ISPC-2026

April 24-25, 2026, Tbilisi, Georgia

II INTERNATIONAL SCIENTIFIC-PRACTICAL CONFERENCE

"Georgian Scientific Pharmacy: Past and Present"

dedicated to Academician Ether Kemertelidze 100th anniversary

ABSTRACT BOOK

Tbilisi State Medical University
TSMU I.Kutateladze Institute of Pharmacochemistry
Association of Scientists and Young Pharmacists of Georgia

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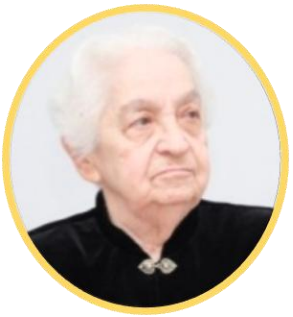

ABSTRACT BOOK

Organized by:
Tbilisi State Medical University
TSMU I. Kutateladze Institute of Pharmacochemistry
Association of Scientists and Young Pharmacists of Georgia

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WELCOME

Dear Colleagues!

The Organizing Committee is pleased and honored to invite you to the II International Scientific-Practical Conference "Georgian Pharmacy: Past and Present" (ISPC 2026) which will be held in honor of Academician Ether Kemertelidze's 100th anniversary, in Tbilisi, Georgia on April 24-25, 2026.

ISPC 2026 aims to bring together a multidisciplinary group of scientists from worldwide to share and debate the most recent advancements in major fields of pharmaceutical science. We look forward to seeing pharmacy professionals, medicinal and synthetic chemists, analysts, pharmacologists, as well as other scientists working in drug research and development.

The scientific program of the ISPC 2026, includes plenary lectures, oral and poster presentations.

The Organizing Committee encourages you to join the ISPC 2026 and looks forward to meeting you in the middle of the ancient Silk Way, historical bridge between Asia and Europe, the capital of Georgia– Tbilisi.

Organizing Committee of the ISPC-2026

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GENERAL INFORMATION

Conference Venue

Tbilisi State Medical University, Address: 33 Vazha Pshavela ave, Tbilisi, Georgia

Registration Desk

Conference Material and Name Badges will be distributed at the Regiatration Desk in the University Hall left to main entrance.

Operating hours:

April 24 8^{30}–10^{00}; April 25 9^{00}–10^{00};

Secretariat and Information Desk

The Secretariat and Information Desk will operate in the registration area to provide any information regarding the Scientific Program, Social Events, transportation, lost & found, etc.

Operating hours:

April 24 8^{30}–17^{30}

April 25 9^{30}–17^{00}

SCIENTIFIC INFORMATION

For Oral Session Speakers

The session room is provided with LCD projector and laptop computer loaded with MS Office Power Point. Speakers are asked to bring their presentation (either on USB sick or CD) and load it during the break prior to the session. Staff will be available in the session room to assist with the operations.

Alloted time for Plenary Lecture will be 40 min, Oral Presentation - 20 min.

For Poster Presentations

The Poster Session will be held in the University hall. Authors are asked to mount posters on boards assigned by Secretariat during the registration. Mounting accessories will be available at the Information Desk.

PROGRAM

	APRIL 24, FRIDAY
9 00–10 00	**REGISTRATION**
10 00–11 30	**OPENING CEREMONY**
11 30– 12 00	**COFFEE-BREAK**
12 00–14 00	**SESSION 1.** **Co-Chairs: M.GETIA, Ö. EMINAĞAOĞLU**
12 00–12 40	**PL–1. NEW INSIGHTS INTO ARTEMISIA AFRA AND A. ANNUA IN THE FIGHT AGAINST MALARIA** – *M. FRÉDÉRICH, University of Liège, Belgium*
12 40–13 00	**OP–1. METABOLIC PROFILING AND IDENTIFICATION STRATEGIES OF SOME INDAZOLE - 3 - CARBOXAMIDE SYNTHETIC CANNABINOIDS USING UPLC - MS/MS** – *M. JOKHADZE, Tbilisi State Medical University, Georgia*
13 00–13 20	**OP–2. ADVANCES IN THE PHARMACOGNOSTIC RESEARCH OF *DAPHNE PONTICA* L. –** – *G. MOSHIASHVILI, Tbilisi State Medical University, Georgia*
13 20–13 40	**OP–3. AN OPTIMIZED HEMP EXTRACTION STRATEGY TO ENHANCE SYNERGISTIC ACTIVITY AGAINST TRIPLE - NEGATIVE BREAST CANCER (TNBC)** *C. HAMANN, University of Liège, Belgium*
13 40–14 00	**OP–4. IMPACT OF SACUBITRIL/VALSARTAN ON CARDIOVASCULAR FUNCTION AND INFLAMMATORY MARKERS IN EXPERIMENTAL HYPERTENSION** – *D. GOLOSHVILI, Tbilisi State Medical University, Georgia*
14 00–15 00	**LUNCH**
15 00 – 17 20	**SESSION 2.** **Co-Chairs: M.JOKHADZE, M. FRÉDÉRICH**
15 00–15 40	**PL–2. THE ROLE OF ALİ NİHAT GÖKYİĞİT BOTANICAL GARDEN IN THE CONSERVATION, CULTIVATION, AND VALUE-ADDED PROCESSING OF MEDICINAL AND AROMATIC PLANTS IN ARTVİN** – *Ö. EMINAĞAOĞLU, Artvin Coruh University, Türkiye*
15 40–16 20	**PL–3. ADHESIVE PLATFORM FOR THE DENTAL DELIVERY OF BIOGENIC ELEMENTS: FORMULATION, TECHNOLOGY, AND BIOPHARMACEUTICAL EVALUATION** – *A. BAKURIDZE, Tbilisi State Medical University, Georgia*
16 20–16 40	**OP–5. ROWAN SPECIES OF TÜRKIYE: MEDICINAL AND AROMATIC VALUE AND GENETIC IDENTIFICATION** – *H. AKYILDIRIM BEĞEN, Artvin Coruh University, Türkiye*
16 40–17 00	**OP–6. FROM SEMINARS TO ESCAPE GAMES: RETHINKING HOW WE TEACH PHYTOCHEMISTRY** – *A. LEDOUX, University of Liège, Belgium*
17 00 - 17 20	**OP–7. PHYTODRUGS AS CHALLENGING MOLECULES: BIOPHARMACEUTICAL LIMITATIONS AND DELIVERY-BASED SOLUTIONS** – *L. TSIKLAURI, Tbilisi State Medical University, Georgia*
17 20–19 00	**FREE TIME**
19 00–21 00	**GALA DINNER**

APRIL 25, SATURDAY	
9^{30}–10^{00}	**REGISTRATION**
10^{00}–12^{00}	**SESSION 3.** **Co-Chairs: K.MULKIJANYAN, A.HOVAKIMYAN**
10^{00}–10^{40}	**PL–4. 4-SULFONAMIDES INCORPORATING PYRAZOLE- PYRIDAZINECARBOXAMIDE AND PYRIDINE MOIETIES AS CARBONIC ANHYDRISE INHIBITORS. SYNTHESIS, IN SILICO AND IN VITRO EVALUATION** **–** *A.GERONIKAKI, Aristotle University of Thessaloniki, Greece*
10^{40}–11^{00}	**OP–8. DISUBSTITUTED PIPERAZINES – SYNTHESIS AND PROPERTIES** **–** *E. HAKOBYAN, Institute of Fine Organic Chemistry, Armenia*
11^{00}–11^{20}	**OP–9. SYNTHESIS AND BIOLOGICAL ACTIVITY EVALUATION OF NOVEL NITROGEN-CONTAINING STEROIDS DERIVED FROM TIGOGENIN** **–** *N.BARBAKADZE, Tbilisi State Medical University, Georgia*
11^{20}–11^{40}	**OP–10. DESIGN AND DEVELOPMENT OF PSEUDO-PROTEINS: ADVANCED BIOMATERIALS FOR VERSATILE MEDICAL APPLICATIONS .....** **–** *N. ZAVRADASHVILI*, **Agricultural University of Georgia**
11^{40}–12^{00}	**OP–11. CAFFEIC ACID-BASED BIOPOLYMERS FROM DIFFERENT SPECIES OF BORAGINACEAE FAMILY AND THEIR SYNTHETIC ANALOGUES** **–** *M. MERLANI, Tbilisi State Medical University, Georgia*
12^{00}–12^{30}	**COFFEE-BREAK**
12^{30}–14^{00}	**SESSION 4.** **Co-Chairs: A.GERONIKAKI, M.MERLANI**
12^{30}–13^{10}	**PL–5. PEPTIDE–DRUG CONJUGATES: BRIDGING PRECISION TARGETING AND POTENT CYTOTOXICITY IN CANCER THERAPY –** *G.GELLERMAN, Ariel University, Israel*
13^{10}–13^{30}	**OP–12. CHEMICAL COMPOSITION AND EVALUATION OF ANTIOXIDANT ACTIVITY OF SOME ESSENTIAL OIL-BEARING PLANTS OF THE GEORGIA FLORA** **–** *T. KORKOTADZE, Tbilisi State Medical University, Georgia*
13^{30}–13^{50}	**OP–13. LC-MS ANALYSIS OF PLANT-DERIVED BIOLOGICAL ACTIVE COMPOUNDS: NEW APPROACHES –** *M.GETIA, Tbilisi State Medical University, Georgia*
13^{50}–14^{10}	**OP–14. AI AS A FORCE MULTIPLIER: A STAGED INTEGRATION FRAMEWORK FOR DRUG DESIGN AND DEVELOPMENT –** *K.MULKIJANYAN, Tbilisi State Medical University, Georgia*
14^{10}–15^{00}	**LUNCH**
15^{00}–16^{30}	**POSTER SESSION & EXHIBITION**
16^{30}–17^{00}	**CLOSING CEREMONY**

PLENARY LECTURES

PL–1. NEW INSIGHTS INTO ARTEMISIA AFRA AND A. ANNUA IN THE FIGHT AGAINST MALARIA

M. Frédérich

Pharmacognosy Laboratory, Center of Interdisciplinary Research on Medicine (CIRM), University of Liège, Belgium

Corresponding author e-mail:

Malaria is a global public health concern, and natural products have been investigated as potential treatments. Extracts of *A. afra* and *A. annua* remain widely used in Cameroon and in other African countries for healthcare purposes, notably to prevent and/or treat malaria but without pharmacological quality control. Additionally, the modes of action of these plant extracts remain unclear, with contradictory reports regarding the presence and role of artemisinin in both plants. This study explores the phytochemical diversity and identifies differences in the antimalarial mode of action of *A. afra* and *A. annua* sourced from distinct geographical locations within Cameroon, aiming to define the optimal chemical composition in terms of anti-plasmodial activity. Extracts prepared from plants collected from diverse regions in Cameroon during both the rainy and dry seasons and metabolic contents were analyzed by TLC, HPLC, and GC. Additionally, HPLC-MS metabolomic analysis was done on in vitro-cultured Plasmodium falciparum trophozoites to elucidate the potential modes of action. The activity profiles of the samples were associated with their environment, with distinct phytochemical compositions observed for each sample based on its geographical origin and season. Traces of artemisinin were detected in some of the *A. afra* samples, but present in the *A. annua* samples at a significantly higher concentration, especially in the rainy season samples. *A. afra* elicited a different parasite metabolic response compared to *A. annua* which correlated closely with the parasite response profile elicited by purified artemisinin. *A. annua* impacted parasite glutathione metabolism in agreement with the established redox activity of artemisinin, while *A. afra* had an effect on lipid precursors. This study reveals that *A. afra* and *A. annua* have divergent effects on P. falciparum metabolism. And the selection of a suitable Artemisia sample for use as a potential antimalaria treatment should take into consideartion it geographical origin and period of collection.

Keywords: Malaria, metabolite, *Artemisia afra*, *Artemisia annua*, Artemisinin

PL–2. THE ROLE OF ALİ NİHAT GÖKYİĞİT BOTANICAL GARDEN IN THE CONSERVATION, CULTIVATION, AND VALUE-ADDED PROCESSING OF MEDICINAL AND AROMATIC PLANTS IN ARTVİN

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Artvin is recognized as one of Türkiye's leading provinces in plant diversity, hosting about 2,727 taxa, including nearly 850 species with medicinal and aromatic significance [1,2]. However, the growing demand for these plants has led to uncontrolled harvesting from natural habitats, increasing the risk of depletion and making it necessary to develop domestication efforts, sustainable production methods, and conservation-oriented strategies. In response to these needs, the Ali Nihat Gökyiğit Botanical Garden (ANGBG) was established in 2018 within Artvin Çoruh University as a living plant museum, a scientific research facility, an educational center, and a conservation institution. The garden is one of the 13 botanical gardens in Türkiye that are members of the BGCI platform [3, 4]. Supported by national and international projects—including those funded by the Presidency of Strategy and Budget, the ANG Foundation, and the Interreg VI-B NEXT Black Sea Basin Programme under the European Union's Cohesion Policy—ANGBG carries out comprehensive scientific and applied studies aimed at conserving the region's botanical richness.

Fig. 1. Greenhouse in ANGBB

ANGBG functions as a central platform for research, education, production, and outreach activities focused on medicinal- aromatic plants (MAPs). Its training laboratories provide hands-on instruction in essential oil and hydrosol extraction, as well as in the preparation of dried herbal products, while molecular analyses are used to ensure accurate species identification. The cultivation areas, designed as model gardens, include a 700 m² R&D and Exhibition Greenhouse, a 500 m² production greenhouse, and 50 raised plant beds, supporting the cultivation of both ornamental plants and a wide range of medicinal and aromatic species. This infrastructure enables controlled cultivation trials that contribute to academic research and, at the same time, supports rural development through farmer training and advisory services. Within the scope of project activities, an inventory of Artvin's medicinal-aromatic plant species (MAPs) has been established, seeds have been collected, and traditional ethnobotanical knowledge has been documented. In addition, the botanical garden hosts demonstration gardens for medicinal and aromatic plants, a fruit species gene garden, and laboratories where in vitro propagation studies are carried out.

Fig. 2. Extraction and freze-drying processing system

The Plant Processing and Product Development Center, equipped with distillation, extraction, evaporation, and spray-drying systems, facilitates the transformation of region-specific plants into high-value products such as essential oils, hydrolates, and freeze-dried fruits. The facility features 500-liter extraction and distillation units, along with purified water systems and advanced process control modules, which allow the production of high-quality extracts and powders derived from different plant parts. The center also supports the development of encapsulated oils, flavorings, functional compounds, and mineral products. As the next stage of development, a 1,000 m² production and storage facility was constructed and processing lines were procured to expand operational capacity. This facility will enable the production of marmalades, jams, fruit purées, and fruit juices, with the option of aseptic filling.

Fig. 3. MAPs production greenhouse and fruit production and storage facility

Taken together, these research, conservation, cultivation, and processing activities make a substantial contribution to ANGBB's scientific capacity, support local economic development, promote environmental sustainability, and enhance Artvin's ecotourism potential.

References

[1] Eminağaoğlu, Ö. (ed.) 2015, Artvin'in Doğal Bitkileri (Native Plants of Artvin), İstanbul: Promat, 456.
[2] Eminağaoğlu, Ö. (ed.) 2023, Artvin'in Tıbbi-Aromatik Bitkileri (Medicinal-Aromatic Plants of Artvin), Artvin: Zafer press.
[3] Eminagaoglu, Z., Eminağaoğlu, Ö. 2024, Planning and design principles of Artvin Çoruh University Ali Nihat Gökyiğit Botanical Garden in a sustainable approach, Biological Diversity and Conservation, vol. 17, no. 2, pp. 160-174.
[4] Eminagaoglu, Ö., Eminağaoğlu, Z. 2018, Some thoughts on botanical garden establishment in Artvin, International Journal of Ecosystems and Ecology Science, Vol. 8, no. 4, pp. 767-776.

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PL–3. ADHESIVE PLATFORM FOR THE DENTAL DELIVERY OF BIOGENIC ELEMENTS: FORMULATION, TECHNOLOGY, AND BIOPHARMACEUTICAL EVALUATION

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Dental caries, a disease of the hard tissues of the teeth—enamel, dentin, and cementum—is one of the most common diseases in the world that significantly impacts the quality of human life [1]. Despite the implementation of large-scale measures aimed at combating the formation and spread of caries and advancing treatment methods, this dental disease still remains the number one problem in dentistry. The disease starts with the damage of the tissue covering the tooth crown, enamel. Though this acellular, avascular, and highly mineralized structure is the hardest tissue in the human body, acids produced by acidogenic bacteria cause the breakdown of its inorganic skeleton, resulting in the formation of a cavity. The process of breakdown of the mineral skeleton is called demineralizationand although the processes of de- and remineralization in tooth structures are continuous, disruption of the buffer balance, the proportion of micro- and macroelements, and the permeability of enamel in the oral cavity contribute to the prevalence of demineralization. The strategy for successful caries management is based on holistic and comprehensive approaches, among them the most important are antimicrobial therapy, the implementation of remineralizing agents, and the improvement of methods for their infiltration into the hard tissues of the tooth. that the modern concept of caries prevention and treatment is based largely on maximizing tissue infiltration and minimal preparation. This is not possible without enriching the tooth tissues with elements such as calcium, magnesium, phosphorus, fluoride, zinc, and others.

Significant interest in nanoparticles of biogenic elements is largely due to their unique physicochemical and biological properties, which differ from those of the bulk elements. Their nanoscale form provides higher bioavailability.

Biosynthesized nanoparticles of biogenic elements are generally biocompatible, which facilitates their further use in biomedical devices.

Nanoscale biogenic elements penetrate deeper layers of the damaged tooth area, ensuring the restoration of damaged enamel [2,3,4].

To deliver active pharmaceutical ingredients to the tooth tissue, a gel is often used as a carrier, which significantly prolongs the contact time between the active ingredient and the enamel, allowing biogenic elements to fill small lesions and cavities [5].

It should be noted that in many cases the gel can be washed off by saliva, and while being used, it is also impossible to avoid changes in the concentration of the API (fluctuations, instability) within the tooth tissue.

