoids analysis [1]: chloroform – methanol – formic acid anhydrous (48:2:2), chloroform – methanol – water (26:14:3), ethyl acetate – dichloromethane – formic acid anhydrous – acetic acid – water (20:5:2:2:2,2), formic acid anhydrous – methyl ethyl ketone – water – ethyl acetate (10:10:30:50) on the TLC-plates with a layer of Silica gel F254 after spraying with the solution of 10 g/l of the diphenylboronic acid aminoethyl ester in methanol and 50 g/l of macrogol 400 in methanol (UV light, 365 nm).

Results: The best separation of the chromatographic zones of the extracts, made from vegetative and generative black poplar buds is reached in the mobile phase chloroform – methanol – formic acid anhydrous (48:2:2). The obtained chromatographic profiles of the different buds species do not differ in the location and colour of the chromatographic zones. However, for the quantitative estimation of the active substances content it is necessary to conduct the research by other chromatographic methods.

Conclusions: In the result of the experimental research of vegetative and generative black poplar buds by a TLC method the most optimal separation conditions were chosen and it was found out that the chromatographic profiles of the different buds species do not differ from each other.

References
Root alkylamide profile comparison between *Echinacea purpurea* (L.) Moench plants grown in different *in vitro* conditions

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**Introduction:** *Echinacea purpurea* (L.) Moench is a traditional medicinal plant used by North American Indians. It can be used as an immunostimulant for the common cold and various infectious diseases [1]. *E. purpurea* is one of the most cultivated, best-selling herbs in the world [2]. It is necessary to look for a new viable cultivation method in order to increase growth productivity of these medicinal herbs. Consequently, is important to investigate the composition of the phytochemical compounds that determine the pharmacological properties of herbal material grown in an innovative environment. The aim of experiment is to compare alkylamide profile in *E. purpurea* (L.) Moench plant roots grown on different agar media composition.

**Materials and methods:** 1. *E. purpurea* (L.) Moench seeds were sterilized and germinated in Petri dishes on two different medias: Murashige and Skoog (MS) media supplemented with sucrose, 6-benzylaminopurine (BAP) (0,2ml/l), α-naphtalene acetetic acid, gelrite and MS with sucrose and, gelrite. After month, plants were transferred on two medias, with and without growth regulators: MS+BAP, and MS. Photoperiod in growth chamber at 24°C ±2°C was 16 hours of light and 8 hours of darkness.

2. Separation of alkylamides in *Echinacea* samples was carried according to modified method of Žvikas et all, 2016. Positive electrospray ionization was applied for analysis with the following settings: capillary voltage – 3.5 kV, source temperature –150°C, desolvation temperature –400°C, desolvation gas flow – 700 l/h, cone gas flow – 20 l/h. Mass spectra was recorded in range from 50 to 1000 m/z

**Results:** 1. Plants grown on media with growth regulators had more leaves and fewer roots than plants grown on media without growth regulators.

2. Alkylamide profile in tested samples was identical, except one isoform of alkylamide compounds, which was expressed more extensively in MS+BAP media grown plant root samples.

**Conclusions:** 1. Different compositions of media had a non-identical effect on *E. purpurea* plants.

2. Tested different compositions of agar media had a minor effect on in vitro grown *Echinacea purpurea* (L.) Moench plant root alkylamide profile.

**References:**


The excipients’ effect on the biopharmacy of diclofenac sodium capsules

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Introduction: Diclofenac sodium (Na-DFC) is a non-steroidal anti-inflammatory, analgesic drug, which is used in the treatment of rheumatic pain and disorders [1, 2]. It exists in its acidic form in an acidic solution such as gastric juice, and is practically insoluble in water (~3.6 µg/ml), but soluble in intestinal fluid (~26 mg/ml) [3]. It is relevant to produce slowly dissolving capsules with Na-DFC, to avoid irritating effect on gastrointestinal tract mucosa and to ensure the solubility of diclofenac salt in gastrointestinal fluids. Capsules was a chosen pharmaceutical form for this study. Carboxymethylcellulose sodium (CMC) was used in a formulation as a prolongator of the process of active drug substance release.

Materials and methods: Disintegration and dissolution tests were performed according to the methods provided by European Pharmacopoeia. The quantity of Na-DFC was determined by the spectrophotometric method; the wavelength was 275 nm. Also, we investigated the statistical properties by using the Student’s t-test, utilizing IBM SPSS Statistics 20 software.

Results: The produced capsules contain 100 mg of Na-DFC and 200 mg of excipients. Capsules of 6 different compositions, containing CMC (20-35%) were produced in order to prolong the release of an active drug substance. The study showed, that as the quantity of CMC in capsule was increasing, the release of active drug substance kept slowing down. When capsule composition contained 20% CMC, the Na-DFC dissolved up to approx. 28% within 15 min, approx. 52% within 45 min, approx. 78% within 60 min, and approx. 105% within 120 min. When capsule composition contained 35% CMC, the Na-DFC dissolved even more slowly – up to approx. 24% only within 30 min, approx. 34% within 45 min, approx. 54% within 60 min, and approx. 97% within 120 min. The difference between these two samples is statistically significant (p=0.002). As the quantity of CMC in a capsule was increasing, the disintegration time kept slowing down.

Conclusions: The results of this study proved, that CMC is an appropriate excipient for prolonging the release of an active drug substance. Na-DFC release and disintegration rate depends on the quantity of CMC in a capsule.

References
Comparative analysis based on protein content in different vegetation periods of the raw material of (*Baptisia australis* (L.) R. Br ex Ait f.) roots

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Introduction: *Baptisia australis* (L.) R. Br ex Ait f., is a perennial legume of the Fabaceae family. Roots of this plant accumulate biologically active substances. The main ones are alkaloids, flavonoids, saponins. For example, alkaloid sparteine gives anti-arrhythmic and flavonoids – anti-inflammatory effects. Roots also accumulate protein, but it was not quantified. In this research protein concentration was evaluated based on the different vegetation periods of the raw material of *Baptisia australis* (L.) R. Br ex Ait f. [1].

Materials and methods: Material - fresh *Baptisia australis* (L.) R. Br ex Ait f. roots collected in Vytautas Magnus University Botanical garden medical herbs section during different vegetation periods – intense growth, butonization, intense flowering, seed maturity. Methods: protein extraction was made using phosphate buffer solution (PBSx10) prepared from Na₂HPO₄, NaH₂PO₄, NaCl and deionized water; protein precipitation using ammonium sulfate (AS); resuspension using PBSx1; spectrophotometric (at 595 nm) protein determination by Bradford method [2]; statistical analysis based on SPSS 17.0 and Microsoft Excel.

Results: During the first phase analysis, the sample had to be diluted 3 times to reduce the concentration of the substance in the solution. The average μg of protein in 1 g root sample decreased with each phase. During the intense growth (roots were collected 2⁰ of May) it was 416,04 ± 0,744 μg/g DW, during butonization (15⁰ of May), almost four times less – 105,56 ± 0,848 μg/g DW, at vigorous flowering (29⁰ of May) protein quantity decreased even more and was – 62,69 ± 0,227 μg/g DW and during seed maturity (11⁰ of June) roots accumulated the least amount of protein that was 40,12 ± 0,241 μg/g DW.

Conclusion: After a quantitative analysis of the proteins isolated from the roots of *Baptisia australis* (L.) R. Br ex Ait f., it was found that the highest protein content was extracted from the first investigated phase - intense growth (2⁰ of May).

References


Effect of beta adrenoblockers on human breast cancer cell migration and invasion in vitro

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Introduction: Beta blockers are class of drugs that are usually prescribed to treat hypertension by blocking the effects of epinephrine. Beta adrenergic blockade, because of the relationship between stress and cancer, may play a role in the prevention and treatment of cancer [1]. Recent studies show that beta-blockers inhibit matrix metalloproteinases, protein kinase A, reduce expression of vascular endothelial growth factor (VEGF), that have an impact for cancer cells ability to proliferate, metastasize [2,3].

The aim of the research was to evaluate the antimetastatic activity of beta blockers in human breast cancer cell cultures.

Materials and methods: Experiments were performed on two human breast cancer cell lines: MDA-MB-231 and MCF-7. Four beta blockers (atenolol, betaxolol, pindolol and propranolol) have been tested. The effect of beta blockers on cell viability was evaluated by MTT assay after 72 hours of incubation, and EC₅₀ values were calculated. The in vitro antimetastatic activity of compounds was evaluated using 3D invadopodia formation and 3D inverse invasion assays.

Results: The most active anticancer compound against all breast cancer cell lines was propranolol (EC₅₀ values on MDA-MB-231 and MCF-7 cell lines were 69.7 ± 15.5 μM and 62.5 ± 3.2 μM, respectively). Using 3D cell culture assays, we found that pindolol showed the strongest effect on MDA-MB-231 cells invasion (invasion decreased to 63%). Among tested compounds propranolol had the greatest effect on cell migration. It inhibited breast cancer cells migration through invadopodia approximately 15% when compared to control. MCF-7 cell line, as non-invasive, during experiments did not form invadopodium and did not pass through the filter membrane.

Conclusions: Tested compounds, especially propranolol, possess anticancer activity on human breast cancer cell lines. They inhibit the viability of cells, migration and invasion, and may be worthy of further studies.

Acknowledgment: This research has been done during summer research practice „Evaluation of beta adrenoblockers effect on breast cancer cell migration and invasion in vitro“, funded by Research Council of Lithuania according to the Measure 09.3.3-LMT-K-712 of the Operational Programme for the EU Fund.

References
The protective effect of aqueous and non-aqueous propolis extracts in primary rat brain cell culture against hypoxia

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Introduction: Propolis is one of the most fascinating honey bee (Apis mellifera L.) products. The constituents of propolis are flavonoids, phenolic acids, terpenes, aromatic acids and others, most of them are soluble in ethanol and that is why propolis is commonly used as ethanolic extract. Water-based propolis extracts are more biocompatible and could be applied more safely but they have significantly smaller range and quantity of active substances (1). Propolis is known to have antioxidative, anti-inflammatory, antimicrobial, immunomodulatory, neuroprotective and other effects (2). The aim of this study is to determine the effect of different propolis extracts to the primary rat brain cell culture after 24 hours hypoxia.

Materials and methods: Crude propolis was grounded into powder and macerated in different solvents (water, 20% polyethylenglycol/water and 70% ethanol) by shaking. Extraction time - 5 hours in room temperature. Propolis sample-to-solvent ratio was 1:10 (w/v). After extraction, extracts of propolis were filtered through paper filter and stored at 4 °C (1). The primary rat brain cell culture was incubated for 24 hours in hypoxic conditions. The vitality of cell culture was measured using Propidium Iodide/Hoechst method.

Results: After 24 hours of hypoxia, control group had 21,7% necrotic cells and 1,2% apoptotic cells. Different concentrations of ethanolic extracts and the lowest concentrations of aqueous extracts (3 μg/ml of phenolic compounds (PC) and 6 μg/ml PC) had no protective effect. The tendency to protect cells against hypoxia was seen when the concentration of aqueous extracts was higher (12 μg/ml PC; 18 μg/ml PC) – count of necrotic cells was 9,7% and 7,7%, apoptotic cells - 1,8% and 1,1%. The highest protective effect was achieved using 5 μg/ml PC – 32 μg/ml PC concentration aqueous-polyethylenglycolic extracts (necrotic cells – 2,4-11,85%, apoptotic cells – 0,6-1,65%).

Conclusions: Aqueous and aqueous-polyethylenglycolic propolis extracts protect cells against hypoxia. Aqueous-polyethylenglycolic extract showed the greatest protective effect compared with other propolis extracts.

References:
Application of microwave-assisted extraction method to the phenolic compounds from Lithuanian propolis

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Introduction: A microwave-assisted extraction (MAE) method uses microwaves, which supply a large amount of energy for the extraction process and it is an effective way to obtain a higher extraction yield and shorten the extraction time [1, 2]. The aim of this study was to apply MAE method to extract phenolic compounds more efficiently from Lithuanian propolis using water as a solvent.

Materials and methods: Raw Lithuanian propolis was used and it was grounded. A MAE method was applied using a domestic microwave oven at 1:20 sample-to-solvent ratio, 5 min of extraction time and 472 W, 636 W, 800 W microwave power settings. For comparison, an extraction by stirring method was chosen and performed at 1:20 sample-to-solvent ratio, 1 hour of extraction time, 70°C temperature and 500 rpm stirring setting, using a magnetic stirrer with hotplate. The contents of phenolic compounds (vanillic, p-coumaric, caffeic, ferulic acids and vanillin) were determined applying a validated high-performance liquid chromatography (HPLC) method.

Results: The extract prepared by stirring method was around 2.7 times lower in concentration (at 126.33 µg/ml) than MAE extracts. Our data revealed that the higher microwave power was used – the bigger amounts of phenolic compounds were extracted – at 472 W power setting the concentration was at 348.05 µg/ml, at 636 W – 567.32 µg/ml, and at 800 W – 666.44 µg/ml.

Conclusions: The MAE method is a suitable and an effective way to extract phenolic compounds from Lithuanian propolis while using water as a solvent.

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Investigation of the influence of gelling agents on rheological properties of gels

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Introduction: Gelling agents undergo a high degree of cross-linking or association when hydrated, forming an interlaced three-dimensional structure that provides stiffness to a solution or dispersion [1]. The rheological properties of gels depend on many factors such as concentration, temperature, degree of dispersion, dissolution and electrical charge [2]. The aim of the present study was to determine the rheological properties of gels with different gelling agents.

Materials and methods: Three different gels were formed in the assay using xanthan gum (1%), carbomer C940 (0.75%) and poloxamer P407 (16%). In the preparation of the gels, the gelling agents C940 and P407 were spread on the water surface and left to hydrate for 24 hours. Triethanolamine 10% was used to form the carbomer gel. The xanthan gum was dispersed with glycerol, poured with purified water and left to swell for 24 hours. The rheological properties of the resulting gels were investigated on a rheometer Anton Paar® GmbH, Modular Compact Rheometer, MCR 102 (Austria). The Flow curve test was used during the study, shear rate was 0.1-100 1/s. The flow index (n) and the consistency coefficient (K) were calculated using the Ostwald de Waele mathematical model. Microsoft Office Excel 2013 and IBM SPSS statistics 20 softwares were used for the statistical analysis.

Results: The K and n of the modeled gels were studied using a rheometer and a cone-plate geometry system. Indicators were measured at 18°C, 30°C and 40°C (±0.05°C). Temperature changes were statistically insignificant on xanthan gel (p>0.05), while temperature has statistically significant effect on carbomer and poloxamer gels (p<0.05). However, the sharpest change in K and n was found for the poloxamer gel: at 18°C K = 0.02558 ± 0.004 (Pa x s)^n, 30°C K = 99.7073 ± 4.979 (Pa x s)^n, and at 40°C K = 131.0133 ± 3.597 (Pa x s)^n. Accordingly, n was: 0.961803 ± 0.049; 0.063925 ± 0.004; 0.038937 ± 0.006. The study showed that with increasing consistency coefficient, the flow index decreases, indicating changes in the viscosity of the formulation. The poloxamer gel becomes more viscous as the temperature increases and its structure is stronger.

