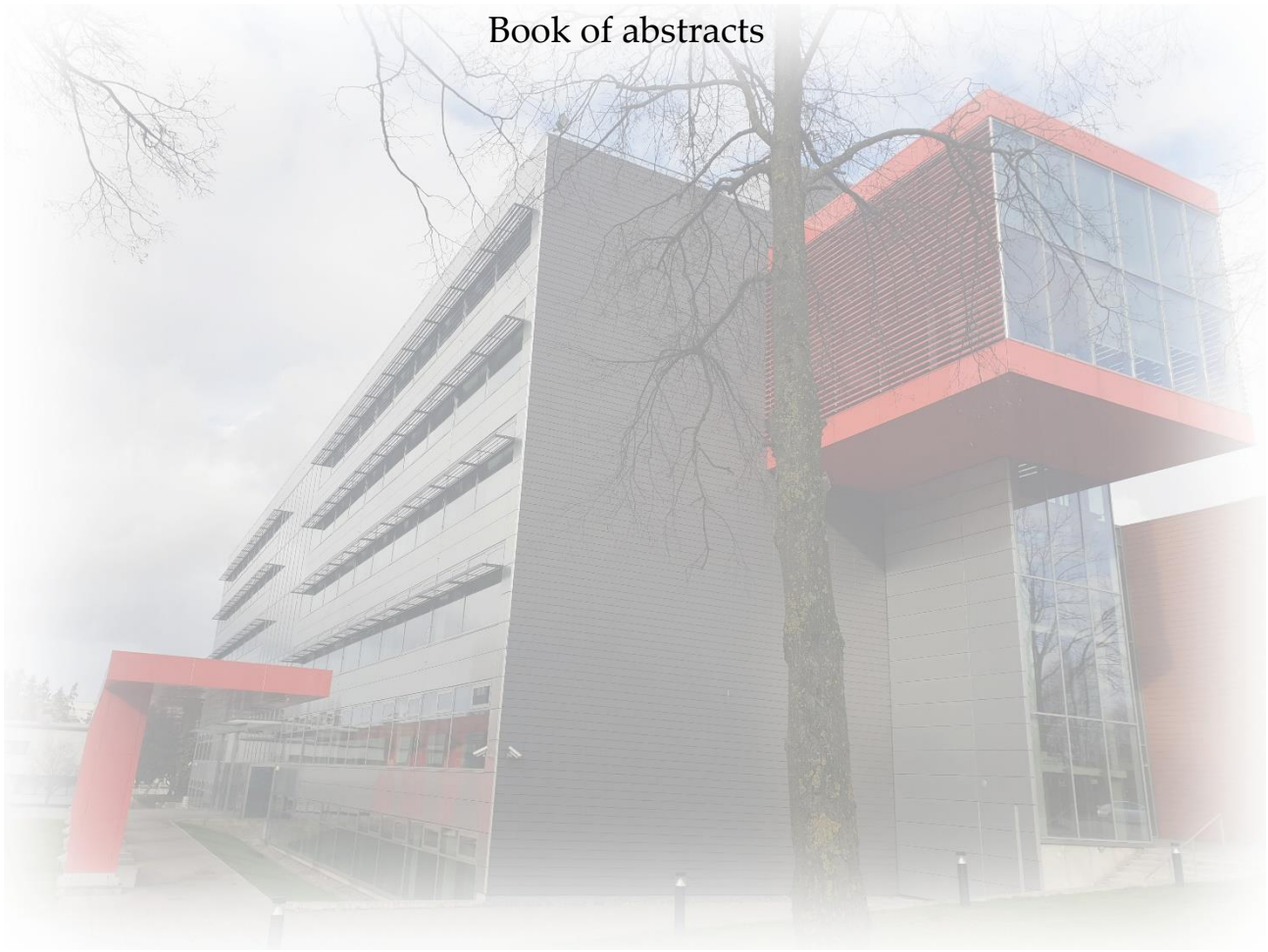
International conference of the Lithuanian Pharmaceutical Association

ACHIEVEMENTS OF PHARMACEUTICAL SCIENCE AND PRACTICE

Tarptautinė mokslinė-praktinė konferencija, skirta pirmojo farmacijos žurnalo išleidimo Lietuvoje 200 metų sukakčiai ir habil. dr. Eugenijos Šimkūnaitės šimtmečiui pažymėti

FARMACIJOS MOKSLŲ IR PRAKTIKOS PASIEKIMAI

Book of abstracts



October 16, 2020
Kaunas, Lithuania

The International scientific-practical conference „ACHIEVEMENTS OF PHARMACEUTICAL SCIENCE AND PRACTICE“ is organized by Lithuanian Pharmaceutical Association.

Organizational Scientific Committee of the International Scientific Conference

Chair of Organizing committee:
Prof. Eduardas Tarasevičius
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Prof. Vilma Petrikaitė
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PROGRAMME

10:00-16:00 PLENARY SESSION **Chair:** Prof. Vilma Petrikaitė, President of the Lithuanian Pharmaceutical Association (LPA) **Co-Chair**: Pharm. Eglė Rasa Dieninytė, Chair of Organizing committee	
10:00	**Opening of the LPA International Conference** Prof. Eduardas Tarasevičius, VicePresident of LPA, Lithuania Prof. Vilma Petrikaitė, President of LPA, Lithuania
10:10	**„Pamiętnik Farmaceutyczny Wilenski" Pharmaceutical Journal and its importance to the society** Prof. Anita Magowska, Medical University of Poznan, Poland
10:40	**Importance of „Farmacijos žinios" Journal for Lithuanian readers** Assoc. Prof. Vilma Gudienė, Faculty of Pharmacy, LUHS, Lithuania
11:10	**Pharmacist Practice. Ability to teach and learn throughout life** Indrė Trečiokienė, Vilnius University, Lithuania
11:40	**Development of medicinal (aromatic) plants research and their application in Lithuania 1785-2020** Prof. Ona Ragažinskienė
12:10-13:00 Break / Presentation of posters	
13:00	**Regulatory Practice for Clinical Trials of New Medicines in the European Union** Dr. Rima Minkutė, Faculty of Pharmacy, LUHS, Lithuania
13:30	**Drug Interaction with Food – Pharmacological Assessment** Laimis Akramas, UAB Aksada, Lithuania
14:10	**Experience of distance selling of prescription drugs in Estonia and other EU countries** Pharm. Kaidi Sarv Vendla, Estonian Pharmacists Association, Estonia
14:40	**Pharmacoeconomics and pharmacies** Indrė Brazauskaitė, UAB TAMRO/BENU, Lithuania
15:20	**Discussions**

16:00-17:00 LPA annual meeting

- Discussion of LPA activities in the previous year.
- Perspectives of LPA in organizing professional development of LPA members through conferences, forums (BaltPharm), congresses (FIP, EHPA).
- Increasing the prestige of the profession of pharmacist and spreading it among the society and youth.
- Perspectives of training a clinical pharmacist in Lithuania, taking into account the program provided by the Government.
- Pharmacist's stand (opinions of LPA members, comments on the organization's activities).
- Increasing LPA membership to include young pharmaceutical professionals.

PROGRAMA

10:00-16:00 PLENARINĖ SESIJA **Pirmininkauja:** Prof. Vilma Petrikaitė, Lietuvos farmacijos sąjungos (LFS) prezidentė Vaist. Eglė Rasa Dieninytė, organizacinio komiteto pirmininkė	
10:00	**LFS tarptautinės konferencijos atidarymas** Prof. habil. Dr. Eduardas Tarasevičius, LFS viceprezidentas, Lietuva Prof. Vilma Petrikaitė, LFS prezidentė, Lietuva
10:10	**Farmacijos žurnalo "Pamiętnik farmaceutyczny Wilenski" tematika ir jo svarba visuomenei** Prof. habil. Dr. Anita Magowska, Poznanės medicinos universitetas, Lenkija
10:40	**"Farmacijos žinių" žurnalo reikšmė Lietuvos skaitytojams** Doc. Vilma Gudienė, LSMU Farmacijos fakultetas, Lietuva
11:10	**Vaistininko praktika. Gebėjimas mokyti ir mokintis visą gyvenimą** Indrė Trečiokienė, Vilniaus universitetas, Lietuva
11:40	**Vaistinių (aromatinių) augalų tyrimų plėtra ir taikymas Lietuvoje 1785-2020 m.** Prof. Ona Ragažinskienė, Vytauto Didžiojo universitetas, Lietuva
12:10-13:00 Pertraukėlė / Stendinių pranešimų pristatymas	
13:00	**Naujų vaistų klinikinių tyrimų reglamentavimo praktika Europos Sąjungoje** Dr. Rima Minkutė, LSMU Farmacijos fakultetas, Lietuva
13:30	**Vaistų sąveika su maistu – farmakologinis vertinimas** Vaist. Gyd. Laimis Akramas, UAB Aksada, Lietuva
14:10	**Receptinių vaistų nuotolinio platinimo patirtis Estijoje ir kitose ES šalyse** Vaist. Kaidi Sarv Vendla, Estijos vaistininkų asociacija, Estija
14:40	**Farmakoekonomika ir vaistinės** Indrė Brazauskaitė, UAB TAMRO/BENU, Lietuva
15:20	**Diskusijos**
16:00-17:00 LFS suvažiavimas • LFS praėjusiųjų metų veiklos aptarimas. • LFS perspektyvos organizuojant LFS narių kvalifikacijos kėlimą per konferencijas, forumus (BaltPharm), kongresus (FIP, EHPA). • Vaistininko profesijos prestižo didinimas ir sklaida visuomenės bei jaunimo tarpe. • Klinikinio vaistininko rengimo Lietuvoje perspektyvos, atsižvelgiant į Vyriausybės numatytą programą • Vaistininko tribūna (LFS narių nuomonės, pastabos dėl organizacijos veiklos) • LFS narių gausinimas, įtraukiant jaunuosius farmacijos specialistus.	