The objective of the study was to investigate the possibility of using antimicrobial bioadhesive for targeted dental delivery of nanoparticles of biogenic elements.

The study was counducted using UV-vis spectroscopy, transmission electron microscopy, inductively coupled plasma optical emission spectrometry (ICP-OES) and nanosizer.

The biosynthesis of nanoparticles of biogenic elements: calcium, magnesium, fluorine and zinc was carried out.

When examined using transmission electron microscopy and a nanosizer, it was determined that the nanoparticles of biogenic elements are uniform and their sizes range within 65-100 nm.

The formulation of a bioadhesive containing nanoparticles of biogenic elements is provided, the preparation technology is developed and the quality parameters are determined.

In order to determine the potential for the use of the proposed composition in dental practice, in particular, the delivery of biogenic nanoelements to tooth tissue, the main characteristics have been studied and it has been established that the adhesion strength to enamel is 214±7.2%, pH–7.05±0.12, while the rheological characteristics of the composition and, accordingly, its consumer properties are within the optimal range.

The release kinetics of biogenic elements from the bioadhesive were studied using Franz diffusion cells. It has been established that almost 75% of calcium, magnesium, zinc and fluorine are released within 3 hours.

Based on the conducted biopharmaceutical studies, the biosynthesis of calcium, magnesium, zinc and fluorine nanoparticles has been carried out and their characteristics have been determined. The formulation of a bioadhesive containing nanoparticles of biogenic elements has been provided and the technology has been developed. The dynamics of the release of biogenic elements from the bioadhesive have been examined using Franz diffusion cells.

References

[1] Peres, M. A., Macpherson, L.M.D., Weyant, R.J.,Daly, B., Venturelli, R., Mathur, M. R., et al. (2019). Oral diseases: A global public health.

[2] Xu J, Shi H, Luo J, Yao H, Wang P, Li Z and Wei J (2022), Advanced materials for enamel remineralization. Front. Bioeng. Biotechnol. 10 [98]5881. doi: 10.3389/fbioe.2022.985881.

[3] Li, Y.; Liu, M.; Xue, M.; Kang, Y.; Liu, D.; Wen, Y.; Zhao, D.; Guan, B. Engineered Biomaterials Trigger Remineralization and Antimicrobial Effects for Dental Caries Restoration. Molecules 2023, 28, 6373. https://doi.org/10.3390/ molecules28176373.

[4] Qingyi Yang, Fan Li, Yangyang Ye and Xu Zhang* Antimicrobial, remineralization, and infiltration: advanced strategies for interrupting dental caries https://doi.org/10.1515/mr-2024-0035 Received April 30, 2024; accepted August 2, 2024; published online August 23, 2024.

[5] Khonina, T. G., Chupakhin, O. N., Shur, V. Y., Turygin, A. P., Sadovsky, V. V., Mandra, Y. V., et al. (2020). Silicon-hydroxyapatite glycerohydrogel as a promising biomaterial for dental applications. Colloids Surfaces B Biointerfaces 189, 110851. DOI: 10.1016/j.colsu rfb.2020.110851...

PL–4. 4-SULFONAMIDES INCORPORATING PYRAZOLE- PYRIDAZINECARBOXAMIDE AND PYRIDINE MOIETIES AS CARBONIC ANHYDRISE INHIBITORS. SYNTHESIS, IN SILICO AND IN VITRO EVALUATION

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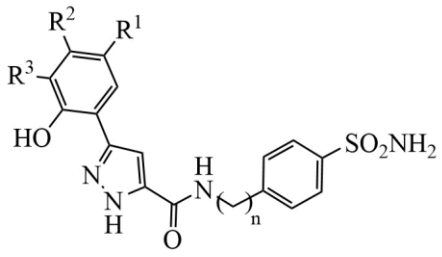
A series of benzenesulfonamides incorporating pyrazole- and pyridazinecarboxamides decorated with several bulky moieties has been obtained by original procedures. The new derivatives were investigated for the inhibition of four physiologically crucial human carbonic anhydrase (hCA, EC 4.2.2.1.1) isoforms, hCA I and II (cytosolic enzymes) as well as hCA IX and XII (transmembrane, tumor-associated isoforms). Examples of isoform-selective inhibitors were obtained for all four enzymes investigated here, and a computational approach was employed for explaining the observed selectivity, which may be useful in drug design approaches for obtaining inhibitors with pharmacological applications useful as antiglaucoma, diuretic, antitumor or anti-cerebral ischemia drugs.



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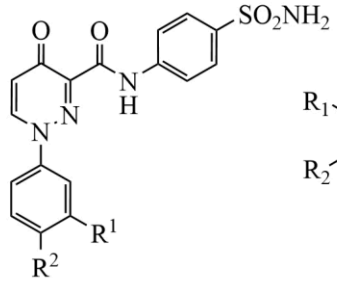

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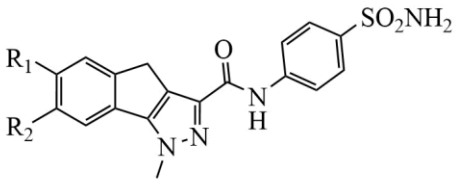

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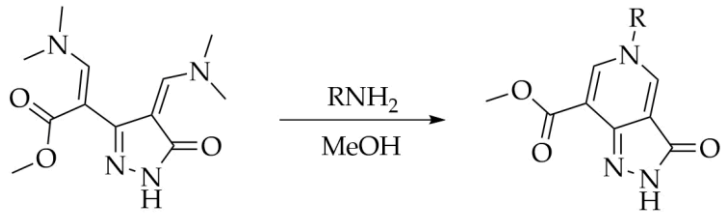

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PL–5. PEPTIDE–DRUG CONJUGATES: BRIDGING PRECISION TARGETING AND POTENT CYTOTOXICITY IN CANCER THERAPY

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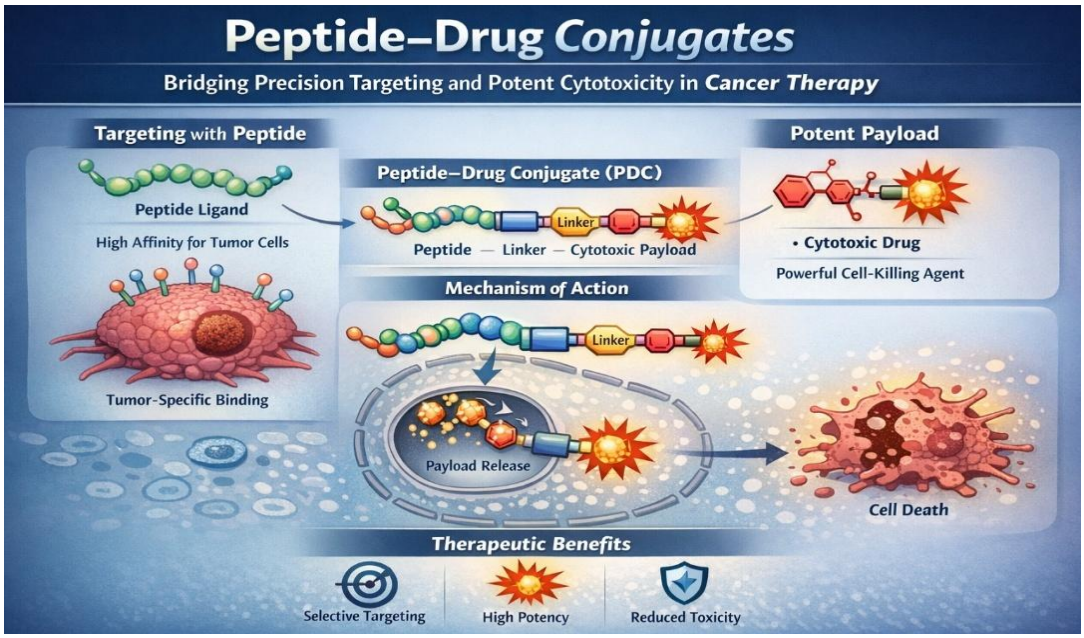
– Peptide–drug conjugates (PDCs) are an emerging targeted therapeutic modality that integrate the tumor-selective recognition of peptides with the high potency of cytotoxic small-molecule drugs. Designed to improve the therapeutic index of anticancer agents, PDCs consist of a targeting peptide, a linker, and a cytotoxic payload, enabling selective delivery to tumor cells or the tumor microenvironment. Upon binding to cancer-associated receptors, PDCs undergo receptor-mediated internalization or controlled drug release, resulting in localized cytotoxicity and reduced off-target effects. Compared with antibody–drug conjugates, PDCs offer several advantages, including smaller molecular size, improved tumor penetration, lower immunogenicity, and enhanced synthetic flexibility. Advances in peptide engineering, linker chemistry, and payload optimization have accelerated the development of PDCs, with multiple candidates progressing into clinical evaluation. This presentation highlights the rationale, design principles, mechanisms of action, and current clinical landscape of peptide–drug conjugates, underscoring their potential as a next-generation precision therapy in oncology.



References

[1] Bazylevich, A., Gellerman, G., et all. Novel Cyclic Peptide–Drug Conjugate P6-SN38 Toward Targeted Treatment of EGFR Overexpressed Non-Small Cell Lung Cancer. *Pharmaceutics* 2024, 16, 1613.

[2] Redko B., Gellerman, G, et all. Toward the development of a novel non-RGD cyclic peptide drug conjugate for treatment of human metastatic melanoma. *Oncotarget*. 2017 Jan 3;8(1) [75]7-768.

[3] Gilad, Y., Firer, M., Gellerman, G. Recent Innovations in Peptide Based Targeted Drug Delivery to Cancer Cells. *Biomedicines* 2016, 4, 11.

[4] Redko, B., Gellerman, G. et all., Synthesis, drug release, and biological evaluation of new anticancer drug–bioconjugates containing somatostatin backbone cyclic analog as a targeting moiety. *Biopolymers*, 2015,104: 743-752

ORAL PRESENTATIONS

OP–1. METABOLIC PROFILING AND IDENTIFICATION STRATEGIES OF SOME INDAZOLE - 3 - CARBOXAMIDE SYNTHETIC CANNABINOIDS USING UPLC - MS/MS

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Introduction: Indazole-3-carboxamide synthetic cannabinoids remain a major challenge in forensic and clinical toxicology because of their high potency, structural diversity and extensive biotransformation after intake. In urine, the parent compounds are frequently absent or present only at trace levels, consequently, analytical confirmation depends mainly on characteristic metabolites.

Indazole-3-carboxamide synthetic cannabinoids remain important forensic toxicology targets because they are highly potent, structurally diverse, and extensively metabolized. In urine, parent compounds are often absent or detected only at trace levels; consequently, analytical confirmation depends mainly on characteristic metabolites. This is particularly relevant for AB-CHMINACA, AB-FUBINACA, and AB-PINACA, whose urinary marker profiles are shaped by hydrolysis, hydroxylation, and oxidation. For this reason, metabolite-centered UPLC-MS/MS screening offers greater diagnostic value than parent-drug testing alone and is especially useful for routine confirmation of exposure to closely related synthetic cannabinoids [1-4].

Objective: To present a targeted UPLC-MS/MS strategy for urinary identification of selected indazole-3-carboxamide metabolites, namely AB-CHMINACA metabolites M4, M6, and M7, AB-FUBINACA metabolites 3 and 4, and the AB-PINACA 3-carboxyindazole metabolite.

Methods: Urine samples underwent beta-glucuronidase hydrolysis followed by solid-phase extraction on Oasis HLB cartridges (3 cc, 60 mg). Analysis was performed on an Agilent 1290 Infinity UPLC coupled to an Agilent 6460 triple quadrupole mass spectrometer in positive ESI mode with multiple reaction monitoring. Separation was achieved on a Zorbax Eclipse Plus C18 column (100 x 3.0 mm, 1.8 um) using 0.1% formic acid in water (A) and 0.1% formic acid in acetonitrile (B) under gradient elution at 0.5 mL/min with a 5.0 uL injection volume. The targeted transition set included AB-CHMINACA M4 (m/z 259.0>241.0 and 259.0>145.0), AB-CHMINACA M6 (387.4>370.5, 387.4>241.3, 387.4>145.0), AB-CHMINACA M7 (388.3>370.4, 388.3>97.3, 388.3>145.1), AB-FUBINACA metabolite 3 (370.2>324.2, 370.2>253.1, 370.2>109.0), AB-FUBINACA metabolite 4 (271.1>253.1 and 271.1>109.0), and AB-PINACA 3-carboxyindazole metabolite (232.2>215.2, 232.2>145.0, 232.2>90.0). Identification criteria included retention-time agreement, monitoring of at least two transitions per analyte, acceptable ion-ratio matching, and negative blank and carryover controls [2-5].

Study objects: The selected analytes represent diagnostically informative urinary metabolites of indazole-3-carboxamide synthetic cannabinoids. AB-CHMINACA M4, M6, and M7 reflect major hydrolytic and oxidative biotransformation pathways; AB-FUBINACA metabolites 3 and 4 are recognized urinary exposure markers; and the AB-PINACA 3-carboxyindazole metabolite represents an analytically useful hydrolyzed indazole-carboxylic acid marker.

Results: In the validated urinary workflow, the analytical range was 2-100 ng/mL with correlation coefficients above 0.995. The limit of detection was 1 ng/mL and the lower limit of quantification was 2 ng/mL. Intra-day accuracy ranged from 89.3-110.2% and inter-day accuracy from 93.2-109.5%, while precision remained < 11.8%. No significant carryover was observed, and the monitored metabolites remained stable in urine after room-temperature, refrigerated, freeze-thaw, and long-term storage conditions. Within the extended panel, the use of multiple transitions per target improved selectivity and provided reliable confirmation of the included AB-CHMINACA, AB-FUBINACA, and AB-PINACA urinary markers under a short chromatographic run.

Discussion: The data support a metabolite-centered identification strategy for indazole-3-carboxamide synthetic cannabinoids in urine. For this structural class, the most informative approach is to combine structure-based metabolite selection with multi-transition MRM confirmation rather than to rely on the parent compounds, which are frequently absent in urine. A panel that includes hydrolyzed, oxidized, and carboxylated metabolites improves analytical sensitivity and helps distinguish closely related analogues with overlapping metabolic behavior. In this context, simultaneous targeting of AB-CHMINACA M4, M6, and M7, AB-FUBINACA metabolites 3 and 4, and the AB-PINACA 3-carboxyindazole metabolite strengthens forensic interpretation by linking exposure assessment to characteristic biotransformation patterns .

Conclusions: A urine-based UPLC-MS/MS workflow using hydrolysis, SPE cleanup, and targeted MRM detection provides a selective and practical approach for confirming exposure to indazole-3-carboxamide synthetic cannabinoids. The proposed metabolite panel is suitable for routine forensic toxicology screening and confirmatory analysis.

References

[1] Roque-Bravo, R., Silva, R.S., Malheiro, R.F., Carmo, H., Carvalho, F., Dias da Silva, D. & Silva, J.P. 2023, 'Synthetic Cannabinoids: A Pharmacological and Toxicological Overview', *Annual Review of Pharmacology and Toxicology*, vol. 63, pp. 187-209.

[2] Navarro-Tapia, E., Codina, J., Villanueva-Blasco, V.J., Garcia-Algar, O. & Andreu-Fernandez, V. 2022, 'Detection of the Synthetic Cannabinoids AB-CHMINACA, ADB-CHMINACA, MDMB-CHMICA, and 5F-MDMB-PINACA in Biological Matrices: A Systematic Review', Biology, vol. 11, no. 5, article 796.

[3] Minakata, K., Hasegawa, K., Nozawa, H., Yamagishi, I., Suzuki, M., Kitamoto, T., Suzuki, O. & Watanabe, K. 2021, 'Quantification of Major Metabolites of AB-FUBINACA in Solid Tissues Obtained from an Abuser', Journal of Analytical Toxicology, vol. 45, no. 6, pp. 555-565.

[4] Minakata, K., Hasegawa, K., Yamagishi, I., Nozawa, H., Suzuki, M., Kitamoto, T., Suzuki, O. & Watanabe, K. 2021, 'In Vivo Metabolites of AB-PINACA in Solid Tissues Obtained from Its Abuser: Comparison with In Vitro Experiment', Journal of Analytical Toxicology, vol. 44, no. 9, pp. 1027-1035.

[5] Scientific Working Group for Forensic Toxicology 2013, 'Scientific Working Group for Forensic Toxicology (SWGTOX) standard practices for method validation in forensic toxicology', *Journal of Analytical Toxicology*, vol. 37, no. 7, pp. 452-474.

OP–2. ADVANCES IN THE PHARMACOGNOSTIC RESEARCH OF *DAPHNE PONTICA* L.

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Daphne pontica L. (*Thymelaeaceae*) has recently attracted attention as a phytochemically and pharmacologically significant species within the genus *Daphne*, owing to its rich diversity of secondary metabolites and associated biological activities. The species, being native to parts of southeastern Europe and Western Asia, has been traditionally used in folk medicine, particularly in Turkey and Iran, for the management of pain, diarrhea, and inflammatory conditions. In recent years, comprehensive phytochemical and biological research conducted by various teams using revealed a structurally diverse array of constituents found in the aerial parts of the plant and various biological activities exhibited by extracts and fractions obtained from all parts of the plant.

Among the most prominent metabolites identified are daphnane-type diterpenoids, a characteristic class of highly oxygenated diterpenes found within the *Daphne* genus and known for their potent biological properties. More than 30 distinct daphnane diterpenoids have been detected, with several compounds tentatively characterized as novel based on spectral data [1]. In addition to diterpenoids, phytochemical profiling has identified significant quantities of phenolic acids and flavonoids, as well as

biflavonoids, coumarins, lignans, dilignans, and various glycosidic derivatives including a potentially novel glycosidic tricoumarin [2-3].