Conclusions: Strong inverse correlation (r_carbomer = -0.917; r_poloxamer = -0.9) between the K and n was found in the carbomer and poloxamer gels, both of which were statistically significantly dependent on temperature (p<0.05).

References
Activity of statins on human breast cancer cell proliferation and migration

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Introduction: Statins are a type of drugs that are used to lower cholesterol level in blood. Their mechanism of action is related to the inhibition of enzyme known as 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase. [1] Since the early 1990’s, it has been known that statins could be successfully used in cancer therapy. They show different effects depending on cell line, statin concentration, duration of exposure of cells to statins and the type of statin being used. [2] The aim of our research was to evaluate the anticancer activity of statins on human breast cancer cell proliferation and migration.

Materials and methods: We tested four different commercially available statins: lovastatin, mevastatin, pitavastatin and simvastatin. Experiments have been done in two different human breast cancer cell lines: MDA-MB-231 (not expressing ER and PR) and MCF-7 (expressing ER and PR). Cell viability was tested using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 hours of incubation with compounds. EC₅₀ values that represent the concentration of a compound causing 50% reduction of cancer cell metabolic activity has been calculated. Cell migration was analyzed by wound healing assay. Images of “wounds” have been taken every 24 hours for 3 days, and the effect was evaluated by measuring the size of the “wound” area.

Results: All statins showed a greater anti-proliferative effect on MDA-MB-231 than MCF-7 cell line. The most effective compound on both cell lines was pitavastatin (EC₅₀ values in MDA-MB-231 and MCF-7 cell lines were 0.243 ± 0.04 and 2.231 ± 0.12 µM respectively). All statins, especially pitavastatin, inhibited MCF-7 cell migration. In MDA-MB-231 cancer cell line, only concentration of 90% EC₅₀ values of mevastatin and pitavastatin had an effect on cell migration (the size of “wound” area was 20% bigger than in control group after 72h of incubation).

Conclusions: Statins, especially pitavastatin, could be developed as anticancer compounds with anti-migratory effects against MDA-MB-231 and MCF-7 breast cancer cell lines.

References:
Effect of apple-tree growth regulation on variance of quantitative composition of phenolic compounds in samples of apples (cv.'Rubin')

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Introduction: Phenolic compounds are important biologically active compounds found in apples. In intensive apple gardens is applied regulation of fruit tree growth, which ensures a better quality fruit harvest. The use of fruit tree growth regulators is known to influence the quantitative composition of phenolic compounds [1].

Materials and methods: In this study were investigated biological replicates of apples (cv.'Rubin') grown using trunk incision, root pruning on one/two side of the fruit tree, summer pruning, use of growth regulator prohexadione calcium (Pro-Ca) under different conditions (spraying once/twice/twice on top of fruit-tree), a control group was also included. There were performed 3 biological replicates, one of each contained 10 apples. Samples of lyophilised apple fruits were extracted with 70% ethanol (v/v) for 20 min at 40°C temperature using ultrasonic bath. The ethanol extracts of apple fruits were analyzed by the HPLC method [2].

Results: The highest amount of quercetin glycosides was detected in the control apple samples (293.67±4.33µg/g). Using Pro-Ca twice increased the amount of flavan-3-ols (2001.96±16.41µg/g), floridzin (102.70±17.22µg/g), while the use of the same amount of Pro-Ca once reduced the levels of flavan-3-ols (1523.87±34.93µg/g), floridzin (79.44±1.69µg/g), chlorogenic acid (424.69±22.91µg/g). The highest amount of phenolic compounds was found in control apple samples (2924.20±38.55µg/g). The total amount of phenolic compounds tested in apple fruits grown using Pro-Ca once was about 24% lower than in the control apple samples and using the same amount of Pro-Ca twice, the total amount of phenolic compounds was similar to the control apple samples.

Conclusions: The regulation of fruit tree growth had a significant effect on the composition of apple phenolic compounds. Studies by other scientists investigating the use of Pro-Ca once have shown a negative effect on the accumulated phenolic compounds [1,3]. This study showed that the application of the same amount of Pro-Ca twice could have a positive effect.

References
Determination of protein content extracted from lyophilized biomass of Kirchneriella sp. Schmidle

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Introduction: Green algae contains lipids, carbohydrates, minerals, vitamins, amino acids etc. Algae proteins can be used as an alternative to the source of proteins [1]. The aim of the study – to determine the quantity of protein extracted from biomass of Kirchneriella sp. Schmidle.

Materials and methods: Lyophilized biomass of green algae Kirchneriella sp. Schmidle was received from the Nature Research Centre, Laboratory of Algology and Microbial Ecology. Lyophilized green algae were swelled in the purified water (1 mL of purified water was poured on 0.2 g of lyophilized biomass of algae). 8.0 mL of 0.2 M NaOH solution was poured on swollen algae. Extraction was carried out by ultrasound sonication at 30°C for 25 min. The sample was cooled (to the 22±2°C) and centrifuged at 8500 rpm for 20 min at 4°C degrees. Precipitate was discharged and supernatant was used in further experiments. 5.58 g of (NH₄)₂SO₄ was added into the supernatant and left for extraction for 16 h at 4°C under constant stirring. After that the sample was centrifuged at 8500 rpm for 20 min at 4°C. Precipitate was resuspended in 200-400 µL PBS (by phosphate buffered solution – 7.6 mM Na₂HPO₄, 2.3 mM NaH₂PO₄, 0.15 mM NaCl, pH 7.4).

Repeatability of this experiment – 5 tests.

Loss on drying of Kirchneriella sp. Schmidle biomass was determined in accordance with the European Pharmacopoeia Article 2.2.32.

The protein content was determined by Bradford method. Concentration of isolated proteins was based on the calibration curve of bovine serum albumin (BSA): 0.125; 0.25; 0.5 ir 1.0 mg/mL (in the PBS buffer) standard. Research results were statistically processed by using MS Excel software [2].

Results: One mg of lyophilized algal biomass contained 0.39±0.23 µg of proteins.

Conclusion: It has been found that in lyophilized biomass of Kirchneriella sp. Schmidle was 39,02 % of proteins.

References:
The effect of branched chain amino acid metabolism on breast and colon cancer cells

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Introduction: Altered metabolic pathways, compared to normal tissue, is a hallmark of cancer. [¹] Multiple studies have found, that branched chain amino acid transaminase (BCAT) – an enzyme that breaks down three essential amino acids: leucine, isoleucine, and valine, is overexpressed in numerous cancer cell lines. [²,³] The aim of this study is to evaluate the effect of mitochondrial BCAT2 activity on breast and colon cancer cell proliferation, viability and mitochondrial membrane potential (ΔΨm).

Materials and methods: Three commercial cell lines: MCF-7 – breast cancer, MCF-10A – normal mammary cells, HCT116 – colon cancer and BC4 – cell culture, isolated from breast tumor, were used for the assay. BCAT2 gene was knocked down by transfection using a concentration of 5nM BCAT2 siRNA (Invitrogen™, USA) and a respective amount of jetPRIME transfection reagent (Polyplus-transfection® SA, France) according to manufacturer's instructions. The cells were incubated in 37°C, 5% CO₂ for 24 hours. 7-aminoactinomycin D (7-AAD; Invitrogen™, USA) fluorescent dye (1μl/ml) was used for viability assessment and 1μl/ml of JC-1 fluorescent dye (EMD Millipore Corp., USA) was used to determine ΔΨm. Quantification was performed by Guava PCA flow cytometer (Millipore, USA) and the data was analysed by guavaSoft 2.7 software.

Results: A significant decrease of proliferation was observed in MCF-7 (28,4%), BC4 (13,8%) and HCT116 (15,3%), compared to mock transfection. Viability also decreased by 7,1% in MCF-7, 9,51% in BC4 and 2,72% in HCT116. After silencing BCAT2 gene – mitochondria hyperpolarized, the measurement of ΔΨm in red/green fluorescence ratio increased from 2,05 to 3,78 (84,4%) in MCF-7, from 7,20 to 13,55 (88,2%) in BC4 and from 4,35 to 5,45 (25,3%) in HCT116. No significant effect on proliferation of MCF-10A was observed.

Conclusions: Branched chained amino acids are necessary for breast and colon cancer cells to proliferate normally and to maintain viability. Increased ΔΨm may be due to transfection.

References
Study of the influence of the lipophilic phase on the stability and texture of semisolid o/w emulsion

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Introduction: Emulsions are heterogeneous systems composed of at least two immiscible liquids, oil and water, one of which is usually uniformly dispersed as fine droplets throughout the other liquid phase by a mechanical agitation process [1]. Emulsions are not stable systems and emulsifiers (surfactants) are used to stabilize them [2]. Texture is one of the most important parameters for assessing the quality and stability of the produced emulsion. The aim of this study was to evaluate the o/w quality of semi-solid emulsion systems with different amounts of lipophilic phase.

Materials and methods: Three emulsion systems were prepared with different percentage of vegetable oils 8%, 10%, 12% in the liquid lipophilic phase using the same amount of Behentrimonium Methosulfate, Cetearyl alcohol Sodium Cetearyl Sulfate and Glycerol monostearate as emulsifiers. Semi-solid emulsion systems o/w were made using automatic mixer IKA EUROSTAR (Germany); homogenizer Ultra Turrax (Germany). The kinetic stability studies were conducted with a SIGMA Laborzentrifugen Centrifuge (Germany) at 3000 and 10000 rpm for 5 minutes. Texture studies were performed using TA.XT plus Texture Analyser (United Kingdom). Microsoft Office Excel 2013 software was used for statistical analysis.

Results: The produced emulsion systems remained stable during the centrifugation test. The emulsion extrusion test gave different results. The firmness of first composition with 8% of dispersion phase was 224.75±7.5g; consistency 840.22±8.84g/sec; viscosity index -215.94±9.1 g/sec; cohesiveness -136.08±5.01 g/sec. The firmness of the second composition with 10% of dispersion phase was 229.51±1.08g; consistency 895.14±3.28g/sec; viscosity index -171.64±2.93g/sec; cohesiveness -155.1±0.35g/sec. The composition with 12% of dispersion phase showed these results: firmness 237±4.7g; consistency 771.2 ±5.44g/sec; viscosity index -153±1.9g/sec; cohesiveness -118.8±5.97g.

Conclusions: The concentration of the oily phase did not affect the stability of the emulsion system, but changed the texture indices statistically significantly. Correlation values between oil phase concentration and the firmness r=0.991; consistency r=-0.55; cohesiveness r=-0.475; viscosity index=0.973.

References:
Factors affecting qualitative parameters of bigels

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Introduction: Bigels contain two immiscible phases in which one of them is hydrogel and another one is oleogel [1]. Due to the composition of hydrogels and oleogels, bigels are being utilized as carriers or vehicles for combined delivery of both hydrophilic and lipophilic drugs [1]. Hydrogels and oleogels concentrations could affect bigels qualitative parameters [2]. The aim of this study was to determine which factors affect physical and mechanical properties of bigel.

Materials and methods: The subjects of our study were different concentration bigels. There were three bigels consist of hydrogels and oleogels. Hydrogels were prepared with purifiend water and carboxymethylcellulose sodium salt was used as a gelification agent at the concentrations 4, 4.5, and 5 percent. Meanwhile oleogels consist of sea buckthorn (Hippophae rhamnoides L) and marigold (Callendula officinalis L) oils (1:1) mixture and as a gelificators, stearic acid and sorbitan monostearate with the concentrations 6, 9 and 12 percent, were used. Spreadability test, work of shear, firmness, stickiness and ease of spread were measured to determine mechanical properties. These parameters were determined using texture analyzer (TA.XT.plus, UK,). To measure the viscosity of the preparations rotational viscometer was used (Fungilab, USA). Statistical analysis was performed using Student’s t test. The results are presented as mean ± standard deviation, a value of p<0.05 was taken as level significance.

Results: Firmness of bigels with different concentration of hydrogels and oleogels increased from 104.7 g till 156.7 g and work of shear varied from 174.88 g/sec till 251.065 g•sec. Viscosity of bigels increased from 227195 mPa•s till 314191 mPa•s. The spreadability and consistency testing results presented that bigel with the hydrogel concentration 4 percent and oleogel concentration 6 percent is the less thick that other samples. The viscosity test exposed that the higher concentration of the hydrogels and oleogels were used, the higher viscosity of bigels was measured.

Conclusions: The main factor than affects bigels qualitative parameters is the concentration of gelificators of bigel components (hydrogel and oleogel) (p<0.05).

References

SCIENTISTS SECTION
Interactions with the pharmaceutical industry: attitude of physicians, patients' organisations in Lithuania

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Introduction: Despite the same goal of improving patients’ health, a collaboration between physicians and pharmaceutical companies is usually seen in a negative perspective by society. Collaboration lets doctors participate in continuous-medical-education, receive royalties, but at the same time it is also associated with irrational drug use, the threat for patient’s health needs while off-label drugs are used, increased expenses for drugs, decreased patient-trust in their doctors [1-3].

Materials and methods: A qualitative research method interview was applied. 27 qualitative, semi-structured interviews were conducted with the aim to explore their attitudes towards physician and pharmaceutical industry relationship. Content analysis was done by using programme „Atlas.ti“, results were grouped and discussed.

Results: Physicians have a positive attitude towards the relationship with the pharmaceutical industry, because of possibilities to improve qualification, receive information, option for honoraria. Main negative aspects include risk of patient's distrust in a physician, disturbing doctors’ working hours, unpleasant experience when doctors are urged to prescribe medication. Physicians do not feel their prescribing habits are influenced neither by information provided by drug representatives nor by any items received from the industry: gifts, free drug samples. The increased prescription rate might be related with: better-informed decisions, professional curiosity, memorising medication name by the constant repeat, especially in conditions when drug options are wide. Content of pharma-funded conferences are evaluated by doctors as unbiased, but some of the presentations contain tendentious information. Although, representatives of patient's organisations do not endorse drug representatives visits to doctors office especially during working hours. Respondents believe doctor under the influence can prescribe not the most effective or suitable medication for their patients. Respondents care the most about patient well-being. Pharmaceutical representatives express only positive aspects of collaboration. Doctors receive information about drugs, innovative treatment is implemented quicker, physicians’competences being raised with the help of industry.

Conclusions: Interactions with the pharmaceutical industry is covered by a range of positive and negative attitudes of physicians and patients'organisations. Some of the aspects, such as continuous medical education, providing information about drugs and improved quality of patient care, are positive. Despite that collaboration faces challenges – continuous medical education might contain biased information of the sponsors' drug, risk of patient’s distrust in a physician, irrational use of medication.

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Validation of assay of glucose and chlorides in peritoneal dialysis solutions according to the State Pharmacopoeia of Ukraine approach

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Introduction: Analytical procedures validation should be based on justified criteria taking into account a risk of wrong decisions on compliance to specifications (1). The State Pharmacopoeia of Ukraine (SPhU) introduced the criteria that ensue from target uncertainty for main pharmacopoeial tests (2). The aim of our work was to perform validation of the glucose and chlorides assay in peritoneal dialysis solutions based on these criteria.

Materials and methods: Direct argentometric and iodometric methods for assay of chlorides and glucose, respectively, and statistics method were used.

