SFUS
Savez farmaceutskih udruženja Srbije

SEKCIJA ZA FARMACEUTSKE NAUKE

ČETVRTI NAUČNI SIMPOZIJUM SAVEZA FARMACEUTSKIH UDRUŽENJA SRBIJE

sa međunarodnim učešćem

Budućnost farmaceutskih nauka: Kreativni ljudi i inovativne ideje u vremenu izazova

30. oktobar 2025. • Divčibare, Srbija

PROGRAM SIMPOZIJUMA

4th SCIENTIFIC SYMPOSIUM OF THE PHARMACEUTIAL ASSOCCIATION OF SERBIA

with international participation

The Future of Pharmaceutical Sciences: Creative People & Innovative Ideas in Challenging Times

October 30th 2025. • Divčibare, Serbia

SYMPOSIUM PROGRAMME

"Science lives in curiosity, in resilience and in persistence to keep asking questions."

L. Tabellini Pierre, Parse Biosciences

ČETVRTI NAUČNI SIMPOZIJUM SAVEZA FARMACEUTSKIH UDRUŽENJA SRBIJE

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ZBORNIK SAŽETAKA / BOOK OF ABSTRACTS

Sažeci radova sa Četvrtog naučnog simpozijuma Saveza farmaceutskih udruženja Srbije sa temom „Budućnost farmaceutskih nauka: Kreativni ljudi i inovativne ideje u vremenu izazova."– 30. oktobar 2025. Divčibare, Srbija

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Editorial

Dear colleagues, dear friends,

In a time of rapid change and remarkable progress in science and technology, pharmaceutical sciences are expected to provide answers and solutions to the increasingly complex healthcare needs of modern society and individual patients. How scientific discoveries enable novel therapies and improved patient health outcomes, what is needed to achieve such transformative innovations, and how to integrate them in professional practice are some of the topics addressed during the 4th Scientific Symposium of the Pharmaceutical Association of Serbia entitled "The Future of Pharmaceutical Sciences: Creative People & Innovative Ideas in Challenging Times."

The symposium program includes two plenary lectures, six invited lectures, five oral presentations, a poster session and a panel discussion devoted to current challenges and untapped opportunities for strengthening partnership between the research sector and the pharmaceutical industry. Particular attention is given to various models of collaboration, the role of the state in fostering innovation and the potential of science to drive sustainable change in healthcare and the pharmaceutical sector.

We would like to thank all the participants who, through their ideas, scientific contributions and dedication, help shape a shared vision of pharmaceutical sciences and create the environment necessary for their further advancement.

Sincerely,
Jelena Parojčić
president od the Scientific committee
Branislava Miljković
president of the Pharmaceutical Association of Serbia

Uvodnik

Poštovane koleginice i kolege, dragi prijatelji,

U vreme ubrzanih promena i snažnog napretka nauke i tehnologije, od farmaceutskih nauka se očekuje da pruže odgovore i rešenja za složene zdravstvene potrebe savremenog društva i individualnih pacijenata. Kako naučna otkrića doprinose unapređenju terapijskih pristupa i zdravstvenih ishoda pacijenata, koji su ključni preduslovi za nastanak transformativnih inovacija i na koji način se one mogu integrisati u savremenu profesionalnu praksu – pitanja su kojima se bavi Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije, organizovan pod sloganom „Budućnost farmaceutskih nauka: Kreativni ljudi i inovativne ideje u vremenu izazova".

Program skupa obuhvata dva plenarna predavanja, šest predavanja po pozivu, pet usmenih saopštenja, poster sesiju i panel diskusiju posvećenu aktuelnim izazovima i neiskorišćenim prilikama za snažnije povezivanje istraživačkog sektora i farmaceutske industrije. Poseban akcenat stavljen je na različite modele saradnje, ulogu države u podsticanju inovacija i potencijal nauke da pokrene održive promene u zdravstvu i farmaciji.

Zahvaljujemo se svim učesnicima koji svojim idejama, naučnim rezultatima i posvećenošću doprinose oblikovanju zajedničke vizije farmaceutskih nauka i stvaranju podsticajnog okruženja za njihov dalji razvoj.

Srdačno,

Jelena Parojčić

predsednica Naučnog odbora

Branislava Miljković

predsednica Saveza farmaceutskih udruženja Srbije

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https://doi.org/10.5937/arhfarm-61879

IZAZOVI U RAZVOJU BIOTEHNOLOŠKIH LEKOVA – PERSPEKTIVA PROIZVOĐAČA LEKOVA

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Zahvaljujući inovativnim lekovima pacijenti danas žive duže i kvalitetnije, zdravstveni sistemi beleže uštede u delu budžeta koji se ne odnosi na lekove, a zajednica ima korist od pacijenata čija je bolest dovoljno dobro kontrolisana da ostaju produktivni članovi društva. Broj novoregistrovanih inovativnih lekova raste iz godine u godinu, ali je opet nedovoljan da pokrije sve oblasti u kojima i dalje imamo nepovoljne ishode lečenja. Razlozi za to su višestruki. Sa jedne strane, proces razvoja jednog inovativnog leka traje veoma dugo, dok sa druge strane troškovi razvoja takve terapije sve više rastu. Međutim, glavni uzrok zbog kojeg nemamo više inovativnih terapija je ogromna neizvesnost koja prati razvoj jednog takvog leka. Šta su najveći izazovi u razvoju ovih terapija na strani inovativnih farmaceutskih kompanija, kako se efikasnije mogu otkloniti administrativne prepreke u razvoju novih lekova i da li postoji način da ove terapije budu dostupnije neka su od pitanja kojima se bavi ovo predavanje.

4th Scientific Symposium of the Pharmaceutical Association of Serbia
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CHALLENGES IN THE DEVELOPMENT OF BIOTECHNOLOGICAL DRUGS – THE PERSPECTIVE OF DRUG MANUFACTURERS

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Thanks to innovative medicines, patients are now living longer and better lives, health systems are saving on the non-drug part of the budget, and the community benefits from patients whose disease is controlled enough to remain productive members of society. The number of newly registered innovative drugs is growing year by year, but it is not enough to cover all areas in which we still have unfavorable treatment outcomes. The reasons for this are multiple. On the one hand, the process of developing an innovative drug takes a very long time, while on the other hand, the costs of developing such therapy are increasing. However, the main reason why we do not have more innovative therapies is the enormous uncertainty that accompanies the development of such a drug. What are the biggest challenges in the development of these therapies on the part of innovative pharmaceutical companies, how can administrative obstacles in the development of new drugs be removed more efficiently and is there a way to make these therapies more accessible are some of the questions addressed in this lecture.

Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 7–8 **PL 2**
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PERSONALIZOVANA FARMAKOTERAPIJA - POMACI U PREVAZILAŽENJU TERAPIJE NA OSNOVU POKUŠAJA I GREŠAKA

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Personalizovana farmakoterapija predstavlja savremeni koncept u kojem se odluke o izboru i doziranju lekova donose na osnovu relevantnih karakteristika pacijenata sa ciljem da se postigne maksimalna efikasnost, bezbednost i komfor terapije. Ključni izazov ovog pristupa jeste konverzija velikog broja prikupljenih parametara (od anamnestičkih, antropometrijskih i biohemijskih, preko genotipa i polifarmacije, do životnih navika pacijenta) u kredibilne i klinički primenljive odluke. Predavanje će, kroz primer devetogodišnjeg istraživanja i više kliničkih studija sa fokusom na personalizovanu terapiju escitalopramom, prikazati čitav životni ciklus jedne inovacije iz oblasti personalizovane farmakoterapije: od bazične nauke, preko razvoja i validacije mehanizama za donošenje odluka, pa sve do implementacije u kliničku praksu. Poseban akcenat biće na ulozi farmaceuta u ovom procesu, kao stručnjaka koji svojim znanjem i pozicijom u zdravstvenom sistemu mogu značajno doprineti uspešnoj primeni personalizovane medicine u praksi.

4th Scientific Symposium of the Pharmaceutical Association of Serbia
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PHARMACOTHERAPY - ADVANCES IN OVERCOMING THERAPY BASED ON TRIAL-AND-ERROR

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Personalized pharmacotherapy is a modern concept in which decisions on drug selection and dosing are based on relevant patient characteristics, with the goal of achieving maximum efficacy, safety, and treatment convenience. The key challenge of this approach lies in converting a large set of collected parameters (ranging from anamnestic, anthropometric, and biochemical data, to genotype, polypharmacy, and lifestyle factors) into credible and clinically applicable decisions. This lecture will, through the example of nine years of research and several clinical studies focusing on personalized escitalopram therapy, present the entire life cycle of an innovation in personalized pharmacotherapy: from basic science, through the development and validation of decision-making mechanisms, to implementation in clinical practice. Special emphasis will be placed on the role of pharmacists in this process, as professionals whose expertise and position within the healthcare system can significantly contribute to the successful application of personalized medicine in practice.

PREDAVANJA PO POZIVU / INVITED LECTURES

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 10–11 **IL 1**

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ODRŽIVOST KROZ DIZAJN – NOVA PARADIGMA U UPRAVLJANJU ŽIVOTNIM CIKLUSOM LEKA

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Koncept održivog razvoja zasniva se na principu da "se potrebe sadašnjeg društva zadovolje bez ugrožavanja mogućnosti budućih generacija da ostvare svoje potrebe" [1]. Ostvarivanje ovog principa zahteva promenu načina razmišljanja i postupanja, kako na ličnom, tako i na profesionalnom planu. Od istraživača u svim oblastima nauke očekuje se integracija principa održivosti u naučni i stručni rad, proučavanje tema povezanih sa održivim razvojem i formulisanje rešenja usmerenih ka prevazilaženju izazova u postizanju održivosti [2, 3].

Paradigma "Održivost kroz dizajn" u farmaceutskim naukama podrazumeva integraciju principa održivog razvoja u sve faze životnog ciklusa leka. U ovom radu razmatrane su ključne dimenzije koncepta "Održivost kroz dizajn" u različitim fazama životnog ciklusa leka, odgovarajući alati i aktivnosti:

- **Istraživanje i razvoj** zasnovani na: (i) prediktivnom modelovanju efikasnosti i bezbednosti, (ii) primeni principa zelene hemije, (iii) dizajnu proizvoda usmerenom na pacijenta, (iv) ranu procenu uticaja na životnu sredinu.
- **Proizvodnja i distribucija** sa minimizovanim uticajem na životnu sredinu kroz: (i) upotrebu obnovljivih resursa i smanjenje otpada, (ii) primenu biorazgradivih aktivnih farmaceutskih supstanci i ekscipijenasa, kao i reciklabilnih materijala za pakovanje, (iii) digitalizaciju procesa.
- **Klinička primena** koja podrazumeva: (i) racionalno propisivanje lekova, (ii) precizno doziranje, (iii) unapređenje adherence i (iv) integraciju digitalnih alata, što omogućava optimizaciju terapije i poboljšanje zdravstvenih ishoda uz izbegavanje prekomerne upotrebe lekova, kao i smanjenje otpada.

Paradigma "Održivost kroz dizajn" u farmaceutskim naukama predstavlja savremen, interdisciplinarni koncept koji prevazilazi okvire laboratorijskih istraživanja i tradicionalnih proizvodnih procesa, sa ciljem da se inovacije usklade sa širim prioritetima očuvanja životne sredine, farmakoekonomske efikasnosti i unapređenih zdravstvenih ishoda pacijenata.

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4th Scientific Symposium of the Pharmaceutical Association of Serbia
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SUSTAINABILITY BY DESIGN – A NEW PARADIGM FOR DRUG PRODUCT LIFE-CYCLE MANAGEMENT

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The essential principle of sustainable development is to "meet the needs of the present without compromising the ability of future generations to meet their own needs" [1]. In order to achieve this, a paradigm shift is necessary in the way we think and act as citizens and professionals. Scientists in different disciplines are expected to integrate sustainability principles in their work, investigate topics associated with sustainable development and provide solutions for sustainability challenges [2, 3].

The Sustainability by Design (SbD) in pharmaceutical sciences emphasizes the integration of sustainability principles across the entire drug product life cycle. In this work, key dimensions of SbD in different stages of pharmaceutical product life cycle, relevant tools and points of action are reviewed:

- **Research and development** based on: (i) predictive modelling of pharmaceutical safety and efficacy, (ii) green chemistry principles, (iii) patient-centric product design, and (iv) early environmental impact assessment.
- **Manufacturing and distribution** incorporating the principles of ecological footprint minimization through employment of: (i) renewable resources and waste minimization, (ii) biodegradable, recyclable active pharmaceutical ingredients, excipients and packaging materials, and (iii) process digitalization.
- **Clinical use** guided by: (i) rational prescribing; (ii) precision dosing, (iii) enhanced adherence, and (iv) incorporation of digital health tools, leading to therapy optimisation and improved health outcomes, while avoiding pharmaceuticals overuse and reducing waste.

SbD paradigm in pharmaceutical sciences is an advanced, interdisciplinary concept which extends beyond the laboratory benchtop and manufacturing site to align pharmaceutical innovation with the broader objectives of environmental stewardship, pharmacoeconomic efficiency, and improved patient health outcomes.

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UNAPREĐENJE FARMACEUTSKIH INOVACIJA KROZ INSTITUCIONALNU TRANSFORMACIJU: SAIGE PROJEKAT U INSTITUTU ZA MEDICINSKA ISTRAŽIVANJA

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Institut za medicinska istraživanja Univerziteta u Beogradu (IMI) od 2022. godine sprovodi proces institucionalne transformacije uz podršku projekta *Serbia Accelerating Innovation and Growth Entrepreneurship* (SAIGE), koji je usmeren na razvoj inovacione infrastrukture i jačanje kapaciteta za translaciju naučnih rezultata u društveno i komercijalno relevantne proizvode. Ključni strateški stubovi transformacije obuhvataju izvrsnost u nauci, razvoj ljudskih resursa, modernizaciju istraživačke infrastrukture i snažniji fokus na inovacije i transfer tehnologija. U okviru inovacionog portfolija IMI, posebno su od strane SAIGE podržani *Proof of Concept* (PoC) i *Cross-the-Gap in Technology Transfer and Commercialization* (CtG) projekti sa farmaceutskom i biomedicinskom relevantnošću, koji reflektuju različite paradigme translacione nauke i održivog razvoja. Razvoj stabilizovanih čvrstih formulacija hem-gvožđa iz nusproizvoda mesne industrije predstavlja model cirkularne bioekonomije i održive valorizacije bioloških resursa; platforma za rast ćelija pacijenata obolelih od multiplog mijeloma je korak ka personalizovanoj onkološkoj medicini; ekstrakti suvih semena novih sorti boba i organskim kalcijumom obogaćeni voćni sokovi doprinose inovacijama u oblasti funkcionalne hrane i dijetetskih suplemenata; *in-house* razvijeni ELISA testovi omogućavaju nova rešenja u kliničkoj dijagnostici, dok tkivni derivati placente otvaraju nove mogućnosti u razvoju 3D štampanih mukoadhezivnih filmova za regeneraciju oralnih tkiva. Ovi projekti ilustruju transformativni kapacitet IMI da kroz interdisciplinarni pristup i strateško upravljanje inovacijama integriše akademsku izvrsnost sa primenljivim rešenjima u oblasti savremenih farmaceutskih istraživanja i razvoja.