Biological evaluation of crude extracts obtained from all parts of the plant, enriched fractions and isolated compounds has demonstrated a range of biological effects. A strong antioxidant activity was demonstrated in multiple *in vitro* assays, correlating with high phenolic and flavonoid content. Cytotoxic screening against several human cancer cell lines including HeLa, A-549, DU-145 and LNCaP has revealed selective antiproliferative and pro-apoptotic effects, suggesting the involvement of daphnane diterpenoids and related compounds. Furthermore, enzyme inhibitory assays have shown activity against targets such as acetylcholinesterase, butyrylcholinesterase, and α-amylase, highlighting potential relevance in the context of neurodegenerative and metabolic disorders. Additional investigations report antimicrobial activity, DNA-protective effects, anti-inflammatory and anti-oxidant activities [2-6].

Overall, the available phytochemical and pharmacological evidence underscore *D. pontica* as a chemically rich and biologically active species with notable potential for natural product-based drug discovery for anticancer, antioxidant, enzyme-modulating, and anti-inflammatory applications. While current findings are primarily derived from *in vitro* studies, they provide a robust foundation for further bioactivity-guided isolation, structural elucidation, and *in vivo* pharmacological evaluation. Further and more thorough research integrating advanced analytical chemistry, molecular pharmacology, and toxicological assessment will be essential to fully characterize the therapeutic potential and safety profile of *Daphne pontica* L.

References

[1] Onder, A.A., Otsuki, K., Li, W., et al. 2025, 'Qualitative analysis of daphnane diterpenoids in various parts of Daphne pontica L. by UHPLC-Q-Exactive-Orbitrap MS', Phytochemical Analysis, vol. 36, no. 2, pp. 805-818.

[2] Celik Altunoglu, Y., Can, T. H., Tufekci, E. F., Altunoglu, B. D., Baloglu, M. C., Llorent-Martínez, E. J., & Zengin, G. 2022. Comprehensive approaches on chemical composition and biological properties of Daphne pontica L. extracts. Plant Biosystems - An International Journal Dealing with All Aspects of Plant Biology, vol. 156, no. 1, pp. 116–129.

[3] Avcı, E., Zengin, G., Bakar Ateş, F., & Önder, A. 2025. Antioxidant, enzyme inhibitory, and cytotoxic activity screening of Daphne pontica L. (Thymelaeaceae). Journal of Research in Pharmacy, vol. 29, no 4, pp. 1675-1681.

[4] Nikahd, M., Amirghofran, Z. & colleagues 2022, 'Phytochemical analysis of Daphne pontica L. stems with their pro-apoptotic properties against DU-145 and LNCaP prostate cancer cells', Scientific Reports, vol. 12, no. 1, pp. 85–101.

[5] Moshiashvili, G., Pichette, A., Legault, J. et al. 2022. Chemical Composition and Cytotoxic Activity of Daphne glomerate and D. pontica. Chemistry of Natural Compounds no. 58, pp. 329–331.

[6] Kupeli, E., Yesilada, E. & co-authors 2007, 'Assessment of anti-inflammatory and antinociceptive activities of Daphne pontica L.', Journal of Ethnopharmacology, vol. 113, no. 2, pp. 152–154

OP–3. AN OPTIMIZED HEMP EXTRACTION STRATEGY TO ENHANCE SYNERGISTIC ACTIVITY AGAINST TRIPLE - NEGATIVE BREAST CANCER (TNBC)

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Triple-negative breast cancer (TNBC) remains a major therapeutic challenge due to its aggressiveness and limited treatment options. Cannabis sativa L. has gained increasing interest for its potential anticancer properties, notably through the potential of cannabinoids and terpenes. In this study, we developed and characterized a custom-formulated hemp extract (Felina 32 variety) designed to obtain a rich phytochemical composition, with high levels of cannabidiol (CBD) and terpenes, based on our

previous research on synergistic interactions to enhance the entourage effect. This work aimed to evaluate the impact of this extract on the growth of TNBC cells and its potential impact on lymphangiogenesis.

Cannabinoid content was quantified using a validated HPLC method, while terpenes profiles were analyzed by GC, with quantitative assessment of key constituents. Antiproliferative effects were monitored kinetically over 72 hours using live-cell imaging (Incucyte SX-5, Sartorius). The extract significantly inhibited the growth of MDA-MB-231 cells, with a growth rate value of 0.18 ± 0.06 at 72 hours, indicating a near-cytostatic activity compared to control cells (GR=1.00). Holotomographic microscopy (CX-A, Nanolive) revealed clear morphological alterations in response to treatment (loss of adherence and formation of apoptotic bodies), providing dynamic insights into cellular responses. Given the established role of lymphangiogenesis in TNBC metastasis, additional tests were conducted on lymphatic endothelial cells (LEC) to investigate the influence of the extract on these cells. Reduction in LEC proliferation and morphological alterations were observed. Preliminary toxicity screening was performed using zebrafish embryo models to evaluate safety profiles.

These findings support the therapeutic potential of optimized hemp extracts for TNBC management and highlight the importance of preserving the complete phytochemical profile to harness potential synergistic effects.

Keywords: bioactive; cannabinoids; extraction; synergy; MDA-MB-231; lymphangiogenesis.

OP–4. IMPACT OF SACUBITRIL/VALSARTAN ON CARDIOVASCULAR FUNCTION AND INFLAMMATORY MARKERS IN EXPERIMENTAL HYPERTENSION

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Arterial hypertension is a major modifiable risk factor for cardiovascular disease. It is estimated that approximately 10–15% of patients with hypertension exhibit resistance to currently available antihypertensive therapies. Therefore, the development of novel therapeutic strategies and intensified research efforts is essential to improve blood pressure control and enhance protection of target organs.

The study aims to investigate alterations in cardiovascular parameters in hypertensive Wistar rats and to assess their association with inflammatory cytokines, vasoactive mediator production, and melatonin levels.

The experiments were conducted on 40 male rats weighing 200–250 g. The rats were housed in the controlled environmental conditions (temperature 23 ± 1°C, relative humidity 50 ± 5%, 12 h light/12 h dark cycle). The rats were randomly assigned to four experimental groups (n = 10 per group): I - control group received saline solution with1% NaCl plus 0.2% KCl in drinking water for 4 weeks. II - hypertensive group received deoxycorticosterone acetate (DOCA) at 25 mg/kg intraperitoneally and 1% NaCl plus 0.2% KCl in drinking water for 4 weeks. III - DOCA and Sacubitril/Valsartan, delayed treatment received Sacubitril/valsartan at an oral dose of 30 mg/day for 2 weeks, which was started after 25 mg/kg DOCA intraperitoneally and 1% NaCl + 0.2% KCl in drinking water for 4 weeks (n=10); IV - DOCA and Sacubitril/Valsartan, concomitant treatment received sacubitril/valsartan (30 mg/day, orally) concomitantly with DOCA (25 mg/kg, intraperitoneally) and 1% NaCl plus 0.2% KCl in drinking water for 4 weeks.

After 4 weeks of DOCA administration, hypertensive rats exhibited a significant increase in blood pressure (BP) and heart rate (HR), accompanied by a marked reduction in baroreflex sensitivity (BRS) compared with normotensive controls. These hemodynamic alterations were associated with elevated

plasma levels of proinflammatory cytokines, including interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), and nuclear factor kappa B (NF-κB), as well as increased concentrations of the vasoconstrictor agents endothelin-1 (ET-1) and angiotensin II (Ang II). In contrast, plasma melatonin (MT) levels were significantly reduced in hypertensive animals.

Two-week treatment with sacubitril/valsartan restored the levels of these biomarkers toward the normal range. In the fourth group, concomitant administration of sacubitril/valsartan exerted a significant preventive effect, as evidenced by the absence of increases in inflammatory cytokines and vasoconstrictor agents, along with preservation of melatonin levels. Melatonin levels demonstrated a negative correlation with inflammatory markers. Therefore, the sacubitril/valsartan–induced restoration of melatonin may represent a contributory mechanism in delaying the development of chronic inflammation.

Treatment with the combination of sacubitril/valsartan, initiated at an early stage of arterial hypertension, prevents the progression of the disease mediated through modulation of inflammatory pathways, attenuation of vasoconstrictor activity, and preservation of melatonin levels. These results suggest that sacubitril/valsartan may represent a promising therapeutic strategy for mitigating hypertension-associated cardiovascular and inflammatory alterations.

OP–5. ROWAN SPECIES OF TÜRKIYE: MEDICINAL AND AROMATIC VALUE AND GENETIC IDENTIFICATION

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Rowan species and related taxa within the Rosaceae (including *Aria, Hedlundia, Sorbus*, and *Torminalis*) constitute an important but still underutilized plant group in Türkiye with considerable medicinal and aromatic potential. Traditionally, several of these taxa have attracted attention due to their bioactive compounds, antioxidant properties, and possible applications in herbal medicine, functional foods, and natural product industries [1, 2]. However, the effective and safe utilization of these resources is strongly dependent on accurate species identification, as the group is taxonomically complex and characterized by frequent hybridization, polyploidy, and high morphological similarity [3].

In this context, this study integrates morphological assessments with molecular phylogenetic analyses based on chloroplast and nuclear DNA markers to ensure reliable identification of rowan-related taxa in Türkiye. The molecular results provide higher resolution than morphology alone, allowing clearer delimitation of closely related species and the clarification of taxonomic uncertainties. This robust taxonomic framework is essential for correctly linking specific genetic lineages with their medicinal and aromatic properties and for avoiding misidentification in pharmacological, phytochemical, and applied studies.

By combining genetic identification with an evaluation of the medicinal and aromatic significance of these taxa, the study establishes a scientific basis for their sustainable use, conservation, and valorization. The findings support future research on bioactive compounds, product development, and cultivation strategies and contribute to the responsible exploitation of Türkiye's rowan diversity as a valuable natural resource for medicinal and aromatic applications.

References

[1] Arvinte, O.M., Senilă, L., Becze, A. & Amariei, S., 2023, Rowanberry–A Source of Bioactive Compounds and Their Biopharmaceutical Properties, Plants, vol. 12, no. 12, pp. 3225–3242.

[2] Neagu, E., et al., 2025, Antidiabetic and Anti-Inflammatory Potential of Sorbus aucuparia Extracts, Applied Sciences, vol. 15, no. 23, pp. 12585–12598.

[3] Hummer, K.E. and Janick, J., 2009, Rosaceae: Taxonomy, economic importance, genomics, Plant Genetics and Genomics: Crops and Models, vol. 6, no. 1, pp. 1–17.

OP–6. FROM SEMINARS TO ESCAPE GAMES: RETHINKING HOW WE TEACH PHYTOCHEMISTRY

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The teaching of phytochemistry in pharmacy curricula often remains fragmented, oscillating between theoretical instruction and applied laboratory practice. This communication explores how two complementary pedagogical innovations, a cross-year interdisciplinary seminar and a gamified escape game, can be combined to rethink how phytochemistry is taught and experienced by students.

First, a spiral, cross-year seminar was designed to bridge pharmaceutical chemistry and pharmacognosy by engaging second- and third-year students in collaborative problem- solving tasks. Through progressive exercises linking acid–base chemistry, solubility, and natural product extraction, students developed a more integrated understanding of how foundational chemical principles underpin pharmacognostic applications. This approach enhanced perceptions of interdisciplinarity, curricular coherence, and peer learning.

Second, an immersive escape game was implemented within a third-year laboratory module to teach pharmacognosy quality control. Students worked in teams to solve analytical challenges based on pharmacopeial methods (microscopy, TLC, GC), simulating real-world decision-making in herbal drug evaluation. While practical performance remained stable, a significant improvement in final exam scores suggested deeper conceptual understanding and enhanced data interpretation skills.

Together, these approaches illustrate a shift from passive knowledge transmission to active, student-centered learning environments that promote integration, engagement, and higher-order thinking. By combining vertical integration, near-peer collaboration, and game-based learning, this work proposes a coherent pedagogical framework for teaching phytochemistry as a dynamic and connected discipline. These findings support the broader adoption of innovative, experiential teaching strategies to better prepare pharmacy students for professional practice.

OP–7. PHYTODRUGS AS CHALLENGING MOLECULES: BIOPHARMACEUTICAL LIMITATIONS AND DELIVERY-BASED SOLUTIONS

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Phytodrugs demonstrate a broad spectrum of pharmacological activities; however, their successful development into effective dosage forms is frequently hindered by inherent biopharmaceutical and technological limitations, including poor aqueous solubility, chemical and physical instability, volatility, efflux transporter–mediated reduction in bioavailability, hygroscopicity, and formulation-related challenges. To overcome these limitations, delivery-oriented approaches employing natural and hybrid biomaterials have attracted considerable scientific interest [1, 2].

This work summarizes advanced formulation strategies developed for bioactive compounds derived from Georgian natural resources, with particular emphasis on bentonite - based polymer hybrid systems, nanostructured carrier platforms, and solid-state pharmaceutical technological approaches aimed at improving physicochemical stability, processing performance, and bioavailability.

Tikha-Ascane (Georgian bentonite clay) was extensively investigated as a multifunctional inorganic component in hybrid delivery formulations due to its layered structure, high specific surface area, ion-exchange capacity, and swelling behavior. Polymer–clay composites incorporating natural and synthetic polymers were prepared using gelation and dispersion techniques to stabilize and deliver volatile and chemically labile phytoconstituents, including essential oils, plant extracts, and royal jelly. The influence of polymer-to-clay ratio, processing parameters, and compositional modifications on intercalation, microstructure, and macroscopic properties was systematically evaluated. Fourier transform infrared spectroscopy (FTIR) confirmed the establishment of polymer-clay interactions and the formation of intercalated hybrid networks, while microscopic analysis demonstrated the development of dense, homogeneous, and composition-dependent morphologies. Rheological characterization revealed thixotropic and viscoelastic behavior, indicating structural stability and suitability for topical and intranasal administration [3].

Bentonite-based delivery systems were designed and evaluated as multifunctional carrier matrices for nasal, topical, oral, and semisolid pharmaceutical applications. The incorporation of structural modifiers and plant-derived bioactive compounds significantly influenced the internal architecture of the systems, thereby modulating rheological behavior, and release kinetics. Bentonite-based hydrogels and bio-hybrid composites demonstrated improved physical stability, compositional uniformity, and controlled release of essential oils and aqueous plant extracts of *Matricaria chamomilla* L., enabling the development of topical formulations and nasal spray systems with optimized pH, sprayability, and mechanical performance. Royal jelly-loaded bentonite creams, as well as sea buckthorn oil–based ointments and emulsions, exhibited enhanced physicochemical stability and preservation of biological activity, confirming the protective and stabilizing function of the clay matrix [3, 4].

In addition, solid-state formulation technologies involving rational selection of functional excipients, modification of particle morphology, and application of direct compression approaches were utilized to improve processing characteristics and tableting performance of moisture-sensitive non-hormonal anabolic and hypocholesterolemic substance, derived from *Tribulus terrestris.*

Nanostructured delivery systems, including liposomal, PEGylated, thiomer-modified, and tetraether lipid-based vesicular carriers, were developed to overcome permeability and efflux-related barriers of plant-derived flavonoids and alkaloids. These nanocarriers improved encapsulation efficiency, physicochemical stability, controlled release behavior, and intestinal transport characteristics, leading to enhanced *in vitro* bioavailability of bioactive phytocompounds such as hypoazotemic flavonoid glycoside and anti-arrhythmic sum of indoline alkaloids, isolated from Georgian plant sources [5].

In conclusion, the developed delivery systems provide a scientifically grounded approach for overcoming the biopharmaceutical limitations of phytodrugs by improving physicochemical stability, solubility, and bioavailability. These findings support the rational design of advanced phytopharmaceutical formulations with enhanced therapeutic potential.

References

[1] Sanjai, C., Gaonkar, SL., Hakkimane, S S. 2024, Harnessing Nature's Toolbox: Naturally Derived Bioactive Compounds in Nanotechnology Enhanced Formulations. *ACS omega*, vol.9 no 43, pp. 43302–43318.

[2] Swain, R., Nandi, S., Mohapatra, S., Mallick, S. 2024, Engineered Clay-Polymer Composite for Biomedical Drug Delivery and Future Challenges: A Survey. *Current drug delivery*, vol. 21, no. 5, pp. 645–661.

[3] Tsiklauri, L., Janezashvili, A., Getia, M. 2026, Georgian bentonite clay–polymer system as a carrier for volatile oil in topical applications, *Journal of the Serbian Chemical Society*, vol. 91, no.1, pp. 71–84.

[4] Tsiklauri, L., Tsagareishvili, G. 2011, *Gastroenterological and dermatological soft drug formulations containing Georgian bentonite clay preparation–Thicha-ascanae*. Universal, 89 p.

[5] Tsiklauri L., Bernkop-Schnürch A., Allémann E. 2024, Oral delivery systems of phytobioactive ingredients from Georgian flora. Proceedings of *the* GEORGIA - ISRAEL BILATERAL SYMPOSIUM "TRENDS IN DRUG DISCOVERY AND DEVELOPMENT, 20-25 September, Tbilisi, Georgia, pp. 28 -29

OP–8. DISUBSTITUTED PIPERAZINES – SYNTHESIS AND PROPERTIES

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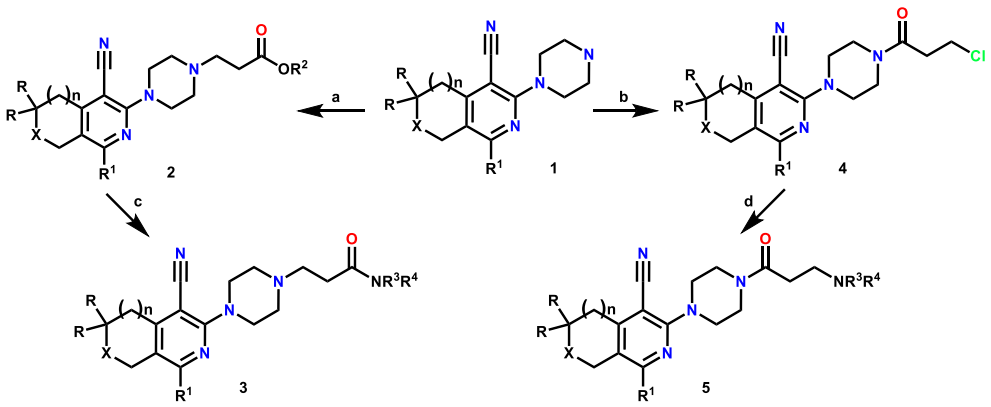
Literature data indicated that piperazine derivatives are characterized by high biological activity [1–7]. In our previous works we have described the synthesis, antimicrobial activity [4] and psychotropic properties [5–7] of some disubstituted piperazines. These studies revealed that some of these compounds showed low toxicity and high activities than the reference drugs [4].