Results: The SPhU approach put the following criteria to analytical procedure validation: concentrations for linearity study should be in the range of 80-120%; correlation coefficient (r) should be not less 0.9981; residual standard deviation (s0/b) and an y-intercept of a regression line should not exceed 0.84 and 2.6, respectively; one-sided 95% confidence limits (ΔZ) in precision study should not exceed a critical value of 1.6%. The linearity of the analytical procedures was found in the glucose amount of 76.9 to 115.4 mg in a titration sample with the regression equation of y=0.972•X+2.57 and r of 0.9994, and in the concentration range of 76 to 114 mmol/L of chloride ions with the regression equation y=1.0029•X-0.23 and r of 0.9989. The s0/b of the calibration curves was 0.52 and 0.65. The mean recovery (Z±SD) was found as 99.82±0.55% and 100.07±0.62% for the assay of glucose and chlorides, respectively. The precision study also showed low values of one-sided 95% confidence limits (ΔZ) 1.02% and 1.15%. The accuracy studies also demonstrated that the deviations δ (%) of the value Z from 100% (99.82% and 100.07%) did not exceed their confidence interval 0.34% and 0.38%, respectively, for the assay of glucose and chlorides (3).

Conclusions: Validation criteria of the developed analytical procedures met the requirements of the SPhU.

Acknowledgement. Co-author Natalia Hudz is grateful to the International Visegrad Fund for providing scholarship for studies related to solutions for dialysis therapy.

References
In vitro release kinetics of phenolic compounds from semisolid formulations designed with bee products and microbiological activity

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Introduction: The most important thing is to develop such a semisolid system would have natural base. As the main ingredients for modeling semisolid preparations there were beeswax, olive oil and honey chosen. They are natural origin and contain flavonoids, antioxidants, antibacterial and anti-fungal ingredients. When applied topically, these substances affect the production of cytokines in skin cells. The main objective of investigation was to design semisolid formulations from bee products and evaluate the quality of them using a biopharmaceutical research method in vitro.

Materials and methods: The investigation focuses on the study of microbiological activity and the evaluation of their physical characteristics, the pH values and the determination of total phenolic compounds spectrophotometrically. Propolis as an active component was introduced to semisolid bases in soft extract form. Ointment bases contain honey, olive oil and yellow beeswax.

Results: The research has established that the composition of bases has an impact on their stability and the releases of the active substances. There were stable semisolid formulations containing bee products which had acceptable organoleptic properties made. The biopharmaceutical experiment in vitro demonstrates that the quantity of beeswax influences the release of phenolic compounds from formulation. The increase of the quantity of wax cause the lower release of phenolic compounds from ointment. All the studied ointments have inhibited the growth of gram-positive S. aureus and Enterococcus faecalis in vitro, inhibited the growth of standard culture of spore bacteria Bacillus cereus. The growth of Pseudomonas aeruginosa, Proteus mirabilis and Klebsiella pneumoniae was inhibited by ointment containing honey. The Gram-negative bacterium Escherichia coli has been the most resistant to the effect of ointment specimens. Biopharmaceutical and antimicrobial study results showed that modeling ointment bases are suitable carriers for propolis soft extract used as an active ingredient.

Conclusions: The results confirmed that the biopharmaceutical research is an effective way to evaluate the quality of semisolid preparations. The phenolic compounds which are released from the stable semisolid preparations have an antimicrobial effect.

References
Berry pomace powder increase the functionality of fruit leathers

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Introduction: Fruit leathers (FL) are restructured products made from fresh fruit and berry pulp by dehydration. Berry by-products (pomace) contain various bioactive substances, such as phenolic compounds, which are strong antioxidants and might reduce the risk of cancer and cardiovascular diseases. For increasing the amount of natural antioxidants in the diet, foods can be enriched with active fractions of concentrated polyphenolic plant substances. The aim of this study was to enrich apple and black currant FL with freeze-dried sea buckthorn, raspberry and black currant pomace powders, and evaluate their effect on chemical composition, the content of vitamin C, total phenolics, total anthocyanins, antioxidant activity (AA) and texture of FL.

Materials and methods: The FL were enriched with 1% of sea buckthorn (SB) and with 1% of raspberry (R) and black currant (BC) freeze-dried pomaces powders. The chemical composition of berry pomaces (P) and FL was determined by AOAC methods; total phenolics were measured with Folin-Ciocalteu reagent; total anthocyanins by pH differential method and AA by in vitro DPPH• scavenging and ferric reducing antioxidant power FRAP assays.

Results: The highest lipid content was determined in SB-P, while BC-P was richest in vitamin C. The content of total phenolics varied from 1339 to 2019 mg GAE 100 g⁻¹ in SB-P and R-P, respectively. The BC-P was rich in total anthocyanins, 2539 mg CGE/100 g⁻¹. The moisture content in FL varied from 19.4 to 20.9%, which is within recommended level of 20%. Higher contents of total phenolics, total anthocyanins, as well as total minerals, lipids and vitamin C were found in FL enriched with pomaces. The addition of pomaces also increased AA of the tested FL. The highest AA was obtained of FL enriched with SB-P and it was by 9.5% and 10.4% (DPPH and FRAP assay, respectively) higher compared to the control. The addition of R-P and BC-P increased the AA by 4.9% (DPPH) and 13.0% (FRAP). The high AA of R-P could be attributed to the presence of ellagitannins; anthocyanins were the main contributors to AA of BC [1,2]. The addition of pomaces reduced firmness of the FL.

Conclusions: Berry pomaces are promising ingredients for increasing the nutritional value and antioxidant potential of fruit leathers.

References

Acknowledgement
This work was supported by the European Regional Development Fund under Measure No. 01.2.2-LMT-K-718.
Situational marketing analysis of nasal preparations for topical application in Ukraine

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Introduction: Nasal preparations for topical application (NPTA) comprises medicines for local treatment of nasal congestion (e.g. sympathomimetics) or for prophylaxis and treatment of allergic rhinitis (e.g. corticosteroids, cromoglicate medicines).

Materials and methods: The objects of the study were the State Register of Medicinal Products (SRMP) of Ukraine, the prices of producers, wholesalers, and retailers of the medicines for NPTA in Ukraine. Methods of data retrieval and generalisation, mathematical and statistical analysis were used.

Results: 140 trade names and 180 medical forms including different dosages and packaging of NPTA were included into the SRMP of Ukraine in September 2019. All the analysed medicines were based on 20 active pharmaceutical ingredients and were divided into 5 subgroups of the forth level according to the ATC classification system. The biggest part of all the trade names of these medicines belonged to the subgroup R01AA “Sympathomimetics” (65.7%). It was followed by the subgroups R01AD “Corticosteroids” (12.9%), R01AB “Sympathomimetics, combinations excluding corticosteroids” (10.7%), R01AX “Other nasal preparations” (8.6%) and R01AC “Antiallergic agents excluding corticosteroids” (2.1%). 72.9% of the all registered medicines contain only four active pharmaceutical substances (xylometazoline (33.6%), oxymetazoline (24.3%), mometasone (7.9%) and xylometazoline, combinations (7.1%)). Nasal sprays (62.1%) and drops (32.9%) occupied the first and the second places among all the dosage forms of NPTA. 36% of them were locally manufactured. The registered producers’ prices for 31 medicines were higher compared to their wholesale and retail prices.

Conclusions: The special characteristics of Ukrainian market of NPTU are defined due to the assortment of these medicines, the type of dosage forms, assortment dependence upon the import and peculiarities of their pricing at different levels. The obtained results are important for the further forming of the assortment and the price policy of NPTU.
Application of HPTLC fingerprints method for evaluation of polyphenols and terpenoids in some Lamiaceae species

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Introduction: The quality of any medicinal product depends primarily on the presence and content of certain ingredients with proved biological activity. High-Performance Thin Layer Chromatography (HPTLC) method has become increasingly practiced for evaluation of active compounds in herbal drugs. However, this method was not applied for some promising herbal materials belonging to Lamiaceae Family representatives.

Materials and methods: Plant raw materials (herbs) and essential oils obtained from Lophanthus anisatus, Monarda fistulosa, Ocimum americanum, Dracocephalum moldavica and Satureja hortensis (Lamiaceae). HPTLC method was applied according to [1] using the CAMAG analytical system.

Results: HPTLC chromatograms obtained with the reference solutions of polyphenols and the test solutions of investigated herbs showed the most intense UV-light blue zones at Rf=0.75 in the mobile phase ethyl acetate – formic acid – water (15:1:1) corresponding to rosmarinic acid reference; weaker light blue zones of caffeic acid were presented in all tested tracks at Rf=0.79. Furthermore, additional zones in different shades of blue and yellow colors corresponding to phenolic compounds were detected in the specific for each species positions. Presence and sequence of terpenoids in the chromatograms of essential oils after developing in two mobile phases were very characteristic for each investigated species and there were not found their common dominant components as in the case of polyphenols.

Conclusions: HPTLC method was developed for evaluating the qualitative parameters of standardization of investigated herbs and essential oils.

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**Introduction:** Identification and quantitative determination of hydroxycinnamic acids of *Calluna vulgaris* (L.) Hull. and *Betonica peraucta* Klok. was conducted with the purpose of rational use of herbal raw material. The results of the study of hydroxycinnamic acids using the methods of HPLC are presented.

**Materials and methods:** The object of study was the herb of *Calluna vulgaris* and *Betonica peraucta* harvested during the mass flowering in Ivano-Frankivsk region in 2016. The analysis was conducted by HPLC on Agilent Technologies 1200 (USA) chromatograph in combination with personal software Agilent ChemStation. Separation of hydroxycinnamic acids was performed by the reverse phase chromatography using the chromatographic column Discovery C18 on silica gel with modified octadecyl groups. Orthophosphoric acid and acetonitrile were used as the mobile phase [1,2].

**Results:** The results of study indicate that caffeic, p-coumaric, ferulic and chlorogenic acids were identified in the *Calluna vulgaris* herb; chlorogenic, rosemarinic, caffeic, ferulic and p-coumaric acids were identified in the *Betonica peraucta* herb. In the herb of *Calluna vulgaris* chlorogenic acid prevailed – 0.1736%; in *Betonica peraucta* herb rosemarinic acid was the dominant – 2.142%.

**Conclusions:** As the result of the HPLC study the qualitative and quantitative content of hydroxycinnamic acids in the herb of *Calluna vulgaris* and *Betonica peraucta* was determined. This makes it possible to develop drugs with the predicted pharmacological activity on the basis of this medicinal plant raw material.

**References**


Study of microbiological purity of the complex mixture with anthelminthic activity

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Introduction: Parasitic infections are widely spread around the world and are one of the most acute and urgent problems of the modern society. According to the recent findings, helminthiasis affect all, without exception, age groups and are met in each country of the world, regardless of the general level of well-being and development of medicine [1]. Pharmacotherapy of helminthiasis usually consists of a preparatory phase, causal treatment and correction of the consequences and complications of adjourned helminthiases [2, 3]. The extemporal mixture containing the aqueous and aqueous-glycerol extracts of tansy flowers, wormwood herb, flax seeds, walnut leaves, chamomile flowers, centaury grass, peonies rhizomes and roots, ginger rhizome, ginseng roots was proposed for use in the third phase of treatment of helminthes of the digestive system. To determine its microbiological purity the proper study was conducted.

Materials and methods: The research was conducted according to the requirements of the State Pharmacopoeia of Ukraine (SPhU) 2 ed. (ar. 2.6.12, p. 251) by the two-layer sowing method [4]. The examined samples of the mixture must meet the criteria for acceptability of microbiological purity of non-sterile ready-made herbal remedies for oral use (category C) (SPhU 2 ed., p. 795).

Results: The study of microbiological purity of complex mixture samples showed that the total amount of viable aerobic microorganisms does not exceed 860 CFU/ml (norm 10^5 CFU/ml) and the total number of yeast and mold fungi does not exceed 420 CFU/ml (norm 10^4 CFU/ml). The further incubation of the mixture samples on McConkie agar and deoxycholate agar with xylose and lysine showed the absence of bacteria Escherichia coli and Salmonella in 1 ml of the studied samples.

Conclusions: The results obtained showed that the examined samples of complex mixture fully comply with the requirements of the SPhU by the indicator of the microbiological purity.

References
Identification of the risks for quality of compounding ointments

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Introduction: The main difference between compounding preparations and other medicines is absence of their state registration process. According to the requirements of the general article “Pharmaceutical preparations” of the European Pharmacopoeia and the State Pharmacopoeia of Ukraine during their production a suitable level of risk assessment must be undertaken. In pharmaceutical branch management process of the risks for quality regulates by ICH Q9 guideline [1] implemented in Ukraine in 2011. General requirements for this process are regulated by several ISO standards also implemented in Ukraine [2-3]. According to the requirements of all these documents, the first step of risk assessment is risk identification, when it is determined what may go wrong and why. So the aim of our research was risks for quality of compounding ointments identification.

Materials and methods: General risks assessment methods B.1 «Method of brainstorming » and B.17 «Analyzing of cause and effect relationships» (the Ishikawa diagram) (according to the ISO/IEC 31010:2009 guideline) were used for the risks identification.

Results: The most successful and visual method for risks identification is the Ishikawa diagram [4]. We were guided by its principles to achieve our goal. Whole process of compounding ointments production; requirements of the regulatory framework of Ukraine for their quality; storage conditions; usage and quality control were analyzed for the risks for quality identification. Six main categories that can affect the quality of compounding ointments have been determined. Among these categories are personnel; active pharmaceutical ingredients and excipients; equipment and premises; manufacturing technology; stability and quality control. These categories have been selected due to their direct ability to influence the quality of the final product. Factors that can cause compounding ointments quality deterioration also have been identified for each of these categories. Two categories (stability and quality control) are characterized by the largest number of such factors.

Conclusions: Six major categories which are the source of risks for the quality of compounding ointments were identified by Ishikawa diagram construction. The principal factors which specify appropriate level of the final product quality were determined for each of them. Consideration of these factors during the compounding ointments production will allow constantly producing a product of good quality.

References
1. ICH guideline Q9 on quality risk management. 2015;20 p.
New approaches to prevent toxic effects of chemotherapy

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Introduction: Due to the attempts to modify the chemical structure of anthracyclines, the adverse effects of this group of chemotherapy drugs have been somewhat reduced. However, the problem of pharmacotherapeutic prevention, primarily of specific myocardial damage, remains unresolved [1].

Materials and methods: Adult Wistar rats (weight: 180-220 g); doxorubicin-KMP (5,0 mg/kg once a week IM 5 weeks); coordination compounds of germanium with nicotinic acid (5,0; 10,0; 30,0 mg/kg IP 35 days) in comparison with niacin in same dosage. In the myocardial and liver homogenates were investigated products of lipid (conjugated dienes, TBA – active compounds and Schiff bases) and protein peroxidation (total, protein-bound and non-protein SH-groups), energy metabolism by ATP-ADP-AMP level and the activity of superoxide dismutase and catalase. Statistical processing of results was performed using t-test or Mann-Whitney test. Quantum-chemical characteristics of molecules were calculated by the "HyperChem rel.7".