CONTENT

WELLCOME SPEECH

Dear participants of the XXXV Congress of the LPA and the International Scientific-Practical Conference,

This year marks the 200th anniversary of the publication of the first issue of 'Vilnius Pharmacy Handbook' (Pamiętnik farmaceutyczny Wilenski), the first magazine in Eastern Europe to be published by the prof. Johan Wolfgang. It contained articles from various fields of pharmaceutical science and practice, and their authors were both researchers and pharmaceutical practitioners. The significance of this publication was also appreciated by pharmaceutical historians from many European countries, who organized an international conference in Paris, which was attended by LITHUANIAN REPRESENTATIVES Alfonsas Kaikaris, Tauras Mekas and Eduardas Tarasevičius. Another important anniversary is the centenary of habil. dr. Eugenija Šimkūnaitė's birth. She was an active member of the LPA and published articles in the magazine 'Lietuvos Farmacijos žinios'. Thus, the LPA Congress and Conference are dedicated to mark these anniversaries. I congratulate all the participants in this event, and in particular the rapporteurs, who will present the latest news in pharmaceutical science. Participants in a remote event will learn a lot of useful knowledge and thus improve their professional qualifications. Special thanks to the foreign speakers from Poland and Estonia.

I wish all participants a good mood and a successful listening to the conference presentations.

On behalf of the organising committee
VicePresident of Lithuanian Pharmaceutical Association
Prof. Eduardas Tarasevičius

SVEIKINIMO KALBA

Gerbiami LFS XXXV-ojo suvažiavimo ir Tarptautinės mokslinės praktinės konferencijos dalyviai,

Šiais metais sukanka 200 metų nuo prof. Johano Volfgango pastangomis pradėto leisti pirmojo Rytų Europoje žurnalo „Vilniaus farmacijos žinyno“ („Pamiętnik farmaceutyczny Wilenski“) pirmojo numerio pasirodymo. Jame buvo patalpinti straipsniai iš įvairių farmacijos mokslų ir praktikos sričių, o jų autoriai buvo ir mokslininkai, ir farmacijos praktikai. Šio leidinio reikšmę įvertino ir daugelio Europos šalių farmacijos istorikai, Paryžiuje surengę tarptautinę konferenciją, kurioje dalyvavo LIETUVOS ATSTOVAI Alfonsas Kaikaris, Tauras Mekas ir Eduardas Tarasevičius. Kita svarbi sukaktis – tai habil. dr. Eugenijos Šimkūnaitės gimimo šimtmetis. Ji buvo aktyvi LFS narė, spausdino straipsnius „Lietuvos farmacijos žinių“ žurnale. Taigi, LFS suvažiavimas ir konferencija skirti šioms sukaktims pažymėti. Sveikinu visus šio renginio dalyvius, o ypač pranešėjus, kurie pateiks naujausias farmacijos mokslų naujienas. Nuotoliniu būdu organizuojamo renginio dalyviai sužinos daug naudingų žinių ir tuo būdu pakels savo profesinę kvalifikaciją. Ypatingai dėkojame užsienio pranešėjams iš Lenkijos ir Estijos.

Linkiu visiems dalyviams geros nuotaikos ir sėkmingo konferencijos pranešimų išklausimo.

Lietuvos farmacijos sąjungos (LFS) viceprezidentas
Konferencijos organizacinio komiteto pirmininkas
Prof. habil. dr. Eduardas Tarasevičius

"Pamiętnik Farmaceutyczny Wileński" – the first pharmaceutical journal in Vilnius and its importance to the society

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Introduction. This paper focused on the journal "Pamiętnik Farmaceutyczny Wileński" (in English: Vilnius Pharmaceutical Journal), published in Vilnius in 1820-1822, and its contribution to the development of pharmacy in the territories of Polish-Lithuanian Commonwealth annexed by the Russian Empire at the end of the 18th century.

Materials and Methods. The copies of the journal from the library of Poznan Society of Friends of Learning, Poznan, Poland, were investigated. Numerous studies by Witold W. Głowacki, Barbara Kuźnicka, and others are the secondary literature. The content of the journal was analyzed qualitatively in the social and scientific context.

Results and discussion. The publishing of the journal was a timeless achievement of the Pharmaceutical Division of the Vilnius Medical Society, established in 1819 by, amongst others, apothecaries Jerzy Gutt (1769-1836), Karol Wagner and Jan Fryderyk Wolfgang (1775-1859). The Division proved to be very dynamic and ambitious what may come from the fact that Gutt, Wagner, and Wolfgang were members of the Masonic lodge Gorliwy Litwin (in English: the Zealous Lithuanian), reactivated in Vilnius in 1816. Bartłomiej Gryzer (died 1822), Michał Macewicz (died 1820), Fryderyk Woelck (died 1856), Michał Machnauer (died 1828) and Maciej Szulc were other editors of the journal. The last two were former Wolfgang's students and members of the lodge, which meetings were organized in the University Pharmacy run by J. F. Wolfgang at the time. Fascination with the freemasonry ideals of continuous professional and personal self-improvement influenced the concept of "Pamiętnik…". The journal was arranged to disseminate the progress of pharmaceutical sciences (pharmacognosy, applied pharmacy, technique, natural sciences, pharmaceutical manufacture) and deontology in the best way. The editorial staff consisted of eight Vilnius pharmacists who were the principal authors and first readers of the journal as well. Most of the readers originated from the Polish Kingdom, founded in 1815 by the Versailles Treaty, and, so-called, the Western Country of Russia. They were doctors, lawyers, clerks, or wealthy aristocrats. Surprisingly, few residents of Vilnius subscribed the journal. In total, it was about 60 subscribers, too little to make the publishing cost-effective. In 1822, Wolfgang gave up further publishing of the first Polish specialized periodical. Excerpts and statements from German, French, British, and Swiss pharmaceutical and chemical periodicals prevailed in the journal. Publications of such eminent scholars as Johann W. Döbereiner (1780-1849), Christoph W. Hufeland (1762-1836), Johann Trommsdorff (1770-1837) and Louis N. Vauquelin (1763-1829) were cited and discussed. Pharmacists' floristic observations and comments on the pharmaceutical practice was the second-largest group of articles. In this way, pharmacists and other readers from the Russian partition of the Polish-Lithuanian Commonwealth were familiarizing with the newest achievements of European pharmacy and botany; moreover, they were more and more prepared to take up scientific work. It is worth to mark that J. W. Wolfgang wrote articles on the newly invented machines using devices brought by him from abroad to the University Pharmacy in Vilnius. The periodical was the first platform for discussion on deontology and social integration of pharmacists and naturalists residing in the Russian partition.

Conclusions. Tquarterly spread the culture of Vilnius University and was the significant achievement of Prof. Wolfgang and his former students. From today's perspective, "Pamiętnik Farmaceutyczny Wileński" provides knowledge on efforts to modernize pharmacies and pharmaceutical profession in Eastern Europe, especially in Lithuania.

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Žurnalo „Farmacijos žinios" svarba Lietuvos vaistininkų bendruomenei

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Įvadas. Vaistininkų periodinis žurnalas – tai profesinės bendruomenės komunikacijos priemonė, tarnaujanti mokslo žinių sklaidai, diskusijoms, informacijos perteikimui. Šiais metais minime 200-ąsias metines, kai Lietuvoje buvo išleistas pirmasis farmacijos žurnalas *Pamietnik Farmaceutyczny Wilenski* (leistas 1820-1822 m.). Jis gyvavo du metus ir leidyba nutrūko. Tik praėjus šimtmečiui, 1923 m., vaistininkų bendruomenė laikinojoje sostinėje Kaune pradėjo leisti profesinį žurnalą „Farmacijos žinios". Šis žurnalas gyvavo 18 metų, iki 1940 m., pažymėtų esminėmis permainomis Lietuvoje.

Šaltiniai: Pranešime bus apžvelgiama profesinės periodikos istoriografija ir *Farmacijos žinių* publikacijų (1923–1940) istorinio tyrimo rezultatai.

Rezultatai: Dvi organizacijos – Lietuvos vaistininkų draugija ir Lietuvos farmaceutų sąjunga – buvo *Farmacijos žinių* leidėjos**,** išėjo 138 žurnalai. Leidinį redagavo keturi vaistininkai, ilgiausiai Steponas Nasvytis. 1926 m. leidyba buvo nuostolinga ir sąnaudos 2000 litų viršijo pajamas, 1928 m. leidinys davė 1500 litų pelną. Palaipsniui *Farmacijos žinios* tapo pelningu, populiariu ir įtakingu leidiniu.
Žurnale aptariamas temas galima suskirstyti į kelias grupes: 1. farmacijos administravimo klausimai, teisinė reglamentacija; 2. profesinių draugijų veikla; 3. farmacijos mokslas; 4. pasaulio farmacijos aktualijos; 5. diskusijos – nuomonės; 6. bendra informacija, naujienos ir kt. Pirmaisiais metais žurnalo leidėjai daugiau dėmesio skyrė farmacijos reikalų administravimo klausimams, diskusijoms apie valstybės institucijų priimamus sprendimus, apie rengiamą Farmacijos įstatymą, valdžios institucijų ir vaistininkų požiūrio į problemas savitumus. Palaipsniui vis daugiau publikuota mokslinių straipsnių.

Išvados: Profesinis žurnalas *Farmacijos žinios* tarpukario metais buvo svarbiausia ir populiari farmacininkų bendruomenės komunikacijos, informavimo, profesinės kompetencijos tobulinimo priemonė. Žurnalo turinys atskleidžia požiūrio į aktualiausias bendruomenei problemas kaitą: pirmuosiuose numeriuose daugiau diskutuota apie farmacijos reglamentavimą, kasdienes problemas, vėliau reikšmingai daugiau skiriama dėmesio farmacijos mokslui. Publikacijų autoriai – ne tik redakcijos nariai, draugijų valdybų atstovai, bet ir vaistininkai praktikai iš Lietuvos provincijos. Visa tai rodo, kad žurnalas buvo diskusijų, problemų aptarimo tribūna, reikšminga visai profesinei bendruomenei.

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Pharmacist Practice. Ability to teach and learn throughout life.

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The importance and usefulness of competency frameworks (CFs) in pharmacy professional development is recognized globally. The International Pharmaceutical Federation (FIP) Global Competency Framework in 2012 introduced four domains and competencies for pharmaceutical services which focus population, patient, health system and professional/personal practice. Scientific knowledge is essential, yet the key competencies of the professional services are so cold soft skills including communication, continuing professional development and self – management.

The role and contribution of pharmacists in the overall context of health care delivery is changing dramatically on a global level. In 2014 FIP alerted both practitioners and those in pharmacy education to challenging times ahead as the practice of pharmacy continued to become more complex and demanding. Pharmaceutical care, a model focusing on patient wellbeing and optimal outcomes from medication usage, demands a new level of professionalism in its practitioners. Pharmacists' focus on assuming a greater responsibility for the safe, effective and responsible use of medications by patients and populations, with the main goal of optimizing therapeutic outcomes. New competencies as clinical and communication skills, decision-making and critical thinking, leadership, innovation and research abilities for practices as medication therapy management, evidence-based pharmacy, collaborative practice, independent prescribing, and rational and responsible use of medicines are needed.