Taking into account above, new series of *N*-substituted derivatives of piperazinopyridines **2–5** were synthesized, which differ in the α and γ positions of the carbonyl group relative to the piperazine ring. The synthesis of target compounds was carried out on the basis of 3(6)-piperazinopyridines **1** [4, 6] according to the scheme below. The *N*-alkyl derivatives **2** were synthesized using copper oxide nanoparticles as a catalyst. *N*-acyl compounds **4** were formed between the reaction of compounds **1** and 3-chloropropanoyl chloride. After starting from these compounds **2** and **4** the corresponding amino derivatives **3** and **5** were synthesized. Preliminary biological results showed that the final compounds have high antitumor activity.



(a) H_2C=CH-$COOR^2$, CuO, EtOH; (b) $ClCH_2CH_2COCl$, C_6H_6, Py; (c) NHR^3R^4, EtOH; (d) NHR^3R^4, EtOH.
R = H, alkyl; R^1 = alkyl, aryl; R^2 = Me, Et; R^3, R^4 = H, alkyl, $R^3 + R^4$ = cycloalkyl

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References

[1] Romanelli MN., Braconi L., Gabellini A., Manetti D., Marotta G., Teodori E., 2024, Synthetic Approaches to Piperazine-Containing Drugs Approved by FDA in the Period of 2011–2023, Molecules, vol. 29, pp. 68.

[2] Rizwan M., Noreen S., Asim S., Liaqat Z., Shaheen M., Ibrahim H.,2024, A comprehensive review on the synthesis of substituted piperazine and its novel bio-medicinal applications, Chem. Mater., vol. 2, pp. 100041.

[3] Sumalatha S., Venkataramaiah CJ., 2022, Design, synthesis, in vitro and in silico bioactivity profiles of new urea/thiourea derivatives of 2-pyridyl piperazine as potent antioxidant and antimicrobial agents: chemo-bio-computational approach, Biomol. Struct. Dyn., vol. 41, pp. 4786–4797.

[4] Sirakanyan SN., Kartsev VG., Spinelli D., Geronikaki A., Petrou A., Ivanov M., Glamoclija J., Sokovic M., Hakobyan EK., Hovakimyan AA., 2021, Synthesis and antimicrobial activity of new 2-piperazin-1-yl-N-1,3-thiazol-2-ylacetamides of cyclopenta[*c*]pyridines and pyrano[3,4-*c*]pyridines, Arch. der Pharm., vol. 354, pp. 2000208.

[5] Sirakanyan SN., Spinelli D., Geronikaki A., Hakobyan EK., Petrou A., Kartsev VG., Yegoryan HA., Paronikyan EG., Zuppiroli L., Jughetsyan HV., Paronikyan RG., Arakelyan TA., Hovakimyan AA., 2024, New triazole-based hybrids as neurotropic agents, RSC Adv., vol. 24, pp. 32922–32943.
[6] Sirakanyan SN., Akopyan EK., Paronikyan RG., Nazaryan IM., Akopyan AG., Ovakimyan AA., 2019, Synthesis and neurotropic activity of piperazino-derivatives of pyrano[3,4-*c*]pyridines, Pharm. Chem. J., vol 53, pp. 495–499.
[7] Sirakanyan SN., Spinelli D., Petrou A., Geronikaki A., Kartsev VG., Hakobyan EK., Yegoryan HA., Paronikyan EG., Zuppiroli L., Zuppiroli R., Ayvazyan AG., Paronikyan RG., Arakelyan TA., Hovakimyan AA., 2023, New bicyclic pyridine-based hybrids linked to the 1,2,3-triazole unit: synthesis via click reaction and evaluation of neurotropic activity and molecular docking, Molecules, vol. 28, pp. 921.

OP–9. SYNTHESIS AND BIOLOGICAL ACTIVITY EVALUATION OF NOVEL NITROGEN-CONTAINING STEROIDS DERIVED FROM TIGOGENIN

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Steroids are a class of natural compounds that play a key role in the homeostasis of living organisms. Even a slight change in their structure can radically alter the activity of these compounds. The synthesis of new pharmacologically active derivatives through targeted chemical modification of the steroid structure is a major task for scientists working in the field of drug development. Therefore, the search for biologically active steroid compounds, their chemical modification, and biological screening remain highly relevant today.

Among synthetic nitrogen-containing steroid compounds, semicarbazones, thiosemicarbazones, hydrazones, pyrazolines, and triazoles are of particular interest to researchers because they are characterized by high biological activity [1,2].

In order to obtain new potential biologically active compounds, a series of new nitrogen-containing 5α-steroids was synthesized based on tigogenin, a raw material for the synthesis of 5α-steroids, isolated from the plant *Yucca gloriosa*, which has been introduced in Georgia [3–5].

In vitro studies of our synthesized compounds have shown that they are characterized by significant antiviral, cytotoxic, antibacterial, antifungal, anti-inflammatory, and antitumor activity. The broad biological activity of androstane and pregnane compounds indicates that they could serve as key starting points for the development of new drugs.

References

[1] Gan, C. Cui, J. Su, S. Lin, Q. Jia, L. Fan, L. Huang, Y. 2014, Synthesis and antiproliferative activity of some steroidal thiosemicarbazones, semicarbazones and hydrozones, Steroids, vol. 87, pp. 99-107.
[2] Shamsuzzaman, Khanam, H. Dar, Siddiqui, N. Rehman. S. 2016, Synthesis, characterization, antimicrobial and anticancer studies of new steroidal pyrazolines, J. of Saudi Chemical Society, vol. 20, no. 1, pp. 7–12.
[3] Nadaraia, NSh. Amiranashvili, LSh. Merlani, MI. Kakhabrishvili, ML. Barbakadze, NN. Geronikaki, A. Petrou, A. Poroikov, V. Ciric, A. Glamoclija, J. Sokovic. M. 2019, Novel antimicrobial agents' discovery among the steroid derivatives, Steroids, vol. 144, pp. 52-65.
[4] Merlani, M. Nadaraia, N. Barbakadze, N. Amiranashvili, L. Kakhabrishvili, M. Petrou, A. Carević, T. Glamočlija, J. Geronikaki. A. 2024, Steroidal hydrazones as antimicrobial agents: biological evaluation and molecular docking studies, SAR and QSAR in Environmental Research, vol. 35, no. 2, pp. 137-155.
[5] Eerlings, R. Barbakadze, N. Nguyen, T. Nadaraia, N. Smeets, E. Moris, L. Handle, F. Kharraz, SE. Devlies, W. Voet, A. Dehaen, W. Claessens, F. Helsen. Ch. 2022, Small-molecule profiling for steroid receptor activity using a universal steroid receptor reporter assay, Journal of Steroid Biochemistry and Molecular Biology, vol. 217, p.106043.

OP–10. DESIGN AND DEVELOPMENT OF PSEUDO-PROTEINS: ADVANCED BIOMATERIALS FOR VERSATILE MEDICAL APPLICATIONS

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Among naturally occurring biodegradable polymers, proteins play a central role in advanced medical applications due to their intrinsic tissue affinity, enzymatic degradability, and ability to release α-amino acids (α-AAs) that support tissue regeneration [1]. However, their clinical use as biomaterials is limited by drawbacks such as immunogenicity related to their native molecular structure (Fig.1, A). To address these limitations, a new class of α-AA-based biodegradable polymers - artificial analogues of natural proteins known as pseudo-proteins (PPs) has been developed [2]. PPs exhibit low immunogenicity, high biocompatibility, and intrinsic biological activity. Owing to their distinct molecular architecture (Fig.1, B), PPs overcome key limitations of natural proteins while retaining essential advantages, including tissue compatibility and the capacity to promote cell proliferation and regeneration upon biodegradation [2,3].

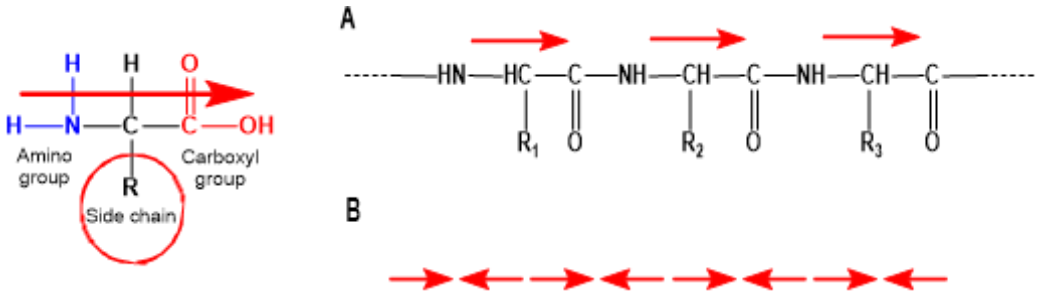

Fig. 1. Possible orientations of α-amino acids (α-AAs) in (A) proteins and (B) pseudo-proteins (PPs)

The key monomers used in the synthesis of PPs are diamine-diesters derived from α-amino acids (α-AAs) and diols [5]. Based on these building blocks, various classes of PPs, including both regular and functional types, have been developed, exhibiting a broad range of material properties. In addition to peptide bonds, PPs incorporate diverse chemical linkages that permit tailoring of their physicochemical characteristics for various biomedical applications [2–7], including coatings for vascular stents with controllable drug release (already implemented in the clinic through a collaboration between Royal DSM, Netherlands, and Svelte Medical Systems, USA [8]), as well as polymer-bacteriophage composites (in the form of films and gel-forming drug-loaded microspheres), and spray-on wound dressings effective for the treatment of burns, tropical ulcers, and post-surgical wounds. Ongoing studies are also focused on PP–based nanocontainers coated with a polyethylene glycol (PEG) cloud, which are resistant to phagocytosis and show great potential for targeted drug delivery [9-10].

References

[1] Stie, M.B., Kalouta, K., Vetri V. and Foderà, V. 2022, "Protein materials as sustainable non-and minimally invasive strategies for biomedical applications," *J. Control. Release*, vol. 344, pp. 12-25. https://doi.org/10.1016/j.jconrel.2022.02.016

[2] Zavradashvili, N., Puiggali, J. and Katsarava, R. 2020, "Artificial polymers made of α-amino acids-poly (amino acid)s, pseudo-poly (amino acid s, poly (depsipeptide)s, and pseudo-proteins," *Curr Pharm Design,* vol. 26, no. 5, pp. 566-593. https://doi.org/10.2174/1381612826666200203122110.

[3] Ksovreli, M., Kachlishvili, T., Skhvitaridze, M., Nadaraia, L., Goliadze, R., Kamashidze, L., Zurabiani, K., Batsatsashvili, T., Kvachantiradze, N., Gverdtsiteli, M., Kantaria, T., Piot, O., Courageot, M.P., Terryn, C.,

Tchelidze, P., Katsarava R. and Kulikova, N. 2024, "Wound Closure Promotion by Leucine-Based Pseudo-Proteins: An In Vitro Study," *Int. J. Mol. Sci.* vol. *25*, pp. 9641. https://doi.org/10.3390/ijms25179641.

[4] Zavradashvili, N., Kobauri, S., Puiggali, J. and Katsarava, R. 2021, Functional Pseudo-Proteins. Book chapter in "Functionalized Polymers: Synthesis, Characterization and Applications" (1st ed.). CRC Press. Chauhan, N.P.S. (Ed.) https://doi.org/10.1201/9780367821913.

[5] Katsarava, R. and Gomurashvili, Z. 2011, "Biodegradable Polymers Composed of Naturally Occurring α-Amino Acids", *Handbook of Biodegradable Polymers - Isolation, Synthesis, Characterization and Applications*, Lendlein, A. and Sisson, A., Eds., pp. 107-31. Wiley-VCH Verlag GmbH & Co. KGaA. https://doi.org/10.1002/9783527635818.ch5.

[6] Zavradashvili, N., Sarisozen, C., Titvinidze, G., Otinashvili, G., Kantaria, T., Tugushi, D., Puiggali, J., Torchilin, V. P. and Katsarava, R. 2019, "Library of cationic polymers composed of polyamines and arginine as gene transfection agents," *ACS omega*, vol. 4, no. 1, pp. 2090-2101. https://doi.org/10.1021/acsomega.8b02977.

[7] Wang, Y., Zavradashvili, N., Wang, Y., Pietropaolo, A., Song, Z., Bando, M., Katsarava, R. and Nakano, T. 2020, "Optically Active Polymers with Cationic Units Connected through Neutral Spacers: Helical Conformation and Chirality Transfer to External Molecules," *Macromolecules*, vol. 53 no. 22, pp. 9916-9928. https://doi.org/10.1021/acs.macromol.0c02199.

[8] Verheye, S. 2017, „Evaluation of the Svelte Medical systems SLENDER IDS Sirolimus-eluting coronary stent-on-a-wire integrated delivery system for the treatment of coronary artery disease". *Expert Review of Medical Devices,* vol. 14, no. 9, pp. 669–683. https://doi.org/10.1080/17434440.2017.1364990

[9] Makharadze, D., Kantaria, T., Yousef, I., Del Valle, L. J., Katsarava R. and Puiggalí, J. 2024, "PEGylated Micro/Nanoparticles Based on Biodegradable Poly (Ester Amides): Preparation and Study of the Core–Shell Structure by Synchrotron Radiation-Based FTIR Microspectroscopy and Electron Microscopy," *Int. J. Mol. Sci.*, vol. *25,* no. 13, pp. 6999. https://doi.org/10.3390/ijms25136999.

[10] Makharadze, D., Kantaria, T., Kantaria, T., Kupatadze, N., Zavradashvili, N., Kirtadze, L., Puiggali, J., del Valle L.J., Katsarava, R. 2025, "Pseudoprotein-Poly(ethylene glycol) Multi-purpose Graft Copolymers *via* Michael Addition Reaction" *Europ. Polym. J*. vol. 236, 114103. https://doi.org/10.1016/j.eurpolymj.2025.114103.

OP–11. CAFFEIC ACID BASED BIOPOLYMERS FROM DIFFERENT SPECIES OF BORAGINACEAE FAMILY AND THEIR SYNTHETIC ANALOGUES

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Previously, we reported on the isolation of a biologically active polymer - poly-[3-(3,4-dihydroxyphenyl)glycerine acid] (PDHPGA) (Fig.1,1) from various species of plants of Boraginaceae family: *Symphytum asperum* (SA)*, S. caucasicum* (SC), *S. grandiflorum* (SG), *S. officinale* (SO), *Anchusa italica* (AI), *Cynoglossum officinale* (CO), *Borago officinalis* (BO), *Paracynoglossum imeretinum* (PI) and *Trachistemon orientalis* (TO). Distinguished from PDHPGA-SA, PDHPGA-SC, PDHPGA–SO, and PDHPGA–CO most of the carboxylic groups of PDHPGA-SG, PDHPGA-AI, and PDHPGA-BO are methylated (Fig.1,2). The attempt of the polymerisation of caffeic acid derived glycidates (Fig .1, 3-5) under mild and environmentally-friendly conditions using lipases from two different sources - *Candida rugosa* (*C. rugosa*) and *Penicillium camemberti* (*P. camemberti*) showed that lipase from *C. rugosa* was the most efficient in inducing the ring-opening polymerization of MDBPO (3) while the enzyme from *P. camemberti* was not active under the polymerization conditions chosen (Scheme 1). Catalytic debenzylation of PMDBPO (6) using H_2 on Pd/C yields poly[2-methoxycarbonyl-3-(3,4-dihydroxyphenyl)oxirane] (PMDHPO) (2) - the first synthetic analogue of natural biopolymer with 80% yield..

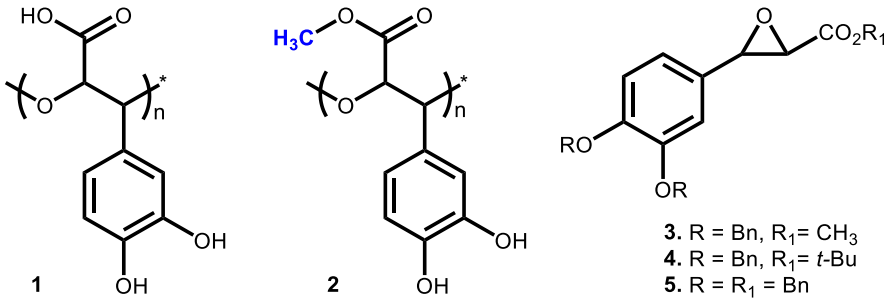
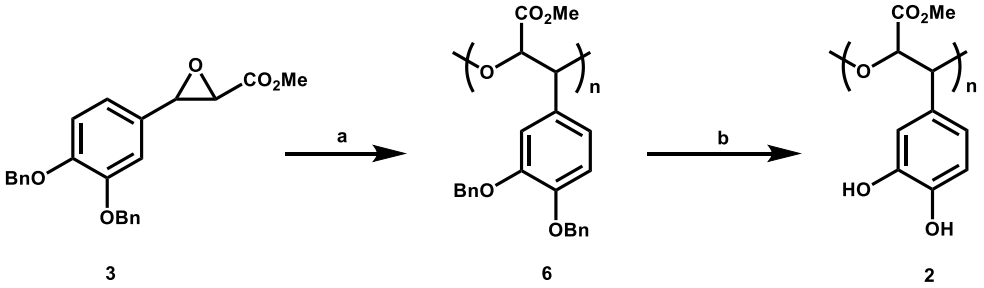


Figure 1. Poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDHPGA) (1) and poly[2-methoxycarbonyl-3-(3,4-dihydroxyphenyl)oxirane] (PMDHPO) (2)



Scheme 1. Enzymatic polymerization of MDBPO and modification of the polymer: a) *C. rugosa lipase*, toluene, 80°C, 7 days b) Pd/C, H_2, THF/EtOH

The reactions with BDBPO and TBDBPO did not show any trace of polymer, most probably due to the steric hindrance by the benzyloxy- and t-butyloxy groups

OP–12. CHEMICAL COMPOSITION AND EVALUATION OF ANTIOXIDANT ACTIVITY OF SOME ESSENTIAL OIL-BEARING PLANTS OF THE GEORGIA FLORA

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Antioxidants are compounds that protect cells from damage caused by unstable molecules known as free radicals. Numerous studies have demonstrated that oxidative stress plays a significant role in the pathogenesis of diabetes, cancer, Alzheimer's disease, inflammatory and cardiovascular disorders, as well as immune system dysfunction [1]. Among plant secondary metabolites, essential oil and phenolic compounds, such as flavonoids, are characterized by significant antioxidant capacity [2,3]. The flora of Georgia is characterized by a high diversity of essential oil–bearing medicinal plants. Members of the Lamiaceae family are particularly rich in essential oil [4]. The Lamiaceae family is one of the largest botanical families in terms of species diversity [5]. In Georgia, 160 species belonging to 37 genera of the Lamiaceae family are distributed, including 9 species endemic to Georgia and 17 endemic to the Caucasus. In the study, two species of the genus Thymus L. within the family Lamiaceae were selected as the objects of investigation. In traditional medicine, the leaves and flowers of *Thymus* species have long been used as tonic, antiseptic, analgesic, anti-inflammatory, and antitussive agents [6]. Numerous studies have demonstrated that *Thymus* species and their essential oils possess a wide range of biological activities, including antimicrobial, antioxidant, anticarcinogenic, cardioprotective, neuroprotective, fungicidal, anti-inflammatory, and hypoglycemic effects [7].