Results: The coordination compounds of germanium with nicotinic acid in the presence of intoxication with the doxorubicin reduces the degree of oxidative stress, as evidenced by an increase in the activity of the antioxidant system enzymes, inhibition of lipid and protein peroxidation and normalization in the level of ATP of myocardial and liver tissues (P<0.05). Niacin had less pharmacological effect, than as the bioligand with metal. The increased pharmacological activity of coordination compounds of germanium with nicotinic acid versus free nicotinic acid is confirmed by the quantum chemical analysis result.

Conclusions: The results provide a rationale for further studies of coordination compounds of germanium as a potential cytoprotector in chemotherapy with anthracycline antibiotics. Based on the established “structure-action” relationship, the targeted synthesis and the study of new substances of this line with the specified action become promising.

References

Modern technologies in the search for herbal anticonvulsants

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Introduction: Nowadays, the problem of increasing the number of neurological pathologies, in particular, epilepsy, remains relevant. The use of herbal remedies may be appropriate and justified, given the complex impact on mechanisms of seizures and mild psychotropic effects, which is significantly important against development of epileptic personality changes symptoms. Given the above mentioned information, development of new algorithms for the search of herbal remedies with proven anticonvulsant activity is appropriate and relevant [1].

Materials and methods: A complex phytochemical study of the content of biologically active substances of herbs-members of Ukrainian flora was carried out to determine their influence on the anticonvulsant activity of the studied herbs. The obtained results of in vitro and in vivo pharmacological studies were used for correlation analysis. In silico prediction of anticonvulsant activity of biologically active compounds was performed using PASS, BuildQSAR and molecular docking software.

Results: Quantitative content of flavonoids, hydroxycinnamic acids, amino acids, polyphenols and alkaloids was determined in the studied herbs. According to pharmacological screening results on the model of pentylenetetrazole-induced seizures, it was found that 11 dry extracts have high anticonvulsant potential. In silico prediction has shown that alkaloid protopin, flavonoid rutin and fumaric acid have the highest anticonvulsant activity. Molecular docking research resulted that none of the investigated substances showed affinity for active site proteins. Based on the obtained results, a general algorithm as a decision tree was offered to optimize the search for promising herbal anticonvulsants. The original software "AntiConvulsant_Test" was developed. It is able to calculate the probability of anticonvulsant potential of herbs, taking into account the ratio of different groups of biologically active substances. During software testing, it was found that calculation results of the potential activity of herbs correlated with previously obtained experimental data.

Conclusions: According to the generalized results, the algorithm of the selection of herbs with anticonvulsant potential depending on its chemical composition was developed. Original software was developed and tested to calculate the likely anticonvulsant potential of the studied herbs.

References
Anti-allergic inflammatory activities of saffron extracts

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Introduction: In traditional medicine, saffron (Crocus sativus L.) stigma has been used for the treatment of heart disease, depression, stress and sleep disorders, but also to treat asthma, cough, or psoriasis [1]. Saffron was reported to have antioxidant, anti-inflammatory and anticancer effects but antiallergic properties of saffron are largely unknown. Flavonoids in herbal extracts possess anti-allergic activities by suppression of degranulation and inhibition of cytokines synthesis in mast cells [2].

Materials and methods: The aim of this study was to investigate anti-allergic activity of aqueous and 70% ethanolic extracts of saffron stigma, leaf, corm and perianth collected in Ukraine. The samples were subjected to anti-allergic degranulation assay based on β-hexosaminidase release in RBL-2H3 mast cells induced by calcium ionophore (A23187) or antigen (IgE plus DNP-BSA) [3]. For the chemical analysis, HPLC-DAD method was used [4]. Elastase release (degranulation) and superoxide anion generation (respiratory burst) assays were used to evaluate anti-inflammatory activity in human neutrophils [5].

Results: The results showed that both aqueous and ethanolic extracts of saffron corms markedly inhibited degranulation of mast cells stimulated by A23187 or antigen, with IC50 range 38-79 µg/mL. Saffron corms showed profound inhibition of degranulation induced by calcium ionophore-induced (which bypasses receptor interaction) suggesting that the extracts may rather act via calcium signaling pathway than suppression of FcεRI, a high affinity IgE receptor. Saffron flowers and leaves inhibited superoxide anion generation in human neutrophils. The HPLC fingerprint revealed presence of apigenin and genistein as major components in the active saffron corms extracts. The content of identified components in aqueous and ethanolic extracts varied. It was found that the quantitative content of flavonoids in the ethanolic extracts was higher in comparison with aqueous extracts.

Conclusions: Saffron corms exerted promising anti-allergic activity and further evaluation is needed to understand the active ingredients responsible for the effects.

References

The development of medicated chewing gums as a rational dosage form for use in dentistry

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Introduction: Currently formulation of drugs into medicated chewing gums (MCGs) is promising trend in modern pharmaceutical technology, as this dosage form is well perceived by patients, convenient in use and characterized by high bioavailability [1]. Owing to comparatively long retention time in the oral cavity MCGs are attractive dosage form for the use in dentistry [2, 3]. The purpose of our work is the development of MCGs containing lysozyme hydrochloride (LH) and ascorbic acid (AsA) obtained by compression method with Health in Gum® (HiG) PWD 01 as a gum base.

Materials and methods: Objects of the study are LH (Bouwhuis Enthoven B.V., Netherlands), AsA (Foodchem International Corporation, China), HiG® PWD 01 (Cafosa Gum SA, Spain) and mass for pressing. During the experiment physical-chemical, technological and statistical research methods were used.

Results: Taking into account fine dispersion and insufficient flow properties of LH, which may cause its inhomogeneous distribution in MCGs, two different methods for preparation of gum mass were tested. The first method was simple dry mixing of all ingredients as it is usually practiced in direct compression technology. The second method included the step of wet granulation of three-component mixture, viz. LH, intensive sweetener and taste additive. AsA was not considered to undergo wet granulation because of its satisfactory flow properties and also in order to avoid its oxidation upon contact with the granulating liquid. Therefore, AsA powder was mixed with the granulate and gum base, after that the rest excipients were added. A microscopic analysis was carried out and the technological properties of the blends were investigated.

Conclusions: Based on studies which were conducted it has been established that for obtaining compressed MCGs of a high quality LH should be added into chewing gums using pre-granulation technique, and AsA – by premixing with lysozyme granulate and gum base.

References
Parameters of the quantitative determination when standardizing *Salvia grandiflora* leaves

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**Introduction:** By the results of the earlier chemotaxonomic study of sage of the flora in Ukraine it has been found that *S. grandiflora* is one of the most promising species. Since the State Pharmacopoeia of Ukraine (SPhU) and the European Pharmacopoeia does not have monographs concerning *S. grandiflora* leaves, it is advisable to develop the parameters of its standardization according to the requirements of the SPhU.

**Materials and methods:** The study object was *Salvia grandiflora* leaves. It has been proposed to determine the qualitative composition and the quantitative content of terpenoids by gas chromatography, while phenolic compounds – by high-performance liquid chromatography (HPLC).

**Results:** The dominant compounds of terpenoid nature in *S. grandiflora* leaves are 1,8-cineol, α- and β-pinenes, p-cimene, limonene, camphene, camphor, borneol, pinocarvone, α-copaene and α-amorphene. Therefore, we propose to use the content of these terpenoids as one of the standardization parameters for *S. grandiflora* leaves. The content of 1,8-cineol should be not less than 50 mg/100 g of the raw material, α-pinene – not less than 300 mg/100 g, β-pinene – not less than 170 mg/100 g, camphor – not less than 140 mg/100 g, and borneol – not less than 80 mg/100 g.

The dominant compound of phenolic nature in *S. grandiflora* leaves is rosmarinic acid, therefore, its content in leaves is also proposed to be used as a parameter for standardization of the raw material. The content of rosmarinic acid should be at least 400 mg/100g of the raw material.

**Conclusions.** Five batches of the raw material have been analyzed. All of them corresponded to the standardization parameters proposed. The standardization parameters developed for *S. grandiflora* leaves will serve as a basis for elaborating the normative documentation for this raw material according to the SPhU.
Development of the composition and technology of cerbroprotector action capsules

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Introduction: Treatment of brain remains an urgent problem in the health system in Ukraine, due to the wide prevalence of the most common as a result of this disease causes cerebrovascular diseases, including atherosclerosis and hypertension, leading to a narrowing of the blood vessels of the brain and decreased cerebral blood flow.

Materials and methods: An alternative method of treatment of cerebrovascular diseases it is expected pharmacological effect, which is achieved through use in medicines herbal drug that exhibits antyarytmichal, sedative, tranquilizing, antispasmodic effects. According to literature data types such therapeutic activity black horehound grass, nettle herb wormwood and compatible whose presence leads to a potentiation of pharmacological action due to the fact that the components of the content biologically active substances (BAS) show a complex impact on different parts of body systems and increase reliability and predictable therapeutic effect.

Results: The aim of this work is the theoretical basis structure and development of technology for rational drug cerebroprotective action in the form of hard gelatin capsules based on dry extracts medical plant material (MPM), namely black horehound grass, nettle herb, sage herb.

Conclusion: On the basis of experimental studies, we have proved the composition of masses for encapsulation of drug in the form of hard gelatin capsules number 0. Composition per capsule: a mixture of dry extracts MPM – 400 mg; aerosil – 50 mg; lactose monohydrate – 50 mg. The weight of the contents of the capsule – 500 mg.

References
Introduction: Vegetable marrow and Zucchini (Cucurbitaceae family) grown as vegetables. The both species are annual herbaceous plants with sturdy running stalks; the leaves large hispid and lobed, are supported by long, thick, completely hollow petioles. The fruits are cylindrical in shape, creamy, light green, yellow or dark green in color [2].

Materials and methods: The raw Zucchini, Vegetable marrow fruit with skin a rich source of water 95%, protein 1%, fats 0.1%, minerals (Ca, Fe, Mg, P, K, Na, Zn, Cu, Mn), vitamins (C, B1, B2, PP, B5, B6, E, K), fiber 0.9%, carbohydrates 2-3%, amino acids, carotenoids, etc. [1, 2]. Fruits of the both species possess antisclerotic and diuretic activity. They also are recommended in dietary food for people with strict diets and infants. These fruits are also appreciated for their culinary properties [2]. The objects of the research were Vegetable marrow and 2 varieties of Zucchini (with yellow and green fruits) leaves.

Results: We determined the following technological parameters of the studied plant material: weight loss on drying, total ash, ash insoluble in 10% hydrochloric acid, volumetric, bulk and specific density, porosity, separation and spare volume of the layer [3].

Conclusions: The obtained values of technological parameters will be further used for the quality control methods development for the plant material studied.

References
Development of the method for determination of metoprolol in human plasma

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Introduction: The method development process can be broken down into components with a logical progression. In practice, the process is more a series of iterative and interlinked steps that may often need to be revisited and adjusted to finally arrive at the best method. The present study was aimed to develop a rapid, specific and sensitive method based on LC-MS/MS method was developed for the determination of metoprolol.

Materials and methods: Chromatography was achieved on Discovery C18, 50 × 2.1 mm, 5 μm column. Samples were chromatographed in a gradient mode (eluent A (acetonitrile – water – formic acid, 5 : 95 : 0.1 v/v), eluent B (acetonitrile – formic acid, 100 : 0.1 v/v)). The initial content of the eluent B of 8%, which increases linearly to 1.0 min to 100%, is maintained up to 1.5 minutes and returned to the original 8% to 1.51 minutes. The mobile phase was delivered at a flow rate of 0.400 ml/min into the mass spectrometer ESI chamber. The sample volume was 4 μl [1-3].

Results: The total chromatographic run time was 2.0 minutes. A linear response function was established at 1 - 100 ng/ml for metoprolol and IS in human plasma. The % mean recovery for metoprolol in LQC, MQC and HQC was 104.1 %, 100.0 % and 97.4 %. The lowest concentration with the RSD <20% was taken as LLOQ and was found to be 1.03 ng/ml for metoprolol. The within-run coefficients of variation ranged between 0.271 % and 0.478 % for metoprolol. The within-run percentages of nominal concentrations ranged between 99.12 % and 100.21 % for metoprolol. The between-run coefficients of variation ranged between 0.388 % and 0.601 % for metoprolol. The between-run percentages of nominal concentrations ranged between 98.78 % and 101.11 % for metoprolol.

Conclusions: A highly sensitive, specific, reproducible, rapid and high-throughput LC-MS/MS assay was developed and validated to quantify metoprolol in human plasma as per the regulatory guidelines. Due to the sensitivity of the developed method, it can be applied to the monitoring of plasma levels in the analysis of drug in preclinical and clinical pharmacokinetic studies. All the parameters and results were found within the acceptance limit as given in the validation protocol.

References
Researches in the field of $1H$-2,1-benzothiazin-4($3H$)-one 2,2-dioxide and 1,2-benzoxathiin-4($3H$)-one 2,2-dioxide chemistry

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**Introduction:** So-called privileged scaffolds have been playing significant role in pharmaceutical chemistry while searching for a new bioactive molecule. These scaffolds represent a frame which is commonly used as a core-structure for further transformations. There are a lot of such skeletons known at the time. Our research group headed by prof. Leonid Shemchuk became interested in creation of novel nonsteroidal anti-inflammatory substances based on such privileged scaffolds as benzosultams and derivatives similar to them. This research was seen to be relevant because of obvious disadvantages of known representatives of this group of medicines.

**Materials and methods:** $1H$-2,1-benzothiazin-4($3H$)-one 2,2-dioxide, 1,2-benzoxathiin-4($3H$)-one 2,2-dioxide and a set of chemicals either synthesized by known procedures or obtained from commercial sources were used. While carrying out the research standard methods of organic synthesis were also applied.

**Results:** $1H$-2,1-benzothiazin-4($3H$)-one 2,2-dioxide and 1,2-benzoxathiin-4($3H$)-one 2,2-dioxide are being regarded by us as isosteres for 2,3-dihydro-4$H$-1,2-benzothiazin-4-one 1,1-dioxide. The latter underlies the famous group of NSAIDs – oxicams. Moreover, being a structural analogue of cyclic 1,3-dicarbonyls, the mentioned heterocycles seemed to be promising and convenient materials to construct novel molecules possessing NSAID activity. Application of different synthetic methodologies such as multicomponent approach and microwave-assisted transformations, we have been able to construct fused and/or $\sigma$-linked $4H$-pyran, 3,4-dihydro-2$H$-pyran, 2$H$-pyran-2-one (and their 2-imino derivatives), 2-pyridone, 1,4-dihydropyridine and pyridine derivatives [1,2]. Pharmacological screening of the compounds synthesized revealed substances with promising analgesic and anti-inflammatory activities [3].

**Conclusions:** Collected results reveal indisputable prospects of this research direction and encourage us to push ahead with further investigations in the field of $1H$-2,1-benzothiazin-4($3H$)-one 2,2-dioxide, 1,2-benzoxathiin-4($3H$)-one 2,2-dioxide and related SO$_2$-containing compounds.