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ADVANCING PHARMACEUTICAL INNOVATION THROUGH INSTITUTIONAL TRANSFORMATION: THE SAIGE PROJECT AT THE INSTITUTE FOR MEDICAL RESEARCH

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Since 2022, the Institute for Medical Research, University of Belgrade (IMI), has been implementing an institutional transformation supported by the *Serbia Accelerating Innovation and Growth Entrepreneurship (SAIGE)* project, aimed at developing innovation infrastructure and strengthening the capacity for translating scientific results into socially and commercially relevant products. The key strategic pillars of transformation include scientific excellence, human resource development, modernization of research infrastructure, and a strengthened focus on innovation and technology transfer. Within the IMI innovation portfolio, the *Proof of Concept (PoC)* and *Cross-the-Gap in Technology Transfer and Commercialization (CtG)* projects supported through SAIGE reflect diverse paradigms of translational science and sustainable innovation. The development of stabilized solid formulations of heme-iron derived from meat industry by-products embodies the principles of circular bioeconomy and sustainable bioresource valorization; the platform for the growth of multiple myeloma patient-derived cells marks a step toward personalized oncology; extracts from new faba bean varieties and organically calcium-enriched fruit juices contribute to advances in functional food and dietary supplement innovation; in-house developed ELISA tests provide novel solutions in clinical diagnostics, while placenta-derived tissue derivatives open new avenues in the design of 3D-printed mucoadhesive films for oral tissue regeneration. These projects illustrate the Institute's transformative capacity to integrate academic excellence with practical innovation through interdisciplinary collaboration and strategic innovation management, bridging science and application in contemporary pharmaceutical research and development.

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FROM INNOVATION TO PATIENTS: AI-DRIVEN DRUG DISCOVERY AND THE ROLE OF INTELLECTUAL PROPERTY RIGHTS

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Artificial intelligence (AI) is reshaping drug discovery with direct implications for patients. Drug candidates such as LP-284 for relapsed or refractory non-Hodgkin's lymphoma [1] and INS018_055 for fibrosis [2] entered clinical trials in record time, showing that AI can help bring innovative treatments to patients much more quickly, particularly valuable in diseases with limited therapeutic options. Beyond speed, AI helps design safer and more effective drugs by predicting toxicity and metabolism early in development, reducing potential failures in later phases. This could lower adverse effects, enable personalized therapy, and expand options for diseases like Alzheimer's, cancer and rare disorders.

However, major intellectual property (IP) challenges remain. The DABUS (Device for the Autonomous Bootstrapping of Unified Sentience) cases in many jurisdictions have shown that current law does not recognize AI as an inventor, creating uncertainty over ownership and the patentability of AI-created molecules. These disputes underscore the gap between rapid technological progress and slower legal adaptation. In addition, questions of novelty, non-obviousness, and data provenance complicate legal protection, raising the risk that promising discoveries may be delayed in their translation into therapies for patients [3].

For patients to benefit from AI-driven discoveries, scientific advances must be supported by legal clarity and ethical responsibility. Achieving this balance will require close collaboration between researchers, policymakers, and regulatory bodies, ensuring that innovations are transformed into therapies that reach patients. Flexible IP laws can undoubtedly improve access to novel medicines, helping innovative treatments reach patients more quickly and equitably.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 15–16 ***IL 4***
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KOGNITIVNO OŠTEĆENJE I ANHEDONIJA KAO POTENCIJALNE KOMPLIKACIJE DIJABETESA TIPA 2: PREKLINIČKA PERSPEKTIVA

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Dijabetes tipa 2 (T2D) predstavlja veoma često metaboličko oboljenje koje je snažno povezano sa nezdravim životnim navikama i gojaznošću. Ipak, hiperglikemija i poremećaj u signalizaciji insulina ne dovode samo do komplikacija u perifernim organima, već utiču i na funkciju mozga. T2D je jedan od glavnih faktora rizika za razvoj demencije, pri čemu su efekti potencijalno zavisni od pola. U skladu s tim, kognitivno oštećenje je u novijoj naučnoj literaturi sve više prepoznato kao nova komplikacija dijabetesa tipa 2 [1]. Pored toga, depresija se često javlja zajedno sa T2D zbog preklapanja faktora rizika, naročito onih povezanih sa životnim stilom i genetikom. Međutim, molekularni mehanizmi koji stoje u osnovi promena u mozgu izazvanih metaboličkim disbalansom u T2D i dalje su nedovoljno istraženi. Dodatno, antidijabetik semaglutid je u novijim studijama pokazao povezanost sa ublažavanjem kognitivnog oštećenja [2, 3] što ukazuje na njegov mogući efekat na modulaciju moždanih funkcija. U skladu s prethodno navedenim, cilj naše studije je bio da se istraži uticaj T2D na mozak putem bihejvioralne procene kod T2D modela pacova oba pola. Takođe, ispitali smo efekte terapije semaglutidom u ovom modelu. Zaista, kognitivna oštećenja i anhedonija su uočeni kod T2D model životinja u poređenju sa kontrolnim grupama, dok je semaglutid pokazao ohrabrujuće, polno-zavisne efekte na ove poremećaje. Zaključno, translaciono relevantan model T2D zajedno sa proširenom bihejvioralnom analizom može ponuditi opsežnije razumevanje uticaja ove bolesti i semaglutida na centralni nervni sistem, koje se dalje može povezati sa potencijalnim molekularnim promenama u moždanim strukturama uzrokovanim T2D.

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COGNITIVE IMPAIRMENT AND ANHEDONIA AS POTENTIAL DIABETES TYPE 2 COMPLICATIONS: A PRECLINICAL PERSPECTIVE

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Diabetes type 2 (T2D) is a very common metabolic disorder strongly associated with poor lifestyle choices and obesity. However, hyperglycemia and impaired insulin signalling not only lead to complications in the periphery but also affect brain function. T2D is one of the main risk factors for the development of dementia, as it suggested, in a sex-dependent manner. In line with this, cognitive impairment has received attention as an emerging complication of T2D in recent scientific literature [1]. Similarly, depression may also co-occur with T2D due to overlapping lifestyle and genetic factors. However, the molecular mechanisms underlying brain changes caused by metabolic imbalance in T2D remain largely unexplored. Furthermore, the antidiabetic drug semaglutide has shown potential in treating cognitive impairment in recent studies [2, 3] suggesting an effect on brain modulation. Thus, we investigated how T2D affects the brain through behavioral testing in a rat T2D model of both sexes. In addition, we have evaluated the effects of semaglutide treatment in this model. Indeed, both cognitive impairment and anhedonia were observed in T2D animals compared to controls, while semaglutide showed promising sex-dependent effects on these conditions. In conclusion, the translationally relevant T2D model, combined with an extensive behavioral test battery, may offer a comprehensive understanding of the disease and the effects of semaglutide on the central nervous system, which could be further linked to potential molecular changes in brain structures caused by T2D.

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CHEDO: DIGITALNI PRATILAC KROZ PROCES VTO - OD IZAZOVA KA NOVIM MOSTOVIMA

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Infertilitet je značajan zdravstveni izazov u oblasti reproduktivnog zdravlja koji je fragmentisan, sa velikim obimom podataka i snažnim emotivnim opterećenjem. CHEDO je digitalni pratilac zasnovan na dokazima, kreiran sa pacijentima i stručnjacima radi unapređenja kontinuiteta i kvaliteta nege tokom postupka vantelesne oplodnje (VTO). Rešenje počiva na tri stuba: (i) interaktivnom kalendaru za praćenje ciklusa VTO, terapije i laboratorijskih analiza, strukturisane izveštaje za jedan i više ciklusa za nesmetan prenos informacija između zdravstvenih profesionalaca; (ii) edukativnom delu pisanom od strane eksperata; i (iii) „izazovu endokrinih ometača" koji prevodi toksikološke uvide u praktične, fazne promene ponašanja ka zdravijim navikama. Pored toga, CHEDO pruža sažete smernice zasnovane na nauci o dugovečnosti, kako bi podržao zdrav životni vek žena tokom i nakon VTO. Uključivanje partnera putem bezbednog zajedničkog profila i razvoj moderirane zajednice odgovaraju na psihosocijalne potrebe. Ključni izazovi obuhvatili su prevođenje složenih kliničkih puteva u razumljive tokove za pacijente, zaštitu privatnosti i interoperabilnost, i dizajn održivog poslovnog modela. Prepreke smo prevazilazili iterativnim razvojem prototipa, testiranjem upotrebljivosti i usavršavanjem B2B platforme za klinike (u izradi) radi integrisanog pristupa podacima i povratne komunikacije. Prvi pilot projekti ukazuju na bolju informisanost pre/tokom procesa VTO, lakši transfer između klinika, uz istovremeno isticanje potrebe za personalizacijom sadržaja. Budući rad fokusira se na evaluaciju ishoda (informisanost, stepen adherence, kontinuitet nege), razvoj marketinške strategije i optimizaciju poslovnog modela, kao i postepenu integraciju sa kliničkim sistemima. CHEDO ilustruje kako farmaceutski vođena inovacija može ujediniti različite oblasti farmaceutske ekspertize, reproduktivnu medicinu i personalizovan pristup u podršci parovima tokom procesa VTO [1-3].

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CHEDO: IVF DIGITAL COMPANION - FROM CHALLENGES TO NEW BRIDGES

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Infertility is a major challenge in reproductive health—fragmented, data-intensive, and emotionally demanding. CHEDO is an evidence-based digital companion co-created with patients and specialists to enhance continuity and quality of care during in-vitro fertilisation (IVF). The solution rests on three pillars: (i) an interactive calendar for tracking IVF cycles, medication, and laboratory results that also produces structured single- and multi-cycle reports to support seamless information handover between healthcare professionals; (ii) an expert-written educational hub; and (iii) an "endocrine-disruptor challenge" translating toxicology insights into practical, phased behaviour change towards healthier habits. In addition, CHEDO provides concise longevity-science guidance to support women's healthspan during and after IVF. Partner inclusion via a secure shared profile and the development of a moderated community address psychosocial needs. Key challenges included translating complex clinical pathways into patient-readable workflows, safeguarding privacy and interoperability, and designing a sustainable business model. We addressed these through iterative prototype development, usability testing, and refinement of a clinic-facing B2B platform (in development) to enable integrated data access and feedback loops. Early pilots indicate improved pre/in-treatment understanding and smoother transfers between clinics, while underscoring the need for content personalisation. Future work focuses on outcome evaluation (treatment literacy, adherence, continuity of care), marketing strategy and business-model optimisation, and progressive integration with clinical systems. CHEDO illustrates how pharmacy-led innovation can unite diverse pharmacy expertise, reproductive medicine, and a personalised, human-centred approach to support couples throughout IVF [1-3].

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USMENA PREDAVANJA / ORAL PRESENTATIONS

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OP 5

Hemotaksonomija roda *Hypericum* sekcije *Drosocarpium* bazirana na analizi hemijskog sastava etarskih ulja

Chemotaxonomy of *Hypericum* (sect. *Drosocarpium*) species: patterns in essential oil composition

Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 21–22 **OP 1**
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PRIMENA *ZoomLab*® VIRTUELNOG ASISTENTA U RAZVOJU DIREKTNO-KOMPRESIBILNIH FORMULACIJA: MOGUĆNOSTI I OGRANIČENJA

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Razvoj lekova zahteva poznavanje složenih odnosa između karakteristika aktivnih supstanci (AS) i ekscipijenasa, procesnih parametara i ciljnog profila kvaliteta proizvoda, koje je teško pouzdano predvideti. Unapređenje naučnih saznanja u ovoj oblasti, dostupnost velikih baza podataka i primena mašinskog učenja doveli su do razvoja digitalnih platformi sa naprednim algoritmima koji podržavaju i omogućavaju brži razvoj formulacije.

U ovom istraživanju ispitivana je mogućnost primene platforme *BASF Virtual Assistant ZoomLab*® [1] kao alata za razvoj direktno-kompresibilnih formulacija, uz korišćenje kofeina i rivaroksabana kao model aktivnih supstanci. Sprovedena je uporedna analiza eksperimentalno dobijenih podataka i podataka integrisanih u platformu u okviru aplikacija *Tabletabilnost* i *Procesabilnost* aktivne supstance i tabletne smeše, a potom faza razvoja formulacije, korišćenjem aplikacije *Formulation Wizard*.

Razmatranje svojstava AS u okviru platforme ukazivalo je na slabu procesabilnost, odnosno mogućnost obrade kofeina i rivaroksabana, što implicira na poteškoće prilikom direktne kompresije. Međutim, u aplikaciji *Formulation Wizard* predložen je sastav formulacija sa dobrom procesabilnošću. Formulacije, odabrane na osnovu predviđene povoljne protočnosti ili tabletabilnosti, pokazale su dobru gustinu, protočnost i kompresibilna svojstva, a izrađene tablete pokazale su zadovoljavajuće mehaničke karakteristike (čvrstina i friabilnost) i kratko vreme dezintegracije.

Zahvaljujući integrisanim algoritmima, kao i bazama podataka AS i ekscipijenasa, *ZoomLab*® platforma predstavlja koristan alat i vodič za razvoj formulacije. Međutim, baza ekscipijenasa ograničena je na odabrane proizvode kompanije BASF. Iako primena hibridnog pristupa može doprineti razvoju proizvoda u kraćem vremenu, uz manji utrošak materijala, potrebno je kritički razmotriti dostupne podatke i optimizovati sastav formulacije na osnovu sprovedenih eksprimenata.

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EXPLORING THE BENEFITS AND LIMITATIONS OF THE ZoomLab® VIRTUAL ASSISTANT IN DIRECTLY COMPRESSIBLE FORMULATION DEVELOPMENT

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Pharmaceutical development is based on complex relationships between active pharmaceutical ingredients (APIs) and excipients material properties, process parameters and targeted product performance which are difficult to model and predict. With advancement of the knowledge base in the field, availability of large datasets and machine learning, digital platforms have been created providing advanced algorithms to simplify and accelerate formulation development.

In this study, the applicability of BASF Virtual Assistant ZoomLab® [1], as a tool for development of directly compressible formulations was investigated, using caffeine and rivaroxaban as model drugs. Comparative evaluation of the experimentally obtained and built-in data has been performed using the API and Powder Blend *Tabletability* and *Processability* applications followed by *Formulation Wizard* guided formulation selection.

Based on API characteristics evaluation, both caffeine and rivaroxaban presented poor processability, indicating that direct compression into tablets would be challenging. However, *Formulation Wizard* identified a number of prospective formulations with good processability. Powder blends, selected based on predicted favorable flowability or tabletability, exhibited good flowability, powder density, and compression-related properties. The obtained tablets exhibited good mechanical properties (hardness and friability), as well as fast disintegration.

ZoomLab® built-in algorithms, as well as the API and excipient databases represent useful preformulation tool and provide insights which could guide formulation development. However, the excipients database is limited to the selected BASF products. Relevant outputs should be critically assessed and further optimized based on experimental observations leading to hybrid approach which would accelerate product development while minimizing time and resources consumption.