The aerial parts of *Thymus tiflisiensis* and *Thymus collinus* endemic to the Caucasus, were collected in Georgia during the full flowering stage (Kartli floristic region, altitudes: 485 and 649 m above sea level; voucher specimen numbers: TBPH-21351 and TBPH-22303).

Essential oils were isolated from the aerial parts by hydrodistillation using a Clevenger-type apparatus. After essential oil extraction, the residual aqueous phase was lyophilized, and the dried plant material was successively extracted with chloroform and methanol. Essential oil composition was determined by gas chromatography–mass spectrometry (GC MS) using an Agilent Technologies 7890B GC coupled to an Agilent Technologies 5977A MSD. In the non-volatile extracts, phenolic compounds were identified by HPLC MS/MS (Agilent Technologies 1290 Infinity LC system coupled to an Agilent Technologies 6460 Triple Quadrupole MS) based on retention times and mass spectral data of reference standards.

The antioxidant activities of the essential oil (volatile fraction) and the non-volatile aqueous, methanolic, and chloroform extracts were evaluated using the oxygen radical absorbance capacity (ORAC) assay, the human skin fibroblast (WS1) cell-based assay and the DPPH radical scavenging assay. Trolox, quercetin and gallic acid were used as reference standards.

The essential oil of *T.collinus* is rich in oxygenated monoterpenes, whereas *T.tiflisiensis* is characterized by a high content of sesquiterpene hydrocarbons. In the non-volatile extract of *T.tiflisiensis*, phenolic compounds were identified, including flavones, flavonoid glycosides, flavanols, and phenolic acids such as hydroxybenzoic and hydroxycinnamic acids. The essential oil and aqueous extract of *T.collinus* exhibited high antioxidant activity. The aqueous and chloroform extract of *T.tiflisiensis* also demonstrated strong antioxidant activity.

The essential oils and extracts of *T.tiflisiensis* and *T.collinus* exhibit strong antioxidant activity, reflecting their diverse chemical compositions. These findings support their traditional medicinal use and suggest their potential as natural antioxidant sources.

References

[1] Shaaban, H.A.E., El-Ghorab, A.H. & Shibamoto, T., 2012, Bioactivity of essential oils and their volatile aroma components: Review, Journal of Essential Oil Research, vol. 24, no. 2, pp. 203–212.

[2] Napoli, E.M., Di Vito, M., 2021, *C*hemical Composition and Biological Activities of Essential Oils, MDPI Books.

[3] Tzima, K., Brunton, N. and Rai, D. 2018, Qualitative and Quantitative Analysis of Polyphenols in Lamiaceae Plants—A Review. Plants, vol. 7, no. 2, pp. 1-30.

[4] Ramos da Silva, L.R., Ferreira, O.O., Cruz, J.N., Jesus Pereira Franco, C. de, Oliveira dos Anjos, T., Cascaes, M.M., Almeida da Costa, W., Helena de Aguiar Andrade, E. & Santana de Oliveira, M., 2021, Lamiaceae Essential Oils, Phytochemical Profile, Antioxidant, and Biological Activities, Evidence-Based Complementary and Alternative Medicine, vol. 2021, no. 1, pp. 1–18.

[5] Çelik, G., Kılıç, G., Kanbolat, Ş., Özlem Şener, S., Karaköse, M., Yaylı, N. & Karaoğlu, Ş.A., 2021, Biological activity, and volatile and phenolic compounds from five Lamiaceae species, Flavour and Fragrance Journal, vol. 36, no. 2, pp. 223–232.

[6] Li, X., He, T., Wang, Xiuhuan, Shen, M., Yan, X., Fan, S., Wang, L., Wang, Xiaoping, Xu, X., Sui, H. & She, G., 2019, Traditional Uses, Chemical Constituents and Biological Activities of Plants from the Genus *Thymus*, Chemistry & Biodiversity, vol. 16, no. 9.

[7] Aouam, I., El Atki, Y., Taroq, A., El Kamari, F. & Abdellaoui, A., 2019, Chemical composition, antimicrobial, and antioxidant activities of two moroccan Thymus essential oils, Asian Journal of Pharmaceutical and Clinical Research, vol. 12, no. 1, pp. 447-451.

OP–13. LC-MS ANALYSIS OF CRUDE EXTRACTS FROM THE PLANTS GROWING IN GEORGIA

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The analysis and standardization of pharmaceutical products require continuous updates, particularly when dealing with multi-component herbal medicines and other pharmaceutical preparations. TSMU Iovel Kutateladze Institute of Pharmacochemistry studies natural products of plant irigin. The active constituents are typically represented as complex mixtures of diverse plant secondary metabolites such as terpenoids, phenolic compounds, alkaloids, lipids et al. Therefore, analysis of the compounds represents challenging issue from scientific and practical viewpoints [1-7].

This study aims to summarize the general challenges in the analysis (LC-MS and GC-MS) of extracts and mixtures containing terpenic compounds, flavonoids and essential oils derived from some species growing in Georgia.

Methods and techniques of extraction, separation and purification of crude extrats needs improuvement. Content of phenolic compounds was quantified using a validated HPLC method, while terpenes and aromatic profiles of essential oils were analyzed by GC-MS, with quantitative assessment of key constituents. Various stationary phases, solvents and technics of separation biologically active compounds were used to enhance the selectivity of developed analytical methods for standartization of the herbal products obtained at Iovel Kutateladze Institute of Pharmacochemistry.

The use of mass spectrometry and diode-array detectors (DAD) detectors facilitated the identification and quantification of active constituents in natural products. UV and IR spectroscopy allowed rapid, simultaneous qualitative and quantitative analysis of mixtures of terpenes and flavonoids without destructive sample preparation.

In this study are described validated methods of analyses essental oils and crude extract derived from the species of the family Rosaceae and Araliaceae and the main problems in method development of the crude extracts.

Keywords: HPLC separation, GC-MS, standardization, natural products

References

[1] Lloyd R. Snyder, Joseph Jack Kirkland, Joseph L. Glajch. Practical HPLC Method Development. 1997. Second edition. New York. 765 pages
[2] Validation of analytical procedures: Text and methodology - International Conference on Harmonisation. ICH Q2(R2) Validation of analytical procedures - Scientific guideline.
[3] Hill, C. B., & Roessner, U. (2013). Metabolic profiling of plants by gas chromatography–mass spectrometry (GC-MS). Methods in Molecular Biology, 1062, 77–89.
[4] Lisec, J., Schauer, N., Kopka, J., Willmitzer, L., & Fernie, A. R. (2006). Gas chromatography mass spectrometry–based metabolite profiling in plants. Nature Protocols, 1(1), 387–396.
[5] Fiehn, O. (2008). Metabolomics—the link between genotypes and phenotypes. Plant Molecular Biology, 48(1–2), 155–171.
[6] Dettmer, K., Aronov, P. A., & Hammock, B. D. (2007). Mass spectrometry-based metabolomics. Mass Spectrometry Reviews, 26(1), 51–78.
[7] D'Auria, J. C., & Gershenzon, J. (2005). The secondary metabolism of Arabidopsis thaliana: growing like a weed. Current Opinion in Plant Biology, 8(3), 308–316.

OP–14. AI AS A FORCE MULTIPLIER: A STAGED INTEGRATION FRAMEWORK FOR DRUG DESIGN AND DEVELOPMENT

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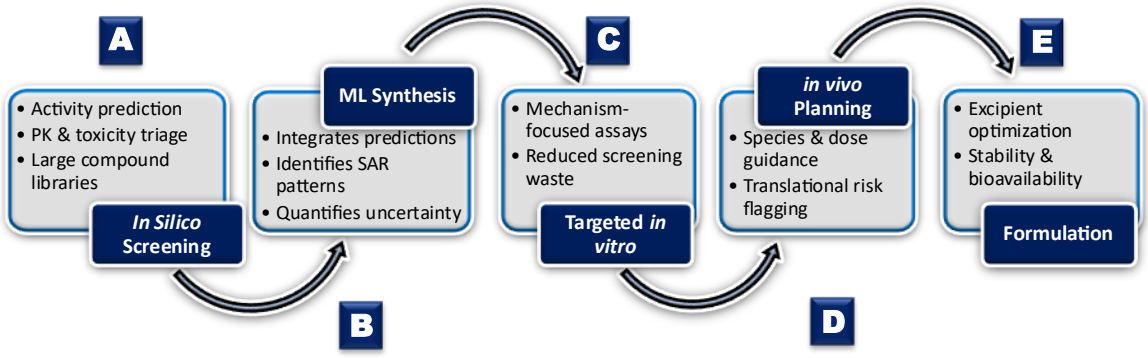
Contemporary drug discovery remains constrained by attrition rates exceeding 90% and development cycles spanning a decade or more. Rather than positioning artificial intelligence (AI) as a disruptive replacement for established science, we aim to propose a pragmatic integration framework where AI functions as a force multiplier—accelerating decision points while preserving essential human expertise.

We tried to answer a foundational question: can AI meaningfully enhance drug design and development (DDD) without displacing domain expertise? Evidence suggests yes - when deployed selectively. Machine learning algorithms now assist in target identification by analysing multi-omics datasets to uncover disease-associated pathways with greater speed than manual curation. In lead optimization, generative AI models design novel molecular structures with desired binding affinities, while graph neural networks predict ADMET (absorption, distribution, metabolism, excretion, toxicity) properties early in development, reducing late-stage losses.

We propose a five-stage pipeline where AI augments, rather than automates, critical transitions across the drug design and development (DDD) continuum.



The workflow begins with *in silico* screening (Stage **A**): lead compounds undergo rapid triage using platforms like PASS [1] for pharmacological activity prediction, SwissADME [2] for pharmacokinetic profiling, and GUSAR for preliminary toxicity estimation. These computational outputs generate multidimensional datasets far exceeding manual analysis capacity. Stage **B** applies machine learning to synthesize these *in silico* results, identifying non-obvious structure-activity relationships and prioritizing compounds with optimal predicted pharmacodynamics. Crucially, AI does not make final selections—it flags high-potential candidates and quantifies uncertainty margins for expert review.

This AI-refined shortlist directly informs Stage **C**: the design of targeted in vitro experiments. Instead of broad phenotypic screening, researchers validate only the highest-probability mechanisms suggested by the model, reducing experimental waste by an estimated 40–60% in pilot studies. Stage **D** extends this logic to in vivo planning: AI correlates *in silico* and *in vitro* outcomes with historical animal model data to recommend species, dosing regimens, and endpoints most likely to yield translatable results—while flagging compounds with predicted species-specific toxicity risks.

Finally, Stage **E** addresses formulation science: generative models propose excipient combinations and delivery matrices optimized for the lead compound's physicochemical properties, stability

requirements, and target tissue bioavailability. Each stage maintains a closed feedback loop—experimental results continuously retrain models, improving predictive accuracy for subsequent iterations.

However, AI's utility remains bounded by data quality, algorithmic transparency, and biological context. Models trained on biased or sparse datasets risk propagating errors, while "black box" decision-making complicates regulatory acceptance. Crucially, AI cannot interpret clinical nuance or ethical implications—tasks demanding human judgment. Our analysis, therefore, positions AI as a force multiplier: it excels at pattern recognition across vast datasets and iterative hypothesis generation, but requires pharmacologists, medicinal chemists, and clinicians to validate outputs, design experiments, and contextualize findings within the realities of therapeutic applications. We further discuss practical implementation challenges: data standardization, interdisciplinary team formation, and evolving regulatory pathways for AI-assisted therapeutics.

In conclusion, AI represents a paradigm shift in how we approach DDD—not what we discover. Its greatest promise lies in accelerating hypothesis generation, prioritizing high-value experiments, and reallocating human expertise toward higher-order scientific reasoning. For academia and industry alike, the imperative is not to chase AI for its own sake, but to integrate it thoughtfully as one instrument among many in the researcher's toolkit. As we navigate this transition, maintaining scientific rigor, transparency, and human oversight will determine whether AI fulfills its potential to deliver safer, more effective medicines to patients faster—without compromising the foundational principles of pharmaceutical science

References

[1] Lagunin A, Stepanchikova A, Filimonov D, Poroikov V. (2000). Bioinformatics, 16(8), 747–748; DOI 10.1093/bioinformatics/16.8.747
[2] Daina A, Michielin O, & Zoete V. (2017). Scientific Reports, 7, 42717; DOI 10.1038/srep42717ES

POSTER PRESENTATIONS

PP–1. BIOLOGICALLY ACTIVE POLYETHYLENE GLYCOL (PEG)-BASED MULTI-CATECHOL-CONTAINING BIOPOLYMER FROM MEDICINAL PLANTS OF THE BORAGINACEAE FAMILY

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Within our ongoing search for biologically active biopolymers in plant species belonging to different genera of the Boraginaceae family, the present study aimed to isolate water-soluble high-molecular-weight mucilage fractions (HMFs) (Mr > 500 kDa) to study the main chemical constituents of HMFs and carry out their structure elucidation.

The HMFs mucilaginous water extracts of medicinal plants *Symphytum asperum* (SA), *S. caucasicum* (SC), *S. grandiflorum* (SG), *S. officinale* (SO), *Anchusa italica* (AI), *Cynoglossum officinale* (CO), *Borago officinalis* (BO), *Paracynoglossum imeretinum* (PI), and *Trachistemon orientalis* (TO) (Boraginaceae family) were fractionated by ultrafiltration with membrane filters of 500 kDa cut-off to remove inactive ballast polysaccharides, yielding water-soluble HMFs.

Based on the data from various NMR spectroscopy techniques, including ^{1}H NMR, ^{13}C NMR, and 2D ^{1}H/^{13}C HSQC spectra, the primary chemical component of HMFs from the plants SA, SC, SO, CO, and PI was identified as a caffeic acid-derived polymer, specifically poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene], also known as poly[3-(3,4-dihydroxyphenyl)glyceryl acid] (P-DGA) (Fig. 1, 2, Table 1). Thus, the polyethylene glycol (PEG) chain forms the backbone of this biopolymer, with a residue of 3-(3,4-dihydroxyphenyl)glyceric acid as the repeating unit (Fig 1).

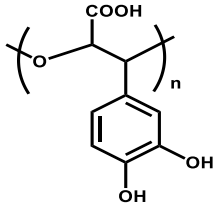
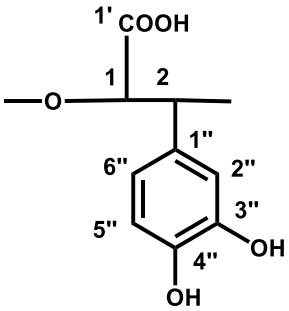


Fig. 1. Poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene], that is poly[3-(3,4-dihydroxyphenyl)glyceric acid] (P-DGA).

Table 1. The total assignments of the signals of the 13C and 1H NMR spectra of P- DGA from SA, SC, SO, CO, and **PI.**



The repeating unit of **P-DGA**

C atom no.	^{13}C chemical shift, δ_C, ppm	^{1}H chemical shift, δ_H, ppm
1'	175.0	
1	77.5	5.7
2	79.6	5.1
1''	130.7	
2''	116.6	7.6
3''	143.9	
4''	143.0	
5''	117.8	7.5
6''	121.5	7.5

3,4-Dihydroxyphenyl (catechol group) (Fig. 2) and carboxyl groups are common substituents at two carbon atoms in the chain. Its basic monomer, glyceric acid, is a natural three-carbon sugar acid, which

is an oxidation product of the simplest common aldehyde, glyceraldehyde. P-DGA represents a new class of natural polyethers.

P-DGA, as a multi-functionalized poly(2,3-glyceric acid ether), belongs to a rare class of carbohydrate-based biopolymers with attached catechol groups (Fig. 2).

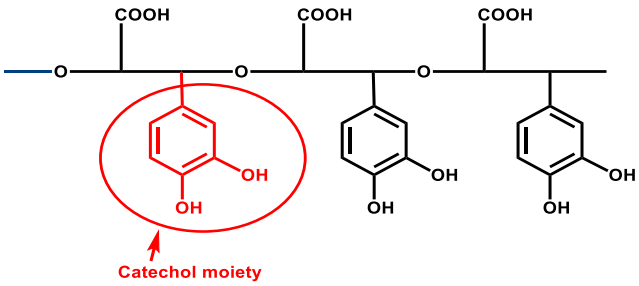
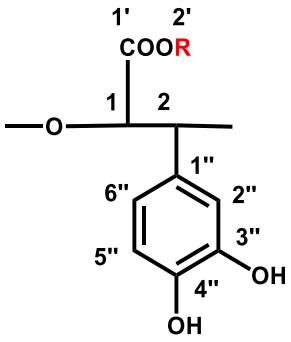


Fig. 2. Catechol moieties and carboxyl groups are regular substituents attached to two carbon atoms in the **PEG** backbone of P-DGA.