FIP Quality Assurance of Pharmacy Education emphasizes changes in the education of pharmacists. In the undergraduate pharmacy education, practice-based experiences are in value to the development of professionalism. For practicing pharmacists Continuing Professional Development (CPD) is emphasized. CPD is considered as self-directed, ongoing, systematic and outcomes-focused approach to lifelong learning that is applied into practice.

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Vaistinių (aromatinių) augalų tyrimų plėtra ir taikymas Lietuvoje 1785-2020 m.

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Įvadas. Sprendžiant augalų įvairovės gausinimo ir jų apsaugos, sveikos gyvensenos bei papildomosios ir alternatyviosios medicinos įstatymo įgyvendinimo problemas – tyrimo objektas yra vaistinių (aromatinių) augalų ir jų biologiškai veikliųjų junginių įvairovė.
Tyrimo tikslas – įvertinti vaistinių (aromatinių) augalų tyrimų raidą Lietuvoje nuo XVII a. iki dabar.

Metodai. Sisteminės teorinės analizės metodai.

Rezultatai ir diskusijos. Lietuvoje vaistinių (aromatinių) augalų tyrimai pradėti XVII a. ir yra susiję su farmacijos mokslo ir vaistažolininkystės raidos pradininkais (liaudies medicinos žinovais – etnobotanikais, klajojančiais vaistų pardavėjais – vengrais, vienuoliais vaistininkais) bei Jėzuitų ordino veikla, tiriant, auginant ir vartojant vaistinius augalus.
1785 m. prof. Juozapas Sartorijus pradėjo skaityti farmacijos kursą, kur pirmą kartą pateikė mokslinius duomenis apie vaistinių augalų pažinimo, jų biologiškai veikliųjų junginių ir vaistų gamybos būdų reišmę gydymui.
Pažymėtina prof. Johano Frydricho Volfgango Europinio lygio Farmacijos mokslo ir studijų veikla. Jis iniciavo Vilniaus Medicinos draugijos farmacijos skyrių, kuris 1820 m. išleido Europinio lygio periodinį žurnalą „*Pamiętnik Farmaceutyczny Wilenski*“ (*Vilniaus farmacijos užrašai*).
1831 m., uždarius Vilniaus universitetą su jame sukurtu botanikos sodu, sužlugo gamtos mokslai Lietuvoje.
Šiuo laikotarpiu Botanikos mokslinių veikalų ir vadovėlių autorius, farmakognozijos mokslo pradininkas Lietuvoje ir liaudies medicinos žinovas, Žemaitijos etnografiniame regione tyrinęs vaistinius augalus ir surinkęs induočių augalų herbarą – Jurgis Ambraziejus Pabrėža.
Po Vilniaus universiteto uždarymo, 1920 m. sausio 27 d. buvo įsteigti Aukštieji kursai Kaune.
1922 m. vasario 16 d. Aukštųjų kursų pagrindu įsteigtas Lietuvos universitetas, vėliau Vytauto Didžiojo universitetas, kuriame veikė Medicinos fakultetas su keturiais skyriais, tarp jų ir farmacijos.
1922 m. prof. dr. Konstantinas Regelis įsteigė Lietuvos universiteto Botanikos soda, o 1924 m. prof. dr. Kazimieras Grybauskas įkūrė Vaistinių augalų skyrių su Vaistinių augalų kolekcijomis ir bandymais. Jos buvo ir yra iki šiol nacionalinio ir tarptautinio bendradarbiavimo su kitomis mokslo institucijomis kompleksinės, tarpkryptinės vaistinių augalų introdukcijos mokslinės–projektinės veiklos ir studijų centras.

Apibendrinimas. Įvertinus vaistinių (aromatinių) augalų tyrimų raidą Lietuvoje nuo XVII a. iki dabar, nustatytas farmacijos ir vaistažolininkėstės mokslo indėlis, sprendžiant vaistinių augalų įvairovės gausinimo ir apsaugos, jų racionalaus naudojimo, sveikos gyvensenos bei papildomosios ir alternatyviosios medicinos įstatymo įgyvendinimo problemas.

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Naujų vaistų klinikinių tyrimų reglamentavimo praktika Europos Sąjungoje

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Klinikiniai tyrimai yra būtini kuriant naujus vaistinius preparatus, patvirtinant naujus gydymo metodus bei diagnostinius testus. Šiuose tyrimuose dalyvauja žmonės, todėl pagrindinis tyrimus reguliuojančių teisės aktų tikslas – užtikrinti tyrime dalyvaujančio paciento teises ir saugumą. Kaip rodo pasaulinis klinikinių tyrimų registras, tyrimų skaičius pasaulyje kasmet didėja maždaug 10 proc. Nors ir Europos Sąjungoje kasmet klinikiniams vaistinių preparatų tyrimams išduodama apie 4000 leidimų, tačiau stebimas tokių tyrimų mažėjimas – apie 25 proc. lyginant 2007 ir 2011 m. Ta pati tendencija matoma ir Lietuvoje – čia 2007 m. – 2018 m. pateiktų paraiškų skaičius klinikinių tyrimų vykdymui sumažėjo 27 proc.

Pagrindinis dokumentas, pagal kurį šiuo metu Europos Sąjungoje (ES) atliekami klinikiniai tyrimai - tai 2001 m. balandžio 4 d. priimta Europos Parlamento ir Tarybos direktyva 2001/20/EB dėl valstybių narių įstatymų ir kitų teisės aktų, susijusių su geros klinikinės praktikos įgyvendinimu atliekant žmonėms skirtų vaistų klinikinius tyrimus, suderinimo. Šio dokumento pagrindu šalyse narėse parengti nacionaliniai teisės aktai atsižvelgiant į geros klinikinės praktikos taisykles, tarptautinę žmogaus teisių konvenciją bei etikos principus. Tačiau, atskirų šalių teisės aktai turi savų ypatumų ir tai apsunkina klinikinių tyrimų vykdymą (pvz. iki 2020 m. sausio 17 d. Lietuvoje galiojęs reikalavimas I ir II fazės klinikinių tyrimų pagrindiniams tyrėjams turėti mokslo laipsnį). Harmonizuojant taisykles visoms šalims narėms, 2014 m. balandžio 16 d. priimtas Europos Parlamento ir Tarybos reglamentas Nr. 536/2014 dėl žmonėms skirtų vaistų klinikinių tyrimų, kuriuo panaikinama Direktyva 2001/20/EB, kuris turėtų suvienodinti reikalavimus ir paspartinti leidimų tyrimams išdavimą. Deja, kol kas reglamentas dar nėra taikomas.

LR biomedicininių tyrimų etikos įstatyme įteisinta sąlyga, kad žmogaus interesai svarbesni už visuomenės ir mokslo interesus, ir tai apima tiek tiriamojo įtraukimą į tyrimą, tiek konfidencialumo bei asmens duomenų apsaugą. 2018 m. gegužės 25 d. įsigaliojęs Europos parlamento ir tarybos reglamentas (ES) 2016/679 dėl fizinių asmenų apsaugos tvarkant asmens duomenis ir dėl laisvo tokių duomenų judėjimo ir kuriuo panaikinama Direktyva 95/46/EB, įnešė papildomų reikalavimų ir vykdant klinikinius tyrimus, ypač jeigu tyrimo duomenys yra perduodami į trečią šalį. Lietuva ir anksčiau buvo vienintelė šalis ES, kuri vykdė priemonių, užtikrinant asmens duomenų apsaugą klinikinio tyrimo metu, vertinimą, ir kurioje tyrimo vykdymui reikėjo gauti Valstybinės duomenų apsaugos inspekcijos (VDAI) leidimą. Dabar, po BDAR įsigaliojimo, sutrumpėjo pasirengimo laikas klinikinio tyrimo vykdymui Lietuvoje, nes nebereikalaujamas VDAI vertinimas ir pakanka reguliojančių institucijų (Lietuvos bioetikos komiteto ir Valstybinės vaistų kontrolės tarnybos) leidimų.

Besiplečiant mokslo žinioms, greta įprastų vaistų egzistuoja ir kita klinikinių tyrimų pakraipa – tai pažangios terapijos vaistinių preparatų (PTVP) klinikiniai tyrimai. Šią sąvoką atitinkantys preparatai – tai somatinių ląstelių preparatai, audinių inžinerijos bei genų terapijos preparatai, kurie galėtų pagerinti lėtinių ar sunkiai pagydomų (pvz. onkologinių) ligų gydymą. Žmogaus ląstelės, audiniai ir genai tampa vaistinių preparatų vystymo medžiaga ir reikalauja atnaujinti arba kurti naujus teisės aktus, apimančius šią sritį. Čia pagrindiniai dokumentai yra nuo 2008 m. gruodžio 30 d. galiojantis Europos parlamento ir tarybos reglamentas (EB) Nr. 1394/2007 dėl pažangiosios terapijos vaistinių preparatų, iš dalies keičiantis Direktyvą 2001/83/EB ir Reglamentą (EB) Nr. 726/2004 bei 2009 m. Europos komisijos patvirtintos geros klinikinės praktikos gairės, susijusios su PTVP (atnaujintos 2019 m.). Skirtingai nuo įprastinių vaistų kūrimo proceso, čia pasitelkiami ir Audinių bankai, tampa reikšmingi donorystę reguliuojantys teisės aktai, o gamintojams ir klinikinių tyrimų užsakovams atsiranda prievolė užtikrinti pilną preparato atsekamumą. Nors preparatai ir yra inovatyvūs, tačiau leidimų išdavimas tokių preparatų klinikiniams tyrimams ES gali užtrukti iki 1 m. ar net daugiau.

Norint pagreitinti PTVP taikymą žmonėms, 1394/2007 reglamento 28 straipsnis leidžia PTVP gaminti konkrečiam ligoniui pagal gydytojo paskyrimą ir vartoti tik sveikatos priežiūros įstaigoje. Lietuvoje tokia galimybė egzistuoja nuo 2010 m. (LR SAM 2010 m. liepos 28 d. įsak. Nr. V-675) ir vykdoma PTVP gamyba.

Nepaisant gana sudėtingo klinikinių tyrimų reglamentavimo, tyrimų organizavimas ir vykdymas plečia mokslininkų bei tyrėjų žinias, o tuo pačiu suteikia galimybę gauti naujo vaistinio preparato naudą ir tyrimuose dalyvaujantiems pacientams.