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METABOLIČKE PROMENE ZAVISNE OD REDOKS STATUSA SU U OSNOVI HEMIOSENZITIVNOSTI U ĆELIJAMA LEUKEMIJE HL-60 I K562

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Oksidativni stres (OS) je odavno prepoznat kao centralni pokretač maligne transformacije i progresije. Kod leukemije, poremećena redoks ravnoteža i metaboličko reprogramiranje utiču na proliferaciju, diferencijaciju i preživljavanje ćelija, kao i na odgovor na terapiju. Povećana produkcija reaktivnih vrsta kiseonika (ROS) u ćelijama ne samo da podstiče razvoj bolesti već doprinosi i citotoksičnoj aktivnosti mnogih hemioterapeutika. U ovoj studiji, ispitali smo efekte dva leka, busulfana i melfalana, koji predstavljaju kondicionirajuću terapiju za transplantaciju hematopoetskih matičnih ćelija, na redoks status i metabolizam u dva različita metabolička *in vitro* modela, HL-60 (promijelocitna linija) i K562 (eritroleukemična linija). U ćelijama multiplog mijeloma melfalan indukuje proizvodnju ROS, smanjuje nivo glutationa (GSH), indukuje oksidaciju proteina i lipida i aktivira antioksidativni odgovor posredovan Nuklearnim eritroidnim faktorom 2 (Nrf-2), ističući njegov uticaj na redoks regulaciju. U našoj studiji smo uporedili bazalne redoks markere u HL-60 i K562 ćelijskim linijama i procenili kako busulfan i melfalan moduliraju stvaranje ROS i citotoksičnost. Takođe smo ispitali i promene u metaboličkim profilima tretiranih ćelija kako bismo definisali promene izazvane lekovima u ključnim metaboličkim putevima, uključujući glikolizu, ciklus trikarboksilne kiseline (TCA), metabolizam aminokiselina i metabolizam glutationa. Naši rezultati ukazuju da hemioterapija dovodi do redoks disbalansa i metaboličkog remodeliranja kod ćelijskih modela leukemije, ukazujući na potencijalne biomarkere hemiosenzitivnosti koji se mogu iskoristiti za poboljšane terapijske strategije kod lečenja mijeloidnih leukemija.

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REDOX-DEPENDENT METABOLIC ALTERATIONS UNDERLYING CHEMOSENSITIVITY IN HL-60 AND K562 LEUKEMIA CELLS

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Oxidative stress (OS) has long been recognized as a central driver of malignant transformation and progression. In leukemia, disrupted redox balance and metabolic reprogramming critically shape cell proliferation, differentiation, and survival, while also influencing response to therapy. An excess of reactive oxygen species (ROS) over the antioxidant defense system (AOS) not only promotes leukemogenesis but also contributes to the cytotoxic activity of many chemotherapeutics. In this study, we investigated the effects of two drugs, busulfan and melphalan, used as conditioning therapy for hematopoietic stem cell transplantation, on OS and metabolism in HL-60 (promyelocytic) and K562 (erythroleukemic) cell lines, two different *in vitro* models with distinct metabolic profiles. In multiple myeloma cells, melphalan has been reported to induce ROS production, deplete glutathione (GSH), enhance protein and lipid oxidation, and activate the Nuclear factor erythroid 2 (Nrf-2)-mediated antioxidant response, underscoring its impact on redox regulation. Here, we compared basal redox markers in HL-60 and K562 cells and assessed how busulfan and melphalan modulate ROS generation and cytotoxicity. Importantly, we complemented these analyses with metabolomic profiling to capture drug-induced changes in key metabolic pathways, including glycolysis, the tricarboxylic acid (TCA) cycle, amino acid metabolism, and glutathione metabolism. Our results indicate that chemotherapy leads to redox imbalance and metabolic remodeling in leukemia cell models, representing potential biomarkers of chemosensitivity that can be exploited to develop improved therapeutic strategies for myeloid leukemias.

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MONTE KARLO SIMULACIJA U FARMAKOKINETICI IMUNOSUPRESIVA

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Optimizacija imunosupresivne terapije kod pacijenata sa transplantiranim bubregom otežana je izraženom interindividualnom varijabilnošću u farmakokinetičkim procesima. Cilj ove studije bio je da se proceni primenljivost i izvrši validacija prethodno objavljenog populacionog farmakokinetičkog modela [1] mikofenolne kiseline (MPA) korišćenjem Monte Carlo (MC) simulacije, u cilju individualizacije doziranja i poboljšanja terapijskih ishoda.

MC numerička analiza sprovedena je kroz 1000 simulacija za svaki analizirani model, kako bi se dobio opseg očekivanih vrednosti klirensa MPA. Kliničke kovarijate su varirane u okviru opsega njihovih standardnih devijacija, a raspodela očekivanih vrednosti klirensa poređena je unutar samog modela i sa objavljenim modelima iz sličnih studija [2, 3]. MC analiza je izvršena korišćenjem softvera Matlab R2017b (MathWorks).

Simulacije su potvrdile robusnost našeg modela i identifikovale starost i koterapiju nifedipinom kao najuticajnije prediktore klirensa MPA. Primena nifedipina povećala je klirens za oko 18%, dok je stariji uzrast bio povezan sa povećanjem klirensa do 50% u analiziranom simulacionom opsegu. Poređenje sa spoljnim modelima pokazalo je dobro slaganje: u studijama gde je albumin bio značajna kovarijata, niže vrednosti albumina bile su povezane sa povećanjem klirensa za oko 15–25%, dok su drugi modeli naglašavali značaj kreatinina i telesne mase. Veći procenat slaganja između spoljnih i našeg modela zabeležen je kod pacijenata koji nisu koristili nifedipin, u odnosu na one sa koterapijom.

MC simulacija se pokazala kao dragocen alat za procenu farmakokinetičkih modela i identifikaciju ključnih prediktora varijabilnosti. Njena primena smanjuje potrebu za opsežnim uzorkovanjem i pruža podršku kliničkoj praksi u određivanju optimalne doze imunosupresiva, čime se potencijalno unapređuju bezbednost i efikasnost posttransplantacione farmakoterapije.

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Zahvalnica

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MONTE CARLO SIMULATION IN IMMUNOSUPPRESSANT PHARMACOKINETICS

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The optimization of immunosuppressive therapy in kidney transplant recipients is challenged by pronounced interindividual pharmacokinetic variability. This study aimed to evaluate the applicability of a population pharmacokinetic model [1] of mycophenolic acid (MPA) using Monte Carlo (MC) simulation to support dose individualization and improve outcomes.

MC numerical analysis was performed with 1000 simulations per model to define the expected range of MPA clearance values. Clinical covariates were varied within their standard deviation ranges, and the distribution of predicted clearance was compared within the model and against published models from similar studies [2,3]. Analyses were conducted using Matlab R2017b (MathWorks).

The simulations confirmed the robustness of our model and identified age and nifedipine co-therapy as the most influential predictors of MPA clearance. Nifedipine co-administration increased clearance by approximately 18%, while advancing age was associated with a rise in clearance of up to 50% across the simulated range. Comparison with external models showed good concordance: in studies where albumin was a significant covariate, lower albumin levels were associated with an increase in clearance of about 15–25%, while other models emphasized the role of creatinine and body weight. A higher percentage of agreement was observed between external models and our model for patients not receiving nifedipine compared with those on concomitant therapy.

MC simulation proved to be a valuable tool for evaluating pharmacokinetic models and identifying key predictors of variability. Its application reduces the need for extensive sampling and supports clinical practice in determining the optimal dose of immunosuppressants, thereby potentially improving the safety and efficacy of post-transplant pharmacotherapy.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 27–28 ***OP 4***

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UTICAJ ANEMIJE NA KONCENTRACIJE INFLIKSIMABA I ISHODE LEČENJA KOD PACIJENATA SA INFLAMATORNIM BOLESTIMA CREVA

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Do 50% pacijenata sa inflamatornom bolešću creva (IBC) ima ekstraintestinalne manifestacije, pri čemu je anemija jedna od najčešćih (prevalencija 6-74%) [1]. Anemija u IBC je prethodno povezana sa lošijim ishodima i smanjenim kvalitetom života [2]. Ovo istraživanje ispitivalo je povezanost anemije i koncentracije infliksimaba (IFX), kao i njenu korelaciju sa kliničkom i biohemijskom remisijom.

Demografske karakteristike, biohemijski i klinički podaci su prikupljeni retrospektivno za svakog pacijenta u dve vremenske tačke: prilikom merenja koncentracije IFX tokom i u odsustvu anemičnog stanja. Pošto je test normalnosti pokazao da podaci nisu normalno distribuirani, neparametarski testovi su primenjeni u *IBM SPPS* v29 (*Wilcoxon* - kontinuirane varijable; *McNemar* - kategoričke varijable). Podaci su podeljeni u dva podskupa na osnovu pola zbog različitih nivoa hemoglobina za postavljanje dijagnoze anemije kod muškaraca i žena.

Baza podataka sastojala se iz 52 pacijenta (40,38% muškaraca, 46,15% Kronova bolest, medijana starosti 39 (18-65) godina). Blago, ali značajno, niže medijane koncentracije IFX primećene su kada je anemija bila prisutna kod muškaraca (5,91 naspram 11,48 mg/L) i žena (3,26 naspram 10,2 mg/L). Svi markeri inflamacije su bili značajno viši kada su pacijenti bili anemični, sa značajnim povećanjem broja leukocita samo kod muškaraca ($p=0,011$). Takođe, muški pacijenti su pokazali značajno ($p<0,02$) bolje ishode lečenja kada anemija nije bila prisutna, dok kod žena nije primećena značajna razlika u ishodima.

Nešto niže koncentracije IFX ukazuju da klirens može biti povećan usled anemije. Rezultati vezani za ishode lečenja su oprečni, te je neophodno da se dalja analiza sprovede na većoj populaciji pacijenata.

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IMPACT OF ANAEMIA ON INFLIXIMAB CONCENTRATIONS AND TREATMENT OUTCOMES IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Up to 50% of patients with inflammatory bowel disease (IBD) experience extraintestinal manifestations, with anaemia being one of the most common (6-74% prevalence) [1]. Anaemia in IBD has previously been associated with poorer outcomes and reduced quality of life [2]. This research explored the relationship between anaemia and infliximab (IFX) concentrations, and its correlation with clinical and biochemical remission.

Demographic characteristics, biochemical and clinical data were retrospectively collected for each patient at two time points: when IFX concentrations were measured during and in the absence of anaemia. Since the normality test indicated data were not normally distributed, non-parametric tests were implemented in IBM SPPS v29 (Wilcoxon – continuous variables; McNemar – categorical variables). Data were divided into two subsets by sex due to different HGB thresholds for diagnosing anaemia in men and women.

The dataset included 52 patients (40.38% male, 46.15% Crohn's disease, median age 39 (18-65) years). Slightly, but significantly, lower median IFX concentrations were observed when anaemia was present in males (5.91 vs 11.48 mg/L) and females (3.26 vs 10.2 mg/L). Each marker of inflammation was significantly higher when patients were anaemic, with a significant increase in leukocyte count only in males ($p=0.011$). Also, male patients showed significantly ($p<0.02$) better treatment outcomes when anaemia was absent, whereas, in females, no significant difference in outcomes was observed.

Slightly lower IFX concentrations suggest that clearance may be increased in anaemia. Findings related to treatment outcomes were inconclusive, indicating the need for further analysis in a larger patient population.

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HEMOTAKSONOMIJA RODA *HYPERICUM* SEKCIJE *DROSOCARPIUM* BAZIRANA NA ANALIZI HEMIJSKOG SASTAVA ETARSKIH ULJA

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Prilikom upotrebe biljnih droga za pripremu bilo kakvog farmaceutskog oblika neophodno je odabrati biljni materijal sa biološkim izvorom propisanim u zvaničnim dokumentima kakva je Farmakopeja. Ponekad, izazovno je propisanu vrstu razlikovati od drugih vrsta iz istog roda. Često mikroskopske i makroskopske tehnike identifikacije ne mogu biti primenjene za reševanje ovog problema, te hemijska karakterizacija često ostaje jedino pouzdano rešenje. Zato, otkrivanje hemijskih taksonomskih markera i primena hemometrijskog pristupa omogućavaju pouzdanu identifikaciju vrsta. Cilj ovog istraživanja je dokazivanje postojanja ovakvih markera na primeru grupe taksona *Hypericum* sect. *Drosocarpium*. Tokom istraživanja dobijeno je petnaest uzoraka etarskih ulja metodom hidrodestilacije. Prinos ekstrakcije etarskih ulja se nalazio u rasponu od 0,01% do 0,1%. Uzorci su analizirani metodom GC-MS, a su poreklom od pet vrsta iz sekcije *Drosocarpium* roda Hypericum. Među dominantnim grupama biomolekula identifikovani su oksidovani alifatični ugljovodonici i oksidovani seskviterpeni, koji su se pokazali kao pouzdani hemotaksonomski markeri. Monoterpeni nisu detektovani, a njihovo odsustvo je rezultat njivove visoke molatilnosti usled manje molarne mase, i dugog vremena čuvanja pre analize. Multivarijantne statističke analize, uključujući analizu glavnih komponenti (PCA) i UPGMA klastersku analizu, pokazale su jasno razdvajanje *H. barbatum* i *H. richeri*, prvenstveno usled prisustva karofilen alkohola, n-dodekanske kiseline i n-dodekanola. Ovi metaboliti se stoga mogu predložiti kao potencijalni hemotaksonomski markeri. Dalja istraživanja su potrebna kako bi se razjasnilo postojanje specifičnih hemotipova ovih balkanskih vrsta *Hypericum*.

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CHEMOTAXONOMY OF *HYPERICUM* (SECT. *DROSOCARPIUM*) SPECIES: PATTERNS IN ESSENTIAL OIL COMPOSITION

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When using herbal drugs for the production of any pharmaceutical dosage form, it is essential to select species listed in official documents such as the Pharmacopoeias. Sometimes it can be challenging to distinguish the designated species from other members of the same genus. Since microscopic and macroscopic identification methods are not always applicable, chemical characterization often remains the only reliable solution. Thus, the detection of chemical taxonomic markers and the application of a chemometric approach provide reliable species identification. The aim of this study was to demonstrate that such markers can be found within the genus *Hypericum*, specifically in sect. *Drosocarpium*. In this study, fifteen essential oil samples were obtained by hydrodistillation from five species belonging to *Hypericum* sect. *Drosocarpium* and subsequently analyzed using GC–MS. The yield of essential oils ranged from 0.01% to 0.1%. Among the dominant groups of compounds were oxidized aliphatic compounds and oxidized sesquiterpenes, which proved to be reliable chemotaxonomic indicators. Monoterpenes were not detected, most likely due to their high volatility caused by smaller molar mass and long-term storage prior to analysis. Multivariate statistical analyses, including principal component analysis (PCA) and UPGMA clustering, revealed distinct separation of *H. barbatum* and *H. richeri*, driven primarily by the presence of caryophyllene alcohol, n-dodecanoic acid, and n-dodecanol. These metabolites can thus be proposed as potential chemotaxonomic markers. Further studies are warranted to clarify the existence of specific chemotypes within these Balkan *Hypericum* species.

POSTER PREZENTACIJE / POSTER PRESENTATIONS

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 36–37 ***PP 1***
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POREĐENJE RAZLIČITIH PRISTUPA ZA DEFINISANJE PROSTORA DIZAJNA: PRIMER METODE ZA ISPITIVANJE STABILNOSTI CITALOPRAMA U TABLETAMA

Jevrem Stojanović[1*], Jelena Andrejić[2], Biljana Otašević[1], Mira Zečević[1], Marija Rašević[1], Anđelija Malenović[1], Ana Protić[1]

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Na osnovu definicije iz ICH Q14, prostor dizajna za analitičke metode može se opisati kao podskup ispitivanih eksperimentalnih uslova za koje se može, sa dovoljnom verovatnoćom, pokazati da metoda ispunjava unapred definisane kriterijume [1]. Distribucija odgovora treba da se simulira, a eksperimentalni uslovi, za koje je verovatnoća da se ključni atributi kvaliteta (CQA) nalaze unutar prihvatljivog regiona iznad željenog nivoa kvaliteta (π), treba da budu uključeni u prostor dizajna. Mogu se primeniti Monte Karlo simulacije, *bootstrap* metode i Bajesova analiza [2], pri čemu se poslednji pristup preferira jer uzima u obzir i nesigurnost parametara modela i korelacije podataka [3]. Cilj ove studije bio je da se ispitaju razlike između tri pristupa za određivanje prostora dizajna hromatografske metode za ispitivanje stabilnosti citaloprama u tabletama. Kao CQAs (Y) izabrani su retencioni faktor nečistoće A (k) i rezolucija između citaloprama i nečistoće E (R_s), a kao kritični procesni parametri (X) sadržaj acetonitrila koncentracija perhlorata u mobilnoj fazi, kao i temperatura kolone. Prihvatljivi region za CQAs definisan je kao $S = \{(k, R_s): k > 1,\ R_s > 2\}$, a prostor dizajna kao $DS = \{x \in \chi \mid P(Y \in S) \geq \pi\}$, pri čemu je π = 0,9. Kontur dijagrami koji prikazuju zavisnost verovatnoće od sadržaja acetonitrila i temperature kolone pri pet različitih koncentracija perhlorata nisu pokazali značajne razlike, što se može pripisati niskoj nesigurnosti parametara modela (0,0015–0,0240) i slaboj korelaciji regresionih reziduala (–0,26). Potrebne je ispitati veći opseg nesigurnosti parametra, korelacije reziduala i slično, kako bi se utvrdile oblasti praktične ekvivalentnosti ispitivanih pristupa.