Additionally, based on data from ^{1}H NMR, ^{13}C NMR, and 2D $^{1}H/^{13}C$ HSQC spectra, the primary chemical component of HMFs from SG, AI, BO, and TO is also P-DGA, however some of its carboxylic groups are methylated (Table 2, Fig. 3).

Table 2. The total assignments of the signals of the ^{13}C and ^{1}H NMR spectra of P- DGA from SG, AI, BO, and TO.



The repeating unit of **P-DGA; R=H, CH_3**

C atom no.	^{13}C chemical shift, δ_C, ppm	^{1}H chemical shift, δ_H, ppm
1' (R=H)	175.5 (-COOH)	
1' (R=CH_3)	173.0 (-COOCH$_3$)	
2' (R=CH_3)	51.9 (-OCH$_3$)	3.7 (-OCH$_3$)
1	79.8	5.6
2	81.8	5.0
1''	132.9	
2''	118.9	7.5
3''	146.2	
4''	145.2	
5''	120.1	7.4
6''	123.8	7.4

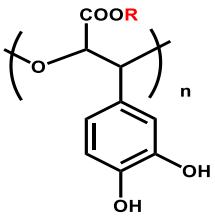


Fig. 3. Poly[3-(3,4-dihydroxyphenyl)glyceric acid] (P-DGA, R=H, CH_3).

Thus, the PEG main chain forms the backbone of P-DGA, with catechol moieties covalently attached as regular substituents. As a result, this macromolecule is a naturally PEGylated, multi-catechol-containing biopolymer with a wide range of biological activity.

PP–2. INVESTIGATION OF F-METALS TETRAOXOARSENATE(V) COORDINATION COMPOUNDS OF N-SALICYLIDENE ANILINE FOR MEDICAL APPLICATIONS

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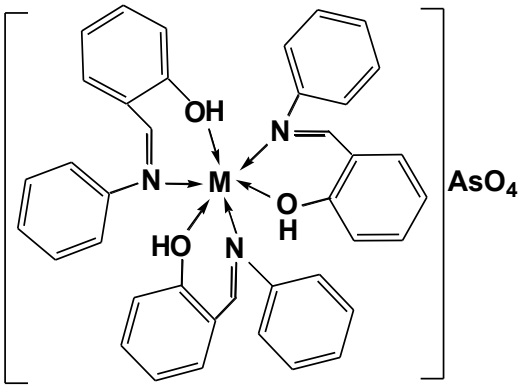
In the human body, metals exist predominantly in the form of coordination compounds. The presence or excess of some of them leads to disruption of normal physiological and biochemical processes and the development of various diseases. Therefore, even in previous centuries, the opinion was expressed that knowledge of influence of coordination compounds on biosystems and understanding of their mechanisms of action would play a major role in the search for effective medicines based on coordination compounds.

The development of research in this regard laid the foundation for the study and discovery of precisely such medicinal products as anticarcinogenic platinum complexes, copper and gold coordination compounds with anti-inflammatory properties, effective anemia treatment agents based on iron and zinc coordination compounds, etc. The wide range of complex-forming metals, as well as of ligands provides great opportunities for the development of research in the field of coordination compounds. In this regard, pnictogens–elements of the main subgroup of group V of the periodic table provide almost inexhaustible opportunities. Also, schiff base ligands contain N, O donor atoms chelated with metal ions forms stable complexes. The use of these products is promising for biological, analytical, industrial and medical purposes [1-3].

Based on the above, the objective of this research was to synthesize coordination compounds of tetraoxoarsenates(V) of Dy(III), Ho(III), Er(III), and Tm(III) metals ions of the N-salicylidene aniline (L) derived by condensation of aniline with salicylaldehyde.



Scheme. The chelation mode of N-salicylidene aniline with Dy(III), Ho(III), Er(III), and Tm(III) metals ions

The prolate-shaped N-salicylidene anilines are employed in a wide range of scientific, technological, industrial domains and possess mesomorphism that have photochromic properties. Complexation of N-salicylidene aniline with some metals initiates a modification of the geometric structure of the molecule and exhibit smectic mesomorphism.

The starting material for the planned research was also sodium arsenate, distinguished by its physiological activity, was obtained by the hydrochemical method–by neutralizing (NaOH) the oxidation product of arsenic (III) oxide, arsonic acid.

The composition and structure of coordination compounds of tetraoxoarsenates(V) of Dy(III), Ho(III), Er(III), and Tm(III) metals ions based on the N-salicylidene aniline have been studied using physico-chemical research methods. The chelation of oxygen, nitrogen of **L** has been shown through the complexation process with used metals ions which supported by spectroscopic data. The data supported also the octahedral geometry formed by the ligands. Thermal analysis studies also served to assess the stability of the compounds.

References:

[1] Zhang, N., Ayral-Kaloustian, S., Nguyen, T., Hernandez, R., Beyer, C. 2007, 2-Cyanoamino-pyrimidines as a class of antitumor agents that promote tubulin polymerization. Bioorg. Med. Chem. Lett., 17, pp. 3003-3005.

[2] Khan, S.A., Asiri, A.M., Al-Amry, K., Malik, M.A. 2014, Synthesis, Characterization, Electrochemical Studies, and In Vitro Antibacterial Activity of Novel Thiosemicarbazone and Its Cu(II), Ni(II), and Co(II) Complexes, Sci. World J., 1, 592375.

[3] Ma, D.Y., Zhang, L.X., Rao, X.Y., Wu, T.L., Li, D.H., Xie, X.Q., Guo, H.F., Qin, L. 2013, Structures, luminescence, and antibacterial studies of two transition metal complexes involving Schiff bases. J. Coord. Chem., vol. 66, no. 18, pp. 3261-3271.

PP–3. SYNTHESIS AND STUDY OF DIFFERENT-LIGAND CHELATES

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Microelements play an important role in human health status preservation. At that, it has been established that the chelate form of microelements is the most advantageous one for filling their deficiency in organism. Amino acids and oxy-acids are the most frequently used as chelating ligands.[1] Taking this circumstance into account, we developed the method and synthesized glycine (Gl) and tartaric acid (Tr) containing manganese, zinc and iron tartrates with molar ratios 1:1:1 and 1:2:1. Some physical and chemical characteristics of the synthesized chelates have been established (Table 1).

Table 1. Some physical and chemical characteristics of glycine containing metal tartrates

#	Compound formula	Mol Mass g/mol	Melting t 0_C	Humidity B (%)	Solubility				Conductometric Survey Results	
					Water	Alcohol	Acetone	DMSO *	Dissociation constant pKa	Coeff. of determination R^2
1	$[Mn{\cdot}Gl{\cdot}Tr]{\cdot}2H_2O$	314.94	230	1.12	+	sl. sol.	sl. sol.	sl. sol.	1.24	0.84
2	$[Mn{\cdot}Gl_2{\cdot}Tr]{\cdot}2H_2O$	390.02	218	1.17	+	sl. sol.	sl. sol.	sl. sol.	2.13	0.92
3	$[Zn{\cdot}Gl{\cdot}Tr]{\cdot}H_2O$	307.17	200	0.46	+	-	-	-	1.29	0.79
4	$[Zn{\cdot}Gl_2{\cdot}Tr]{\cdot}H_2O$	382.24	175	0.95	+	-	-	-	2.17	0.81
5	$[Fe{\cdot}Gl{\cdot}Tr]{\cdot}3H_2O$	333.92	198	0.85	+	-	-	-	1.61	0.73
6	$[Fe{\cdot}Gl_2{\cdot}Tr]{\cdot}H_2O$	372.92	216	0.89	+	-	-	-	1.51	0.75

+ Soluble, - Insoluble, sl.sol - Slightly soluble, DMSO- Dimethylsulfoxide

The identity of the compounds was determined by the diffractometric method. X-ray diffractometer studies were carried out using a DRON-4.07 with Cukα (λ=0.154184 nm) irradiation. The identity of the compounds was also determined by measuring the melting point using a melting point determination device–Melting Point /SMP10/.

Qualitative solubility has been determined in water, alcohol, acetone and dimethylsulfoxide. Conductometric study has been conducted on the device Ph and Conductivity Sensor LE703. Humidity (B) has been established using the analyser AXIS ADGS50.

Biological activity of the synthesized compounds has been studied.[2] For this purpose, the chelate mixtures for 100 kg broiler combined feed have been prepared. According to the zootechnical analogy principle, 20 broilers each have been selected for two test and one control groups. Experiments lasted one month. During a test, bird's live weight has been studied in the beginning and the end of the test. (Table 2). Birds' survival rate has been established as well (Table 3).

Table 2. Live weight change (in grams) during a test

Group	Beginning of the test			End of the test		
	Min	Max	M±m	Min	Max	M±m
Control	1415	1610	1513±65	1430	1620	1525±95
Xnorm	1470	1620	1545±75	1520	1680	1600±80
Xmax	1560	1745	1653±92.5	1550	1660	1605±55

Table 3. Bird's survival rate during a test

Group	Number of birds (wing)		Survival rate %
	Beginning of the test	End of the test	
Control	20	14	75
Xnorm	20	17	90
Xmax	20	20	100

According to experiments carried out in order to study biological activity, it has been established that entry of mixture of microelements' chelates into composition of broilers' combined feed premixes has had a positive effect on live weight gain and bird's survival rate.

Reference:

[1] Hertrampf, E., Olivares M., 2004. Iron Amino Acid Chelates. *International Journal for Vitamin and Nutrition Research*, vol 74, no.6, pp. 435–443, https://econtent.hogrefe.com/doi/epdf/10.1024/0300-9831.74.6.435

[2] Jian S. A., Dasen L. B.,Rubin S, 2015, Supplemental Dietary Iron Glycine Modifies Growth, Immune Function and Antioxidant Enzyme Activities in Broiler Chickens. *Livestock Science* vol.176, pp.129–134, https://www.sciencedirect.com/science/article/abs/pii/S1871141315001328

PP–4. FUNGICIDALLY ACTIVE FRACTION OF *PUERARIA HIRSUTA* ROOT

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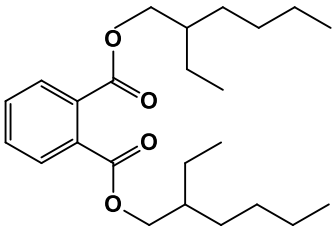
Continuing the study of the chemical components of *Pueraria hirsuta* (Thunb.) Matsum. roots, collected from the Black Sea coast of Georgia [1, 2], a lipophilic fraction with antifungal activity was isolated. Fungicidal efficacy *in vitro* was assessed on *Candida albicans* cells using microdilution method [3]. The results of the biological experiment are presented in Table 1.

Table 1. Fungicidal activity of the lipophilic fraction from the *Pueraria hirsuta* roots against *Candida albicans*

	IC_{50} μg/ml
Fraction	25 ± 3
Amphotericin B	0.8 ± 0.1

GC-MS analysis of the active fraction revealed the presence of some saturated acids, higher fatty alcohols, alkanes, and phthalic acid derivative–bis(2-ethylhexyl)phthalate with predominant content. Multiple chromatography of the active fraction on silica gel column yielded a pale yellowish, viscous, oily liquid with a faint characteristic odour–compound 1. Based on the results of IR, UV, Mass, ^{1}H and ^{13}C spectroscopic analyses and comparison of the obtained data with literature [4, 5], compound 1 was identified as bis(2-ethylhexyl)phthalate or di(2-ethylhexyl)phthalate (Scheme 1).



Scheme 1. Bis(2-ethylhexyl)phthalate

Phthalates, contained in some plants, are not used in industrial production, that proves their formation by biosynthetic pathways and excludes their entry into the body from contaminated soil or air [6]. Many recent studies confirm that living organisms are also capable of biosynthesizing phthalic acid and its esters. Microorganisms and algae are particularly notable in this regard. Endophytes inhabit the roots and leaves of species of the Fabaceae family, including species of the genus Pueraria [7]. Interactions between endophytes and plants are species-specific. They synthesize a variety of biologically active metabolites, including antifungal substances [8]. Phthalic acid esters have been described from various organs of species of the legume family [6]. Analyzing these data, one can come to the logical conclusion that the biosynthesis of phthalates in plants, including species of Pueraria, and also the studied species, is quite possibly carried out by their endophytes. Bis(2-ethylhexyl)phthalate has a fungicidal effect against *Candida albicans* [5]. This can explain the biological activity of the fraction isolated from the roots of *Pueraria hirsuta* (Thunb.) Matsum.

Some phthalates, such as phthalic acid and di-6-octyl phthalate, are compounds with allelochemical properties [6]. *Pueraria hirsuta* (Thunb.) Matsum. is not a native species of Georgian flora. The mild climate of the Black Sea coast of Western Georgia proved favorable; the plant quickly outgrew the boundaries of the botanical garden, spread, and covered a large area, from which it effectively displaced previously existing species [1]. Among all the possible mechanisms of invasion of Pueraria species, the allelopathic, fungicidal, and insecticidal actions of some secondary metabolites (xanthoxins, isoflavonoids, phenylpropanoids) have been proposed [9]. One of the mechanisms underlying *Pueraria hirsuta*'s dominance along the Black Sea coast may be is the presence of bis(2-ethylhexyl) phthalate in its roots. Its release into the rhizosphere, controls the growth and spread of neighboring plants. Bis(2-ethylhexyl) phthalate has been isolated and characterized from the roots of *Pueraria hirsuta* (Thunb.) Matsum. for the first time.

References:

[1] Kavtaradze, NSh. Alaniya, MD. Getia, MZ. Gogitidze, NM. Mushkiashvili, NI. Mulkijanyan, KG. Mskhiladze, LV. Kemertelidze, EP. 2022, Isoflavonoids from roots of Pueraria hirsuta distributed in Georgia and their hepatoprotective activity, Chem. Nat. Compd., vol. 58, pp. 27-31.

[2] Kavtaradze, N. Getia, M. Pichette, A. Legault, J. Mshvildadze, V. 2025, Isoflavonoid bioside from roots of Pueraria hirsuta, Chem. Nat. Compd., vol. 61, pp. 443-446
[3] Korkotadze, T. St-Gelais, A. Berashvili, D. Getia, M. Pichette, A. Legault, J. Sok-Siya Bun-Llopet, Kemoklidze, Z. Mshvildadze, V. 2025, Phytochemical Characterization and In Vitro Assessment of Cytotoxic, Antioxidant, Anti-Inflammatory and Antibacteria Activities of Abies nordmanniana (Stev.) Spach Essential Oil, Grown in Georgia, Journal of Essential Oil Bearing Plants, vol. 28, no. 4, pp. 806-817.
[4] Osama El-Sayed, H. Mohsen Asker, MS. Seham Shash, M. Shimaa Hamed, R. 2015, Isolation, structure elucidation and biological activity of di-(2-ethylhexyl) phthalate produced by Penicillium janthinellum 62, International Journal of ChemTech Research, vol. 8, no. 1, pp. 58-66.
[5] Lotfy, MM. Hassana, HM. Hetta, MH. El-Gendy, AO. Mohammed, R. 2018, Di-(2-ethylhexyl) Phthalate, a major bioactive metabolite with antimicrobial and cytotoxic activity isolated from River Nile derived fungus *Aspergillus awamori*, Beni-Suef University Journal of Basic and Applied Sciences, vol. 7, no. 3, pp. 263-269.
[6] Huang, L. Zhu, X. Zhou, S. Cheng, Z. Shi, K. Zhang, C. Shao, H. 2021, Phthalic acid esters: natural sources and biological activities, Toxins, vol. 13, 495.
[7] Shahrtash, M. Brown, ShP. 2020, Diversity, drivers of foliar fungal endophytic communities of kudzu (*Pueraria montana* var. lobata) in the southeast United States, vol. 12, no. 5, 185.
[8] Gouda, S. Das, G. Sen, SK. Shin, H-S. Patra, JK. 2016, Endophytes: A treasure house of bioactive compounds of medicinal importance, Front. Microbiol. vol. 7, 1538.
[9] Kato-Noguchi, H. 2023, The impact and invasive mechanisms of *Pueraria montana* var. lobata, one of the world's worst alien species, Plants, vol. 12, no.17, 3066.

PP–5. SYNTHESIS AND QUANTUM-CHEMICAL ASPECTS OF THE HYDRIDE ADDITION REACTION OF α,ω-BIS(TRIMETHYLSILOXY)METHYLHYDRIDOSILOXANE WITH TRIETHOXYMETHACRYLOXYSILANE

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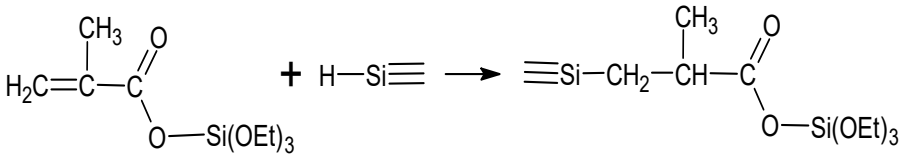
The present study investigates the addition reaction of α,ω-bis(trimethylsiloxy) methylhydridosiloxane with triethoxymethacryloxy silane, utilising density functional theory (DFT). In this study, two possible variants of the bimolecular reaction were considered in accordance with the principles set out by Markovnikov and the Anti-Markovnikov rule 1,2.

For the first time, we discussed a variant of the Farmer's rule.



The dependence of the system energy change (ΔH) on the distance between atoms is shown in Fig.1.