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Vaistų sąveika su maistu – farmakologinis vertinimas

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Įvadas. Vidutiniškai per metus Lietuvoje yra nuperkama 75 mln. vaistų pakuočių. Vidutiniškai vienam gyventojui kasdien tenka daugiau nei viena vaistų dienos dozė, skaičiuojant DDD metodu. Tačiau retas vartotojas perskaito visą vaistų informacinį lapelį, kuriame yra svarbi informacija, su kokiu maistu ar gėrimais nepatartina vartoti konkrečių vaistų. O kartais tiesiog nesusimąstoma apie galimas nepageidautinas vaistų su maistu saveikos pasekmes, kai tabletė užgeriama greipfrutų sultimis ar dietine kola, o po to, vakarienės metu, išgeriama viena ar dvi taurės vyno, o gal ir ko stipresnio.

Šaltiniai: Apžvalga atlikta remiantis mokslinėmis publikacijomis apie dažniausiai pasitaikančias maisto ir vaistų sąveikas.

Rezultatai: Šiame pranešime apžvelgiamos dažniausiai pasitaikančios vaistų ir maisto nepageidaujamoss ir net pavojingos sąveikos.Vaistų ir maisto sąveika mums svarbi tuomet, kai maistas ar jo komponentai paveikia vaisto skaidymo, pasisavinimo kelią, keičia jo koncentraciją organizme arba jo veikimo mechanizmą ir norimą poveikį bei gali sukelti rimtų nepageidaujamų reakcijų, kurios kartais gali baigtis mirtį sukeliančiomis komplikacijomis. Tačiau, kai kuriais atvejais maisto ingradientų ir vaistų sąveika gali būti teigiama- sustiprinamas vaisto terapinis poveikis, sumažėja nepageidautinų reiškinių atsiradimo rizika.

Išvados: Žinant maisto ir vaistų sąveikos dėsningumus, galima pasiekti geresnio ir saugesnio gydymo rezultatus, išvengti gydymo nesėkmių, o kartais net letalinių pasekmių. Siekiant geresnių gydymo rezultatų, galima išnaudoti ir teigiamus maisto ir vaistų sąveikos atvejus. Dažnai vaistų ir maisto sąveika tampa ne mažiau reikšminga, nei sąveika tarp vaistų.

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Experience of distance selling of prescription drugs in Estonia and other EU countries

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Since year 2013 possibility to sell medicinal products via the Internet is open for all community pharmacies in Estonia. Pharmacies that have the right to handle medicinal products in Estonia may create relevant webpages. A company needs an activity licence to trade medicinal products in Estonia. The basic requirement is that the company ensures proper handling of medicinal products, i.e., their storage and dispensing as well as counselling of patients by professionals. The establishment of an online pharmacy is subject to the existence of a pharmacy with premises and professional staff.

An online pharmacy in Estonia may sale both over-the-counter and prescription medicines. Before one can buy a prescription medicine, a medical practitioner needs to have issued a digital prescription which the pharmacist can view in the e-prescription centre and sell to the patient via Internet. The transition to digital prescriptions took place in 2010. Today, more than 99% of all prescriptions in Estonia are issued electronically.

When buying an over-the-counter medicine, one needs to take into account that the age of the patient and the medicinal condition for which the medicinal product is needed must be submitted. Over-the-counter medicines for animals and other health products may be also bought at online pharmacies. Counselling must be guaranteed to a customer wishing to buy a medicinal product over the Internet, i.e. whenever one buys a medicine, a pharmacist will be there to give advice on which product to choose.

Delivery time of medicinal products bought at online pharmacies must be same for urban and rural areas. The maximum time to deliver a medicinal product to the most distant location in Estonia should be no more than three working days. The delivery fees may vary depending on the type (e.g. courier, postal service, automated package delivery systems); however, they must not depend on the address of the patient, specific medicinal product, consignment value or the number of medicinal products or deliveries to a customer.

First distance selling in Estonia started at November 2013 by Terve Pere Apteek OÜ pharmacy (trademarked Apotheka), https://www.apotheka.ee/. In November 2019, second online pharmacy started operating in Estonia: Veerenni apteek OÜ (trademark Südameapteek), https://www.sudameapteek.ee/. From the internet pharmacy, over-the-counter and prescription medicines may be purchased (except narcotic and psychotherapeutic medicine, and anabolic steroids); over-the-counter medicines, medicines for animals and health & beauty products are also available. Delivery takes up to 3 days and delivery fee differs from 0 to 5 €.

Distance selling in other countries (examples). In the European Union it is possible to buy medicines online. Patients should only buy medicines from online retailers registered with the national competent authorities in the EU Member States. The European Commission has introduced a common logo that appears on the websites of these registered retailers. The national flag and the text are an integral part of the logo. Only national flags of an EU Member State, as well as those of Norway, Iceland and Liechtenstein can be displayed.

In the Republic of Latvia only non-prescription medicines can be distributed online. Retail selling of medicines via the internet is allowed only for those general or open type pharmacies which have obtained a specific licence for operation of a general or an open type pharmacy with a special notification in the licence – distribution of non-prescription medicines via the internet. There is 8 online pharmacies in Latvia (5.3.2020).

In Finland, medicines can also be bought in online pharmacies. Products available include both over-the-counter and prescription-only medicines. To buy prescription medicines online, an electronic prescription is needed. Professional consultation is always required when buying medicines. Personal service is also available in online pharmacies by telephone or over a web service. Buying and receiving medicines from outside the European Economic Area is prohibited. The importer or buyer of the medicine is solely responsible for any risks involved in illegal medicine trade. Private individuals may accept medicinal products delivered by post (including express mail and courier deliveries) from the EEA to Finland if the supplier operates legally and the medicinal product has been approved by the authorities of the country in question. Until the end of the Brexit transition period on 31 December 2020, restrictions concerning the import of personal medicines from EEA countries will also be applicable to personal medicines brought from Great Britain. As negotiations between the EU and Britain progress, more detailed information will be provided on what will happen from 1 January 2021 onward when the transition period comes to an end.

Pharma economics and retail pharmacies: coherence and actuality

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Introduction. Based on Ministry of Finance of Republic of Lithuania report on 2020 budget (1), planned expenses on medications were 395.8 million euros. In the context of aging population and increased life expectancy, this amount is expected to grow. Therefore, impact of pharma economic – decisions of all healthcare stakeholders, such as government, retail pharmacies, pharmaceutical manufacturers and distributors, is gaining increased attention and relevance.

Materials and Methods. The content of the thesis consists of a synthesis and meta-analysis of market data (IQVIA reports), state budget assumptions and insights on market development.

Results and discussion. In the context of aging population and increased life expectancy, healthcare budgets are facing growing burden of medical expenses. Two streams, that concern expenses of medications, exist – expenses on generic medications and innovative drugs. Segment of generic medications tend to commoditize, as the prices are being pushed to reduction, and new initiatives, such as frequent changes of reimbursment lists, are being implemented to encourage the competition, liberalize trade and reduce expenses. Yet segment of innovative drugs, tend to be a focus of pharmaceutical manufacturers and wholesalers, while countries tend to invest in more innovative treatment options for critical patients' groups and conditions. Role of pharmacist in both case is distinguished – pharmaceutical service as such is shifting to a service of personal pharmacist with a closer cooperation with patients, physicians and pharmaceutical companies. With growing pressure on healthcare expenses, this tendency is expected to continue.

Conclusions. The increasing cost of healthcare products and services has become a great concern for patients, healthcare professionals, insurers, politicians and the public. Following the existing tendencies in the market, importance of pharma economics in decision making among all stakeholders tend to strengthen. Therefore, exclusion between generics and innovative medicines' segments us going to increase. Numerous drug alternatives and empowered consumers also contribute to the need for economic evaluations of pharmaceutical products. The increasing concern has prompted demand for the use of economic evaluations of alternative healthcare outcomes. This escalation in healthcare spending is due to increased life expectancy, increased technology, increased expectations, increased standards of living and an increased demand in healthcare quality and services, tends to continue.

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Etnobotanikės habil. dr. Eugenijos Šimkūnaitės indėlis farmacijos mokslui Lietuvoje

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Įvadas
Sprendžiant Farmacijos mokslų ir praktikos pasiekimus ir minint pirmojo farmacijos žurnalo išleidimo 200 m. metines, svarbu pažymėti vaistininkės, etnobotanikės habil. dr. Eugenijos Šimkūnaitės indėlį farmacijos mokslui ir vaistažolininkystės plėtrai Lietuvoje.
Tyrimo objektas Habil. dr. Eugenijos Šimkūnaitės autobiografija ir mokslinės – praktinės veiklos rezultatai.
Tyrimo tikslas – įvertinti habilituotos gamtos mokslų daktarės Eugenijos Šimkūnaitės mokslinės- praktinės veiklos rezultatus ir nuopelnus Lietuvoje.

Metodai
Informacija rinkta žinynuose, enciklopedijose, moksliniuose žurnaluose, pritaikant teorinės analizės metodą [1-4].

Rezultatai ir diskusijos
Santraukoje pateikiami vaistininkės, vastažolininkės, etnonobotanikės, Lietuvos nacionalinio kultūrinio paveldo bei tradicinės medicinos puoselėtojos, habilituotos gamtos mokslų daktarės Eugenijos Šimkūnaitės mokslinės- praktinės veiklos rezultatai.
2020-uosius metus Lietuvos Respublikos Seimas paskelbė habil. dr. Eugenijos Šimkūnaitės metais, įvertindamas mokslininkės indėlį į vaistažolininkystės mokslo vystymą ir praktinę reikšmę liaudies medicinai. Ji identifikavo, ištyrė ir aprašė vaistinius augalus, rekomendavo vaistnę augalinę žaliavą ligų prevencijai ir gydymui, moksliškai pagrindė indikacijas, kontraindikacijas bei nepageidaujamą poveikį. Ši vaistininkė ypatingą dėmesį teikdavo gydytojo įvertintai paciento sveikatos būklei ir nustatytai diagnonozei, prieš rekomenduodama gydymui vaistinius augalinius preparatus ir savo sukurtas receptūras.
Mokslininkės praktinės – ūkinės veiklos rezultatas vaistažolininkystės plėtrai – sukurtas Gerdašių eksperimentinis vaistažolių ūkis Lazdijų rajone.