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COMPARISON OF DIFFERENT APPROACHES TO THE DESIGN SPACE COMPUTATION: EXAMPLE OF STABILITY-INDICATING METHOD FOR CITALOPRAM TABLETS

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Based on the ICH Q14 definition, design space for analytical methods can be described as a subset of investigated experimental conditions for which it can be demonstrated, with sufficient probability, that method fulfills predefined criteria [1]. The response distribution should be simulated and the experimental conditions, for which the probability that the critical quality attributes (CQAs) are within acceptance region is above the desired quality level (π), should be included in the design space. Monte-Carlo simulations, bootstrapping, and Bayesian analysis [2] can be applied, with the last approach preferred as it accounts for both model parameter uncertainty and data correlations [3]. This study aimed to investigate differences between the three approaches to derive the design space for a chromatographic stability-indicating method for citalopram tablets. Retention of impurity A (k) and resolution between citalopram and impurity E (R_s) were selected as CQAs (Y), while acetonitrile content, perchlorate concentration in the mobile phase, and column temperature were critical process parameters (X). The acceptance region for CQAs was set as $S = \{(k, R_s): k > 1,\ R_s > 2\}$ and the design space as $\mathrm{DS} = \{x \in \chi \mid P(Y \in S) \geq \pi\}$ with π = 0.9. Contour plots showing the dependence of the probability on acetonitrile content and column temperature at five different perchlorate concentrations showed no significant differences, which can be attributed to the low uncertainty of the model parameters (0.0015–0.0240) and weak correlation of regression residuals (–0.26). A wider range of parameter uncertainties, residual correlations, etc. need to be investigated to determine areas of practical equivalence of the examined approaches.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 38–39 ***PP 2***
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POREĐENJE PRISTUPA PREKLAPANJA PROSEČNIH ODGOVORA, FUNKCIJA POŽELJENIH ODGOVORA I ANALITIČKOG KVALITETA KROZ DIZAJN U OPTIMIZACIJI METODE HAOTROPNE HROMATOGRAFIJE ZA RAZDVAJANJE CITALOPRAMA I NJEGOVIH NEČISTOĆA

Jevrem Stojanović[1*], Jelena Andrejić[2], Biljana Otašević[1], Mira Zečević[1], Milena Rmandić[1], Anđelija Malenović[1], Ana Protić[1]

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Tradicionalni pristupi multikriterijumskoj optimizaciji, kao što su primena funkcija poželjnih odgovora i preklapanje prosečnih odgovora, nisu u skladu sa definicijom prostora dizajna datom u ICH Q14, jer ne pružaju meru osiguranja kvaliteta, tj. verovatnoću da ključni atributi kvaliteta ispunjavaju granične vrednosti prihvatljivosti [1]. Dodatni problem je što ovi pristupi ne uzimaju u obzir nesigurnost u procenjenim vrednostima koeficijenata modela, niti korelaciju reziduala regresionih modela [2]. Cilj ovog rada bio je da se ispita koliko se pomenute teorijske razlike odražavaju na rezultate optimizacije na primeru metode za ispitivanje stabilnosti citaloprama u tabletama. U ovom slučaju, retencioni factor nečistoće A (k) i rezolucija između citaloprama i nečistoće E (R_s) izabrani su kao kritični atributi kvaliteta sa sledećim graničnim vrednostima: $k > 1$ i $R_s > 2$. Kritični parametri analitičke metode bili su sadržaj acetonitrila i koncentracija perhlorata u mobilnoj fazi i temperatura kolone. Upoređeni su region dobijen preklapanjem odgovora, region pri kojem je vrednost funkcije poželjnih odgovora veća od 0,6 i prostor dizajna određen Bajesovom analizom. Na osnovu dvodimenzionalnih grafičkih prikaza utvrđeno je da se optimalni region dobijen tradicionalnim pristupima u velikoj meri poklapa sa prostorom dizajna. Razlog za to može biti slaba korelacija reziduala (–0,26) i male standardne greške koeficijenata modela (0,0015–0,0240). S obzirom na odsustvo komercijalno dostupnih softvera za određivanje prostora dizajna prema ICH Q14, moguća alternativa je da se prikažu mere nesigurnosti parametara i korelacije reziduala zajedno sa rezultatima tradicionalne optimizacije, čime se obezbeđuje dodatna garancija kvaliteta analitičke metode.

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COMPARING OVERLAPPING MEAN RESPONSE, DESIRABILITY FUNCTIONS, AND ANALYTICAL QUALITY BY DESIGN APPROACHES TO THE OPTIMIZATION OF CHAOTROPIC CHROMATOGRAPHY METHOD FOR THE SEPARATION OF CITALOPRAM AND ITS IMPURITIES

Jevrem Stojanović[1*], Jelena Andrejić[2], Biljana Otašević[1], Mira Zečević[1], Milena Rmandić[1], Anđelija Malenović[1], Ana Protić[1]

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Traditional approaches to multicriteria optimization, including desirability functions and overlapping mean responses (OMRs), are not aligned with definition of design space in ICH Q14 because they do not provide a measure of quality assurance, i.e., the probability that critical quality attributes (CQAs) meet acceptance limits [1]. Furthermore, these approaches neglect uncertainty of the model coefficient estimates and correlation of the regression residuals [2]. The aim of this work was to evaluate how such theoretical differences affect the optimization results using the example of a stability-indicating method for citalopram tablets. In this case, the retention factor of impurity A (k) and the resolution between citalopram and impurity E (R_s) were selected as CQAs with the following acceptance limits: k > 1 and R_s > 2. Critical parameters of the analytical method were acetonitrile content, perchlorate concentration in the mobile phase, and column temperature. The region obtained by OMR, the region where the global desirability function exceeded 0.6, and the design space derived by Bayesian analysis were compared. Two-dimensional contour plots showed that the optimal regions obtained by traditional approaches largely overlapped with the design space. This can be explained by the low correlation of the residuals (−0.26) and the low standard errors of the model coefficients (0.0015–0.0240). Since there is no available software to determine the design space according to ICH Q14, a possible alternative is to report the measures of parameters uncertainty and residual correlation along with traditional optimization results, providing an additional measure of analytical method quality.

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PRELIMINARNA HEMOMETRIJSKI PODRŽANA SPEKTROFOTOMETRIJSKA ANALIZA VIŠEKOMPONENTNE FORMULACIJE LEKA

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Analiza višekomponentnih formulacija lekova predstavlja značajan izazov koji proizilazi iz kompleksne prirode ispitivanih jedinjenja. Hemometrija i multivarijantne metode mogu olakšati rad i umanjiti doprinos spektralnih smetnji na koje nailazimo u toku primene spektrofotometrije u kvantitativnoj analizi. Cilj ovog istraživanja je primena *UV* spektrofotometrijskih merenja u kombinaciji sa hemometrijom za kvalitativnu i kvantitativnu analizu tri aktivne farmaceutske supstance: perindopril erbumin, amlodipin besilat i indapamid. Eksperimentalni dizajn koji uključuje procenu uticaja 3 faktora na 5 faktorskih nivoa, izveden uz upotrebu *Design Expert 11.0* (Stat Ease, SAD) softvera. Opseg talasnih dužina je bio od 200 do 400 nm, brzina snimanja 800 nm/min, dok je veličina koraka bila podešena na 1,280 nm sa razrezom od 1,5 nm. Osnovni rastvori su bili pripremljeni u smeši etanola i destilovane vode 50/50, a zatim su radni rastvori razblaženi destilovanom vodom do postizanja radnih koncentracija u opsegu 10-50 μg/mL za sve tri aktivne farmaceutske supstance. Spektralni podaci su snimani pomoću *Cintra* 202 *UV* spektrofotometra (GBC, Australija) čiji rad podržava *Cintral* softver, verzija 2.2. Podaci koji se odnose na preklapanja *UV* spektara su modelovani primenom tehnike parcijalnih najmanjih kvadrata u kombinaciji sa genetskim algoritmom. Ova metodologija je odabrana zbog svoje izuzetne sposobnosti da smanji broj promenljivih tako da zadrži samo one koje poseduju prediktivne sposobnosti, čime se optimizuje tačnost i ponovljivost nagrađenog modela. Razvijena metoda predstavlja isplativiju i vremenski efikasniju alternativu konvencionalnoj *HPLC* metodi koja se uobičajeno koristi u analitici višekomponentnih smeša.

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PRELIMINARY CHEMOMETRIC ASSISTED SPECTROPHOTOMETRIC ANALYSIS OF MULTI-COMPONENT PHARMACEUTICAL FORMULATION

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Multidrug analysis presents significant challenges due to the intricate nature of compounds. Chemometrics and multivariate methods effectively mitigate spectral interference encountered in spectrophotometric techniques for pharmaceutical quantification. This research aimed to employ UV spectrophotometric measurements coupled with chemometrics for both qualitative and quantitative analysis of three active pharmaceutical substances: perindopril erbumine, amlodipine besylate, and indapamide. The experimental design was constructed using Design Expert 11.0 (Stat Ease, USA), employing a 5-level-3-factor design. The wavelength range was from 200 to 400 nm, the speed is set at 800 nm/min, and the step size is precisely set at 1.280 nm, with a slit width of 1.5 nm. Stock solutions were prepared in a 50/50 mixture of ethanol-distilled water. Subsequently, working solutions were diluted with distilled water to achieve a concentration range of 10-50 μg/mL for the three active pharmaceutical ingredients. Spectral data was collected using a Cintra 202 UV spectrophotometer (GBC, Australia), equipped with Cintral software version 2.2. The UV spectral overlapping was recorded and disentangled employing Partial Least Square (PLS) coupled with Genetic Algorithm (GA). This methodology was selected due to its remarkable ability to reduce the number of variables to those that possess predictive capabilities, thereby optimizing the model accuracy and repeatability. The developed method presents a cost-effective and time-efficient alternative to the conventional HPLC standard method.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 42–43 ***PP 4***
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EVALUACIJA EFEKATA TRETMANA SEMAGLUTIDOM NA PROSTORNU MEMORIJU I ANHEDONIJU U MODELU DIJABETESA TIPA 2 KOD PACOVA OBA POLA

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Prostorna memorija može biti narušena kod pacijenata sa dijabetesom tipa 2 (T2D) čak i u ranim fazama bolesti. Pored ovoga, anhedonija se može javiti kod pacijenata sa T2D i negativno uticati na kvalitet života. Agonista receptora za glukagonu sličan peptid 1, semaglutid, pokazao je visoku kliničku efikasnost u regulaciji glikemije, ali noviji literaturni podaci sugerišu njegove efekte i na mozak. Ova studija je imala za cilj da proceni efekte terapije semaglutidom na prostornu memoriju i anhedoniju u modelu dijabetesa tipa 2 i gojaznosti kod starih pacova oba pola. Nakon validacije T2D modela, korišćeni su *Sprague-Dawley* pacovi oba pola koji su bili srednje dobi i koji su hranjeni dijetom sa visokim sadržajem masti i tretirani streptozotocinom. Životinje su dobijale ili vehikulum ili semaglutid i bile su podvrgnute različitim bihejvioralnim testovima, uključujući test preferencije saharoze (SPT) i *Morris*-ov vodeni lavirint (MWM). Tretman semaglutidom nije uticao na vreme potrebno da se pronađe zona platforme u MWM *probe* testu, ali je identifikovan glavni efekat pola, tako da su ženke pokazale veće latence do zone platforme u odnosu na mužjake. Kod T2D ženki, tretman semaglutidom je povećao preferenciju saharoze u poređenju sa vehikulumom. Povećanje preferencije saharoze nakon primene tretmana semaglutidom bi moglo biti relevantno za pacijente sa T2D i promenama raspoloženja, a ovaj model bi mogao poslužiti za dalje istraživanje povezanih molekularnih mehanizama.

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EVALUATION OF SEMAGLUTIDE TREATMENT EFFECTS ON SPATIAL MEMORY AND ANHEDONIA IN DIABETES TYPE 2 RAT MODEL OF BOTH SEXES

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Spatial memory could be compromised in diabetes type 2 (T2D) patients even at early stages of the disease. In addition, anhedonia can co-occur in T2D patients and negatively impact quality of life. The glucagon-like peptide 1 receptor agonist semaglutide has demonstrated advanced clinical efficacy in glycemic regulation, but recent literature suggests its effects may extend beyond this. This study therefore aimed to assess the effects of semaglutide treatment on spatial memory and anhedonia in type 2 diabetes and obesity model in aging rats of both sexes. After validation of the T2D model, middle-aged Sprague-Dawley rats of both sexes, fed a high-fat diet and treated with streptozotocin, were used. They received either vehicle or semaglutide and underwent an extensive behavioral battery, including the sucrose preference test (SPT) and Morris water maze (MWM). Semaglutide treatment did not affect the latency to reach the platform zone in MWM probe test, but main effect of sex was identified, with females having higher values than males. In T2D females, semaglutide increased sucrose preference compared to vehicle. Semaglutide treatment was associated with increased sucrose preference, which could be relevant for T2D patients experiencing mood changes, and this model may serve for further investigation of underlying mechanisms.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 44–45 ***PP 5***
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KVANTITATIVNO ODREĐIVANJE REDUKUJUĆIH ŠEĆERA U HIDROLATIMA VRSTA IZ FAMILIJE LAMIACEAE: KORAK KA NJIHOVOJ FUNKCIONALNOJ I TERAPEUTSKOJ PRIMENI

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Vodeni destilati ili kondenzati, poznati kao hidrolati, nusproizvodi su destilacije vodenom parom biljnog materijala. Predstavljaju vodenu fazu koja preostaje u aparatu za destilaciju nakon izdvajanja etarskog ulja. Hidrolati se, zbog svog hemijskog sastava, smatraju pogodnim za topikalnu i oralnu upotrebu [1, 2].

Cilj istraživanja je bio da se utvrdi sadržaj redukujućih šećera u hidrolatima dobijenim iz nadzemnih delova predstavnika familije Lamiaceae (*Hyssopus officinalis*, *Lavandula intermedia*, *Melissa officinalis*, *Origanum vulgare*, *Ocimum basilicum* i *Thymus vulgaris*). Analiza je sprovedena korišćenjem Dubois metode za kvantifikaciju redukujućih šećera [3], a rezultati su izraženi kao miligrami glukoznih ekvivalenata (GluE) po litru hidrolata, na osnovu kalibracione krive glukoze u opsegu od 0,1 do 1,0 mg/mL.