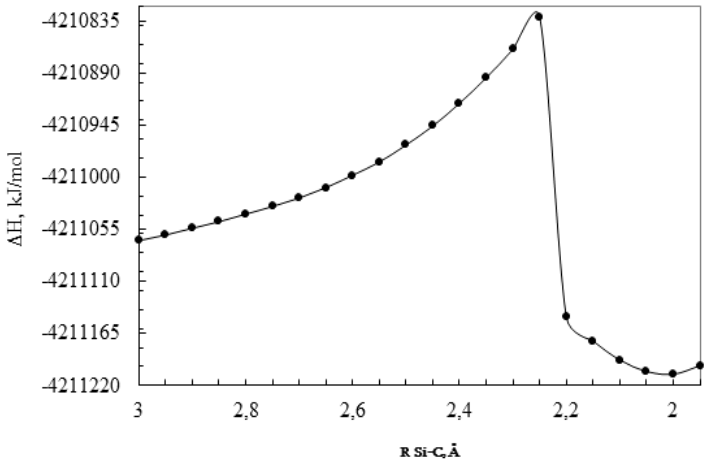
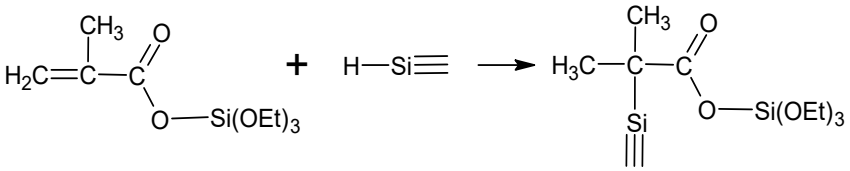


Figure 1. Dependence of system energy change (ΔH) on distance between silicon and carbon atoms $\mathbf{R_{Si-C_1}}$.

Activation energy ΔE*= -236 kJ/mol, and reaction heat effect ΔE= -141. As we can see, the reaction is exothermic.

The second time we discussed the variant of Markovnikov's rule.



The dependence of the system energy change (ΔH) on the distance between atoms is shown in Fig.2.

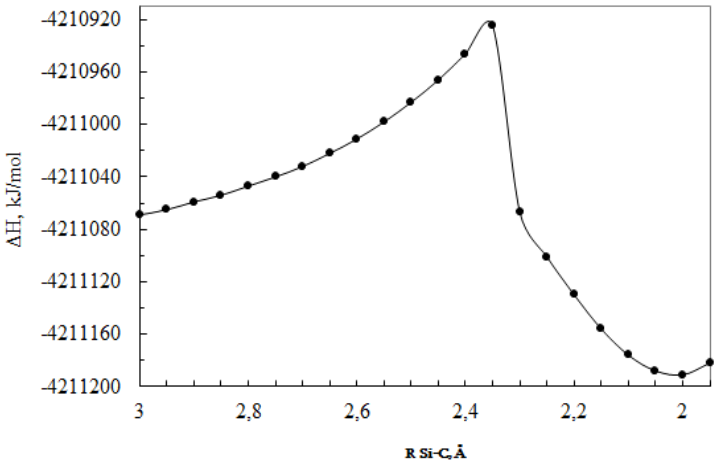


Figure 2. Dependence of system energy change (ΔH) on distance between silicon and carbon atoms R_{Si-C_2}.

Activation energy ΔE*= -113 kJ/mol, and reaction heat effect ΔE= -144 kJ/mol. As can be observed, the reaction is exothermic.

A comparison of the activation energies and heat effects of the reaction indicates that the experiment between α,ω-bis(trimethylsiloxy)methylhydridsiloxane and triethoxymethacryloxysilane is energetically more favourable with the second scheme 3-5. The structure of the synthesised oligomer was confirmed through a combination of analytical techniques, including functional and elemental analysis, as well as infrared IR, proton 1H and carbon 13C NMR spectral data. The order of the hydrosilylation reaction, the rate constants, and the activation energy are determined. The present study utilised DSC, HPLC and wide-angle X-ray methods to investigate the synthesised oligomers. The outcomes demonstrated that the synthesised oligomers are single-phase amorphous systems with a

chain spacing value of d1 ≈ 8.63-8.65 Å. The obtained oligomers are transparent products that are well soluble in common organic solvents (HSP > 0.04). In order to establish the truth, it is necessary to conduct a simple experiment and use more complete non-empirical methods of quantum-chemical calculations.

References:

[1] Laikov D.N., Ustynyuk Yu. A. PRIRODA-04: a quantum-chemical program suite. New possibilities in the study of molecular systems enabled by parallel computing. Russ. Chem. Bull. Int. Ed., 2005, 54, 820-826.
[2] Chikovani, Z. Pachulia, M. Merlani, V. Barbakadze -The Quantum-Chemical Modelling of Synthesis of some Phenylgycidates. Bull. Georg. Natl. Acad. Sci, 2015
[3] Zurab Pachulia, Nana Pirtskheliani „Quantum-Chemical Modelling and Physico-Chemical Research of the Hydride Addition Reaction of α,ω-bis(Trimethylsiloxy)methylhydridsiloxane with Trimethylacryloxysilane“, Apple Academic Press, Publishing quality books in STEM and other fields, Advanced Topics in Polymer Chemistry and Materials Science, Current Strategies and Future Prospects of Nanomedicine. Editors: Tamara Tatrishvili, PhD, Marc Jean Médard Abadie, PhD; 2025, Chapter 27, pp. 351-362.
[4] Omar Mukbaniani, Tamara Tatrishvili, Zurab Pachulia, Levan Londaridze, Nana Pirtskheliani. Quantum-Chemical Modelling of Hydrosilylation Reaction of Triethoxysilane to Divinylbenzene. Chem. Chem. Technol., 2022, Vol. 16, No. 4, pp. 499–506. https://doi.org/10.23939/chcht16.04.499
[5] Mukbaniani O., Pirtskheliani N., Tatrishvili T. „Hydrosilylation Reactions of Methylhydridesiloxane to Trimethylsilylated and Triethoxysilylated“, Modification Reactions of Oligomethylhydridesiloxanes, Nova Science Publishers, Inc., New York, Chapter 3, 2007, pp. 37-56.

PP–6. LANDSCAPE SIGNIFICANCE OF MEDICINAL-AROMATIC PLANTS IN ARTVIN, TÜRKİYE

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The flora of Türkiye comprises 10.460 species, 2.066 subspecies, 888 varieties, and 287 hybrids. Of the approximately 12.000 plant taxa that occur naturally in Türkiye, scientific studies have identified 1.400 taxa with medicinal and aromatic properties; of these, 850 taxa (60%) are naturally distributed in Artvin. Moreover, of the 500 plant speciesused for medicinal–aromatic purposes and subject to trade in Türkiye, 350 species (70%) occur naturally in Artvin [1–4].

Artvin is located both within the “Caucasus– Anatolian–Hyrcanian Temperate Forests”, one of the 200 ecoregions of global conservation priority, and within the “North-eastern Anatolia Plant Diversity Centre” [5].

The province of Artvin, with its wide variety of habitats, an altitudinal gradient of approximately 4000 m, the influence of three different climate types (Mediterranean, continental and oceanic), abundant water resources, and geological and geomorphological heterogeneity, provides suitable conditions for the occurrence of a great number of different plant species. With a total of 2.727 native vascular plant taxa belonging to 137 families and 761 genera, Artvin is the richest province of Turkey in terms of vascular plant diversity. Of these, 198 taxa are endemic and 302 are non-endemic but rare, so that a total of 500 taxa are considered to be under threat [5].

Medicinal-aromatic plants constitute not only an important raw material source for the pharmaceutical industry but also play a significant role in landscape design due to their aesthetic, ecological, functional, and economic values [6-7].

Considering the 850 medicinal- aromatic plant taxa naturally distributed in Artvin, habitat classification was conducted according to the main EUNIS habitat groups. The results indicated that the highest number of records was observed in EUNIS H (rocky and stony habitats) with 606 records. This was followed by EUNIS D/C (wetlands and riparian habitats) with 276 records. A total of 203 records were identified in EUNIS F (shrublands and pseudomaki habitats), 134 records in EUNIS E (grasslands and

pastures), 47 records in EUNIS G (forest and forest understory habitats), and 19 records in EUNIS E/H (alpine and subalpine habitats). The total number of habitat records exceeds the total number of taxa, as some species occur in more than one habitat type.

Analysis of life forms has revealed that most species are perennial herbaceous plants (546 species). Woody species (trees and shrubs) rank second with 154 species, while annual and biennial herbaceous species are represented by 112 species. Perennial creeping/ground-covering herbaceous species are represented by 17 taxa, while climbing/creeping/ground-covering species are represented by 21 taxa.

Additionally, the phytogeographical distributions, endemism status, and IUCN risk categories of the species were evaluated.

When medicinal-aromatic plant species are evaluated using the AHP (Analytic Hierarchy Process) method, it is anticipated that species with high landscape potential can be identified. Perennial herbaceous medicinal and aromatic plants, which are concentrated in open and semi-natural habitats, are considered to be among the species groups that can be prioritized in landscape designs due to their ability to provide aesthetic continuity, their high ecological adaptation capacity, and their low maintenance requirements.

References

[1] Özhatay FN, Kültür Ş, Gürdal B (2022). Check-list of additional taxa to the supplement of flora of Turkey X. Istanbul Journal of Pharmacy 52(2), 226-249.
[2] Eminağaoğlu Ö, Akyıldırım Beğen H (2023). Tıbbi-Aromatik Bitkiler Hakkında Genel Bilgiler. In: Eminağaoğlu Ö (Ed), Artvin'in Tıbbi-Aromatik Bitkileri, Artvin: Zafer press.
[3] Eminağaoğlu Ö, Yalçın E, Özkaya MS (2022). Forest vegetation of the Beşpare ecovillages in the western lesser Caucasus corridor (Artvin/Türkiye). Rendiconti Lincei. Scienze Fisiche e Naturali 33: 739–756.
[4] Eminağaoğlu, Ö. (ed.) 2023, Artvin'in Tıbbi-Aromatik Bitkileri (Medicinal-Aromatic Plants of Artvin), Artvin: Zafer press.
[5] Eminağaoğlu, Ö. (ed.) 2015, Artvin'in Doğal Bitkileri (Native Plants of Artvin), İstanbul: Promat, 456.
[6] Faydaoğlu, E., Sürücüoğlu, M. (2011). Geçmişten günümüze tıbbi ve aromatik bitkilerin kullanılması ve ekonomik önemi. Kastamonu Üniversitesi Orman Fakültesi Dergisi, 11 (1), 52-67.
[7] Karaşah, B. (2025). Koku Bahçelerinde Değerlendirilebilecek Bazı Tıbbi ve Aromatik Bitkiler ve Sağladıkları Ekosistem Hizmetleri. Bahçe, 54(Özel Sayı 1), 419-428.ES

PP–7. CHEMICAL AND BIOLOGICAL EVALUATION OF PINUS SYLVESTRIS L. (P. SOSNOWSKYI NAKAI) NEEDLES ESSENTIAL OIL FROM GEORGIA

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Introduction. The Pinaceae family is one of the most diverse and pharmaceutically valuable groups of medicinal plants. In traditional medicine, its members are used as antiseptics, tonics, expectorants, and treatments for rheumatic pain and skin diseases. Numerous studies on the pharmacological activities of pine (Pinus) species have demonstrated their antioxidant, antiviral, analgesic, cytotoxic, antimicrobial, and anti-inflammatory properties [1,3,5].

Pinus sylvestris L. is one of the most widespread and ecologically significant species of the pine family [2]. It typically reaches a height of 20-35 m and is a pyramidal or conical shaped tree. The needles occur in pairs and are elongated, measuring on average 3-7 cm in length and 1.5-2 mm in width [2]. Its natural distribution extends from Northern Europe to the mountainous regions of Central Asia [4].

The aim of the study. Needles of Pinus sylvestris were collected during the 2024 growing season from three sites in the Kartli Floristic Region of Georgia at elevations of 489, 900, and 1700 m above sea

level. The study aimed to evaluate the chemical composition and biological activities of essential oils extracted from the needles.

Research methods. Essential oils were obtained by hydrodistillation for two hours using a Clevenger type apparatus. Their chemical composition was analyzed by Gas Chromatography-Mass Spectrometry (GC-MS), with mass spectra recorded in scan mode at 70 eV.

The anti-inflammatory activity was evaluated in vitro by measuring the inhibition of nitric oxide (NO) production, with N-nitro-L-arginine methyl ester hydrochloride (L-NAME) serving as a positive control. Cytotoxic effects were determined using Hoechst and Resazurin assays on three cell lines-A-549, DLD-1, and WS1-using daunorubicin as a reference compound.

Results: The essential oils of P. sylvestris needles collected at different altitudes above sea level contained α-pinene, germacrene D, and caryophyllene as the predominant constituents. In addition, β-pinene (13.57%) was a major component of the oil obtained from needles collected at 1700 m. The essential oils from needles collected at 900 m and 1700 m exhibited moderate inhibitory activity against lung carcinoma (A-549) and rectal adenocarcinoma (DLD-1) cells in the Hoechst assay. Furthermore, the essential oils demonstrated notable anti-inflammatory activity by inhibiting nitric oxide (NO) production. At 160 µg/ml, oils from needles collected at 900 m and 489 m inhibited NO production by 98% and 91%, respectively, while the oil from needles collected at 1700 m inhibited NO production by 69% at a lower concentration of 80 µg/ml.

Conclusion: The essential oils of Pinus sylvestris needles from Georgia exhibited a rich chemical composition, with α-pinene, germacrene D, and caryophyllene as the dominant constituents, and β-pinene notably present in the high-altitude (1700 m) sample. The oils demonstrated moderate cytotoxic activity against A-549 and DLD-1 cancer cell lines. Importantly, they exhibited strong anti-inflammatory activity, with significant inhibition of nitric oxide production. These findings highlight the pharmacological potential of P. sylvestris needle essential oil as a source of bioactive compounds with anti-inflammatory, and selective cytotoxic properties.

References

[1] Elcocks, E. R., Spencer-Phillips, P. T. N. and Adukwu, E. C. 2020, Rapid bactericidal effect of cinnamon bark essential oil against Pseudomonas aeruginosa. Journal of Applied Microbiology, vol. 128, no. 4, pp.1025–1037.

[2] Ergül Bozkurt, A., Coşkunçelebi, K. and Terziog˘lu, S. 2021, Population variability of scots pine (Pinus sylvestris L.) in Turkey according to the needle morphology, Šumarski list, vol. 145 no. 7–8, pp.347–354.

[3] Hassan, W., Rehman, S., Noreen, H., Gul, S., Neelofar, N. and Ali, N. 2016, Gas Chromatography Mass Spectrometric (GCMS) Analysis of Essential Oils of Medicinal Plants, Advances in Animal and Veterinary Sciences, vol. 4, no. 8, pp.420–437.

[4] Nassonova, E., Vasileva, Yu., Prishnivskaya, Ya. and Zhulanov, A. 2019, Molecular-Genetic Identification and Analysis of Pinus sylvestris L. Populations in Kirov Oblast and Perm Krai., Bulletin of Science and Practice, vol. 5, no. 4, pp.47–57.

[5] Sharifan, A., Etebari, M., Zolfaghari, B. and Aliomrani, M. 2021, Investigating the effects of bark extract and volatile oil of Pinus eldarica against cisplatin-induced genotoxicity on HUVECs cell line, Toxicology Research, vol. 10, no. 2, pp.223–231.

PP–8. IRON OXIDE NANOPARTICLE–BASED HYPERTHERMIA FOR MODULATION OF THE TUMOR MICROENVIRONMENT

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Background: In recent years, nanotechnology has introduced new horizons in oncology. Among them, Iron oxide nanoparticles (IONPs), also known as ferromagnetic or magnetic nanoparticles (MNPs), are of particular interest because they can generate localized heat and serve as drug-delivery vehicles. Beyond using IONP hyperthermia as a cancer treatment in combination with radiation, chemotherapy, and immunotherapy, researchers are investigating how localized heating can modify the tumor microenvironment.

Objective: The primary objective of this paper is to assess the feasibility of using IONP hyperthermia as a triggering mechanism to modify the tumor microenvironment and thereby enhance drug delivery and nanoparticle uptake in cancer cells. In this work, we modeled IONP-induced hyperthermia, including temperature rise and spatial distribution, using a realistic mouse model under alternating magnetic field exposure, and assessed the effects of IONP on Ehrlich carcinoma growth and survival in BALB/c mice.

Methodology: Temperature rise was modeled in a realistic 12-week-old mouse model using the bioheat equation at 151 kHz for two IONP dosages (2 mg and 4 mg) within a 1 cm^3 tumor. The mouse was positioned inside a 10-cm-diameter, 10-turn coil. Magnetic and electric fields, used to evaluate eddy-current effects, were calculated analytically. Temperature increases due to both eddy currents and IONP heating were quantified.

In parallel, Ehrlich carcinoma–bearing laboratory mice were divided into two groups: G4 (experimental) and G5 (control). On day 21 of tumor growth, mice in group G4 received an IONP inoculation without an external alternating magnetic field at a dose of 4 mg per 1 cm^3 tumor volume. Tumor volume and survival were monitored over 53 days, and survival was analyzed using the Kaplan–Meier method.

Results: Temperature modeling demonstrated that therapeutic tumor temperatures (42–43 °C) can be achieved without harming surrounding tissues, with heating patterns dependent on tumor size, tissue properties, nanoparticle concentration, and applied alternating magnetic field. In vivo studies showed no significant difference in tumor volume between groups at day 21 ($p=0.857$). Following magnetic nanoparticle inoculation, transient tumor growth suppression was observed, although differences in tumor volume were not statistically significant at day 34 ($p=0.587$). Survival analysis revealed a significant extension in lifespan for treated mice compared with controls (mean survival 47.7 vs. 39.1 days; $p < 0.01$), with treated animals maintaining 100% survival until day 36.