Apibendrinimas
Habil. dr. Eugenijos Šimkūnaitės mokslinės ir praktinės veiklos pagrindu, pirmą kartą Lietuvos Respublikos Seimo istorijoje, atkreiptas dėmesys į farmacijos mokslo – Farmakognozijos sritį – vaistinių augalų tyrimą ir jų praktinį pritaikymą.

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Nutmeg (*Myristica fragrans*) Essential Oil Yield Using Magnesium Aluminometasilicate as Excipient

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Introduction. Nutmeg seeds are better known as a spice, but their essential oil may have a pharmacological effect. Scientific sources say that nutmeg has antibacterial, antioxidant, anticancer, antidepressant, and other effects [1, 2]. Nutmeg essential oil is colorless to pale-yellow with a specific odor. The essential oil yield may be more than 10% and varies by 5-15% [3, 4]. Hydrodistillation is the most popular method that is used to obtain essential oil. It is cheap because it mostly uses water as a solvent. The equipment is not expensive, most commonly a Clevenger-type apparatus is used. We found few studies where the excipients are used in hydrodistillation (NaCl salt solution, sea water, and non-ionic surfactants) [5, 6]. So, we decided to use a new material – magnesium aluminometasilicate – as a new excipient in hydrodistillation. It has the ability to absorb materials, so we predicted that it can increase the yield of essential oil.

Materials and Methods

In this research, nutmeg seeds from Grenada were used for the production of essential oil. Magnesium aluminometasilicate (Neusilin® US2, Fuji Chemical Industries Co., Japan) was used as excipient. Distilled water was used throughout the study. The yield of the essential oil was measured using scales.
Hydrodistillation was carried out in 4 hours by using Clevenger-type apparatus. The samples were prepared using nutmeg powder, distilled water, and excipient. The amount of excipient was based on water quantity, its concentration was from 0% to 2%. All samples were prepared using 15 g of nutmeg powder and 300 mL of distilled water. The essential oil was collected in an airtight bottle and stored in a refrigerator at 4 °C.

Results and discussion

We prepared 4 samples of nutmeg essential oil. The excipient quantity was: 0%, 0.5%, 1%, and 2%. We determined the essential oil yield was 5.25 ± 0.04% of pure essential oil without excipient. When we used 0.5% of the excipient, the yield was 7.9 ± 0.05%. The mass of the essential oil with 2% of magnesium aluminometasilicate was 1.565 g, pure essential oil – 0.789 g.

Conclusions

The yield of the essential oil from nutmeg seeds was significantly higher when an excipient was used. In other researchers' studies, the yield of essential oil did not increase significantly. However, our study showed that by using 2% of magnesium aluminometasilicate, the yield increased by almost two times compared to pure essential oil (0% excipient). The excipient improves the absorption of volatile compounds and increases the yield of essential oil.

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Activity of *Crocus sativus L.* extracts on human brain cancer cell lines

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Brain tumours can strike at any age and rather more than 50 per cent of them are malignant with poor prognosis. (1,2) Conventional and newly emerging treatment procedures have not succeeded in reversing the outcome of cancer diseases to any drastic extent which has led researchers to investigate alternative and less toxic treatment options. (3)

The pharmacological effects of aqueous or ethanolic extracts of *Crocus sativus L.* (Saffron) have been described in the literature and comprise a wide spectrum of activities, including anticancer properties (4). There are scientific data showing that therapeutic doses of saffron exhibits no significant toxicity (5). The aim of our research was to evaluate the anticancer activity *in vitro* of *C. sativus L.* extracts produced at National University of Pharmacy, Ukraine.

In our experiments as a cancer model system, we used two brain cancer cell lines U-87 and SK-N-BE(2). MTT assay has been used to evaluate the metabolic activity of cells after their treatment with tested extracts. Half-maximal effective concentration (EC_{50}) value that represents the concentration of a compound causing 50% reduction of cancer cell metabolic activity has been assessed.

All eight examined extracts of *C. sativus L.* inhibited the viability of tested cancer cells and demonstrated higher activity against SK-N-BE(2) cell line. The most active was ethanolic extract of saffron corms, its EC_{50} value against SK-N-BE(2) cells was 0.018 ± 0.002 mg/ml, and 0.02 ± 0.002 mg/ml against U-87 cells. Ethanolic extracts of saffron flowers and leaves were more active than aqueous extracts against both cell lines. Aqueous extract of saffron stigma possessed higher activity than ethanolic one against both cell lines.

In conclusion, all tested *Crocus sativus L.* extracts are more active against SK-N-BE(2) neuroblastoma cell line compared to U-87 glioblastoma cell line and could be developed as anticancer agents against brain cancer.

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Trend of Antihypertensive Medicine Use in the Baltic States between 2008 and 2018

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Introduction. High blood pressure is the most important risk factor contributing to death and disability rates. High prevalence of hypertensions is seen in all three Baltic States, thus making prevention and selection of drugs important for therapy. The aim of this study is to compare utilization of antihypertensive medicines in Estonia, Latvia and Lithuania during the last 11-years.

Materials and Methods. Wholesale data was used to calculate the use of antihypertensive medicines in 2008-2018. Data was obtained from the National retail audit IQVIA. The ATC/DDD methodology was used to calculate utilization of (RAS) inhibitors, including angiotensin converting enzyme inhibitors -ACEi (C09A and C09B) and angiotensin II receptor blockers - ARBs (C09C and C09D), beta receptor blockers (C07), calcium channel blockers (C08), diuretics (C03) and other antihypertensives (C02). The results were expressed in DDD per thousand inhabitants per day (DDD/TID). Time series analysis was used to analyze trends and ANOVA tests were used to test differences between countries.

Results and discussion. The total use of antihypertensive drugs was 372.0 DDD/TID in Estonia, 379.5 DDD/TID in Lithuania and 267.0 DDD/TID in Latvia in 2018. Respectively the utilization of antihypertensive's increased by 10.88 DDD/TID (95% CI: 7.13 – 14.63, P= 0.0001, R^2= 0.827), 8.04 DDD/TID (95% CI: 4.57 – 11.52, P= 0.0005, R^2= 0.753) and 6.42 DDD/TID (95% CI: 2.44 – 10.41, P= 0.005, R^2= 0.597) annually. The use of all classes increased, except the calcium channel blockers. The most frequently used class in 2018 was inhibitors of the RAS, followed by beta-blockers in all three Baltic countries. In 11 year's use of fixed-dose combinations has increased by quarter to third from 30.3 to 94.9, from 33.7 to 87.1 and from 28.2 to 106.6 DDD/TID respectively in Estonia, Latvia and Lithuania. The use of older central acting antihypertensive's was significant between countries with 30.9 DDD/TID in Lithuania compared to 3.01 DDD/TID in Estonia and 16.17 DDD/TID in Latvia (p=0.000001) in 2018.

Conclusions. The use of antihypertensive medicines increased in Estonia, Latvia and Lithuania. The increase was mostly driven by RAS inhibitors, beta-blockers and fixed-dose combinations in all three countries. Further research is needed to detect health impact of differences in use of antihypertensive drug classes in Estonia, Latvia and Lithuania.

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Anticancer activity of beta adrenoblockers in pancreatic cancer cells lines

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Pancreatic cancer remains one of the most lethal malignant tumors that caused 432,242 new deaths (4.5% of all deaths caused by cancer) in 2018 (GLOBOCAN 2018 estimates). Despite advancements in the knowledge of potential risk factors that cause pancreatic cancer and newly available tools for early diagnosis and treatment of pancreatic cancer, the 5-year survival rate still is only 9% [1]. Thus it is very important to investigate new potential ways of pancreatic cancer treatment and control.

In vitro studies have suggested a potential role of beta-blocade in the regulation of several cancers, including pancreatic, prostate, breast, colon, and ovarian [2]. Beta adrenoblockers can inhibit multiple processes of tumor progression and metastasis, including the inhibition of tumor cell proliferation, migration, invasion [3].

To investigate beta adrenoblockers anticancer activity *in vitro*, we selected two pancreatic cancer cell lines – MIA PaCa-2 and Panc-1. These cell lines are primary tumors currently used as *in vitro* models to study pancreatic ductal adenocarcinoma carcinogenesis [4]. We also selectecd two non-selective beta adrenoblockers (propranolol and pindolol) and two beta-1 adrenoreceptor selective antagonists (atenolol and betaxolol). MTT assay was used to evaluate the viability of cancer cells after the treatment with these compounds. The half-maximal effective concentration value (EC_{50}) represents the concentration of a compound causing 50% reduction of cancer cell metabolic activity.

The results of MTT assay experiment have shown that propranolol had the **greatest** effect on cell viability inhibition in both cell lines, its EC_{50} value against MIA PaCa-2 cells was 53.33 ± 5.77 μM and 35.67 ± 4.04 μM against Panc-1 cell line. In addition, selective beta adrenoblocker betaxolol suppressed cell viability at higher concentrations than propranolol, its EC_{50} value against MIA PaCa-2 cells was 206.67 ± 11.55 μM and 108.33 ± 20.21 μM against Panc-1 cells. Panc-1 cell line was more sensitive to both beta adrenoblockers than MIA PaCa-2 cell line. The other two compounds, pindolol and atenolol, showed the weakest effect on cell viability inhibition in both cell lines, their EC_{50} values were higher than 500 μM.

In conclusion, propranolol has the greatest effect on cell viability inhibition in both pancreatic cell lines. The second most active compound in both cell lines was betaxolol. These two beta adrenoblockers could be used for the development of new agents for the treatment of pancreatic cancer.

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Activity of new sunitinib analogues on colon cancer cell lines

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Colon cancer is the second cause of death between all cancers [1]. Chirurgical interventions and chemotherapy are the most used treatments in the case of colon cancer [2]. Despite the progress in cancer treatment, there is still a need for advanced and more effective anticancer agents. Kinase inhibitors regorafenib and sunitinib are used to treat colon cancer [3] and there are scientific data showing that kinase inhibition is related to the anticancer effect [4]. The aim of our research was to evaluate the anticancer activity *in vitro* of new sunitinib analogues synthesized at Cagliari University, Italy.

In our experiments as a cancer model system we used two colon cancer cell lines HT-29 and HCT116. MTT assay was used to evaluate the metabolic activity of cells after their treatment with tested compounds. Half-maximal effective concentration (EC_{50}) value that represents the concentration of a compound causing 50% reduction of cancer cell metabolic activity has been established for the most active compounds. Sunitinib was used as a comparative compound.

At first we performed anticancer activity screening of 17 compounds by MTT assay and identified the most active ones for more detailed studies. CompoEunds #1, #6 and #7 showed the highest activity against both cell lines.