**References**

Validation characteristics research of the hydroxyanthracene glycosides assay procedure in the combination drug “Picosen”

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Introduction: The biological activity of the new medicinal product (MP) “Picosen” in a capsule form is connected with the active ingredients of Cassia leaves dry extract (Cassiae folium extractum siccum) and sodium picosulfate. The hydroxyanthracene glycosides (sennosides) are the active ingredients of the extract. They inhibit the adsorption of fluid and stimulate the peristalsis of the intestinal walls. Sodium picosulfate is a contact stimulant laxative. Cassia leaves dry extract has been standardized for sennosides equivalent to sennoside B, the content of which in capsules is 10 mg. The aim of this work was validation and assessment criteria of acceptability of the hydroxyanthracene glycosides assay procedure by the spectrophotometry method in the new MP “Picosen” [1, 2].

Materials and methods: The spectrophotometric quantitation procedure of the hydroxyanthracene glycosides lies in the following: anthracene derivatives from the raw material are extracted with an aqueous solution; then possible anthrons and dianthrones are oxidized to anthraquinone by the reaction with ferric chloride (III), further acid hydrolysis converts anthroglycosides into aglycones, which are extracted with ether and the residue, after evaporation of the ether, is dissolved in a solution of magnesium acetate, this produces colored chelate compounds. The optical density of the colored solutions was measured at a wavelength of 515 nm.

Results: The assessment results of validation parameters for quantitative determination of the hydroxyanthracene glycosides are given in Tab. 1.

Table 1. The assessment results of validation parameters and criteria of acceptability of an analytical procedure

<table>
<thead>
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<th>Requirements, %</th>
<th>Reported value, %</th>
<th>Criterion satisfaction</th>
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<td>Background absorption</td>
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<td>│a│</td>
<td>≤ 5,1</td>
<td>0,8987</td>
<td>Satisfied</td>
</tr>
<tr>
<td>S0</td>
<td>≤ 1,69</td>
<td>1,32</td>
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</tr>
<tr>
<td>r</td>
<td>&gt; 0,9924</td>
<td>0,9987</td>
<td>Satisfied</td>
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<tr>
<td></td>
<td>Z −10d</td>
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</tr>
</tbody>
</table>

Conclusions: The quantification procedure validation of the hydroxyanthracene glycosides, in the new MP “Picosen” was carried out. The validation characteristics met the acceptability criteria.

References
Synthesis and biological properties of some pteridine derivatives

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Introduction: Pteridines and their derivatives are an interesting group of biologically active compounds of natural and synthetic origin with large pharmacological potential. Most of the pteridines that inhibit the folate's metabolic pathways have been used as antibacterial, antimalarial and anticancer agents. Approaches to the targeted search and synthesis of chemotherapeutic drugs among pteridines are based on the structural modification of this system [1].

Materials and methods: Synthetic methods of organic chemistry were used for preparation of studied compounds. Physicochemical methods of analysis (IR, $^{1}$H-, $^{13}$C-NMR-spectroscopy, gas chromatography-mass spectrometry, mass-spectrometry) were used to verify structure and purity of obtained compounds. Dihydrofolate reductase inhibiting [2], free radical scavenging [3], cytotoxic [4], antimicrobial and antifungal activities were studied in vitro.

Results: Therefore, a combinatorial library of substances was synthesized by the [4+2]-cyclocondensation reaction of 1,2,3-substituted 5,6-diaminoracils with 1,2-dicarbonyl compounds. The synthesis of 6-(2-hydroxy-2-aryl(heteryl)ethyl)-1-methylpteridine $^{1}$H,$^{3}$H,$^{8}$H)-triones by the reduction of the corresponding ketones and the peculiarities of conversion of the synthesized alcohols to $^{(E)}$-1-methyl-6-(2-aryl(heteryl)ethenyl)pteridine $^{1}$H,$^{3}$H,$^{8}$H)-triones were reported. It was shown, that intramolecular cyclization of 3-(1-methyl-2,4,7-trioxo-1,2,3,4,7,8-hexahydro-pteridin-6-y1)propanoic acid led to the formation of 1-methyl-6,7-dihydro-2$^{H}$-pyran[3,2-g]pteridine-2,4,8-(1$^{H}$,3$^{H}$)-trione. Reactions of the latter with $^{N}$-nucleophiles gave a series of amides – structural analogs of antifolates. Biological studies shown, that some of the synthesized compounds reveal antioxidant activity comparable or higher than ascorbic acid. It was established, that the synthesized compounds showed cytotoxic effects against human hepatocellular carcinoma (HepG2) cells and may be of interest for further studies of their antitumor activity against other cell lines. Screening for antibacterial and fungicidal activity in vitro revealed a mild antimicrobial effect against Staphylococcus aureus and Pseudomonas aeruginosa and a high antifungal activity against Candida albicans, which in some cases exceeded the activity of the drug "Ketoconazole."

Conclusions: This work describes synthetic methods of formation and modification of the pteridine system, that allowed to obtain the combinatorial library of promising bioactive molecules.

References
The irrigator is a modern device for professional oral care

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Introduction: Infectious diseases of the oral cavity are the most common problem which affects people throughout their lives causing pain, discomfort and resulting in distortion and even tooth loss [1]. Using an irrigator is twice as effective as toothpastes and toothbrushes: up to 70% of soft dental plaque is cleaned. Numerous studies have confirmed that daily using of an irrigator improves oral health [2].

Materials and methods: A review of the scientific literature, using the descriptional, searching and logical methods.

Results: A professional irrigator greatly exceeds some usual toothbrushes in the process of cleaning hard-to-reach places on account washed with a strong stream of water and that by removal of food debris, dental deposits. If there are crowns, dentures, implants, braces in the oral cavity, that using an irrigator is more than justified, and even recommended by dentists. The principle of working of the irrigator is that a stream of water is supplied to the oral cavity under pressure and by that washing out of food debris and pathogens microorganism. Using an irrigator ensures the most complete removal of soft dental plaque and gum care. In severe forms of periodontal disease, instead of purified water, irrigators can be used as disinfectant solutions or decoctions of medicinal plants.

As a treatment solution can be used, not only antiseptics, but also other composition that are designed to additional strengthen tooth’s enamel.

Conclusions: Scientifically it is proven that constant using of the irrigator let us to carefully clean not only the surface of the teeth, but also to penetrate into hard-to-get places, to clean the space between the teeth; it helps make away with stuck food debris; prevents the appearance of frequent diseases of the teeth directly such as stomatitis, caries, stones, soft dental plaque on the teeth and unnatural color of tooth’s enamel.

References
Introduction: The plants from Lamiaceae Family are used worldwide as herbal raw materials, herbal medicinal products or dietary supplements. Many of them are aromatic due to volatile oils, but also contain phenols, flavonoids, terpenoids, etc., that are used for identification purpose (1–4). The High-performance thin-layer chromatography (HPTLC) – is a modern and specific method for qualitative determination. Recently, HPTLC became official, it was included in pharmacopoeial analysis for identification of herbal raw materials in USP and European Pharmacopoeia (1,4). Today HPTLC procedure is being included in the State Pharmacopoeia of Ukraine. The aim was comparison of HPTLC chromatographic profiles of several Lamiaceae species, that grow in Ukraine.

Materials and methods: Instruments: CAMAG HPTLC Herbal System – ATC 4, ADC 2, Visualizer 2, Derivatization Dip, Vision Cats. Reagents: analytical grade. Chromatography conditions: Stationary Phase – HPTLC plates Si 60 F254. Mobile phase – Formic acid anhydrous-water-ethylacetate (1:1:15); Reference standards – rosmarinic acid, caffeic acid, hyperoside, rutin; Derivatization – NP/PEG; Detection. 366 nm. The samples of herbal raw materials were properly authentificated according to pharmacopoeia requirements (2).

Results: The chromatographic profiles of the herbal raw materials of ten plants from Lamiaceae species, such as Mentha × piperita L., Melissa officinalis L., Rosmarinus officinalis L., Salvia officinalis L., Origanum vulgare L., Thymus vulgaris L., Orthosiphon stamineus Benth., Hyssopus officinalis L., Agastache foeniculum Kuntze, Lavandula angustifolia Mill. were compared at the same chromatographic conditions; determination of characteristic fingerprints and specific marker zones were conducted.

Conclusions: The method allows to detect herbal raw materials of low quality and gives the possibility to differentiate most of the analysed species. For the plants that show similar chromatographic fingerprints in these conditions, for instance, Salvia officinalis L. and Thymus vulgaris L., the usage of additional HPTLC test is recommended. The finding could be used for differentiation analysis to predict falsification of herbal raw materials.

References
The main consumer characteristics of ultrasonic nebulizers

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Introduction: In studying the topic “Commodity analysis of nebulizers and inhalers” at the Department of Commodity Science, National University of Pharmacy, students study the main consumer characteristics of various types of nebulizers: compressor, membrane (or «mesh-nebulizers) and ultrasonic. We will stop in more detail on the last type and consider it with the example of firm «Doctor little» (Singapore), brand LD-250U.

Materials and methods: In carrying out these studies, we have used such empirical and theoretical methods: observation, analysis of literature data of consumer questioning, classification, generalization, description.

Results: Ultrasonic nebulizer is used to treat and prophylactic of diseases associated with the respiratory system and human lungs with aqueous solutions of drugs. Use this type of nebulizer both at home and in medical institutions. The standard set of the nebulizer brand LD-250U consists of: a nebulizer, an inhalation mask for adults, an inhalation mask for children, nozzles for the nose, an inhalation mouthpiece, instructions for use and packaging. The main advantages that consumers distinguish include: relative noiselessness compared to compressor nebulizers, portability, minimal residual volume of a nebulizer chamber. With their help, you can spray large volumes of liquids (20-30 ml). The main disadvantages include: with this type of nebulizer you cannot use a range of drugs (for example, antibiotics, hormones, essential oils, decoctions and infusions of medicinal herbs) because their molecular structure breaks down during ultrasonic treatment, resulting in the descend effectiveness of the treatment; ultrasonic nebulizer can work in a continuous regime for about 15 minutes after which it must be turned off and allowed to rest for about 20 minutes; high cost of the device.

Conclusions: we reviewed main consumer characteristics of ultrasonic nebulizers and determined their main advantages and disadvantages.

References
Amino Acids of *Galium boreale* Herb

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**Introduction:** *Galium boreale* L., or northern bedstraw, is widespread over the temperate and subarctic regions of Europe, Asia and North America. In Ukraine it is to be found all over the territory, except the arid southern areas. *Galium boreale* herb possesses sedative properties, used in folk medicine for treatment of cardiac conditions, liver and kidney problems [1]. The aim of the present research was to study the composition of the amino acids of *Galium boreale* herb.

**Materials and methods:** The plant material was harvested in the Botanical gardens of V. N. Karazin Kharkiv National University in June 2017. The analysis of the amino acid composition of the samples was carried out with the use of a HPLC chromatograph, Agilent Technologies (Model 1100). For the assay of the amino acids, the ZORBAX-SB C-18 chromatographic column (4.6 x 50 mm) filled with octadecylsilyl sorbent (in 1.8 μm particles) and a guard column as well as standard solutions of amino acids (TC 6-09-3147-83) were used. The chromatographic conditions were described in previous publications [2, 3].

**Results:** In *Galium boreale* herb, 21 amino acids were identified. The free amino acid content equaled 0.16%, 0.038% of which fell on essential amino acids, whereas the content of bound amino acids amounted to 8.62%, 3.64% of which fell on essential amino acids. Prevailing among bound amino acids were nonessential aspartic (with 15.22% of the total of bound amino acids) and glutaminic acids (13.53%), whereas among essential bound amino acids, dominating were arginine (9.14%), threonine (7.50%) and leucine (6.43%). Prevailing among free amino acids were nonessential amino acids alanine (with 13.45% of the total of free amino acids), serine (12.95%) and proline (9.90%). Prevailing among essential free amino acids were threonine (5.35%) and methionine (4.48%).

**Conclusions:** Presence of aspartic and glutaminic acids in *Galium boreale* herb may account for sedative effect.

**References**

Study of emulsion bases

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Introduction: Today, the process of development of extemporaneous formulations is observed in Ukraine. More and more domestic pharmacies are introducing extemporaneous dosage forms into the list of sold drugs, among which semi-solid dosage forms (SSDF) occupy about 26% [1]. On this basis, the development of the universal emulsion bases is an important task for the further development of the extemporaneous production of ointments and creams [2].

Materials and methods: To determine the texture of these samples the texture analyzer model TA.XT.plus (Stable Micro Systems Ltd, Godalming, Surrey, UK) with 1.0 g of load sensitivity was used. Using the Exponent computer program, the texture parameters were measured: the force required to deform the sample, (maximum force), and shear (area under the curve). The cone-shaped HDP / SR probe was used for the measurement. Selected parameters: 15 mm depth, 3.0 mm / s speed. Each test was repeated 3 times, averaged and standard deviation calculated. All tests were conducted at room temperature (25 ± 2 ° C).

As samples the following emulsion bases were used, containing: № 1 - OLIVEM® 1000 (Cetearyl Olivate / Sorbitan Olivat) 5.0%; 15% corn oil; purified water to 100% № 2 - OLIVEM® 1000 (Cetearyl Olivate / Sorbitan Olivat) 4.0%; 10% corn oil; purified water to 100%

Results: According to the findings it was found that: Consistency Sample №1 - 174,145 (g.sec); Sample №2 - 156,946 (g.sec); Firmness sample №1 - 160,539 (g) Firmness sample №2 - 83,9201 (g) Cohesiveness sample №1 - 81,6855 (g) sample №2 - 62,0446 (g) Index of Viscosity sample №1 - 30, 9606 (g.sec), sample №2 - 28,5174 (g.sec)

Conclusion: The samples are characterized by flow at an applied voltage, samples the transition from elastic to plastic state, they have sufficient cohesive properties and can be used as bases for SSDF.

References.
Synthesis of new Mannich bases containing 1,2,4-triazole and piperidine moiety

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Introduction: The 1,2,4-triazole nucleus forms the basis of a series of compounds of both therapeutic and chemical interest. 1,2,4-triazole derivatives possesses antiviral, antibacterial, antitumor, antidepressant, antihypertensive activity etc. [1-3]. Substituted 1,2,4-triazole-3-thiones can be used as substrats containing active hydrogen for Mannich reaction. Mannich reaction is important for the construction of nitrogen-containing compounds. The literature studies enlighten the fact that Mannich bases are very reactive and recognized to possess potent diverse activities like anti-inflammatory, antibacterial, anti-HIV, antimalarial, antitubercular, analgesic, antipsychotic activities and so forth [4-5]. In view of this, the aim of our work was to synthesize new Mannich bases in order to find biologically active substances.

Materials and methods: The synthesis of new Mannich bases namely 5-(4-bromophenyl)-4-(R-phenyl)-2-(1-piperidylmethyl)-1,2,4-triazole-3-thiones was carried out by one-pot multicomponent Mannich reaction. Target compounds were obtained by interaction of substituted 1,2,4-triazole-3-thiones, piperidine and formaldehyde in ethanol medium at room temperature for 12 hours with pre-stirring of the reaction mixture for 1 hour. The yields of target compounds were 68-73%. The structure, individuality and purity of the compounds synthesized were confirmed by data of ¹H NMR and ¹³C NMR-spectra. The purity of compounds additionally was controlled by thin-layer chromatography.