Kvantitativna procena sadržaja redukujućih šećera pokazala je vrednosti u rasponu od 125,12 ± 8,33 (*O. basilicum*) do 1047,13 ± 24,80 (*L. intermedia*) mg GluE/L hidrolata. Nisu uočene statistički značajne razlike u sadržaju redukujućih šećera između *H. officinalis* i sledećih vrsta: *O. basilicum*, *O. vulgare* i *T. vulgaris* ($p > 0,05$ i $p > 0,01$).

Kada se hidrolati koriste u čistom obliku u kozmetici ili su prisutni u značajnoj meri u hrani i pićima, a posebno sa stanovišta funkcionalne hrane, neophodno je kvantifikovati njihov sadržaj redukujućih šećera jer je to važno za osobe sa dijabetesom. Ovakva analiza do sada nije sprovedena, a važna je za karakterizaciju ove vredne sirovine, koja se ranije smatrala otpadnim proizvodom.

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QUANTITATIVE DETERMINATION OF REDUCING SUGARS IN HYDROLATES OF LAMIACEAE SPECIES: A STEP TOWARDS THEIR FUNCTIONAL AND THERAPEUTIC UTILISATION

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Aqueous distillates or condensates, commonly known as hydrolates, are by-products of the steam distillation of plant materials. They represent the residual water phase that remains in the distillation apparatus after the essential oil has been separated. Due to their chemical composition, hydrolates are considered suitable for both topical and oral application [1, 2].

The aim of this study was to determine the content of reducing sugars in hydrolates obtained from the aerial parts of Lamiaceae species (*Hyssopus officinalis*, *Lavandula intermedia*, *Melissa officinalis, Origanum vulgare*, *Ocimum basilicum* and *Thymus vulgaris*). The analysis was performed according to the Dubois method for the quantification of reducing sugars [3], with results expressed as milligrammes of glucose equivalents (GluE) per litre of hydrolate based on a glucose calibration curve ranging from 0.1 to 1.0 mg/mL.

Quantitative evaluation of the reducing sugar content yielded values between 125.12 ± 31.22 (*O. basilicum*) and 1047.13 ± 8.33 (*L. intermedia*) mg GluE/L hydrolate. No statistically significant differences in the content of reducing sugars were found between *H. officinalis* and the following species: *O. basilicum*, *O. vulgare*, and *T. vulgaris* ($p > 0.05$ and $p > 0.01$).

When hydrolates are used in pure form in cosmetics or are present to a significant extent in food and beverages, it is essential from a functional food perspective to quantify their reducing sugar content, as this is important for people with diabetes mellitus. Such an analysis has not yet been carried out and is important for the characterisation of this valuable raw material, which was previously considered a waste product.

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ISPITIVANJE *IN VITRO* ANTIOKSIDATIVNE I ANTIHIPERGLIKEMIJSKE AKTIVNOSTI VODENO-ETANOLNIH EKSTRAKATA VRSTE *HYPERICUM OLYMPICUM* L., HYPERICACEACE

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Hypericum olympicum L. (Hypericaceae) je višegodišnja vrsta koja se tradicionalno koristi u lečenju gastrointestinalnih tegoba, rana i inflamatornih stanja. S obzirom na porast interesovanja za prirodne proizvode sa antioksidativnim i antihiperglikemijskim svojstvima, cilj ovog istraživanja bio je hemijska karakterizacija vodeno-etanolnih ekstrakata *H. olympicum* i procena njihovog biološkog potencijala primenom različitih *in vitro* metoda. Tri uzorka nadzemnih delova biljke *Hypericum olympicum*, sakupljena na području Severne Makedonije, ekstrahovana su 70% etanolom i analizirana u pogledu sadržaja ukupnih fenola i flavonoida, antioksidativne aktivnosti i sposobnosti inhibicije enzima uključenih u metabolizam ugljenih hidrata [1, 2].

Dobijeni ekstrakti sadržali su značajne količine ukupnih fenola (113–136mg EGK/g s.e.) i ukupnih flavonoida (29–36mg EK/g s.e.). Antioksidativni potencijal ispitan je pomoću više testova, uključujući neutralizaciju DPPH, OH i NO radikala, inhibiciju lipidne peroksidacije i FRAP-test. Svi uzorci pokazali su snažnu neutralizaciju DPPH radikala (RSC_{50}=3,12–3,43μg/mL), umerenu neutralizaciju OH i NO radikala i dobru redukcionu moć u FRAP testu (178–201mg ekvivalenata askorbinske kiseline/g s.e), dok inhibicija lipidne peroksidacije nije bila značajna. U pogledu antihiperglikemijskog potencijala, ekstrakti su pokazali slabu inhibiciju α-amilaze (IC_{50}=2892–5109μg/mL), dok su u slučaju α-glukozidaze ispoljili snažan inhibitorni efekat (IC_{50}=27–42 μg/mL), izraženiji čak i od standardnog inhibitora akarboze (IC_{50}=42,87 μg/mL).

Dobijeni rezultati ukazuju da vodeno-etanolni ekstrakti *H. olympicum* poseduju značajnu sposobnost neutralizacije slobodnih radikala i izraženu inhibiciju α-glukozidaze, što sugeriše njihovu potencijalnu primenu u prevenciji poremećaja povezanih sa oksidativnim stresom i postprandijalnom hiperglikemijom. Dalja istraživanja su neophodna radi izolacije i identifikacije aktivnih jedinjenja odgovornih za ove efekte.

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IN VITRO EVALUATION OF THE ANTIOXIDANT AND ANTIHYPERGLYCEMIC ACTIVITIES OF HYDRO-ETHANOLIC EXTRACTS OF *HYPERICUM OLYMPICUM* L., HYPERICACEAE

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Hypericum olympicum L. (Hypericaceae) is a species traditionally used in the treatment of gastrointestinal disorders, wounds, and inflammatory conditions. Considering the increasing interest in natural products with antioxidant and antihyperglycemic properties, the aim of this study was the chemical characterization of hydroethanolic extracts of *H. olympicum* and the evaluation of their biological potential using different *in vitro* methods. Three samples of aerial parts of *H. olympicum*, collected in North Macedonia, were extracted with 70% ethanol and analyzed for total phenolic and flavonoid content, antioxidant activity, and the ability to inhibit carbohydrate-metabolizing enzymes.

The obtained extracts contained significant amounts of total phenolics (113–136mg GAE/g dry extract) and total flavonoids (29–36mg QE/g d.e.). Antioxidant potential was assessed by several assays, including DPPH, OH and NO radical scavenging, lipid peroxidation inhibition, and FRAP-test. All extracts demonstrated strong DPPH radical scavenging activity (RSC_{50}=3.12–3.43μg/mL), moderate neutralization of OH and NO radicals, and significant reducing power in the FRAP-assay (178–201mg AAE/g d.e.), while lipid peroxidation inhibition was not significant. Regarding antihyperglycemic potential, the extracts exhibited weak α-amylase inhibition (IC_{50}=2892–5109μg/mL), whereas in the case of α-glucosidase they exerted a strong inhibitory effect (IC_{50}=27–42μg/mL), even more pronounced than the standard inhibitor-acarbose (IC_{50}=42.87μg/mL).

The results indicate that hydroethanolic extracts of *H. olympicum* possess significant radical scavenging capacity and pronounced α-glucosidase inhibition, suggesting their potential application in the prevention of disorders related to oxidative stress and postprandial hyperglycemia. Further investigations are necessary to isolate and identify the active compounds responsible for these effects.

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IN VITRO ISPITIVANJE PERMEACIJE I ANTIMIKROBNE AKTIVNOSTI ALKIL-POLIGLUKOZIDNIH EMULZIJA SA SPIRONOLAKTONOM

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Androgeni, zajedno sa infekcijom bakterijom *C. acnes*, predstavljaju ključne faktore u patogenezi akni. Spironolakton (SP) se odnedavno koristi kao *off-label* topikalna terapija akni (1). Emulzije zasnovane na alkil–poliglukozidima (APG) koje sadrže 5% SP pokazale su prihvatljiv bezbednosni profil za primenu na koži (2). Cilj ovog rada bio je da se ispita permeacija SP kroz kožu iz APG emulzija sa ili bez glikolne kiseline (GA), kao i da se istraži potencijalna aktivnost ovih emulzija prema *C. acnes*.

Pripremljena su dva različita uzorka. *In vitro* ispitivanje oslobađanja sprovedeno je korišćenjem Francovih difuzionih ćelija. Za određivanje sadržaja SP primenjena je HPLC tehnika. Za antimikrobno ispitivanje korišćen je *C. acnes* (ATCC 6919). Minimalna inhibitorna koncentracija (MIC) određena je metodom mikrodilucije u skladu sa preporukama Nacionalnog komiteta za standarde kliničkih laboratorija (3).

Oba ispitivana uzorka pokazala su zadovoljavajuće profile permeacije SP. Permeacija SP iz oba uzorka bila je gotovo linearna, što ukazuje na ujednačeno oslobađanje iz obe emulzije. Naša studija pokazuje da GA može povećati permeaciju SP iz APG emulzija. Obe emulzije su ispoljile izvestan antimikrobni potencijal prema *C. acnes*; vrednosti MIC za SP iznosile su 0,78 mg/g za uzorak F1 i 0,39 mg/g za uzorak F2.

SP je pokazao zadovoljavajući profil permeacije iz APG emulzija, kao i prihvatljivu antimikrobnu aktivnost prema *C. acnes*. GA se pokazala kao pogodan penetracioni enhenser i adekvatan dodatak antimikrobnoj aktivnosti SP.

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IN VITRO PERMEATION STUDY AND ANTIMICROBIAL ACTIVITY OF ALKYL POLYGLUCOSIDE – BASED EMULSIONS WITH SPIRONOLACTONE

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Androgens, alongside *C. acnes* infection, are key factors in the pathogenesis of acne. Recently, spironolactone (SP) was introduced as *off-label* topical acne therapy [1]. Alkyl polyglucoside (APG)-based emulsions with 5% of SP showed acceptable skin irritation profiles [2]. This work's objective was to examine the SP permeation through skin from APG-based emulsions with or without glycolic acid (GA), as well as to investigate the potential activity of these emulsions against *C. acnes*.

We prepared two different samples. *In vitro* release study was performed using Franz diffusion cells. HPLC technique was used for determination of SP content. *C. acnes* (ATCC 6919) was used for antimicrobial bioassay. Minimum inhibitory concentration (MIC) was determined by a microwell dilution method according to the recommendations of the National Committee for Clinical Laboratory Standards [3].

Both tested samples showed satisfactory SP permeation profiles. SP permeation from both samples was almost linear, which indicates its uniform release from both emulsions. Our study shows that GA can enhance SP permeation from APG-based emulsions. Both emulsions showed certain antimicrobial potential against *C. acnes*; MIC values of SP were 0.78mg/g for F1 and 0.39mg/g for F2.

SP showed a satisfactory permeation profile from APG-based emulsions, as well as acceptable antimicrobial activity against *C. acnes*. GA proved to be an acceptable penetration enhancer and adequate addition to the antimicrobial activity of SP.

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IN VITRO ISPITIVANJE ANTIMIKROBNOG I ANTIADHEZIVNOG DEJSTVA PROBIOTIKA U LEČENJU *ACNE VULGARIS*

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Akne su jedan od najčešćih kožnih poremećaja sa estetskim i psihološkim posledicama. Iako su probiotici poznati po koristima u gastrointestinalnom traktu, sve češće se razmatra njihova primena u dermatologiji. Cilj rada je bio *in vitro* procena antimikrobnog i antiadhezivnog dejstva paraprobiotičkih derivata laktobacila protiv *Cutibacterium acnes*.

U radu su korišćeni *C. acnes* i sojevi laktobacila *Lactobacillus salivarius* BGHO1 i *Lactobacillus paracasei* BGSJ2-8. Paraprobiotici su dobijeni termičkom inaktivacijom 30 min na 95 °C (*heat killed* - HK). Agar difuzija: meki BHI 0,7% inokulisan sa 20 µl prekonoćne kulture *C. acnes*; bunarići sa 50 µl preparata laktobacila 1×10^8 CFU/mL; inkubacija 24 h na 37 °C anaerobno; merenje zona u ImageJ. Antiadhezija: HaCaT 10^6 ćelija po bunariću koinkubirane 1 h sa 50 µl *C. acnes* 5×10^6 CFU/mL i 50 µl HK 5×10^6 CFU/mL; pranje tri puta PBS, tripsinizacija, zasejavanje na BHI, inkubacija 24 h na 37 °C; brojanje adherentnih CFU u odnosu na kontrolu.

U agar difuzionom testu na podlozi inokulisanoj *C. acnes*, termički inaktivisani *L. salivarius* BGHO1 i *L. paracasei* BGSJ2-8 formirali su zone inhibicije. U testu adhezije na HaCaT ćelijama broj adherentnih *C. acnes* smanjen je na 15 CFU/mL uz HK *L. salivarius* BGHO1 i na 25 CFU/mL uz HK *L. paracasei* BGSJ2-8, što odgovara smanjenju adhezije za 85% i 75% u odnosu na netretiranu kontrolu.

Ispitivani paraprobiotici ispoljavaju difuziono antimikrobno i antiadhezivno dejstvo prema *C. acnes*, što ukazuje na potencijal inovativnih, održivijih, neantibiotskih topikalnih strategija, ali i potrebu za daljim istraživanjima u cilju identifikacije aktivnih komponenti.

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IN VITRO EVALUATION OF THE ANTIMICROBIAL AND ANTIADHESIVE EFFECTS OF PROBIOTICS IN THE TREATMENT OF ACNE VULGARIS

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Acne is among the most common skin disorders with aesthetic and psychological consequences. Although probiotics are known for benefits in the gastrointestinal tract, their dermatologic use is increasingly explored. The aim was to assess *in vitro* the antimicrobial and antiadhesive activity of paraprobiotic derivatives of two lactobacillus strains against *Cutibacterium acnes*.

We used *C. acnes* and the strains *Lactobacillus salivarius* BGHO1 and *Lactobacillus paracasei* BGSJ2-8. Paraprobiotics were obtained by thermal inactivation for 30 min at 95 °C. Agar diffusion: soft BHI 0.7% inoculated with 20 µL *C. acnes*; wells with 50 µL lactobacillus preparations at 1×10^8 CFU/mL; incubation 24 h at 37 °C anaerobically; zones measured in ImageJ. Antiadhesion: HaCaT 10^6 cells per well coincubated 1 h with 50 µL *C. acnes* 5×10^6 CFU/mL and 50 µL heat killed paraprobiotics 5×10^6 CFU/mL; washed three times PBS, trypsinized, plated on BHI, incubated 24 h at 37 °C; adherent CFU counted vs control.

In agar diffusion on *C. acnes* lawns, heat killed *L. salivarius* BGHO1 and *L. paracasei* BGSJ2-8 formed inhibition zones. In HaCaT adhesion assays, adherent *C. acnes* decreased to 15 CFU/mL with *L. salivarius* BGHO1 and to 25 CFU/mL with *L. paracasei* BGSJ2-8, corresponding to 85% and 75% reductions versus untreated control.

The investigated paraprobiotics exhibit diffusional antimicrobial and antiadhesive effects against *C. acnes*, indicating the potential for innovative, more sustainable, nonantibiotic topical strategies, as well as the need for further research to identify the active components.

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ODREĐIVANJE SADRŽAJA NIACINAMIDA U KOZMETIČKIM PROIZVODIMA IZRAĐENIM U APOTECI

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Personalizovani kozmetički proizvodi predstavljaju individualno pripremljene formulacije koje omogućavaju prilagođavanje sastava, kao i koncentracije aktivnih supstanci potrebama potrošača, čime se postiže viši stepen efikasnosti i bolja tolerancija u poređenju sa komercijalno dostupnim kozmetičkim proizvodima [1]. Niacinamid se često koristi u ovim formulacijama, međutim postoje samo preporuke, ali ne i striktna ograničenja njegove koncentracije u kozmetičkim proizvodima [2]. Preporučene koncentracije niacinamida u kozmetičkim proizvodima su u opsegu 3,5-5,0% [3]. Cilj rada bio je ispitivanje sadržaja niacinamida u kozmetičkim proizvodima izrađenim u apoteci.