All three tested compounds statistically significantly stronger inhibited the viability of tested cancer cells compared to sunitinib. Their activity was from 3 to 26 times higher against HT-29 cell line and from 11 to 58 times higher against HCT116 cell line. The most active compound was #1, its EC_{50} value against HT-29 cells was 76.7 ± 9.4 nM, and 91.7 ± 20.1 nM against HCT116 cells. Compounds #1 and #6 possessed a very similar activity against both cell lines, and compound #7 was more active against HCT116 than HT-29 cell line.

In conclusion, sunitinib analogues #1, #6 and #7 are more active against colon cancer cell lines HT-29 and HCT116 compared to sunitinib, and could be developed as anticancer agents against colon cancer.

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Žurnalo „Vilniaus farmacijos žinynas" svarba Lietuvos farmacijai

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Įvadas. 2019 m. Lietuvos farmacijos sąjungos iniciatyva buvo organizuota tarptautinė konferencija, skirta pirmosios profesinės farmacijos draugijos įkūrimo 200-osioms metinėms pažymėti. Šios draugijos įkūrėjas prof. Johanas Fridrichas Volfgangas 1820 m. pradėjo leisti žurnalą „Vilniaus farmacijos žinynas" lenkų kalba (*Pamiętnik Farmaceutyczny Wilenski, Wilno pharmaceutical diary).* Tai buvo pirmasis Rusijos imperijoje žurnalas farmacijos klausimais

Šaltiniai: Straipsnyje apžvelgiama profesinės periodikos pradininko *Vilniaus farmacijos žinyno* publikacijų (1820-1822) svarbos istoriografija.

Rezultatai: *Vilniaus farmacijos žinyno* leidėjas buvo Vilniaus medicinos draugijos farmacijos skyrius. Leidinį redagavo prof. Johanas Fridrichas Volfgangas. 1820-1822 metais išėjo aštuoni žurnalai, kurių apimtis sudarė 1247 puslapius. Dėl lėšų stokos tolimesnis žinyno leidimas nutrūko. Žinyno tyrėjai nustatė, kad prenumeratorių skaičius siekė 300 asmenų. Jų tarpe buvo farmacijos ir medicinos specialistai, kurie dirbo universitetuose (Vilniaus, Varšuvos, Krokuvos), o didesnė dalis žinyno skaitytojų buvo vaistininkai, dirbusieji 24 gubernijose. Vertinant žinyno turinį, tyrinėtojai nurodė, kad užsienio farmacijos naujienos sudarė 53 procentus visų publikacijų, o originalūs straipsniai sudarė 47 procentus. Žinyne talpinama medžiaga buvo suskirstyta į septynias rubrikas: farmakognozija, farmacija ir farmacinė chemija, farmacinė technologija ir taikomoji farmacija, fizika ir gamtos chemija, farmacijos literatūra, farmacinės gamybos priemonės, farmacijos kronika, įvairūs pranešimai ir naujienos. Žinyne buvo atspausdinta daugiau nei 160 straipsnių. Išsamūs šio žinyno tyrimų rezultatai buvo pateikti tarptautiniame koliokviume, vykusiame Paryžiuje 1990 m., kuriame dalyvavo ir Lietuvos farmacijos istorijos tyrėjai.

Išvados: Pirmasis Rusijos imperijoje profesinis žurnalas *Vilniau farmacijos žinynas* prieš du šimtus metų atliko svarbų vaidmenį, informuojant farmacijos ir medicinos specialistus apie farmacijos mokslų ir praktikos naujienas Vokietijoje, Prancūzijoje ir Rusijoje. Tai buvo reikšminga vaistininkų bendravimo ir profesinės kvalifikacijos kėlimo priemonė. Straipsniuose buvo pateikiami mokslinių tyrimų rezultatai, daug dėmesio buvo skiriama vietinės farmakognostinės žaliavos aprašymui ir vaistų gamybos technologijų tobulinimui. Šio leidinio pasirodymas prieš du šimtmečius padėjo pagrindus farmacijos periodinių leidinių atsiradimui 20 amžiuje: *Farmacijos žinių* ir *Lietuvos farmacijos žinių* žurnalams.

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Phenolic compounds and antioxidant activity in *Hippophae rhamnoides L.* leaves extracts during different vegetation periods

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Introduction: *Hippophae rhamnoides L.*, also known as sea buckthorn, is a member of the *Elaeagnaceae* family. Various pharmacological activities have been reported such as anti-inflammatory, adaptogenic, tissue regeneration, strong anti-viral, anti-tumor, antioxidative and hepatoprotective [1,2]. These therapeutic effects and antioxidant potential of *Hippophae rhamnoides L.* mostly are related to the high amounts of flavonoids and phenolic acids derivatives. Studies have shown that predominant flavonoids in sea buckthorn leaves are rutin, quercetin, kaempferol, isorhamnetin and their glucosides. The main phenolic acids are gallic, caffeic, p-coumaric and ferulic acids [3]. The individual ontogenesis has a significant effect on the content of antioxidant compounds in the leaves [2]. The aim of the study is to determine total phenolic composition content and antioxidant activity of *Hippophae rhamnoides L.* leaves during different vegetation periods.

Materials and Methods: Leaves of *Hippophae rhamnoides L.* were collected in their natural habitat in the fields near the town of Žeimelis (coordinates: 56°15'48.3"N 23°59'26.3"E). They were collected in different vegetation periods from May to the end of September during the year 2019. The extracts were prepared using 0.2 g of dry matter and 20 ml of 70% ethanol, and the extraction was performed in an ultrasonic bath for 15 minutes. Total phenolics were determined by spectrophotometric Folin–Ciocalteu method and total antioxidant capacity – by ABTS and FRAP assays.

Results and discussion: The results have shown that the highest total amount of phenolic compounds was determined in sea buckthorn leaves collected in June (112,96 ± 12,56 mg GAE/g DW). The greatest antioxidant capacity measured of sea buckthorn leaf extracts with FRAP assay was 1250,11 ± 85,1 μmol trolox equivalent (TE)/g and with ABTS assay - 2123,45 ± 235,38 μmol (TE)/g during the leaf's expansion period in June. The lowest radical scavenging and reducing activities were determined at the end of the vegetation period, 657,9 ± 69,74 μmol (TE)/g and 1030,8 ± 91,12 μmol (TE)/g, respectively.

Conclusions: Phenological phases have a great impact on the fluctuations in the amounts of phenolic compounds and antioxidant activity of leaf extracts. The phase of intensive leaf development distinguishes with the highest contents of phenolic compounds and the greatest radical scavenging and reducing effects.

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Natūralios kilmės antimikrobinės priemonės rezistentiškumo kartai

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Įvadas. Atsižvelgiant į didėjantį atsparumą, naujų antibiotikų trūkumas sukėlė daug nerimo. Natūralios antibiotinės priemonės yra evoliucijos produktai, todėl gali padėti įveikti iškilusius bioaktyvumo iššūkius [1]. Antimikrobiškai palankiomis antimikrobinėmis savybėmis pasižyminčių produktų vystymas gali būti vykdomas derinant eterinių aliejų, priešpienio komponentų, vaisių išspaudų ekstraktų bei probiotinėmis savybėmis pasižyminčių pieno rūgšties bakterijų modelius [2,3].
Medžagos. Antimikrobinių savybių tyrimui buvo panaudota 15 patogenų: P. aeruginosa 17-331, A. baumannii 17-380, B. cereus 1801, E. cloacae, S. epidermis, S. haemolyticus, P. multocida, S.enterica 24SPn06, P. mirabilis, S. haemolyticus, K. pneumoniae, MRSA M87fox, E. faecalis 86, E. faecium 103, B. cereus 1801.
Rezultatai ir diskusija. Nustatyta, kad *Thymus vulgaris* eterinis aliejus (EA) yra perspektyvi antimikrobinė priemonė, nes slopino visus tirtus patogenus [4]. *Eugenia caryophyllata* EA slopino visus tirtus patogenus, išskyrus P. aeruginosa. Nustatyta, kad plačiausiu antimikrobinio veikimo spektru pasižymėjo juodųjų serbentų liofilizuoti produktai ir obuolių liofilizuoti produktai (slopino 13 ir 12 patogenų, atitinkamai) [5]. Pieno rūgšties bakterijų (PRB) poveikis patogeninėms bakterijoms ištirtas standžiose terpėse. Nustatyta, kad didžiausiu antimikrobiniu aktyvumu pasižymėjo PRB LUHS210 ir LUHS245 [6]. Nustatyta, kad fermentuojant priešpienio mėginius padidinamas antimikrobinės priemonės funkcionalumas, nes gautas platesnis antimikrobinis spektras [7]. Priešpienio fermentacijai naudojamos PRB įtakoja produkto mikrobiologinės savybes ir imunoglobulinų sudėtį [8].
Išvados. Natūralios kilmės priemonės gali būti naudojamos dėl būdingų antibakterinių savybių. Vaisių perdirbimo šalutiniai produktai yra perspektyvi antimikrobinė priemonė. Priešpienio fermentacija pasirinktomis pieno rūgšties bakterijų padermėmis gali pagerinti šios antimikrobinės priemonės funkcionalumą.
Mokslinis tyrimas finansuotas/finansuojamas Europos regioninės plėtros fondo lėšomis pagal priemonės Nr. 01.2.2-LMT-K-718 veiklą „Aukšto lygio tyrėjų grupių vykdomi moksliniai tyrimai“.

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Investigation of CA IX protein inhibitors as an antimigratory agents

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Introduction. Tumor metastases are related to a poor cancer patient prognosis. Therefore, novel agents preventing cell migration from primary tumor sites are needed. Carbonic anhydrase IX (CA IX) is a tumor-related protein, expressed under hypoxic conditions in order to maintain proper pH, and is also related with cell adhesion [1], invasion and metastases [2]. The aim of our study was to test CA IX inhibitor for its antimigratory properties.

Materials and Methods
Human breast adenocarcinoma cell lines MDA-MB-231 and MCF-7 and human fibroblasts were cultured under normoxia and hypoxia (240 μM of $CoCl_2$) conditions for 48 h. A 35 mm imaging dish with a glass bottom and an imprinted cell location grid (Ibidi, Germany) was covered with 50 μl of rat tail collagen (1 mg/ml) and left to polymerize (1 h, 37 °C). Afterwards, normoxic and hypoxic cells were seeded (16 000 per plate) and left overnight. Then, medium was changed with the one containing 0, 5 or 20 μM of CA IX inhibitor VD11-4-2. Cells were imaged every hour for 6 hours. Images were analyzed by tracking single-cell paths and calculating single cell speeds. Experiments were repeated at least 3 times.