Results: The new Mannich bases containing 1,2,4-triazole and piperidine moiety were synthesized and its structure, purity were confirmed successfully. The data obtained reliably confirm the aminomethylation reaction with the formation of Mannich N-bases. The reaction proceeds via the formation of immonium salt which subsequently attacks the N² atom of triazole giving rise to regioselective Mannich base. It should be noted that the reaction is highly regioselective and furnishes only N-Mannich base, though the intermediate Schiff base can exist in the thiol–thione tautomeric equilibrium.

Conclusions: New 5-(4-bromophenyl)-4-(R-phenyl)-2-(1-piperidylmethyl)-1,2,4-triazole-3-thiones were synthesized and its structure and purity were confirmed by data of modern physicochemical methods of analysis. The synthesis of substances in this series of derivatives continues.

References
Maternal health literacy and the use of information sources in clinic-based pregnant women - pilot study in Serbia

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Introduction: Health literacy is associated with medication safety and few studies explored maternal literacy as critical for the use of medicines and milk formulas at early years [1-2]. Parental health literacy is important for all adults, especially mothers of newborns and small children. The aim was to evaluate the level of maternal pharmacotherapy literacy related to the use of medicines and milk formulas for children as well as maternal attitudes on the sources and information access concerning health-related products for children.

Materials and methods: This was a cross-sectional, pilot study at one maternal clinic in Belgrade (Serbia). We recruited 766 women before and after delivery and assessed maternal health literacy with a validated and adopted Pharmacotherapy Literacy scale for parents of pre-school children [1].

Results: Most of women were in the age from 30-40 years (64.5%), married (80.2%), employed (72.1%), and expected their second child (38%). The adequate level of pharmacotherapy literacy was determined among 22.1% women, marginal (50.9%) and inadequate (27% women). More respondents got the advice for over-the-counter medicines from physician (70.8%) than pharmacists. Almost one-third of women (258) said that pharmacist should explain information on medicines’ use in a plain language. Three quarters of women (74.2%) are seeking for information about medicines’ use and their action in Patient Information leaflet.

Conclusion: A huge number of clinic–based pregnant women and mothers with inadequate health literacy expect to get more information about medicines in pharmacy, which demands further investigations for developing a tailored –based pharmacy services in order to manage their own needs in healthcare system, and their children’s needs.

References
Pharmacotherapy literacy instruments - What do we know so far?

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Introduction: Pharmacotherapy literacy (PHTL) is an individual’s capacity to obtain, evaluate, calculate, and comprehend basic information about pharmacotherapy and pharmacy-related services necessary to make appropriate medication-related decisions, regardless of the mode of content delivery (e.g. written, oral, visual images and symbols) (1). Authors aimed to analyse instruments used to access pharmacotherapy literacy at pharmacy settings.

Materials and methods: Authors conducted a review of original research studies using a structured approach of the following databases PubMed and Kobson in the first two weeks of September 2019. They looked for the pharmacotherapy literacy instruments that can be applied in pharmacy conditions. The key words used were: “pharmacotherapy literacy”, “medication literacy”, “patient”, “healthcare system” and “outcome”.

Results and discussion: The initial search included 12,514 articles, but in the process of viewing the titles and abstracts, removing of duplicates and articles that did not meet the criteria, those that focused on health literacy without investigating the medication literacy, following instruments were identified: PTHL- SR, REALM, REALM-SF (Short Form), NVS and e-HEALS (1-3). Among them the most optimal would be a REALM that serves to quickly assess the level of functional literacy (less than 5 minutes) and is a test of recognition and pronunciation of words. This is an objective test but limited to pronounce words without the ability to measure the patient's understanding of the instructions on the label of the prescribed drug. For patients with limited skills in the functional area, completing a written questionnaire can be difficult. Using an interview format that raises questions may provide insight into pharmaceutical literacy skills and overcome this barrier.

Conclusions: Analysed instruments could play a significant role in facilitating the comprehension of medication information and pharmacy-related services by respondents with marginal or insufficient literature at community pharmacy settings and future research should be directed in investigation applicability of the instruments.

References
The lifestyles of students from the University of Belgrade

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Introduction: Behavioral risk factors are person’s health habits that endanger their own health. The most common reversible health risk factors are tobacco use, unhealthy diet, insufficient physical activity, excessive alcohol consumption, and substance abuse.

Materials and methods: For the purpose of the research, a prospective cross-sectional study was conducted. A custom-made questionnaire was applied to a sample consisting of Belgrade University students.

Results: Total number of respondents was 2918. There was a higher percentage of female students participating in the research (60.8% vs 39.2%). Average age of respondents was 24.7±2.8. The most respondents were of the second year of study (26.1%), and the least of the fifth (10.4%). Calculated BMI values showed that there were 17% of obese and overweight subjects. Salty snacks are consumed by women in greater percentage (82% vs 77.3%). 90.7% respondents consumed sweets, while as many as 65.6% respondents ate at fast food restaurants. 27.3% of surveyed respondents consumed tobacco products. 65.6% respondents consumed alcohol. 72.7% consumed coffee, mostly once a day (46.0%). Only 6.4% of respondents had some form of physical activity organized at their faculties.

Conclusions: The study results indicated significant prevalence of reversible health risk factors among the observed student population. In order to reduce the risk factors and prevent the development of hypertension at the later age, educational programs are necessary as well as preventive measures related to healthy nutritional habits and regular physical activity.

References:
Patients' satisfaction with the introduction of electronic prescribing into pharmacies

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Introduction: E-prescribing (e-Rx) system is growing rapidly caused by technology upgrades, while bringing many benefits for patients and physicians. E-Rx has been suggested as an important strategy for reducing medical errors which may occur in the prescribing processes, while also improving patients' healthcare system and creating savings for the medical sector. In this research, patients' satisfaction with recently introduced e-Rx was evaluated.

Materials and methods: In order to appraise public opinion regarding the e-prescription usage, an anonymous survey which consisted of 12 questions was conducted. SWOT analysis (1) preceded the survey formation and fifty-two patients were interviewed. In addition, Chi square statistical test was employed.

Results: Respondents with their answers supported the most significant strengths of e-prescription implementation which were easier appointment scheduling with chosen doctors (83% of these answers were affirmative, with \( p<0.05 \)), as well as less crowded health care centers (75% of participants of survey expressed their positive opinion, \( p<0.05 \)). Evident weaknesses of this approach were ambiguities regarding deadlines for therapy withdrawing, which were incomprehensible to most of our interrogated subjects (42% of them were appreciative regarding this question, while remaining 58% answered that they didn't understand well, or didn't understand at all aforementioned prescription deadlines; \( p>0.05 \)). Additionally, 75% of patients expressed their contentment with the amount of information obtained from pharmacists, reflecting the most significant opportunity of this approach, since patients' confidence in the pharmaceutical healthcare sector has increased significantly (\( p<0.05 \)). As a threat, healthcare's informational support system remains to be improved.

Conclusions: To resume, patients were mostly satisfied with the introduction of e-Rx, while from their additional survey comments can be concluded that except the inability for remembering prescription withdrawing deadlines, memorizing the amount of medications which one should receive monthly represented significant problem for elderly and this was especially emphasized in cases of polypharmacotherapy.

Research of the professional information environment of pharmacists

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Introduction: With the dynamic development of the pharmaceutical market in Ukraine and the implementation of the principles of Good Pharmacy Practice (GPP), the role of information activity of pharmacy enterprises is growing rapidly [1]. High-quality, reliable and objective information about drugs helps to increase the professionalism of pharmaceutical specialists, public awareness and efficiency of pharmacies in general [2]. Under such conditions, the issues of studying information flows in the professional activities of pharmacists become especially relevant. The purpose of this work is to investigate the information needs of pharmacists and their main sources of decision.

Materials and methods: To achieve this goal, the method of expert assessments was used and 237 employees from 54 pharmacies in one of the pharmacy chains in Kharkov were interviewed. 50 pharmacy managers and 187 pharmacists participated in the survey.

Results: According to the survey, the main motivational factors that encourage pharmacists of the studied pharmacies to research pharmaceutical information are highlighted. It was found that the greatest influence on the specialists has motives such as professional development and customer requests (almost 89% and 78% respectively). Most often pharmacy employees are interested in clarifying information regarding drugs (100%), search for analogues (88.89%), and features of interaction and use of drugs (66.67%).

The analysis and evaluation of the main sources of pharmaceutical information used by employees in their professional activities were conducted. The most important sources on the 10-point scale, which employees prefer, were manufacturers' instructions for medical use of drugs (9.56 points), colleagues (8.33 points) and Internet resources (8.22 points). Among the specialized Internet sources, the majority of the respondents most frequently use the official sites of the State Inspectorate for Quality Control of Medicines, the State Register of Medicines and electronic directories on medicines.

Conclusions: The development of the pharmaceutical market is accompanied by the formation and structuring of information flows, the timely study of which helps to improve the quality of customer service in pharmacies and provides for meeting the needs of the population. The results of the study of the professional information environment of pharmacy employees show the importance of constantly monitoring the level of information awareness and information work of pharmacists.

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Analysis of the pharmaceutical supply of the population with drugs of a chondroprotective action

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Introduction: According to the World Health Organization (WHO), about 4% of the world's population suffer from osteoarthritis (OA), in 10% of cases it is this disease that causes disability. According to official statistics, in 2015 the number of newly registered cases of diseases of the musculoskeletal system and connective tissue was 2919 cases per 100 thousand people, the incidence rate was 1245523 people, which is 4.65% of the total number of diseases. Today, the prevalence of OA in Ukraine is 2200.6 cases per 100 thousand people, i.e., there is a tendency to a decrease in the incidence of [1].

Materials and methods: The system analysis was used in the work, including methods of statistical, structural, graphical and marketing analysis. Data from the State Register of Medicines, research companies and manufacturing enterprises, as well as medical statistics.

Results: Because of the analysis of the assortment of medicines (drugs) of chondroprotective action, it was established that 40 trade names of drugs are represented on the pharmaceutical market of Ukraine [2]. The main share of chondroprotective drugs on the Ukrainian market belongs to the imported manufacturer (52.5%), domestic drugs occupy 47.5%. In general, the nomenclature of Ukrainian drugs is provided by six manufacturing companies. The leaders are three pharmaceutical companies that produce five drugs each (12.5% each): FC Zdorovie, Kharkov, Fitofarm, Artyomovsk, Donetsk Region, Farmak, Kiev. An analysis of the assortment of chondroprotective drugs showed that the largest share was made up of combined drugs containing a combination of chondroitin sulfate and glucosamine – 35%. Monopreparations of the M01AX25 group Chondroitin sulfate – 27.5%, M01AX05 Glucosamine – 17.5%. Of the 40 trade names, drugs are most produced: in the form of tablets coated with a coating of 12 drugs (30%), in the form of solutions for injection – 11 names of drugs (27.5%), in the form of capsules – 7 (17.5%), soft dosage forms – 6 drugs (15%), powders for oral administration – (10%).

Conclusions: Analysis of the assortment of chondroprotectors showed that most of the drugs chondroprotective action (52.5%) are imported. Combined drugs containing a combination of chondroitin sulfate and glucosamine – 35%. Monopreparations of the M01AX25 group Chondroitin sulfate – 27.5%, M01AX05 Glucosamine – 17.5%.

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Determination of standardization parameters of the complex liquid extract for prevention and treatment urolithiasis

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Introduction: Every year, urolithiasis is diagnosed in 10–15% of the European population and 20–25% in Asian countries [1]. Urolithiasis is characterized by impaired metabolism and the formation of stones in the urinary system. The cause of urolithiasis are changes in the urinary tract, endocrine system diseases, a genetic predisposition [2]. Phototherapeutic treatment is an alternative to the prevention and treatment of stone formation by increasing the excretion of urine citrate and reducing the excretion of calcium and oxalate in the urine [2]. Earlier, using the basic principles of herbal medicine we’ve obtained a complex extract from herbs Centaurium erythraea, leaves Rosmarinus officinalis and roots Levisticum officinale, carried out its phytochemical study, and for further preclinical studies it is necessary to standardize the extract. The aim was to determine parameters of standardization for the complex liquid extract.

Materials and methods: The object was the liquid extract from Centaurium erythraea herbs, Rosmarinus officinalis leaves and Levisticum officinale roots (1:1:1) (1:16) (extrahent - 60% ethanol). The identification of the extract was carried out by TLC; the assay – by spectrophotometry; the dry residue – by gravimetric method.

Results: The liquid extract was a turbid liquid, yellow-brown color with a specific odor. The identification of the extract was proposed by TLC in the system (ethyl acetate R - acetic acid glacial R - water R (69:16:16); toluene R - ethyl acetate R (95:5), to identify rosmarinic acid (formic acid anhydrous R - acetone R - methylene chloride R (8.5:25:85). As liquid extract quantitative indicators of quality proposed content of ethanol (55.0% - 62.0%), a dry residue (1.97% - 2.17%), the quantitative content of total polyphenols (19.0 mg – 105.0 mg in terms of pyrogalol in 100 g of the extract).

Conclusions: The parameters for standardization the liquid extract were established. The QCM project was developed. The methods were validated.

References:
Design of novel antibacterial drugs based on the derivatives of 6-imidazo[1,2-a]pyridin-2-yl-5-methyl-3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-diones

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Introduction: The previously reported data confirms the biological activity for the compounds bearing the fragment of imidazo[1,2-a]pyridine; these compounds relive the problems with gastric juice acidity; some of the similar compounds are known as anxiolytics and anticancer drugs. Imidazo[1,2-a]pyridines are able to activate benzodiazepine receptors or act as CXCR-4 α-chemokine receptor antagonists.

Materials and methods: The synthesis of the target molecules was performed using the organic chemistry synthetic methods. The structure of the obtained substances was assumed by NMR 1H, 13C, homo- and heteronuclear correlation NMR methods (NOESY, COSY, HMBC), liquid-chromatography-MS. Antimicrobial activity was studied using the “agar well” diffusion method.

Results: Considering the the promising reported data about the biological activity of imidazo[1,2-a]pyridines, we have decided to modify 3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-dione with this additional moiety in order to obtain the series of compounds suitable for further antimicrobial activity screening. The synthesis was carried out starting form 6-(α-bromoacetyl)-3-phenyl-5-methylthieno[2,3-d]pyrimidin-2,4(1H,3H)-dione 1, which reacted with 2-aminopyridine. The formed quaternary salt was isolated and treated with trimethylamine to afford 6-imidazo[1,2-a]pyridin-2-yl-5-methyl-3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-dione in moderate yield.

The next step of the synthetic scheme was alkylation of the intermediate 6-imidazo[1,2-a]pyridin-2-yl-5-methyl-3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-dione 2 with a verity of alkyl halides, which gave the series of 1-alkyl-6-imidazo[1,2-a]pyridin-2-yl-5-methyl-3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-diones 3.

The results of the antimicrobial activity screening for the compounds 2 and 3 showed their moderate antimicrobial effect against the test strains of S. aureus, E. coli and B. subtilis. The tested compounds 2 and some of 3 were inactive against the other test strains. The compounds 3 with the small alkyl substituents at position 1 of 3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-dione fragment appeared to be active against the strains of P. vulgaris and P. aeruginosa, although they did not inhibit the growth of C. albicans fungi. The same activity against C. albicans was typical for all of tested compounds.