Analizirani su serum, formulisan kao hidrogel, tonik, koji predstavlja vodeni rastvor, i fluid, u formi emulzije, koji sadrže niacinamid. Za njegovu ekstrakciju korišćena je metoda tečno-tečne ekstrakcije, upotrebom vode ili metanola, a kvantifikacija je izvršena RP-HPLC metodom sa UV/VIS detektorom. Mobilnu fazu činili su metanol i fosfatni pufer, 25 mM, pH=4,0, a signal je praćen na talasnoj dužini od 260 nm. Dobijene prosečne koncentracije niacinamida iznosile su 1,6±0,03% u serumu, 5,0±0,07% u fluidu i 6,0±0,05% u toniku.

Niacinamid je nađen u svim analiziranim proizvodima i njegova koncentracija je bila u opsegu od 1,6 do 6,0%. Koncentracija niacinamida u serumu je niža, a u toniku viša od preporučenih vrednosti. Nađena koncentracija niacinamida u fluidu odgovara gornjoj granici preporučenih vrednosti.

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NIACINAMIDE CONTENT DETERMINATION IN COMPOUNDED COSMETIC PRODUCTS

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Compounded cosmetic products represent individually prepared formulations that allow the composition and concentration of the active substances to be tailored to the costumers' need, thereby achieving higher level of efficacy and better tolerance compared to commercially available formulations [1]. Niacinamide is frequently used in those formulations, however there are only recommendations, and no restriction regarding its concentration [2]. The recommended concentrations of niacinamide in cosmetic products range from 3.5 to 5%. [3] The aim of this study was assessment of the niacinamide content in compounded cosmetic products.

A hydrogel-formulated serum, tonic as an aqueous solution, and fluid in emulsion form, containing niacinamide were analyzed. His extraction was accomplished using liquid-liquid extraction with water or methanol, while quantification was performed by the RP-HPLC method with UV/VIS detector. The mobile phase consisted of methanol and phosphate buffer, 25 mM, pH=4.0, and the signal was detected at 260 nm.

The obtained average niacinamide concentrations were 1.6±0.03% in serum, 5.0±0.07% in fluid, and 6.0±0.05% in tonic.

Niacinamide was detected in all analyzed products with concentration ranging from 1.6% to 6.0%. The concentration of niacinamide in serum was below, and in the tonic above recommended concentrations. In the fluid, found niacinamide concentration corresponded to the upper limit of the recommended values.

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RAZVOJ I KARAKTERIZACIJA MUKOADHEZIVNIH BUKALNIH FILMOVA SA PROPILENGLIKOLNIM EKSTRAKTOM PROPOLISA

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Propolis, poznat kao „pčelinji lepak“, predstavlja prirodni proizvod bogat flavonoidima i fenolnim kiselinama, sa dokazanim antioksidativnim, antimikrobnim i antiinflamatornim delovanjem [1]. Zahvaljujući tim osobinama, ekstrakt propolisa se široko primenjuje u prevenciji i lečenju infekcija usne duplje i ždrela, posebno oralne kandidijaze, gingivitisa i parodontalnih bolesti, kao i u jačanju imunog sistema [2]. Bukalni film je savremen farmaceutski oblik koji omogućava laku primenu, fleksibilno doziranje i potencijalno lokalno i sistemsko delovanje [3]. Cilj ovog istraživanja bio je razvoj i karakterizacija inovativnih mukoadhezivnih bukalnih filmova sa propilenglikolnim ekstraktom propolisa, primenom polietilenoksida (PEO), polivinil alkohola (PVA), eritritola i stevije. Filmovi sa 10% ekstrakta propolisa pripremljeni su metodom izlivanja, korišćenjem PEO različitih molekulskih masa (2×10^5 – 1×10^6 Da) u koncentracijama 3 i 3,5%, uz PVA (1,5%), eritritol (3%) i tečnu steviju (1%). Od osam formulacija, pet je zadovoljilo organoleptičke kriterijume i dalje je ispitano u pogledu homogenosti, mehaničkih i mukoadhezivnih svojstava, brzine i mehanizma oslobađanja ukupnih flavonoida. Povećanje molekulske mase i koncentracije PEO značajno je uticalo na homogenost, čvrstoću, elastičnost, mukoadheziju i brzinu oslobađanja katehina. Formulacija F8 (3,5% PEO 1×10^6 Da) pokazala je najpoželjnija svojstva u pogledu mehaničke čvrstoće (1,88 ± 0,28 MPa), elastičnosti (424,57 ± 142,78%), mukoadhezije (F_{max}=2,22 ± 0,19 N; W_{ad}=16,71 ± 4,92 mJ) i brzine oslobađanja katehina (80% za 30 min) koja prati kinetiku prvog reda (R^2=0,9381). Razvijeni mukoadhezivni bukalni filmovi sa propolisom mogu se smatrati savremenim farmaceutskim oblikom koji može da obezbedi lokalni terapijski efekat istovremeno pružajući mogućnost sistemske apsorpcije bioaktivnih supstanci.

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DEVELOPMENT AND CHARACTERIZATION OF MUCOADHESIVE BUCCAL FILMS WITH PROPYLENE GLYCOL EXTRACT OF PROPOLIS

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Propolis, or "bee glue", is a natural product rich in flavonoids and phenolic acids, recognized for its antioxidant, antimicrobial, and anti-inflammatory properties [1]. It is widely used in the prevention and treatment of oral and pharyngeal infections, particularly oral candidiasis, gingivitis, and periodontal diseases, as well as in supporting the immune system [2]. Buccal film represents a modern dosage form with several advantages, including easy administration, dose flexibility, suitability for pediatric, elderly and dysphagic patients, and the potential for both local and systemic effects [3]. This study aimed to develop and characterize mucoadhesive buccal films containing propylene glycol extract of propolis, using polyethylene oxide (PEO), polyvinyl alcohol (PVA), erythritol, and liquid stevia. Films with 10% propolis extract were prepared by solvent casting, combining PEO of different molecular weights (3×10^5 – 1×10^6 Da) at 3–3.5% with PVA (1.5%), erythritol (3%), and stevia (1%). Out of eight formulations, five met organoleptic criteria and were further evaluated for mass uniformity, mechanical and mucoadhesive properties, rate and mechanism of total flavonoid release. Increasing PEO molecular weight and concentration significantly affected film homogeneity, strength, elasticity, mucoadhesion, and catechin release rate. Formulation F8 (3.5% PEO, 1×10^6 Da) showed the most favorable profile, with mechanical strength of 1.88±0.28 MPa, elasticity of 424.57±142.78%, mucoadhesion (F_{max}=2.22±0.19 N; W_{ad}=16.71±04.92 mJ), and catechin release of 80% within 30 min, following first-order kinetics (R^2=0.9381). The developed mucoadhesive buccal films with propolis extract represent an innovative dosage form capable of providing local therapeutic effect with the possibility of systemic absorption of bioactive compounds.

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ISPITIVANJE MOGUĆNOSTI PRIMENE SYLOID® XDP3150 KAO NOSAČA U TEČNO-ČVRSTIM SISTEMIMA SA ATORVASTATIN-KALCIJUMOM

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Tehnologija tečno-čvrstih sistema (TČS) predstavlja efikasan pristup za poboljšanje biološke raspoloživosti slabo rastvorljivih lekovitih supstanci. Jedan od ključnih koraka u razvoju TČS je izbor nosača sa odgovarajućim kapacitetom apsorpcije, koji uz sredstvo za oblaganje omogućava prevođenje disperzije lekovite supstance u suv prašak dobre protočnosti i tabletabilnosti [1]. Cilj ovog istraživanja bio je formulisanje TČS sa nosačem Syloid XDP3150 radi poboljšanja brzine rastvaranja atorvastatin-kalcijuma (ATC) iz tableta. TČS pripremljen je mešanjem tečne faze (2% rastvor ATC u polietilenglikolu 400) sa nosačem, sredstvom za oblaganje (koloidni silicijum-dioksid), superdezintegratorom (kroskarmeloza-natrijum) i lubrikansom (natrijum-stearil-fumarat). Pripremljenoj smeši ispitana je protočnost. Nakon kompresije na laboratorijskom simulatoru kompakcije (500 kg, 60 mm/min), tablete su okarakterisane u pogledu mehaničkih svojstava, vremena raspadanja i brzine rastvaranja ATC. Pripremljena smeša pokazala je dobru protočnost (Karov indeks = 13%). Zatezna čvrstina tableta iznosila je 1,02 MPa, dok su pritisci pri odvajanju i izbacivanju tableta bili 4,32 MPa i 3,05 MPa, redom. Elastični oporavak iznosio je 31,6%. Uprkos visokom udelu tečne faze u sastavu tableta (35%), postignuta su i dobra protočnost i prihvatljiva svojstva pri kompresiji (zatezna čvrstina > 1 MPa; pritisak pri izbacivanju < 5 MPa) [2, 3]. Tablete su pokazale kratko vreme raspadanja (< 3 min). Poređenjem profila brzine rastvaranja uočeno je da se ATC brže i potpunije rastvorio iz TČ tableta (> 90% nakon 10 min) u odnosu na tablete istog sastava, bez polietilenglikola 400 (~50% nakon 60 min). Dobijeni rezultati ukazuju na značajan potencijal TČS sa nosačem tipa mezoporoznog silicijum-dioksida, kao pristupa za postizanje poboljšanog rastvaranja ATC iz tableta.

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Zahvalnica

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INVESTIGATION INTO THE POSSIBILITY OF USING SYLOID® XDP3150 AS A CARRIER IN LIQUISOLID SYSTEMS WITH ATORVASTATIN CALCIUM

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Liquisolid systems (LSS) are an effective approach to improve bioavailability of poorly soluble drugs. A key step in their formulation is selecting a carrier with suitable absorption capacity, which, together with coating agent, converts the drug dispersion into dry powder with good flowability and tabletability [1]. The aim of this research was to improve the dissolution rate of atorvastatin calcium (ATC) from tablets by formulating LSS with carrier Syloid®XDP3150. LSS was prepared by mixing the liquid phase (a 2% solution of ATC in polyethylene glycol 400) with carrier, coating agent/colloidal silicon dioxide, superdisintegrant/croscarmellose sodium, and lubricant/sodium stearyl fumarate, using a pestle and mortar. Flowability of the prepared mixture was tested, and after compression using a laboratory compaction simulator (500 kg, 60 mm/min), the tablets' mechanical properties, disintegration time, and ATC dissolution rate were determined. Prepared mixture showed good flowability (Carr index=13%). Tensile strength was 1.02 MPa, while detachment and ejection stresses were 4.32 MPa and 3.05 MPa, respectively. Elastic recovery was 31.6%. Good flowability and acceptable compaction properties (tensile strength >1MPa; ejection stress <5MPa) [2,3] were achieved despite the high proportion of liquid phase present (35%). Disintegration time was short (<3 min). The dissolution rate profiles showed that ATC dissolved faster and more completely from LS tablets (>90% after 10 min) than from tablets of the same composition without polyethylene glycol 400 (~50% after 60 min). The results demonstrate the significant potential of LSS with a mesoporous silica-type carrier as a method to achieve improved dissolution of ATC from tablets.

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PUT KA LEKOVIMA KOJI SU PRILAGOĐENI PACIJENTU: RAZVOJ I ISPITIVANJE „*PULP-SPOON*“ FORMULACIJA ZA PEDIJATRIJSKU POPULACIJU

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Razvoj lekova prilagođenih deci, kao posebnoj grupi pacijenata, je od ključnog značaja za obezbeđivanje njihove prihvatljivosti i terapijske efikasnosti [1]. Cilj ove studije bio je da se ispita uticaj sastava na osobine „*pulp-spoon*“ formulacija - smeša praškova koje u kontaktu sa vodom bubre i formiraju mekanu masu, laku za gutanje kod pedijatrijskih pacijenata [2].

Kao sastojci formulacija, ispitivani su različiti polimeri (sredstva za geliranje), sredstva za raspadanje, sredstva za dopunjavanje i zaslađivači, uključujući varijacije u njihovim odnosima, pri čemu je karbamazepin korišćen kao model lekovita supstanca. Na osnovu organoleptičkih svojstava izdvojene su četiri formulacije koje su sadržale guar gumu, Prosolv® i manitol, saharozu i/ili steviju u različitim odnosima, a koje su dalje podvrgnute ispitivanjima sadržaja vlage (odmah nakon pripreme i nakon dve nedelje čuvanja), brzine upijanja vode, pH vrednosti vodenih disperzija, sadržaja i brzine rastvaranja lekovite supstance i analizi teksture.

Vodene disperzije su imale blago kiselu pH vrednost, koja se kretala u uskom opsegu za sve formulacije. Početni sadržaj vlage bio je ispod 5% i pokazao je minimalne promene tokom čuvanja. Uočene su određene razlike u brzini upijanja vode i brzini rastvaranja karbamazepina, pri čemu su formulacije sa većim udelom šećera, kao sredstava za dopunjavanje, pokazale sposobnost bržeg upijanja vode i oslobađanje leka, kao i mekšu i glatkiju teksturu. Istovremeno, njihov sadržaj vlage je ostao stabilan tokom perioda čuvanja.

Dobijeni rezultati ukazuju da se *„pulp-spoon“* formulacije mogu jednostavno pripremiti, čak i u uslovima apoteke, i predstavljaju obećavajući, pacijentu prilagođeni farmaceutski oblik leka za pedijatrijsku primenu.

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TOWARD PATIENT-FRIENDLY MEDICINES: DESIGN AND INVESTIGATION OF PEDIATRIC PULP-SPOON FORMULATIONS

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Designing patient-friendly dosage forms for children is crucial for ensuring their acceptability and therapeutic efficacy [1]. The aim of this study was to assess the influence of composition on the properties of pulp-spoons formulations - powder mixtures that readily swell in contact with water to form a soft mass, easy to swallow for pediatric patients [2].

Different polymers (gel-forming agents), disintegrants, diluents, and sweetening agents, including variations in their ratios, were evaluated, and carbamazepine was used as a model drug. Four promising formulations were selected based on organoleptic properties. These formulations, containing guar gum, Prosolv®, and mannitol, sucrose and/or stevia in varying proportions, were subjected to further testing, including moisture content (immediately after preparation and after two weeks of storage), water uptake rate, pH of aqueous dispersions, drug content, dissolution behavior, and texture analysis.

The aqueous dispersions exhibited slightly acidic pH values within a narrow range across all formulations. The initial moisture content was below 5% and showed minimal change during storage. Certain differences were observed in water uptake and carbamazepine dissolution rates, with formulations containing larger proportions of sugar diluents demonstrating faster hydration and drug release, as well as softer and smoother texture. At the same time, their moisture content remained stable over the storage period.

These findings suggest that pulp-spoon formulations are simple to prepare, even in a compounding pharmacy setting, and represent a promising patient-friendly dosage form for pediatric drug delivery.

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UTICAJ ARAPSKE GUME NA REOLOŠKA SVOJSTVA RASTVORA TRAGAKANT GUME

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Danas postoji sve veće interesovanje za upotrebu polisaharida biljnog porekla, kao što su tragakant guma (TG) i arapska guma (AG), zbog njihove široke dostupnosti, relativno niske cene, biokompatibilnosti, biorazgradivosti, jedinstvenih fizičko-hemijskih svojstava i različitih funkcionalnih karakteristika. Posebno su značajna reološka svojstva, zbog njihove sposobnosti modifikovanja reoloških karakteristika vodenih sistema [1, 2].