Results and discussion
CA IX inhibitor VD11-4-2 in concentration of 20 μM reduced migration velocities of hypoxic MDA-MB-231 and MCF-7 cells. Compound started to affect breast cancer cell migration rates after the second hour under hypoxia. Whereas compound did not influence migration speed of CA IX-negative normoxic breast cancer cells and human fibroblasts. This indicates that inhibitor VD11-4-2 perturbs cell migration only in CA IX positive cells.

Conclusions
CA IX is a promising target in the development agents for cancer cell migration prevention.

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Variation of the composition of phenolic compounds in plum fruit of different cultivars

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Introduction. Plums are among the most popular fruit grown in Lithuania and used in the food chain. Plums are used in the manufacturing of food products and are potentially valuable for the development and production of dietary supplements and functional food enriched with biologically active compounds. World plum production has been increasing slightly over the recent years. In 2018, it reached about 12.6 million tons. According to the production scale, plums were in the 7th position among the most cultivated fruit [1].

Materials and methods. The samples taken from 17 different cultivars of the European plum were analysed. The plum trees were grown in the garden of the Institute of Horticulture, Lithuanian Research Centre for Agriculture and Forestry. The slices of pitted plums were lyophilised. The samples were extracted with 83.64 % (v/v) ethanol in an ultrasonic bath for 40 minutes at room temperature. The analysis of the phenolic compounds was performed on the basis of ultra-high-performance liquid chromatography mass spectrometry method. All the results of the experiments were calculated for the absolute dry raw material.

Results and discussion. During the study, the following glycosides of the flavonol group were identified: avicularin, isorhamnetin-3-O-rutinoside, isoquercitrin, hyperoside, rutin, and an aglycone quercetin. In addition, compounds of the flavan-3-ol group were identified, such as (+)-catechin, procyanidin C1, and procyanidin A2, along with chlorogenic acid attributed to phenolic acids and a non-phenolic cyclitol – quinic acid. The highest total amount of the identified phenolic compounds was found in European plum samples of the 'Zarechnaya Ranniaya' cultivar, while the highest amount of quinic acid was found in plum fruit samples of the 'Jubileum' cultivar. Of all the identified phenolic compounds, chlorogenic acid predominated, and its amounts were significantly higher than those of other quantitatively evaluated phenolic compounds. The percentage part of chlorogenic acid in the studied plum fruit samples comprised 6.0% to 62.3% of the total amount of all phenolic compounds. Of all the identified analytes, quinic acid, which does not belong to the group of phenolic compounds, stood out, as its amount in plum fruit samples of some cultivars was even higher than the total amount of the identified phenolic compounds.

Conclusions. In conclusion, the results of this study will provide new knowledge about the composition and content of phenolic compounds in European plum fruit, which will give a wide range of possibilities to employ these plants as a source of phenolic compounds. For this reason, plum fruit have a potential value for the needs of practical medicine, including the isolation of individual compounds with a specific effect and the development and production of preventive phytopreparations, dietary supplements, and functional food.

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Use of complementary and alternative medicine for children with cancer: parents' perspective

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Introduction

Complementary and alternative medicine (CAM) can be defined as healthcare approaches that are not typically a part of conventional medical care or that may have origins outside of usual Western practice, which is being used in Lithuania. Although not a part of mainstream medicine, an increasing number of children with cancer use CAM along with conventional therapies [1]. Parents choose CAM for treatment and cure of cancer in their children [2], and also as a supportive care agent to help minimize side effects of cancer treatment and to improve the general quality of life and well-being [3, 4]. Most commonly used CAM modalities are herbs, diets and nutrition, homeopathy, and prayer [3, 5,].

Materials and Methods

The descriptive qualitative study design was applied. The semi-structures interviews conducted in summer-autumn of 2020. The study population was parents of children 5 - 18 years of age with cancer (non-terminal stage) hospitalized at Clinical Hospital of Lithuanian University of Health Sciences, Pediatrics department. A convenience sample of 9 parents was interviewed face-to-face until data saturation achieved. Qualitative content analysis approach was used for data analysis.
The study was approved by the Committee on Bioethics (permission No. BE-2-68).

Findings and discussion

Parents tended to used CAM for their children. The homeopathy was mentioned several times: "We use herbal preparations. Chelidonium is very good for treating cancer. I give green tea to drink"(M4). Mainly patients were treated by parents "After all, these are not medications. Any mother can be such a doctor"(M4). The main reason parents gave for using CAM was to improve the patient's general health, strengthen the immune system, and improve their chances of cure: "It seemed like we would do anything for our child to get better"(M1). The majority of CAM users thought that CAM therapy had helped "It really works. The child gets better in seconds"(M8), but they didn't consulted with oncologist "We do not consult doctors about it. I think they wouldn't get it. Maybe even make fun of it..."(M8).

Conclusions

Parents often choose complementary and alternative medicine (CAM) to supplement treatment of children and adolescents with cancer. Patients use a broad spectrum of CAM methods, and some may interact with conventional medicine, causing adverse effects. Pediatric oncology patients often use CAM without telling the oncologists or nurses who treat them.
Cooperation between pediatric oncologists, nurses and patients could improve patient care by opening communication, increasing mutual understanding, increasing patient satisfaction, compliance and safety.

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Evaluation of anticancer activity of N-aryl-β-alanine derivatives 58 and 66 in glioblastoma and triple-negative breast cancer cell lines

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Introduction. One of the biggest challenges in clinical oncology is the prevention and treatment of metastatic forms of cancer, that are primary causes of cancer-related deaths worldwide [1]. Glioblastoma (GMB) and invasive triple-negative breast cancer (TNBC) are both the most aggressive forms in their cancer types, characterized with extremely poor survival rates and difficult treatment procedure [2,3]. TNBC also lacks the expression of three genes; estrogen receptors (ER), progesterone receptors (PR) and epidermal growth factor 2 (HER-2) [4], resulting in very limited treatment options. Despite improvements in treatment techniques, patients with GBM often experience early recurrence and eventual death [2]. In search of new compounds that could efficiently target these cancer types, we conducted an *in vitro* experiment that aimed at evaluating the anticancer activity of previously successfully screened and tested N-aryl-β-alanine derivatives on two different cancer cell lines.

Materials and methods. Two cancer cell lines were used as model systems; TNBC cell line MDA-MB-231 and GBM cell line U87; which were further treated with N-aryl-β-alanine derivatives, compounds no. 58 and 66, obtained with permission from scientists of Kaunas University of Technology. After treatment, cancer cell lines were further investigated based on their three properties: 1) their viability was determined using an MTT assay, 2) their ability to migrate was examined via 'wound healing' technique, 3) their ability to form random colonies was investigated via clonogenic assay, as well as the changes in the diameters (μm) of spheroids in 3D cell cultures were also determined. The half-maximal effective concentration values (EC_{50}) represent the concentration of a compound at which the cancer cell metabolic activity is reduced by 50%.

Results and Discussion. Compound no. 58 EC_{50} values on MDA-MB-231 and U87 cell lines were 6.44 ± 0.94 μM and 6.80 ± 0.38 μM, respectively. Compound no. 66 showed a stronger effect on the viability of MDA-MB-231 than U87 cell line (EC_{50} values were 5.55 ± 0.68 μM and 7.10 ± 0.53 μM in MDA-MB-231 and U87 cell lines, respectively). *Wound healing assay* results showed that compound no. 58 had the greatest effect on the migration of the MDA-MB-231 and U87 cell lines. The higher concentration of compound no. 58 reduced the migration of MDA-MB-231 cells 2.6 and 5.6 times, 48 h and 72 h after incubation when compared to the control. *Clonogenic assay* analysis showed that cell lines treated with higher concentration of compound no. 58 reduced the number of colonies by around two folds, 51.12 ± 12.29% ($p<0.001$) and 49.38 ± 13.86% ($p=0.005$), in U87 and MDA-MB-231 cell lines, respectively. Similarly, statistical analysis showed that higher concentration of compound no. 66 had significant impact in the colony growth in both cell lines. Higher concentration of compounds no. 58 and 66 more efficiently reduced the diameter (μm) of spheroids after 8 days of observation compared to the control ones; the diameter decreased by 32.12 ± 2.8% ($p<0.001$) and 30.35 ± 2.15% ($p<0.001$) in U87, and by 15.18 ± 2.45% ($p<0.001$) and 10.61 ± 2.01% ($p=0.006$) in MDA-MB-231 cell lines, treated with compounds no. 58 and 66, respectively. Analysis demonstrated that smaller concentrations of compounds no. 58 and 66 did not make a huge impact on changes in the diameter in both cell lines.

Conclusions. Tested compounds, specifically, compound no. 58, possess anticancer activity on both glioblastoma and breast cancer cell lines. They inhibit the viability of cells, the ability to form colonies, spheroids, migration, and may be worthy of further studies. Furthermore, the mechanisms of action are yet to be investigated.

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Seasonal variation in phenolic compounds and antioxidant activity of hazel (*Corylus avellana* L.) leaves

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Introduction

Hazel *(Corylus avellana L.)* is a common plant in temperate climates, mainly in the northern hemisphere in Europe and Asia [2,4]. Hazel leaves have antimicrobial, cardiovascular and antioxidant effects [1,4,5]. Previous studies have shown that hazel leaves are a rich source of phenolic compounds and total antioxidant activity [2,3,5]. Therefore, it is important to determine their profiles in Lithuanian grown samples.

Materials and Methods

Leaf samples were collected from natural habitats in Lithuania during vegetation period. Spectrophotometric Folin-Ciocalteu method was used for the determination of total content of phenolic compounds in plant material. Spectrophotometric FRAP method was used to determine total antioxidant activity.

Results and discussion

Total phenolic compounds amount in hazel leaves varies from 52.88 ± 1.06 mg/g to 86.02 ± 0,15 mg/g. The highest content of total phenolic compounds was determined in early July during full leaf expansion and in May during leaf growth. The antioxidant activity varies from 264.03 ± 79.03 μmol/g to 1306.63 ± 34.37 μmol/g. The antioxidative activity increase in the middle of July during full leaf expansion, in August at the vegetation period of leaf maturation and decrease in the leaf senescense. The smallest antioxidative activity established at the beginning of vegetation period.

Conclusion

The greatest amount of phenolic compounds and antioxidant activity was determined in *Corylus avellana L.* leaves collected in July during full leaf expansion.