Conclusions: The methods for preparation of 6-imidazo[1,2-a]pyridin-2-yl-5-methyl-3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-diones were developed and it was found that the compounds with small alkyl substituents at position 1 of 3-phenylthieno[2,3-d]pyrimidin-2,4(1H,3H)-dione fragment are active against the strains of P. vulgaris and P. aeruginosa.
Research on the development of the basis of combined gel for mastopathy treatment

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Introduction: The general methodological approach to pharmaceutical drug development is standardized in the ICH Q8 manual. In Ukraine, the harmonized guidance of the Ministry of Health of Ukraine 42-3.0: 2011 “Medicines. Pharmaceutical Development (ICH Q8)”. The purpose of pharmaceutical development is to create a drug of appropriate quality and to substantiate the process of its production in order to constantly produce products with specified functional characteristics [1]. The purpose of the work was the pharmaceutical development of the basis of the gel complex action for the treatment of mastopathy. [2]. Consideration was given to the use as gelling agents of hydroxyethyl cellulose and carbopol. The obtained samples of gel based on carbopol had less satisfactory organoleptic properties than the samples of the GEC gel in terms of transparency and uniformity. For the final selection of the optimum gel-forming agent, the texture of the obtained gels was studied.

Materials and methods: The texture analysis of the developed experimental samples of HPP and carbopol gels was performed at the Department of Pharmacy Technology of Medicines and Social Pharmacy of the Lithuanian University of Health Sciences using TA.XT.plus (Stable Micro Systems Ltd, Godalming, Surrey, UK). Using the computer program Exponent, the texture parameters were measured: the deformation force of the sample, (maximum force), and the shear stress (area under the curve). A cone-shaped probe was used for the experiment. Selected parameters: depth 15 mm, speed 3.0 mm/ s. Each test was repeated 3 times, found the mean, and the standard deviation was calculated.

Results: According to the results of the texture analysis of samples of gel based on HPP and carbopol, the natural origin of hydroxyethyl cellulose, the absence of a stage of neutralization in the technology of gel production, organoleptic and textural characteristics of the samples, it is expedient when developing a drug in the role of a gel. For further research we have previously selected a gel with a concentration of HPP in the amount of 2%.

Conclusion: Based on the research, the type of gel-forming agent and its concentration were selected for further steps in the pharmaceutical development of combination gel for the treatment of mastopathy.

References
Purposeful search of novel anti-inflammatory agents among substituted pyrrolo[1,2-α][1,2,4]azolo-(azino-)[c]quinazolines

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Introduction: For several decades, quinazoline derivatives have been in the focus of researchers developing innovative medicines. This is due to the wide range and high level of biological action of above-mentioned substances, as well as significant opportunities for their chemical modification. Thus, antifungal (Albacanazole), antihypertensive (Doxazosin, Prazosin), sedative (Etapqualon) and anti-inflammatory (Proquazone) drugs were developed and introduced in medical practice.[1]. Despite the fact, that in modern medicinal chemistry quinazoline derivatives mostly considered as promising anticancer agents, the recent studies proved their potential as compounds with high anti-inflammatory activity [2-4].

Materials and methods: Implementation of the concept of searching for innovative anti-inflammatory agents included the design of a combinatorial library of compounds, its formation by organic synthesis methods, in silico screening, determination of free radical scavenging activity, evaluation of enzyme-inhibitory activity (soybean type I-B and human lipoxygenase, COX-2). For the most promising candidates the anti-inflammatory activity in vivo was established.

Result and discussion: Considering the results of previous studies [2-4], the strategy of novel anti-inflammatory compounds searching was elaborated and realized. The target compounds were obtained via tandem heterocyclization of substituted 2-triazolo-(triazino-)anilines with 2-ketoglutaric or 4-ketopimelic acids. The abovementioned transformation allowed to annulate pyrrole cycle to triazolo(triazino)[c]quinazoline system, as well, as to introduce pharmacophore carboxylic group. Obtained compounds were studied for anti-inflammatory activity. The in silico and in vitro methods were used to select promising objects for in vivo studies. It was shown, that a number of the obtained compounds exhibited a pronounced anti-inflammatory effect that was comparable with activity of reference -compound sodium diclofenac [5-7]. It was established that the presence of a triazine cycle and carboxyethyl fragment was essential for the anti-inflammatory effect appearance.

Conclusions: The concept of directed search for anti-inflammatory agents among condensed quinazoline derivatives was developed. The implementation of this concept revealed a number of promising anti-inflammatory agents among the named class of compounds.

References
1. https://www.drugbank.ca/categories/DBCAT000883
Research reaction of [3+2] cycling of isatines, α-amino acid and dipolarophiles based on bis-maleimidines and study of antimicrobial activity of synthesized compounds

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Introduction: Finding new potential of biologically active substances among bis-spiro-2-oxindole-3,3'-pyrrole derivatives by reacting 1,3-dipolar cyclic addition or [3+2] cycling of isatin, α-amino acids and dipolarophiles and studying the effect of such combinations on the manifestation of biological properties is a promising direction in the creation of new, effective dual drugs [1]. In the present work we described the synthesis of symmetric derivatives of bis-spiro-pyrrrolo-2-oxindole via three-component one-pot interaction of isatin with α-amino acids and maleic acid dipolarophiles. We also aimed to investigate antimicrobial activity of the products [2].

Materials and methods: Dipolarophiles used, namely N,N'-hexamethylene-bis-maleimide, N,N'-ethylene-bis-maleimide, N,N'-bis-maleimidoxylalamine, m-phenylene-bis-maleimidine were prepared according to the known method. The structure of received compounds was confirmed by IR- and 1H NMR-spectroscopy, mass-spectrometry and elemental analysis. The microbiological experiment was carried out in accordance with WHO [3] and the Ministry of Public Health of Ukraine recommendations.

Results: A series of new bis-derivatives of spiroindole-3,3'-pyrrolo[3,4-c]pyrrole were synthesized in high yields via three-component domino-interaction of isatin with α-amino acids (alanine, phenylalanine, sarcosine, proline, glycine, tyrosine) and dipolarophiles N,N'-hexamethylene-bis-maleimide, N,N'-ethylen-bis-maleimide, N,N'-bis-maleimidoxylalamine, m-phenylene-bis-maleimidine. It is worth noting that the reaction required a strict maintenance of isatin/amino acid/dipolarophile (2:2:1) ratio. Synthesized compounds were tested for antimicrobial activity against both Gram-positive and Gram-negative bacteria strains as well as against fungal species of C. albicans. Antimicrobial screening of compounds synthesized revealed three the most promising substances which showed significant activity level against S. aureus, E. coli, P. aeruginosa, B. subtilis and C. albicans.

Conclusions: Series of symmetrical derivatives of hexamethylene(ethylene, oxalylamine, m-phenylene)-N,N'-bis(spiroindole-3,3'-pyrrolo[3,4-c]pyrrole-2a',5a'-dihydro-2,2',6'(1H,1'H,5'H)-trione) was syn-thesed for the first time by means of 1,3-dipolar cycloaddition of in situ generated azomethynilides to dipolarophiles containing bis-maleimide fragment.

References
Cyclization of benzylic acid derivatives as the convenient way for creation of new bioactive compounds of lactam structure

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Introduction: It was shown by us previously that interaction of 2-chloro-2,2-diphenylacetyl chloride with methyl 3-aminothiophene-2-carboxylate leads to formation of methyl 3-[(2-hydroxy-2,2-diphenyl-acetyl)amino]thiophene-2-carboxylate [1]. Further treatment of the acylated product with concentrated sulfuric acid supports intramolecular loss of water molecule (acidochromic condensation) and results in methyl 2-oxo-3,3-diphenyl-1H-thieno[3,4-b]pyrrole-6-carboxylate. Based on the latter ester we synthesized a series of 2-oxo-3,3-diphenyl-1H-thieno[3,4-b]pyrrole-6-carboxylic acid amides. Applying 1-R-6-aminoquaricile (acting as amino component) in one-pot interaction with the same acetyl chloride allowed to obtain 1-R-5,5-diphenyl-5,7-dihydro-1H-pyrrolo[2,3-d]pyrimidine-2,4,6-triones. Pharmacological screening revealed promising substances with high levels of anti-inflammatory [2] and antimicrobial activity.

Materials and methods: A set of chemicals either synthesized by known procedures or obtained from commercial sources were used. The structure and purity of compounds synthesized were proved by instrumental methods of analysis. While carrying out the research standard methods of organic synthesis and pharmacological experiment were also applied.

Results: In continuation of the researches mentioned above we significantly extended the series of condensed lactams by utilizing variety of aminoheterocycles in reaction with 2-chloro-2,2-diphenylacetyl chloride. Representatives of such NH₂-containing compounds include methyl 3-amino-4-arylthiophene-2-carboxylates, 3-amino-5-aryl-thiophene-2-carboxylates, ethyl 3-aminobenzothiophene-2-carboxylate, ethyl 3-aminobenzofuran-2-carboxylate which were acylated followed by acid-catalysed intramolecular dehydration as in original protocol. This gave rise to methyl 5-oxo-6,6-diphenyl-4H-thieno[3,4-d][3]benzazepine-3-carboxylate, methyl 4-aryl-2-oxo-3,3-diphenyl-1H-thieno[3,4-b]pyrrole-6-carboxylates, ethyl 6-oxo-7,7-diphenyl-2-thia-5-azatricyclo[6.3.1.04,12]dodeca-1(12),3,8,10-tetraene-3-carboxylate which are lactams condensed with 5-, 6- and 7-membered cycles. At the time we are carrying out investigations aiming to modify ester and NH fragments in the compounds.

Conclusions: We have proposed efficient approach to construction of novel lactams fused with heterocyclic core. Compounds obtained possess different kinds of biological activity. The presence of several reaction centers in their molecules allows further structural modification aiming to find "structure-activity" relationships.

References
Development of transdermal therapeutic system with nicergoline

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Introduction: Nowadays cerebrovascular diseases such as dementia (Alzheimer's disease, Parkinson's disease) which are characterized by a comprehensive violation of cognitive function, progress [1, 2]. In recent years, there have been reports in the scientific literature about the effective use of nicergoline in the treatment of these diseases [3]. Transdermal delivery systems are perspective for use in the treatment of chronic cerebrovascular pathologies.

Materials and methods: In order to develop a transdermal therapeutic system (TTS) for the treatment of cerebrovascular diseases, the substance of nicergoline was selected as the object of study. During the initial preformulation stage of development, the process of in vitro permeability of the selected active substance was investigated by dialysis from model solutions through a semipermeable membrane.

Results: Based on the analysis of the values obtained of the content of the drug substance Xi, its Ci concentration in the sample dialysate and the values increase of specific flux growth in the hour ΔQt was noted that the permeability of nicergoline through a semipermeable membrane in model conditions occurs at a constant speed corresponding to zero order kinetics. All obtained values of the studied parameters are within the confidence interval and vary slightly. The relative uncertainty for the probability of 95% does not exceed the maximum allowable uncertainty of the analysis results (< 8.0%). The correlation coefficient of the linear dependence of nicergoline is 0.9999. These results of the values of the speed steady-state flux rate Is = 0.4598 mg/cm²h and coefficient of the permeability Kp = 0.048 cm/h showed first of all, the ability of molecules of nicergoline to overcome membrane barriers, which practically confirms the choice of this medicinal substance as perspective for the creation of TTS.

Conclusions: Given the lack of TTS with nicergoline in the pharmaceutical market, the relevance of such developments remains high. Carrying out the following stages of the pharmaceutical development of TTS with nicergoline will make it possible to introduce in the medical practice a new transdermal form of the drug for the treatment of cerebrovascular pathologies. This is especially true for a significant improvement in the lives of patients in this group who need long-term treatment.

References
Molecular docking studies of the N-[(2,4-dichlorophenyl)methyl]-2-(2,4-dioxo-1H-quinazolin-3-yl)acetamide of the active site of GABA_A and GABA_AT

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**Introduction:** Molecular docking gives possibility to reduce efforts and time due to carrying out the procedure that is similar to high-performance biological screening. Knowing the structure of the target (receptor or enzyme) and the structure of the ligand it is possible to explain the mechanism of interaction at the molecular level and calculate the strength of binding between them (affinity) [1].

Previously [2], we discovered high anticonvulsant activity of the N-[(2,4-dichlorophenyl) methyl]-2-(2,4-dioxo-1H-quinazolin-3-yl) acetamide using the pentyleneetetrazole-induced seizures model, and indicate GABA-positive properties of the synthesized acetamide. This research aimed at molecular docking between the targets - type-A γ-aminobutyric acid receptor (GABA_A) and γ-aminobutyrate aminotransferase (GABA_AT) and the test ligand to suggest a mechanism of action.

**Materials and methods:** Docking study was carried out by AutoDockTools1.5.6 and Vina [3, 4]. For visualization, Discovery Studio V17.2.0.16349 was used. The crystal structure of GABA_AT (1OHW) and GABA_A (4COF) was obtained from the Protein Data Bank [5].

**Results:** Molecular docking between GABA_AT (1OHW) target and ligand resulted that the studied compound is characterized by significantly less binding energy (high docking scores) comparing to the reference drug vigabatrin binding energy: - 9.0 and - 6.7 kcal/mol, respectively. Ligand completely occupies the active site in the target protein and engages in hydrophobic interaction with valine (Val300), phenylalanine (Phe189, 351), isoleucine (Ile105, 72), histidine (His206) and tyrosine (Tyr 348) and hydrophilic interaction with arginine (Arg 192). Scoring function points to high affinity of ligand to GABA_A receptor active site: -9.7 kcal/mol, while a known agonist GABA_A receptor phenobarbital is characterized by -7.6 kcal/mol value. Ligand engages in hydrophobic interaction with phenylalanine (Phe200), alanine (Ala201), lysine (Lys173) and is additionally stabilized by hydrophilic bonds with residues of the following amino acids: glutamine (Glu64), tryptophan (Thr202), asparagine (Asn41).

**Conclusions:** The estimated affinity of the N-[(2,4-dichlorophenyl)methyl]-2-(2,4-dioxo-1H-quinazolin-3-yl)acetamide to anticonvulsant biotargets allows providing a multifactorial mechanism for anticonvulsant activity implementation: due to the inhibitory effect on GABA aminotransferase and GABA_A receptor agonist.

**References**

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Synthesis of 6-methyl-2-(2-oxo-2-arylethyl)thio)pyrimidin-4(3H)-one derivatives and products of their cyclization as possible anticonvulsants

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Introduction: Derivatives of 2-thiouracil are the subject of close attention of scientists from different countries, which is associated with a significant and varied spectrum of their biological activity. Derivatives of 2-thiopyrimidine-4-one are used in Alzheimer's disease and Parkinson's for the treatment of neurological diseases, migraines, depression and as tranquilizers [1-3]. In previous studies [4], we have synthesized acetamide derivatives of 6-methyl-2-thiopyrimidine-4(3H)-one with significant anticonvulsant activity. In this study, we aimed to synthesize derivatives of 6-methyl-2-[(2-oxo-2-arylethyl)thio]pyrimidin-4(3H)-one and [(4-methyl-6-oxo-1H-pyrimidine-2-yl)thio] methylphenylacetate, which are structural analogues of the previously studied acetamides, and to investigate their anticonvulsant effect on pentylenetrazole seizures in rats.