Cilj ovog istraživanja je bio ispitivanje uticaja dodatka AG na reološko ponašanje rastvora TG. Pripremljeni su vodeni rastvori TG (0,01–1,5%) i smeše sa fiksnim koncentracijama TG (0,5% i 1%) i rastućim koncentracijama AG. Krive proticanja su određene pomoću rotacionog reometra sa koaksijalnom cilindričnom geometrijom na 25 °C u opsegu brzina smicanja 0,001–100 s^{-1}, a dobijeni podaci su fitovani *Ostwald-de Waele* modelom.

Rastvori TG pokazali su Njutnovsko ponašanje pri veoma niskim koncentracijama (do 0,05%), dok su u koncentracijama ≥ 0,1% imali pseudoplastičan karakter, uz porast indeksa konzistencije (K) i smanjenje indeksa protoka (n). Dodavanje AG rastvorima TG značajno je modifikovalo njihova reološka svojstva. U rastvorima sa 0,5% i 1% TG, povećanje koncentracije AG dovelo je do smanjenja K indeksa i porasta n indeksa, što ukazuje na pomak ka ponašanju sličnijem Njutnovskom.

Dobijeni rezultati pokazuju da se pseudoplastičan karakter vodenih rastvora TG menja dodatkom AG zavisno od koncentracije, što ukazuje na prisustvo međumolekulskih interakcija između ova dva polisaharida. Rezultati ovog istraživanja otvaraju mogućnost unapređenja kontrole viskoziteta i teksturnih parametara u višekomponentnim farmaceutskim, prehrambenim i kozmetičkim formulacijama.

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THE INFLUENCE OF GUM ARABIC ON THE RHEOLOGICAL PROPERTIES OF TRAGACANTH GUM SOLUTIONS

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There is a growing interest in using plant-derived polysaccharides, like tragacanth gum (TG) and gum arabic (GA), due to their wide availability, relatively low cost, biocompatibility, biodegradability, unique physicochemical properties, and various functional characteristics. Rheological properties are particularly important due to their ability to modify the rheological characteristics of aqueous systems [1, 2].

The aim of this study was to investigate the effect of GA addition on the rheological behavior of TG solutions. Aqueous TG solutions (0.01–1.5%) and mixtures containing fixed concentrations of TG (0.5% and 1%) with increasing GA concentrations were prepared. Flow curves were determined using a rotational rheometer with coaxial cylinder geometry at 25 °C in the shear rate range of 0.001–100 s^{-1}, and the obtained data were fitted to the Ostwald–de Waele model.

Pure TG solutions exhibited Newtonian behavior at very low concentrations (≤ 0.05%), whereas concentrations ≥ 0.1% showed pseudoplastic character, with increased consistency index (K) and decreased flow index (n). The addition of GA to TG solutions significantly modified their rheological properties. In solutions containing 0.5% and 1% TG, increasing GA concentration led to a decrease in the K index and an increase in the n index, indicating a shift toward more Newtonian behavior.

The obtained results demonstrate that the pseudoplastic behavior of TG aqueous solutions is altered by GA addition in a concentration-dependent manner, suggesting intermolecular interactions between these two polysaccharides. Such findings provide new opportunities for controlling viscosity and texture in multicomponent pharmaceutical, food, and cosmetic formulations.

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STAVOVI I PROFESIONALNA PRAKSA FARMACEUTA U ZBRINJAVANJU PACIJENATA SA ANKSIOZNIM POREMEĆAJEM

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Farmaceuti, kao najdostupniji zdravstveni radnici, imaju važnu ulogu u podršci mentalnom zdravlju. Raste svest o potrebi njihovog aktivnog učešća i većoj odgovornosti u lečenju pacijenata sa anksioznim poremećajima. Cilj istraživanja je da se ispitaju stavovi i percepcije farmaceuta o pružanju farmaceutske zdravstvene zaštite pacijentima sa anksioznošću. Podaci su prikupljeni namenski osmišljenim upitnikom, zasnovanim na srodnim studijama. Za statističku analizu korišćeni su Microsoft Excel i SPSS Statistics, a pouzdanost ankete potvrđena je Cronbach-ovim testom ($\alpha = 0,892$). Ispitivana je povezanost karakteristika ispitanika (pol, stepen obrazovanja, radni staž) i skorova ostvarenih na različitim pitanjima ankete primenom Mann-Whitney U, odnosno Kruskal–Wallis testa. Istraživanje je obuhvatilo 121 diplomiranog farmaceuta (104 žene i 17 muškaraca), prosečne starosti 38,16 ± 10,86 godina i prosečnog staža 12,24 ± 10,72 godina. Većina radi u javnim apotekama (91,74%) i nema poslediplomsko obrazovanje (85,12%). Najveći broj redovno savetuje pacijente o pravilnoj upotrebi lekova (57,02% uvek; 27,27% često) i o rizicima samoinicijativnog prekida terapije (43,8% uvek; 31,4% često). Takođe, 56,2% upućuje pacijente lekaru po potrebi, dok manji deo lično kontaktira lekara (9,92% nikada; 23,97% retko). Približno 23% retko sprovodi rutinsko praćenje pacijenta, a oko 20% ne proverava kontraindikacije redovno. Farmaceuti sa stažom 11–15 godina znatno su spremniji da kontaktiraju lekara nego oni sa 1–5 godina staža, što nije uočeno za ostale kategorije (6–11, 16–20, >20 godina). Rezultati pokazuju da faktori pol i stepen obrazovanja ne utiču značajno na sprovođenje aktivnosti farmaceuta. Uočeni efekat radnog staža na ishode, u pojedinim podgrupama zahteva dalja istraživanja sa ciljem utvrđivanja da li je potrebna veća podrška mlađim farmaceutima u interprofesionalnoj komunikaciji.

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PHARMACISTS' ATTITUDES AND PROFESSIONAL PRACTICE IN PROVIDING CARE TO PATIENTS WITH ANXIETY DISORDERS

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Pharmacists, as the most accessible healthcare professionals, play a key role in supporting mental health. Recognition of the importance of their active involvement in treating patients with anxiety disorders is increasing. This study aimed to examine pharmacists' attitudes and perceptions regarding the provision of pharmaceutical care to patients with anxiety. Data were collected using a specially designed questionnaire adapted from related studies. Statistical analysis was performed in Microsoft Excel and SPSS Statistics. Survey reliability was confirmed with Cronbach's alpha ($\alpha = 0.892$). Associations between respondents' characteristics (gender, work experience, education level) and scores on individual survey items were analyzed using the Mann-Whitney U and Kruskal–Wallis test. The sample consisted of 104 women and 17 men, with a mean age of 38.16 ± 10.86 years and a mean work experience of 12.24 ± 10.72 years. Most work in community pharmacies (91.74%) and lack postgraduate education (85.12%). The majority reported regularly advising patients on the appropriate use of medication (57.02% always; 27.27% often) and on the risks of self-discontinuing therapy (43.8% always; 31.4% frequently). In addition, 56.2% always refer patients to a physician when necessary, while fewer personally contact physicians (9.92% never; 23.97% rarely). About 23% seldom conduct patient follow-up, and roughly 20% do not routinely check for contraindications. Pharmacists with 11–15 years of experience were significantly more willing to contact physicians than those with 1–5 years of experience, while no difference was observed in the other groups (6–11, 16–20, >20 years). Results indicate that neither gender nor education level significantly influences pharmacists' professional activities. The effect of work experience observed in specific subgroups warrants further investigation to determine whether it reflects a genuine need for additional support of younger pharmacists.

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UPOTREBA KARDIOVASKULARNIH LEKOVA KOD DOJILJA: PERSPEKTIVA FARMACEUTA

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Dojenje pruža optimalnu ishranu i poboljšava imunski sistem odojčeta, a uz to ima i dugoročne zdravstvene koristi, kako za odojče, tako i za majku [1]. Većina kardiovaskularnih lekova se može bezbedno koristiti kod dojilja, ali majke te informacije, često ne dobiju [2]. To može dovesti do nepotrebnog prekida dojenja, uprkos odsustvu stvarnog rizika za odojče, ili do toga da majke prekinu terapiju koja im je neophodna [2,3].

Cilj studije je procena upotrebe i bezbednosti kardiovaskularnih lekova kod dojilja i dostupnost savetovanja o bezbednosti upotrebe lekova tokom dojenja.

Podaci su prikupljeni prospektivno u sklopu *Mama Friendly* projekta. Bezbednost lekova u toku dojenja procenjena je primenom *e-lactancia* baze.

Od 1243 pacijentkinje uključene u studiju, 48 (3,86%) je primenjivalo barem jedan kardiovaskularni lek. Ukupno je identifikovano 19 različitih INN, od kojih su 42 (71.19%) bile primene lekova *per os* sa sistemskim dejstvom i 14 (28.81%) rektalnih administracija sa lokalnim dejstvom. Većina lekova za sistemsku primenu (92.86%) bila je bezbedna i kompatibilna sa dojenjem. Verovatno kompatibilni bili su cinhokain (11 primena) i polidekanol (1 primena) za rektalnu primenu, i bisoprolol, indapamid i serapeptaza za sistemsku primenu (po 1 administracija). Od 25 pacijentkinja (52,83%) koje nisu dobile nikakve savete u vezi sa upotrebom lekova tokom dojenja, čak 14 je izjavilo da izbegava uzimanje lekova.

Neophodno je obezbediti da dojilje dobiju adekvatne informacije o bezbednoj upotrebi lekova u periodu dojenja, a upravo farmaceut predstavlja jednog od ključnih zdravstvenih profesionalaca koji treba da pruži uslugu savetovanja.

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USE OF CARDIOVASCULAR DRUGS IN BREASTFEEDING WOMEN: A PHARMACIST'S PERSPECTIVE

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Breastfeeding provides optimal nutrition, immune protection, and long-term health benefits for both infants and mothers [1]. Evidence shows that the majority of cardiovascular drug classes can be used safely in lactating women, yet information about drug safety is often not communicated to the patients [2]. This can lead to unnecessary early cessation of breastfeeding, as well as mothers discontinuing essential cardiovascular therapy [2,3].

The aim of this study was to assess the use and safety of cardiovascular drugs among breastfeeding women and evaluate whether they received advice on medication safety during breastfeeding.

Data were prospectively collected within the *Mama Friendly Pharmacy* project. Safety of drug use was evaluated using the e-lactancia database.

From 1243 patients included in the study, 48 (3.86%) were taking at least one cardiovascular drug. A total of 19 different INNs were recorded, with 42 (71.19%) oral administrations and 14 (28.81%) local (rectal) administrations. Among oral drug administrations, 92.86% were safe and compatible with breastfeeding. Likely compatibility was recorded for cinchocaine (11 administrations) and polydecanol (1 administration) both intended for rectal use, and bisoprolol (1), indamapide (1), and serrapeptase (1), all aimed for oral use. Of the 25 patients (52.83%) who did not receive any advice regarding the use of drug while breastfeeding, 14 reported that they even avoided taking their medication.

Ensuring that breastfeeding women receive evidence–based guidance on drug use is essential, and pharmacists represent a key person for delivering this counselling.

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UTICAJ SUPLEMENTACIJE SUPEROKSID DISMUTAZOM NA REDOKS STATUS REKREATIVNIH SPORTISTA

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Fizička aktivnost pruža brojne benefite za fizičko i mentalno zdravlje. Međutim, naporno vežbanje može dovesti do oksidativnog stresa (OS). Naše istraživanje se bavilo uticajem suplementacije superoksid dismutazom (SOD) biljnog porekla na parametre OS kod rekreativnih sportista. Ukupno 22 učesnika je nasumično podeljeno u eksperimentalnu grupu (n = 10), koja je primala oralno 500 mg (1 mg = 1 IJ SOD) SOD biljnog porekla u kombinaciji sa glijadinom, i kontrolnu grupu (n = 12), koja je primala placebo. Svi učesnici su trenirali 60 minuta, tri dana nedeljno, u teretani. Uzorci venske krvi su uzeti ujutru nakon 24-časovnog perioda odmora na početku studije i nakon šest nedelja suplementacije. Ukupni antioksidativni status (TAS), ukupni oksidativni status (TOS), uznapredovali produkati oksidacije proteina (AOPP), malondialdehid (MDA) i sulfhidrilne grupe (SH grupe) mereni su u uzorcima seruma spektrofotometrijski, a antioksidativni enzimi, Cu/Zn SOD i glutation peroksidaza (GPX), mereni su korišćenjem ELISA testa (Abcam, Boston, MA, SAD). Nije bilo razlika između eksperimentalne i kontrolne grupe na početku studije osim u nivou GPX (52,38 ± 24,68 naspram 101,42 ± 73,82, p = 0,047). Nakon suplementacije, MDA je bio značajno niži u eksperimentalnoj grupi u poređenju sa početnom vrednošću (3,19 ± 0,62 naspram 4,84 ± 0,64, p < 0,001), a TOS je bio viši u kontrolnoj grupi (15,97 ± 5,78 naspram 11,33 ± 5,51, p = 0,047). Ova studija ukazuje na pozitivan efekat suplementacije antioksidansima kod rekreativnih sportista, ali su potrebna dodatna istraživanja kako bi se potvrdili naši rezultati.

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INFLUENCE OF SUPEROXIDE DISMUTASE SUPPLEMENTATION ON REDOX STATUS IN RECREATIONAL ATLETES

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Physical activity provides significant physical and mental health benefits. However, strenuous exercise can lead to oxidative stress (OS). Our investigation evaluated the influence of plant-origin superoxide dismutase (SOD) supplementation on OS parameters in recreational athletes. A total of 22 participants were randomly divided into an experimental group (n = 10) who received orally 500 mg (1 mg = 1 IU SOD) of plant-origin SOD combined with gliadin, and a control group (n = 12) who received a placebo. All participants trained for 60 minutes, three days per week, in a gym. Venous blood samples were taken in the morning after a 24-hour resting period at the beginning of the study and after six weeks of supplementation. Total antioxidant status (TAS), total oxidant status (TOS), advanced oxidation protein products (AOPP), malondialdehyde (MDA), and sulfhydryl groups (SH groups) were measured in serum samples spectrophotometrically, and antioxidant enzymes, Cu/Zn SOD and glutathione peroxidase (GPX), were measured using ELISA kits (Abcam, Boston, MA, USA). There were no differences between the experimental and control groups at the beginning of the study except in GPX level (52.38 ± 24.68 vs. 101.42 ± 73.82, p = 0.047). After supplementation, MDA was significantly lower in the experimental group compared to the initial value (3.19 ± 0.62 vs. 4.84 ± 0.64, p < 0.001), and TOS was higher in the control group (15.97 ± 5.78 vs. 11.33 ± 5.51, p = 0.047). This study indicates a positive effect of antioxidant supplementation in recreational athletes, but future studies are needed to confirm our results.

Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 68–69 ***PP 17***
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NUTRITIVNI ASPEKTI PROSEČNE POTROŠAČKE KORPE U SRBIJI

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Socioekonomski faktori, kao što su prihod, obrazovanje i zanimanje, utiču na ishranu i izbor namirnica u domaćinstvu. Ova veza se ogleda kroz prosečnu potrošačku korpu, čiju strukturu objavljuje Ministarstvo unutrašnje i spoljne trgovine Republike Srbije. Korpa obuhvata 73 prehrambene namirnice raspoređene u devet kategorija: žito i proizvodi od žita, povrće i prerađevine od povrća, voće i prerađevine od voća, sveže i prerađeno meso, sveža i prerađena riba, ulja i masti, mleko, mlečni proizvodi i jaja, bezalkoholna pića i ostali prehrambeni proizvodi.