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The inhibition of CA IX leads to decreased cancer cell migration

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Introduction

Carbonic anhydrase IX (CA IX) is a transmembrane enzyme catalysing the CO_2 hydrolysis reaction to proton and bicarbonate ions [1]. Normally its expression is limited to the epithelia of stomach and duodenum; however, it is highly expressed in various types of cancer. CA IX regulates intracellular pH in hypoxic tumor cells and contributes to extracellular acidosis, cell adhesion, migration and invasion [2,3]. To get better understanding of CA IX involvement in cancer cell migration, we produced triple negative breast cancer cells MDA-MB-231 with a knocked down CA9 gene, and tested the effect of chemical CA IX inhibitor [4] on cell migration using a method of single cell tracking.

Materials and methods

Stable knockdown MDA-MB-231 lines, CA9-1 and CA9-2, were generated using two Sigma lentiviral Ca9 shRNAs [TRCN0000349591 and TRCN0000319003] plasmids. CA IX levels under normoxia (21% O_2) and hypoxia (1% O_2) conditions were determined by imunofluorescence and Western blotting.
For single cell tracking, we seeded the MDA-MB-231 and modified cancer cells (shRNA1) on type 1 collagen coated glass-bottomed Petri dishes. In one group, we added $CoCl_2$ to create hypoxic condition to induce the expression of CA IX. After the cells attached to collagen, we added CA IX inhibitor (VD11) at different concentrations (5 μM, 20 μM), and imaged cells every hour for five hours by conventional bright field microscopy.

Results and discussion

Two stable shRNA cell lines were produced and the levels of CA IX were determined in both. The levels of CA IX in shRNA1 cell line was 10 %, and in CA9-2 was 100 %, of levels in parental MDA-MB-231 cell line. The shRNA2 cell line was used as negative control.
The results showed that decreased expression of CA IX had a significant effect on overall cell motility. ShRNA1 cells migrated slower by 47.6 % ($p < 0.05$) under normoxic conditions and 23.5 % ($p < 0.005$) under hypoxic conditions, compared to the parent MDA-MB-231 cells. Chemical inhibition of CA IX showed that VD11 was able to reduce migration speed in MDA-MB-231 cells under normoxic conditions. Both concentrations of 5 μM and 20 μM decreased the migration speed of cells by 33.04 % and 34.2 %, respectively ($p < 0.05$), though there was no significant difference between the effects in 5 μM and 20 μM treated groups. VD11 did not have any significant effect on shRNA1 cell migration under both normoxic and hypoxic conditions; this could be explained that the compounds acts through the inhibition of CA IX.

Conclusions

Based on our results, CA IX is involved in the migration of breast cancer cells, and the experimental compound VD11 can act as antimigrastatic agent.

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Effect of kinase inhibitors on human breast cancer cell viability *in vitro*

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Introduction. Protein kinases are responsible for regulating different cellular functions, such as proliferation, cell cycle, apoptosis, motility, differentiation. Moreover, many studies have shown a causal role of protein kinase dysregulations or mutations in different human diseases, including cancer [1]. Over 25 kinase inhibitors are approved as anticancer drugs [2]. One of them is sunitinib, which is used to treat kidney cancer and gastrointestinal stromal tumours [3]. However, there is a need to search for the new, more effective agents for treating a cancer. Despite innovations in the treatment of cancer, it is still the second leading cause of death globally. Breast cancer is the most common type of diagnosed malignancy and the second leading cause of cancer death in women around the world [4].
The aim of our study was to evaluate the effect of new sunitinib analogues on human breast cancer cell viability.

Materials and Methods. Experiments were performed on human triple-negative breast cancer cell line MDA-MB-231 and non-malignant cell line – human fibroblasts. 17 kinase inhibitors, which are sunitinib analogues, have been tested. The effect of kinase inhibitors on cell viability was evaluated by MTT assay after 72 hours of incubation. First, we selected the most active kinase inhibitors that reduced cell viability up to 5% or less. Then the EC_{50} values of the most active compounds were evaluated and compared to the sunitinib activity.

Results and discussion. Kinase inhibitors #1, #6, #7, #8 and #17 were the most active ones. These compounds, except #1, more inhibited breast cancer cells viability than non-malignant cells viability. However, among tested compounds, #1 had the greatest effect on cell viability (EC_{50} values after 72 h on MDA-MB-231 and HF was 73.61 ± 5.77 nM and 83.76 ± 4.24 μM, respectively). Most of the other compounds inhibited cancer cells viability at concentrations from 150 to 250 nM. All tested sunitinib analogues were more active than sunitinib.

Conclusions. Tested kinase inhibitors, especially compound #1, demonstrate the inhibitory effect on human breast cancer MDA-MB-231 cell viability, and may be worthy of further studies.

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Anticancer activity of sunitinib analogues in brain cancer models

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Introduction: Glioblastoma (GBM) is the most aggressive type of brain cancer, mostly common in adults. Median survival time for GBM patients is about 12.1 to 14.6 month [1]. Thus, the overall prognosis of GBM remains poor, as there are still extremely limited opportunities of conventional therapy. Tyrosine kinase inhibitors have been used successfully in clinic for other types of cancer since 2001 [2] and currently are considered as perspective targeted therapy for GBM. Kinases belong to the class of enzymes that promote protein phosphorylation, which affects cell apoptosis, proliferation and differentiation. There are numerous studies directly linking changes in kinase activity to carcinogenesis. Tyrosine kinase inhibitors generally target the active site of the kinase and thereby prevent the phosphorylation resulting in inhibition of migration and apoptosis of cancerous cells [2]. One of them is sunitinib, a multi-targeted agent, approved for treatment of kidney cancer and gastrointestinal stromal tumours [3]. Moreover, the new chemical compounds are suggested as more effective sunitinib analogues [4].
The aim of our study was to evaluate the effect of new sunitinib analogues on human brain cancer cell viability.

Materials and Methods: The two human GBM cell lines, U87-MG and A172, and non-malignant cell line-human fibroblasts were used to investigate anticancer activity of 17 sunitinib analogues *in vitro.* The effect of kinase inhibitors on cell viability was evaluated by MTT assay after 72 hours of incubation, and we selected the most active kinase inhibitors that reduced cell viability up to 5% or less. Then the EC_{50} values of the most active compounds were evaluated and compared to the sunitinib activity.

Results and discussion: Kinase inhibitors #1, #6, #7 were the most active ones. All three tested compounds more effectively inhibited brain cancer cell viability of A172 cell line than U87-MG cell line and non-malignant cells viability. It should be noted, that #6 was the only one that had stronger cytotoxic effect on studied cancer cell lines in comparison with non-malignant cells. However, data analysis revealed that #1 had the greatest effect on cell viability ((EC 50 values after 72 h on U87-MG, A172 and HF were 82 ± 6 nM, 72 ± 6 nM and 82 ± 6 nM, respectively). #6 and #7 inhibited studied cells viability at range of average concentrations from 112 to 397 nM. All tested sunitinib analogues were more active than sunitinib.

Conclusions: Tested kinase inhibitors, especially compound #1, demonstrate the inhibitory effect on U87-MG and A172 human brain cancer cell viability, and may be worthy of further studies.

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Chemical composition of essential oils from *Artemisia vulgaris* L.

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Introduction

During the past years, a number of studies have been carried out concerning the application of biologically active compounds from *Artemisia* L. genus. A lot of species of *Artemisia* L. are mentioned in folk and modern medicine, cosmetic and pharmaceutical industry [1]. The special attention for this genus received to content of artemisinin, which used against malaria [2]. The object of investigation was *Artemisia vulgaris* L. - a perennial, medicinal, spice plant of *Asteraceae* (Bercht. & J. Presl) family. As different studies show, extracts from *A. vulgaris* exibit antimicrobial, anti-parasitical and insecticidal properties [3]. The aim of our study was to determine the qualitative and quantitative composition of the essential oils obtained from *A. vulgaris* raw material during different vegetation stages.

Materials and Methods

Artemisia vulgaris L. raw material were colected during different vegetation stages in the Spice - Melliferous Plants Collection *ex situ* of the Botanical Garden at Vytautas Magnus University (VMU) in 2018. Five stages have been separated: growth and leaf production, flower bud development, the beginning of flowering, massive flowering and the end of flowering. The essential oils from dried raw material of *A. vulgaris* were extracted by hydrodistillation and analysed by GC/MS.

Results and discussion

A total of 38 different compounds were found in *A. vulgaris* essential oils. The highest content and diversity of compounds have been obtained from *A. vulgaris* essential oil during the flower bud development stage. We detected twenty-eight constituents of essential oil, representing 66.6% of identified compounds. The principal compounds were found to be isogermacrene D (28.38%), aromandendrene (12.43%), *trans*-sabinyl acetate (5.26%). As results show, isogermacrene D has been found as the first principal component in all vegetation stages (26.12-48.10%).

Conclusions

The chemical composition of essential oils of *Artemisia vulgaris* L. was investigated in 2018-2019. The highest content and diversity of compounds were determined during flower bud development stage. Thirty-eight compounds of the oil were identified, of which isogermecrene D was the major component (26.12-48.10%).

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Phenolic compounds and antioxidant activity of *Artemisia ludoviciana* extracts during different vegetation periods

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Introduction. White sagebrush (*Artemisia ludoviciana* L.) is perennial herbaceous plant that belongs to *Asteraceae* family. Bioactive components such as flavonoids, phenolic compounds have pharmacological properties. In folk medicine *Artemisia* L. could be used to treat scurvy, bronchitis, ulcers. Furthermore, these plants tones, some species could be used as diuretics, antiseptics or antidiabetics preparations [1, 2, 3]. Determination of phenolic compounds and antioxidant activity is an important factor assessing the quality of herbal raw material.

Materials and Methods

The aim of the research was to investigate the antioxidant activity and total phenolic compounds contents of *Artemisia ludoviciana* L. herb during different vegetation periods. Total phenolic compounds content and antioxidant capacity of the white sagebrush were analyzed by spectrophotometric Folin-Ciocalteu and ABTS assays, respectively.

Results and discussion

Results showed that the highest total phenolic compounds content and antioxidant capacity were determined in the extracts of *Artemisia ludoviciana* L. collected in the beginning of vegetation. Total phenolic compounds content ranged from 47,6 ± 2,39 mg/g to 60,94 ± 0,42 mg/g and the highest was in May.

Conclusions

The research showed that it is an important factor, during which vegetation period herbs are collected, because it could affect the quality of the raw material.

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