Materials and methods: The structure and purity of the resulting substances was confirmed by elemental analysis, 1H NMR, 13C NMR spectroscopy and LC/MS.

Results: The alkylation of 6-methyl-2-thioxo-2,3-dihydro-1H-pyrimidine-4-one phenacyl bromides under different conditions was investigated. It was found that during the reaction in the medium of DMF/K2CO3 a mixture of 2-(2-aryl-2-oxoethyl)thio-6-methyl-pyrimidine-4(3H)-one and 3-hydroxy-3-aryl-7-methyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-5-one was formed. The holding of the resulting mixture in the concentrated sulphuric acid leads to the formation of cyclization products - derivatives of 3-aryl-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one with high yields. S-alkylated derivatives – 2-(2-aryl-2-oxoethyl)thio-6-methyl-pyrimidine-4(3H)-one - were obtained by reacting in methanol in the presence of sodium methoxide. Pharmacological screening of synthesized compounds for anticonvulsant activity on the model of pentylenetetrazole seizures in rats was carried out and some regularity "structure-activity" was established.

Conclusions: The conditions for obtaining individual derivatives of (2-aryl-2-oxoethyl)thio-6-methyl-pyrimidin-4(3H)-one are determined. On the PTZ-model seizures in rats, in comparison with reference phenobarbital and lamotrigine, the synthesized compounds did not show significant anticonvulsant activity. It can be stated that compounds with condensed thiazolopyrimidine fragment do not have an anticonvulsant effect. The obtained results in comparison with the previous ones [4] allow confirming the positive effect on the manifestation of the anticonvulsant action of the acetamidic fragment and the reduction of activity as a result of its modification.

References
Features of the introduction of the component piroctone olamine to the foam base

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Introduction: Today, one of the most common diseases associated with the hair part of head is seborrheic dermatitis (SD), its share in the structure of dermatological sickness rate is 10% and its mild clinical degree - dandruff - is observed in more than 20% of people [1].

Materials and methods: The list of medicines based on official sources of information was used in the work; it was processed by generalization, systematization, graphic methods, as well as methods of comparative and structural analysis.

Results: We have been analyzed dermatological drugs for the local treatment of SD. Most often in the composition of such medicines antifungal components are introduced: clotrimazole, ketoconazole and zinc pyrithionate. Following a literature and patent search our attention piroctone olamine which has shown widely fungicidal and antibacterial actions [2]. The aim of our research was to develop a shampoo for the treatment of SD. We have developed an optimal foam base. The next step was the addition of Octopirox, namely, the study of the particularity of its dissolution in a foam base. Identified that the best option for adding Octopyrox to the foam base is its preliminary dissolution in water at a temperature of 20-30 °C at slow turnover of the mixer to form a white suspension. It was experimentally confirmed that the resulting suspension must be added to a solution of detergents at the first stage of preparation of the foam base. We paid attention to that when adding Octopirox in base results in a reduction of foam and foam stability.

Conclusions: With a view to developing a modern shampoo of antifungal action, we conducted an analysis of dermatological means of this group. As a result of the analysis, Octopirox was selected as an antifungal component. Substantiated particular the enactment of Octopirox into the developed foaming base.

References
The aspects of using hydroxycinnamic acids as markers in the pharmacopoeial analysis of the medicinal plant raw material in Ukraine

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Introduction: From the analysis point of view, the medicinal plant raw material (MPRM) is a numerous mixture of organic compounds, many of them can be unknown, and their concentration can vary within a wide range [1]. One of the promising directions for analyzing MPRM is the use of the so-called marker compounds or substance markers [2]. Among substance markers there are both highly specific substances, which presence is typical for only a particular raw material, as well as non-specific substances, which are inherent to many types of the medicinal plant raw material. Phenolic acids, which are present almost in all plants, are referred to the non-specific substance markers. The aim of our work was to carry out an analytical overview of hydroxycinnamic acids used as substance markers in the qualitative and quantitative standardization of the pharmacopoeial medicinal plant raw material [3].

Materials and methods: The study object is the monographs of the European Pharmacopoeia and the State Pharmacopoeia of Ukraine on the medicinal plant raw material, in which hydroxycinnamic acids are used as substance markers. The content analysis was used as the research method for studying the monographs.

Results: Within the framework of the pharmacopoeial quality control while identifying 149 names of the medicinal plant raw material the unified research procedures of TLC analysis are applied for 31 names using hydroxycinnamic acids as markers. Chlorogenic acid (13 names of MPRM), caffeic acid (6 types of MHRM), gallic acid (2 types of MHRM), the amount of chlorogenic and caffeic for 10 types of MHRM (often in combination with flavonoids, which are specific for a particular medicinal plant raw material) are used as standard substances. The quantitative content of the total amount of hydroxycinnamic acids is standardized in the following medicinal plant raw material: Ehinaceae purpurae radix, Ehinaceae purpurae herba, Urticaceae folium, Ballotae nigrae herba, Orthosiphonis folium, Plantaginis lanceolatae folium, Plantaginis majoris folium, Rosmarini folium, Fraxini folium. The total amount of hydroxycinnamic acids is calculated with reference to chlorogenic, rosmarinic, chicory acid or acteoside.

Conclusions: According to the analytical review of standards for the medicinal plant raw material in Ukraine, it has been found that chlorogenic, caffeic, gallic, rosmarinic, chicory acid and acteoside are used as substance markers in quality control of the hydroxycinnamic acid content.

References
Roots of *Rosa majalis* and *Rosa canina* are perspective species of raw medicinal materials

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**Introduction:** The genus of Rose hips has 140 species. There are two types of plants which used in scientific and folk medicine - *Rosa majalis* Herrm. and *Rosa canina* L. The medicinal plant raw material is fruit that is pharmacopoeia raw materials in Ukraine and some countries [1, 3]. Folk medicine is used roots which have choleretic, astringent, anti-inflammatory effect. The chemical composition of the roots has been little studied. It is known that roots contain triterpenoids, tannins, flavonoids, organic acids, ascorbic acid, amino acids, micro- and macroelements but their qualitative composition and quantitative content are missing or different in various sources [2,3,4]. Therefore, pharmacognosy study of the roots of *Rosa majalis* and *Rosa canina* as perspective species of medicinal plant raw materials was actual.

**Materials and methods:** Roots of *Rosa majalis* and *Rosa canina* which had been prepared in spring during the 2014-2018 years in different places in Ukraine were used for research. The quantitative content of sum of organic acids was studied by titration method. The content of the ascorbic acid, flavonoids, hydroxycoric acids and the amount of phenolic compounds was carrying out with using spectrophotometry, polysaccharides – gravimetry and amino acid composition with chromatography mass spectrometry [1, 2,5].

**Results:** In consequence of the study it was found that the quantitative content of substances in the roots *Rosa majalis* and *Rosa canina* is differed slightly and amounted to not less than 3% of the sum of organic acids, 0.11% of ascorbic acid, 1.5% of flavonoids, 4% of hydroxycoric acids, 5% of the sum of phenolic compounds, 10% polysaccharides and 2% amino acids. It was determined that the roots of *Rosa majalis* and *Rosa canina* contain more combined amino acids than free and the biggest content of amino acids was for glutamic acid, aspartic acid, leucine and alanine.

**Conclusions:** As a result of research it is established that the roots of *Rosa majalis* and *Rosa canina* are perspective species of medicinal plant raw material for further research because they can have anti-inflammatory, antimicrobial, diuretic, enveloping and anti-ulcerative action and cardiostimulatory, antiarrhythmic and immunostimulatory activity due to the presence of organic acids, ascorbic acid, flavonoids, hydrochloric acids, polysaccharides and amino acids.

**References**
Perspective about the efficiency of the using of extracts of white willow bark (*Salix alba* L.) in medicine and pharmacy

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**Introduction:** There are about 12 thousand plants that have healing properties and are used in both traditional and folk medicine. In this case, medicinal plants are often combined with other techniques of treatment. To do this, we are trying to review everything, but it has been offered to monitor the pharmaceutical product with the white willow.

**Materials and methods:** The range analysis of the drugs was conducted in accordance with the State Register of Medicines of Ukraine and the WHO classification system. Used Compendium 2017, a weekly Pharmacy.

**Results:** White willow bark contains a large number of biologically active substances: salicin (0.5%) - a compound similar in quality to aspirin, flavonoids (about 2% catechins, flavones, flavonols, flavanones) produce antioxidant and anti-inflammatory effects, glycosides (3%) decrease the level of cholesterol affects the immune processes, tannins (about 12%) have anesthetic, anti-inflammatory effect, tannin (11% -12%) produces astringent effect.

According to research, the following drugs are present on the world pharmaceutical market with white willow bark extracts

Assalix-(Germany), 1 dragee has got dry extract of bark willow (8-14 : 1) – 393.24 mg (with salicin minimum 60.0 mg). Drug helps to eliminate pain in back and joints. Alleviate - for the treatment and prevention of muscle and joint damage; willow bark extract in capsules from New Foods - effective for headaches and arthritis; "Insti" herbal preparation, "Fitol" - recommended for muscle pain and inflammation.

**Conclusions:** The development of new drugs with white willow bark extract which have, powerful anti-inflammatory properties, while being safe, is currently relevant.

**References:**
Introduction: One of the key areas of research in the field of environmental safety is the analysis of pharmaceutical pollutants. A large number of studies show that medicinal substances, as well as their metabolites, were found in surface water, groundwater, and drinking water around the world [1-2]. Environmental safety problems cannot be considered within one country, but at the same time, a detailed study of pharmaceutical pollutants in a particular territory is the task of individual countries. Ukraine is the second-largest country in Europe and the 32nd most populous country in the world. There are more than 100 manufacturers of pharmaceuticals, which produce a large number of unique products for the treatment of various diseases. The aim was to develop approaches to the detailed study of pharmaceutical pollutants in order to further develop appropriate pollution monitoring systems.

Materials and methods: Existing approaches to the study of pharmaceutical pollutants and the availability of appropriate pollution monitoring systems have been studied by analyzing literature and online sources.

Results: Today in Ukraine there is no proper system for monitoring environmental pollution by pharmaceutical pollutants, and the control system of industrial enterprises does not fully minimize the negative impact on the environment. We proposed a number of approaches according to which a detailed study and prediction of the dangers associated with pharmaceutical pollutants are possible. So, at the first stage, it is necessary to conduct a detailed analysis of the production and consumption of medicines in Ukraine, especially those that are specific for Ukraine and produced only on its territory. This analysis will allow selecting the most promising objects for a detailed further analysis and suggesting possible risks. It is also necessary to consider not only the final pharmaceutical products, but also the possible harmful substances used in the synthesis and production process. Based on the data obtained, a further detailed study of the environmental impact of the selected objects is necessary, as well as the development of methods for control the selected pollutants in the environment and forecasting approaches to minimizing and controlling pollution.

Conclusions: The described approaches to a detailed study of pharmaceutical pollutants will be used in the development of appropriate pollution monitoring systems.

References
The study of pharmacological activity of pumpkin lipophilic extract

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Introduction: Currently, the lipophilic fractions of well-known medicinal plants are still understudied despite of contains of unique groups of biologically active substances (chlorophylls, carotenoids, tocopherols, sterols, unsaturated fatty acids, phospholipids, etc.), what is the actual task of modern pharmaceutical science [1, 2]. Benign prostatic hyperplasia is wide-spread disease of urogenital system in middle aged and elderly men today which require well-timed qualitative and modern treatment [3]. The most used drugs for treatment of this pathology are herbal medicines which have a wide therapeutic index along with small range of side effects in comparison with their synthetic analogs. The searching and study most notably the pharmacological activity of new materials of plant origin with perspective of drug development is still essential problem.

To study of antiexudative action and evaluation of anti-inflammatory activity of lipophilic extract of pumpkin seeds and pulp in carrageenin and zymosan-induced edema model in rats.

Materials and methods: The objectives of our study were lipophilic extract obtained from seeds and pulp of pumpkin Cucurbita pepo (L.) family Cucurbitaceae received by various extracting solvents: hexane and freon-22. For the determination of antiexudative action were used models of acute carragenine (was used 1% solution carragenine, as a reference drug was selected herbal medicine with prostate protective effects "Tykveol") and zymosan (was used 2% suspension of zymosan, the reference drug–quercetin) edema. The intensity of the inflammatory process was carried out by the method of A. C. Zaharevsky [4].

Results: The sample of extract of pumpkin pulp extracted by hexane has shown the maximum of anti-inflammatory activity as a result of experiment. The antiexudative activity was 78.4% compared to control pathology in experimental model of acute carragenine edema; in zymosan-induced edema antiexudative activity was 41.0 % compared to control pathology.

Conclusions: Lipophilic extract of pumpkin pulp can be considered a promising substance for obtaining drugs with anti-inflamattory activity.

References
Novel 2-amino-4-aryl-3-cyano-8-methoxycarbonyl-5-oxo-5,6,7,8-tetrahydro-4H-chromenes based on esters of 2-hydroxy-4-oxo-6-arylcyclohexene-2-carboxylic acid

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Introduction: Among chromene derivatives many compounds display a high level of different types of pharmacological activity (anti-inflammatory, antibacterial, anticoagulant, etc.) which causes the relevance of the synthesis of its new derivatives in order to find new biologically active substances [1,2].

In the present work we described the synthesis of derivatives of new derivatives of 2-amino-4-aryl-3-cyanochromenes via three-component one-pot interaction of esters of 2-hydroxy-4-oxo-6-arylcyclohexene-2-carboxylic acid with aromatic aldehydes and malononitrile.

Materials and methods: Starting compounds and reagents: arylidene acetones, dimethyl malonate, aromatic aldehydes, malononitrile, triethylamine, ethanol. The methods of organic synthesis and IR-, ¹H, ¹³C NMR spectroscopy, chromatography-mass spectrometry methods were applied in the course of the research. While carrying out the research standard methods of organic synthesis were also applied.

Results: Interaction between arylidene acetones and dimethyl malonate proceeds in the presence of sodium methylate with refluxing in ethanol for 3 hours as domino transformation by the «Michael addition / Claisen condensation» type. As a result, methyl esters of 2-hydroxy-4-oxo-6-arylcyclohexene-2-carboxylic acid were obtained.

A series of new 2-amino-4-aryl-3-cyano-8-methoxycarbonyl-5-oxo-5,6,7,8-tetrahydro-4H-chromenes were synthesized in high yields via three-component interaction of methyl esters of 2-hydroxy-4-oxo-6-arylcyclohexene-2-carboxylic acid with aromatic aldehydes and malononitrile in the presence of catalytic quantity of triethylamine in ethanol medium.

Conclusions: New 2-amino-4-aryl-3-cyano-8-methoxycarbonyl-5-oxo-5,6,7,8-tetrahydro-4H-chromenes were obtained. These investigations will be a base for further pharmacological researches.

References
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