Cilj ove studije bio je procena unosa nutrijenata/kalorija na osnovu prosečne potrošačke korpe u Srbiji. Za analizu sastava hrane korišćene su baze podataka *CAPNUTRA* i *FoodData Central*. Dnevne količine svake namirnice u korpi pomnožene su sa sadržajem nutrijenata i energetskom vrednošću, a dobijene vrednosti su sabrane kako bi se dobila procena dnevnog unosa pojedinih nutrijenata/kalorija.

Analizom prosečne potrošačke korpe primećeno je da je ishrana stanovništva neuravnotežena (u odnosu na evropske preporuke), sa visokim unosom hleba, brašna i mesnih prerađevina, a nedovoljnim unosom voća, povrća i ribe, što može povećati rizik od hroničnih bolesti. Poređenjem sa referentnim energetskim potrebama odraslih (2000 kcal dnevno, kako je utvrđeno Uredbom (EU) br. 1169/2011) uočeno je da je unos kalorija do 40% viši od preporučenog. Iako procentualna zastupljenost ugljenih hidrata, proteina i masti odgovara prvom principu racionalne ishrane, ukupni unos makronutrijenata i kalorija premašuje dnevne potrebe.

Edukacija i podizanje svesti o zdravim izborima hrane, uz aktivnu podršku institucija i prehrambenog sektora, može imati ključnu ulogu u podsticanju uravnotežene ishrane i unapređenju dugoročnog zdravlja stanovništva.

Zahvalnica

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NUTRITIONAL ADEQUACY OF THE MODERATE-COST SHOPPING BASKET IN SERBIA

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Socioeconomic factors such as income, education, and occupation strongly influence nutrition and household food choices. In Serbia, this relationship is reflected in the national moderate-cost shopping basket, which includes 73 food items grouped into nine categories.

Present study aimed to evaluate the nutritional adequacy of this basket in relation to dietary recommendations. Food composition analysis was conducted using the harmonized CAPNUTRA database and FoodData Central. Daily quantities of each food in the basket were multiplied by nutrient content/energy value of the food and summed to derive an estimate of daily consumption of each nutrient/calorie.

Overall, the diet appears unbalanced when assessed against the European Food-Based Dietary Guidelines, showing excessive consumption of bread, flour, and processed meats, and insufficient intake of fruits, vegetables and fish, which may increase the risk of nutrient deficiencies and chronic health problems. Comparison with reference energy intakes for adults (set at 2000 kcal per day for an average adult, as established by Regulation (EU) No 1169/2011) shows up to 40% higher calorie consumption. Although energy from carbohydrates, protein, and fat falls within recommended proportions (in line with the first principle of a rational diet), total intake of macronutrients and calories exceeds daily needs, indicating that the Serbian moderate-cost shopping basket provides more nutrients than required for a standard diet.

Strengthening nutrition education and raising awareness of healthier food choices, actively supported by institutions and the food sector, could play a key role in encouraging more balanced diets and promoting long-term population health.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 70–71 **PP 18**
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KREATIVNI LJUDI I INOVATIVNE IDEJE U VREMENU IZAZOVA: ZAJEDNIČKA ULOGA U OBRAZOVANJU NOVIH GENERACIJA

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Savremeni javnozdravstveni izazovi zahtevaju da visokoškolske ustanove razvijaju programe koji integrišu zdravstvene sadržaje u širi obrazovni kontekst. Posebno je važno povezivanje humanističkih i medicinskih nauka radi transfera znanja koji je primenljiv u različitim društvenim i profesionalnim okvirima. Kreativni pojedinci i inovativne ideje u procesu učenja postaju ključni pokretači transformacije obrazovnih praksi i institucija. Cilj rada je analiza načina integracije javnozdravstvenih sadržaja u nastavu i kurikulum, kao i procena njihovog uticaja na kompetencije studenata i njihovu povezanost sa potrebama zajednice. Primenjena je analiza sadržaja kurikuluma, pregled relevantnih javnozdravstvenih strategija i primera dobre prakse koji ilustruju uspešnu integraciju kroz multidisciplinarnu saradnju. Poseban akcenat stavljen je na transfer znanja putem tribina, interaktivnih projekata i saradnje sa lokalnom zajednicom, što studentima omogućava povezivanje teorije i realnih javnozdravstvenih izazova. Analiza pokazuje da integracija javnozdravstvenih tema doprinosi razvoju kompetencija, jača angažovanost studenata i stvara održive veze između obrazovanja, zdravstvenog sistema i zajednice. Posebno je istaknuto da obrazovanje ima centralnu ulogu u razvijanju svesti o značaju očuvanja zdravlja i promovisanja zdravih stilova života. Multidisciplinarni pristup u integraciji javnozdravstvenih sadržaja u obrazovanje predstavlja strateški odgovor na savremene potrebe i doprinosi stvaranju stručnjaka sposobnih da povezuju naučna znanja i praksu u cilju unapređenja zdravlja zajednice.

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CREATIVE INDIVIDUALS AND INNOVATIVE IDEAS IN TIMES OF CHALLENGE: A SHARED ROLE IN EDUCATING NEW GENERATIONS

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Contemporary public health challenges require higher education institutions to develop programs that integrate health-related content into a broader educational context. Particularly important is the linkage between the humanities and medical sciences to enable knowledge transfer that is applicable across diverse social and professional settings. Creative individuals and innovative ideas in the learning process become key drivers of the transformation of educational practices and institutions. The aim of this study is to analyze the methods of integrating public health content into teaching and curricula, as well as to assess their impact on student competencies and their alignment with community needs. A curriculum content analysis was conducted, along with a review of relevant public health strategies and best practice examples illustrating successful integration through multidisciplinary collaboration. Special emphasis was placed on knowledge transfer through seminars, interactive projects, and collaboration with local communities, enabling students to connect theoretical knowledge with real public health challenges. The analysis shows that the integration of public health topics contributes to competency development, enhances student engagement, and establishes sustainable links between education, the healthcare system, and the community. Education was highlighted as playing a central role in fostering awareness of the importance of health preservation and the promotion of healthy lifestyles. A multidisciplinary approach to integrating public health content into education represents a strategic response to contemporary needs and contributes to the development of professionals capable of bridging scientific knowledge and practice to improve community health.

Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 72–73 ***PP 19***
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OD TEORIJE DO PRAKSE: NACIONALNI OKVIR KOMPETENCIJA KAO ALAT ZA ODRŽIVE PROMENE U OBRAZOVANJU STUDENATA FARMACIJE

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Razvoj profesionalnih kompetencija u oblasti socijalne farmacije predstavlja ključni preduslov za održive promene u obrazovanju i praksi farmaceuta. Nacionalni okvir kompetencija farmaceuta Srbije (NOKFS) [1] predstavlja strukturisan model koji omogućava povezivanje teorijskih znanja sa praktičnim razvojem veština, pri čemu se samoprocena i samorefleksija izdvajaju kao ključne metakompetencije. Cilj istraživanja bio je upoznavanje studenata farmacije sa NOKFS i metodologijom procene i samoprocene kompetencija, kao i ispitivanje efekata edukativne intervencije na razvoj profesionalnih veština u oblasti socijalne farmacije. Istraživanje je sprovedeno u okviru nastavnog predmeta Profesionalni razvoj i karijerno planiranje. Studenti su sproveli inicijalnu samoprocenu kompetencija na osnovu 24 izjave iz domena socijalne farmacije, potom učestvovali u edukativnoj intervenciji, nakon čega je usledila ponovljena samoprocena. Rezultati su analizirani poređenjem inicijalnih i završnih procena. U prvom krugu samoprocene studenti su najvišom ocenom (4) vrednovali komunikacione veštine (62,90%), uspostavljanje pozitivnih odnosa u timu (37,10%) i primenu informacionih i komunikacionih tehnologija (33,87%), dok je svega 6,45% istom ocenom procenilo javnozdravstvene inicijative i poznavanje pravne regulative. Nakon sprovedene edukativne intervencije registrovan je porast ocena u svim oblastima, pri čemu je najveći napredak uočen u segment promocije zdravlja, zdravih stilova života, prevencije i kontrole bolesti, gde je udeo najviših ocena porastao sa 8,06% na 46,77%. Primena NOKFS u nastavnom procesu potvrđuje njegovu vrednost kao alata za povezivanje teorijskih postavki socijalne farmacije sa praktičnim kompetencijama. Integracija samoprocene i introspektivnog učenja u nastavu doprinosi formiranju profesionalnog identiteta i jačanju kompetencija od strateškog značaja za održivi razvoj farmaceutske profesije.

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FROM THEORY TO PRACTICE: THE NATIONAL COMPETENCY FRAMEWORK AS A TOOL FOR SUSTAINABLE CHANGES IN PHARMACY EDUCATION

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Development of professional competencies in the field of social pharmacy represents a key prerequisite for sustainable changes in pharmaceutical education and practice. National Competency Framework for Pharmacists of Serbia (NCFPS) [1] provides structured model that enables integration of theoretical knowledge with practical skills development, highlighting self-assessment and self-reflection as essential meta-competencies. Objective was to familiarize pharmacy students with NCFPS and methodology of competence assessment and self-assessment, as well as to examine the effects of an educational intervention on development of professional skills in field of social pharmacy. Study was conducted within the course Professional Development and Career Planning. Students performed an initial self-assessment of competencies based on 24 statements related to social pharmacy, participated in educational intervention, and subsequently repeated self-assessment. Results were analyzed by comparing the initial and final assessments. In the first round of self-assessment, students rated their competencies highest (score 4) in communication skills (62.90%), establishing positive team relationships (37.10%), and use of information and communication technologies (33.87%), while only 6.45% rated themselves highest in public health initiatives and knowledge of legal regulations. Following educational intervention, an increase in scores was recorded across all domains, with the most significant improvement observed in health promotion, healthy lifestyle, and disease prevention and control, where proportion of the highest scores rose from 8.06% to 46.77%. Application of NCFPS in teaching process confirms its value as tool for linking theoretical foundations of social pharmacy with practical competencies. Integration of self-assessment and introspective learning into curriculum contributes to formation of professional identity and strengthens competencies of strategic importance for sustainable development of pharmacy profession.

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Četvrti naučni simpozijum Saveza farmaceutskih udruženja Srbije: 74–75 **PP 20**
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ZELENE INOVACIJE ZA ZDRAVIJU I ODRŽIVIJU BUDUĆNOST KROZ PROJEKAT VIVENDI

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Tri četvrtine lekova koji se koriste u borbi protiv kancera potiču iz prirodnih izvora. Međutim, njihova ekstrakcija iz biomase zahteva upotrebu isparljivih i toksičnih organskih rastvarača, što predstavlja značajan rizik po zdravlje ljudi i životnu sredinu. Pored toga, bioaktivna jedinjenja (BAC) često imaju nisku bioraspoloživost, slabu rastvorljivost u vodi i nestabilnost. Projekat VIVENDI (*Green Innovation: Unlocking the Bioactive Potential of Biomass for Enhanced Pharmaceuticals and Foods through Eco-Friendly Sustainable Technologies*), koji se realizuje u okviru poziva Dijaspora2023, razvija integrisanu, ekološki prihvatljivu strategiju ekstrakcije i formulacije. Ova strategija zamenjuje konvencionalne rastvarače održivim alternativama i povećava stabilnost BAC jedinjenja primenom micelarne enkapsulacije.

Po prvi put se primenjuje novi proces tečno–čvrsto membranske ekstrakcije, koji koristi membranski mikromikser za simultanu izolaciju (ekstrakciju) i micelizaciju ciljnih bioaktivnih jedinjenja. Ispituju se dva model sistema: (i) jednostepena ekstrakcija bioaktivnih jedinjenja iz otpada maline korišćenjem bio-baziranih jonskih tečnosti i prirodnih dubokih eutektičkih rastvarača; i (ii) ekstrakcija partenolida iz *Tanacetum parthenium* L. pomoću vodenog bifaznog sistema formiranog biokompatibilnim biopolimerima tipa Pluronic i bio-baziranim jonskim tečnostima.

Stečena znanja tokom realizacije ovog projekta omogućiće valorizaciju biomase i biljnih ostataka nakon prerade, smanjenje industrijskog otpada i razvoj nove, isplative zelene tehnologije za izolaciju i očuvanje bioaktivnih jedinjenja, uz oslanjanje na multidisciplinarnu ekspertizu članova VIVENDI konzorcijuma.

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GREEN INNOVATIONS FOR HEALTHIER AND MORE SUSTAINABLE SOLUTIONS WITHIN THE VIVENDI PROJECT

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Three-quarters of cancer-fighting agents in medical use are derived from natural sources. However, their extraction from biomass requires significant quantities of volatile and toxic organic solvents, posing substantial risks to human health and the environment. Additionally, these bioactive compounds (BACs) often exhibit low bioavailability after administration, insolubility in water, and instability.

Addressing these challenges, the Vivendi project (*Green Innovation: Unlocking the Bioactive Potential of Biomass for Enhanced Pharmaceuticals and Foods through Eco-Friendly Sustainable Technologies*), under the call Dijaspora2023, addresses these challenges by developing an integrated, eco-friendly extraction and formulation strategy that replaces conventional solvents with sustainable alternatives and enhances BAC stability through micellar encapsulation.

A novel liquid–solid membrane extraction process, employing a membrane micromixer, has been applied for the first time to simultaneously isolate and micellize target compounds. Two model systems are investigated: (i) one-step extraction of BAC from raspberry using bio-based ionic liquids and natural deep eutectic solvents, and (ii) extraction of parthenolide from feverfew using an aqueous biphasic system formed with biocompatible Pluronic-type biopolymers and bio-based ionic liquids. To further improve stability, BACs are microencapsulated using different encapsulation techniques (spray and freeze-drying, and Lego-Inspired Microfluidic encapsulation), using different biopolymers, and thoroughly characterized with advanced analytical techniques.

The knowledge generated within the VIVENDI project will enable the valorization of biomass and herbal residues, reduce industrial waste, and establish a novel, cost-effective green technology for BAC isolation and preservation, leveraging the multidisciplinary expertise of the VIVENDI consortium members.

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THE ROLE OF ARTIFICIAL INTELLIGENCE IN DRUG SAFETY

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Pharmacovigilance is a crucial component in ensuring the safety of drugs after they have been licensed and released to the public. Monitoring the adverse effects, interactions, and toxicity throughout the drug life cycle is essential. The World Health Organization defines pharmacovigilance as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem. Artificial intelligence (AI) is increasingly applied in pharmacovigilance to manage large and heterogeneous datasets, predict adverse drug reactions (ADR/ADE), identify drug-drug interactions (DDI), and prioritize safety signals for timely intervention. Natural language processing (NLP) facilitates the extraction of ADR information from electronic health records (EHRs) and social media, thereby enhancing the sensitivity of surveillance systems [1]. Compared to traditional machine learning methods, deep neural networks and graph-based approaches demonstrate improved accuracy in predicting DDIs and ADRs. Outcomes depend on data quality and model architecture [2]. Novel techniques, such as federated learning and health-adapted language models, can help keep data private and scale up analysis; however, concerns remain regarding their transparency, reliability, and regulatory approval. Regulatory and international bodies call for standards, validation, and safeguards against bias and opacity before implementing large-scale pharmacovigilance processes [3]. While AI enhances the efficiency of signal detection and monitoring, proper practical integration requires multidisciplinary validation, reliable data oversight, and clear regulatory pathways to ensure that the benefits outweigh the risks.

Literatura

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