Conclusion: Numerical modeling indicates that iron oxide nanoparticle (IONP) hyperthermia can deliver localized heating to the tumor region with minimal thermal spread to surrounding tissues; however, additional experimental and computational studies are needed to optimize hyperthermia protocols and to correlate modeled temperature distributions with tumor microenvironment changes. Experimental results demonstrate that intratumoral inoculation of IONP inhibits Ehrlich carcinoma progression and significantly prolongs survival in BALB/c mice, although post-treatment tumor volume differences were modest and influenced by selective mortality. Further histopathological and molecular analyses, along with integrated magnetic hyperthermia studies, are required to clarify underlying mechanisms and enhance therapeutic efficacy. This work was supported by Shota Rustaveli

National Science Foundation of Georgia (SRNSFG) NFR-24-7205 "IONP Hyperthermia to Activate Immune Responses and Reprogram Tumor Microenvironment Polarization "

Keywords: Ehrlich Carcinoma, IONP, Ferromagnetic Nanoparticles, Drug Delivery.

References:

[1] Rilan B., Jiuwei Cui. (2022). Development of Immunotherapy Strategies Targeting Tumor Microenvironment Is Fiercely Ongoing. J. Front Immunol. 13: 890166. DOI: 10.3389/fimmu.2022.890166 PMCID: PMC9271663, PMID: 35833121.

[2] Gambashidze K., Sepashvili A., Khorava P., Azaladze T., Jaiani E., Lasareishvili B., Tediashvili M. (2017) Gram-negative bacterial phage lysates in anticancer therapy. J. Med Microb Diagn.; 6:2 (Suppl). DOI: 10.4172/2161-0703-C1-006.

[3] Nicole M. Anderson, M. Celeste S. (2020). Tumor Microenvironment. Curr Biol. 17;30(16):R921-R925. DOI: 10.1016/j.cub.2020.06.081.Curr Biol.

[4] Duan X, He K, Li J, Cheng M, Song H, Liu J, et al. (2018). Tumor-associated macrophages deliver iron to tumor cells via Lcn2. Int J Physiol Pathophysiol Pharmacol., 10 [10]5–14.

[5] Shubitidze F., Ghambashidze K., Hoopes J. (2022). A joint Phagelysate and mNP hyperthermia approach for cancer treatment. European Society for Hyperthermic Oncology 34th Annual Meeting, Sweden. https://www.esho2022.eu/fileadmin/congress/media/esho2022/druckelemente/ESHO22 Abstract_book.pdf.

PP–9. SYNTHESIS OF NEW HETEROCYCLIC SYSTEMS BASED ON FURO[2,3-*C*]-2,7-NAPHTHYRIDINES

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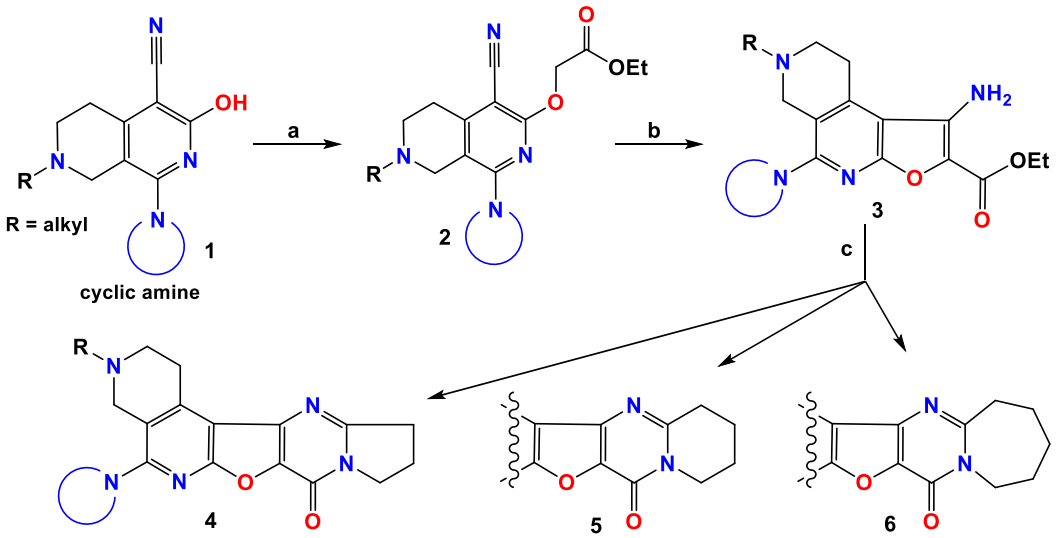
Condensed derivatives of pyrrolo[1,2-*a*]pyrimidines, pyrido[1,2-*a*]pyrimidines and pyrimido[1,2-*a*] azepines exhibit a variety of biological properties [1,2]. In our previous studies [3,4], the synthesis and psychotropic properties of a series of furo[3,2-*d*]pyrrolo[1,2-*a*]pyrimidines, furo[3,2-d]pyrido[1,2-*a*]pyrimidines and furo[3’,2’:4,5]pyrimido[1,2-*a*]azepines were described. The results of these studies showed that some compounds from this series possess potent anticonvulsant properties.

In continuation of these studies, herein we described the synthesis of compounds containing these cycles in their structure. The synthesis of target compounds 4–6 was carried out starting from the 7-alkyl-1-amino-3-hydroxy-5,6,7,8-tetrahydro-2,7-naphthyridines 1 [5] according to the scheme shown below. It should be noted that the synthesized compounds, pyrrolo[1'',2'':1',2']pyrimido[4',5':4,5]furo[2,3-*c*]-2,7-naphthyridines 4, pyrido[1'',2'':1',2']-pyrimido[4',5':4,5]furo[2,3-*c*]-2,7-naphthyridines 5 and azepino[1'',2'':1',2']pyrimido[4',5':4,5]-furo[2,3-*c*]-2,7-naphthyridines 6, represent new heterocyclic systems.



(a) $ClCH_2COOEt$, K_2CO_3/DMF, 75-80°C; (b) NaOEt, EtOH, reflux; (c) lactams, $POCl_3$, $C_2H_4Cl_2$, reflux.

The work was supported by the Science Committee of RA, in the frames of the research project № 21AG-1D036.

References

[1] Ferrara M., Crescenzi B., Donghi M., Muraglia E., Nizi E., Pesci S., Summa V., Gardelli C. 2007, Synthesis of a hexahydropyrimido[1,2-*a*]azepine-2-carboxamide derivative useful as an HIV integrase inhibitor, Tetrahedron Lett., vol. 48, no. 47, pp. 8379–8382.

[2] Zhong Y., Krska SW., Zhou H., Reamer RA., Lee J., Sun Y., Askin D. 2009, Catalytic Asymmetric Synthesis of an HIV Integrase Inhibitor, Org. Lett., vol. 11, no. 2, pp. 369–372.

[3] Sirakanyan SN., Geronikaki A., Spinelli D., Paronikyan RG., Dzhagatspanyan IA., Nazaryan IM., Akopyan AH., Hovakimyan AA. 2016, Pyridofuropyrrolo[1,2-*a*]pyrimidines and pyridofuropyrimido[1,2-*a*]azepines: new chemical entities (NCE) with anticonvulsive and psychotropic properties, RSC Adv., vol. 6, pp. 49028–49038.

[4] Sirakanyan SN., Spinelli D., Geronikaki A., Kartsev V., Hakobyan EK., Petrou A., Paronikyan RG., Nazaryan IM., Akopyan HH., Hovakimyan AA. 2021, New Bicyclic Pyridine-Based Hybrids Linked to the 1,2,3-Triazole Unit: Synthesis via Click Reaction and Evaluation of Neurotropic Activity and Molecular Docking, Molecules, vol. 26, pp. 3320.

[5] Sirakanyan SN., Spinelli D., Geronikaki A., Zuppiroli L., Zuppiroli R., Kartsev V., Hakobyan EK., Yegoryan HA., Hovakimyan AA. 2022, Synthesis of 1-Amino-3-oxo-2,7-naphthyridines *via* Smiles Rearrangement: A New Approach in the Field of Chemistry of Heterocyclic Compounds, Inter. J. Mol. Sci., vol. 23, no. 11, pp. 5904.

PP–10. INVESTIGATION OF ALKALOID CONTENT IN PLANTS OF THE GEORGIAN FLORA

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Biologically active compounds of plant origin are considered a promising source for the development of new pharmaceutical products. Phytochemical studies of Georgian flora have demonstrated that alkaloid-bearing plants contain nearly all major chemical classes of alkaloids [1-4].

The investigated plant material included representatives of the following families: *Papaveraceae, Berberidaceae, Fabaceae, Solanaceae, Fumariaceae, Apocynaceae, Lamiaceae, Asteraceae, Magnoliaceae, Ranunculaceae, Peganaceae*, and *Ephedraceae*.

The aim of the study was to conduct a phytochemical investigation of the selected species for alkaloid content and to evaluate their biological activity.

Within the framework of the study, the preparation and standardization of plant raw materials were carried out. Optimal extraction methods and conditions were selected. Analysis of alkaloid dynamics during plant ontogenesis revealed the productivity of individual vegetative organs, on the basis of which the optimal terms for raw material collection were determined. The research samples were subjected to qualitative and quantitative evaluation using GC/MS and HPLC/MS techniques. As a result of fractionation of total extracts (using polybuffer method, separation based on basicity and column chromatography), fractions enriched with biologically active alkaloids were obtained. Subsequent refractionation of these fractions enabled the isolation of individual compounds. Qualitative analysis of total extracts and fractions was performed by TLC method in comparison with reference standards, using appropriate chromatographic systems. The structures of the individual compounds were confirmed using comprehensive spectroscopic methods (UV, IR), including NMR (^{1}H NMR, ^{13}C NMR, COSY, HMBC, HSQC) analysis. As a result, bologically and pharmacologically active alkaloids belonging to the diterpene, indole, isoquinoline, quinolizidine, steroid, and acyclic classes were identified. Evaluation of total extracts, fractions, and isolated compounds revealed hematopoiesis-stimulating, anticonvulsant, analgesic, antioxidant, anti-inflammatory, antiproliferative, antiarrhythmic, antihypoxic, cerebral blood flow–enhancing, sedative, hypoglycemic, and cytotoxic activities.

The conducted research confirmed the high phytochemical potential of alkaloid-bearing plants from the Georgian flora and their potential for use in the development of novel biologically active substances and pharmaceutical products. Regulatory and technical documentation has been developed for biologically active alkaloid-rich substances.

References:

[1] Kintsurashvili L., Gogitidze N., Mushkiashvili N., Mulkijanyan K. 2024, Alkaloids from the Delphinium flexuosum Bieb. and their Pharmacological Activity, GEORGIAN BIOMEDICAL NEWS, vol. 2, no. 2, pp. 84-87.
[2] Suladze T. 2024, Dynamics of Alkaloid Accumulation in Ephedra Procera aerial Parts According to Phenological Phases, Georgian Scientists, vol. 6, no. 1, pp. 15-19.
[3] Todua N., Chincharadze D., Jokhadze M., Kostyuk V., Mshvildadze V., Legault J., Bakuridze A., Vachnadze N. 2025, Bioactive isoquinoline alkaloids from Mahonia aquifolium (Pursh.) Nutt. acclimatized to natural conditions in Georgia. Natural Product Research, Taylor& Francis Group, pp. 1-5.
[4] Vachnadze V., Jakeli E., Mujiri M., Beshitaishvili L., Kintsurashvili L., Vachnadze N., 2012, Study of alkaloid content in native and introduced plants in Georgia,Tbilisi State Medical University, Collection of Scientific Works, XLVI, pp. 135-144.

PP–11. PHYTOCHEMICAL STUDY OF HYPERICUM HYSSOPIFOLIUM CHAIX GROWING IN GEORGIA

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St. John's wort (*Hypericum*) is a perennial herbaceous plant belonging to the family Hypericaceae, widely distributed throughout the world. In Georgia, 19 species are found. For medicinal purposes, the aerial parts of the plant are used. They contain flavonoids (hyperoside, rutin, quercetin, isoquercetin), carotenoids, hypericin, lipid complexes, essential oils, resins, nicotinic and ascorbic acids, vitamins P and PP, choline, anthocyanins, as well as coloring and tanning substances. The plant exhibits antibacterial, choleretic, diuretic, antiviral, anti-inflammatory, antispasmodic, and antidepressant activities. St. John's wort extract occupy a prominent place in clinical medicine, particularly in dermatocosmetology, where they improve skin regeneration and structure, and in dentistry, where they serve as an effective antiseptic and anti-inflammatory agents [2, 3].

The aerial parts of *Hypericum hyssopifolium* Chaix, collected in the Kartli floristic area during an expedition by the Department of Pharmacobotany of the Iovel Kutateladze Institute of Pharmacochemistry, were investigated for their content of phenolic compounds and anthracene derivatives.

The aerial parts of *Hypericum* were first subjected to preliminary extraction with *n*-hexane to remove lipophilic compounds. The plant material was then extracted with 70% ethanol using a magnetic stirrer at 60°C and 400 rpm. After concentration, a total extract of the aerial parts was obtained, which qualitatively (by TLC analysis) contained anthracene derivatives and the major phenolic compounds.

The presence of hypericin and pseudohypericin in the extract was confirmed using thin-layer chromatography (TLC). Under ultraviolet light at 365 nm, these compounds exhibited red fluorescence, and their Rf values corresponded to literature data [1].

To obtain enriched fractions from the total extract of the aerial parts, a column packed with the synthetic ion-exchange resin Diaion HP-20 was employed. Elution was carried out using increasing concentrations of ethanol (0%, 30%, 50%, 70%, 90%). High-performance liquid chromatography coupled with mass-spectrometric detection (HPLC-MS) of the fractions revealed the presence of pseudohypericin, ferulic acid, rutin, and quercetin.

Within the scope of the present study, anthracene-derivative-enriched fractions isolated from the aerial parts of *Hypericum hyssopifolium Chaix* using the Diaion HP-20 adsorptive resin, represent high-value raw material for the development of innovative therapeutic and preventive agents. This complex of biologically active compounds is characterized by broad therapeutic potential, which determines the prospects for its application in clinical medicine, particularly in dermatocosmetology and pharmaceutical perfumery.

References:

[1] Draves, A. H., Walker, S. E. 2000, Determination of hypericin and pseudohypericin in pharmaceutical preparations by liquid chromatography with fluorescence detection, Journal of Chromatography B: Biomedical Sciences and Applications, vol. 749, no. 1, pp. 57-66.

[2] Karioti, A., Bilia, AR. 2010, Hypericins as potential leads for new therapeutics, Int. J. Mol. Sci., vol. 11, pp. 562–594.

[3] Gagnidze, R. 2005, Vascular plants of Georgia: a nomenclatural checklist, Universal, Tbilisi.

[4] Kikalishvili, B., Sulakvelidze, Ts., Malania, M., Turabelidze, D. 2021, Study of lipids and accompanying biologically active compounds of some plants growing in Georgia, Georgian Medical News, no. 10 (319), pp. 143–14.

PP–12. CHEMICAL STUDY OF *SOLANUM WORONOWII* POJARK. AND *SOLANUM NIGRUM* L. LEAVES COMMON IN GEORGIA

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The family Solanaceae in Georgia is represented by 10 genera and 26 species of plants. Among them, one species - Solanum woronowii Poyark. is endemic to Georgia [1]. We have studied the chemical composition of the leaves of 2 species of Solanum - *S.woronowii* Poyark. and *S.nigrum* L. Along with steroid compounds, the content of flavonoids and alkaloids in them has been established.

One of the classes of secondary metabolites of plants is represented by steroidal glycosides. The identification and study of plants containing them is important in terms of their various pharmacological activity and the possible use of their non-sugar part - sapogenin for the synthesis of steroid hormonal drugs. Species of the Solanaceae genus have been used in traditional medicine of various countries since ancient times [2, 3].

After extraction with 70% methanol and purification from lipophilic substances with chloroform from the leaves of S. woronowii and S. nigrum the total extract yield was 28.3 % and 25.5 %, respectively. By applying a 10 % aqueous solution of the total extract to a Diaion HP-20 column 50 %, 80 % and 100 % methanol fractions were obtained. In both cases, no steroid glycosides were detected in the 50 % methanol eluate, while the 80 % and 100 % methanol eluates were found to be rich in steroid glycosides. Hydrolysis of 80 % methanolic eluate obtained from plant leaves with 8 % hydrochloric acid solution in the presence of benzene on a boiling water bath for 3 hours after neutralization and purification of the benzene layer yielded the sum of steroidal sapogenins in the quantity of 0.6 % and 0.5 % respectively. In total, in the case of S. woronowii, tigogenin - (25R) - 5α- spirostane -3β- ol and chlorogenin - (25R) - 5α- spirostane - 3β, 6α-diol were determined, while in the case of S. nigrum - tigogenin - (25R) - 5α- spirostane -3β-ol and diosgenin - (25R) - 5(6) en-spirostane 3 β-ol.

The total extract obtained from Solanum woronowii leaves exhibits anti-inflammatory and analgesic activity. The antifungal and antioxidant activities of the butanol extract (Fr.1) and the 80 % methanol eluate (Fr.2) obtained from Solanum nigrum leaves were studied at the University of Quebec (Canada). The minimum antifungal activity against Candida albicans is within the concentration of 30.5 ± 0.04μg/ml for Fr.1 and 136 ± 21μg/ml for Fr.2. Amphotericin B was used as a comparative example. The antioxidant activities of the fractions are within the range of 7.1 ± 0.6 μg/ml and 8.1 ± 0.8 μg/ml.

References:

[1] Gagnidze R. 2005, Vascular plants of Georgia A nomenclatural checklist. Tbilisi, 247 p.;
[2] Joseph Sakah Kaunda, Ying-Jun Zhang, 2019, The Genus Solanum: An Ethnopharmacological, Phytochemical and Biological Properties. Review, Natural Products and Bioprospecting, vol. 9, pp. 77–137;
[3] Vinod Kumar Gupta, Aritra Simlai, Manish Tiwari, Kashinath Bhattacharya, Amit Roy. 2014, Phytochemical contents, antimicrobial and antioxidative activities of Solanum sisymbriifolium. Journal of Applied Pharmaceutical Science, vol. 4, pp. 75 - 80.

PP–13. REGIOSELECTIVE NITRATION OF QUERCETIN: PREPARATION AND ANALYSIS

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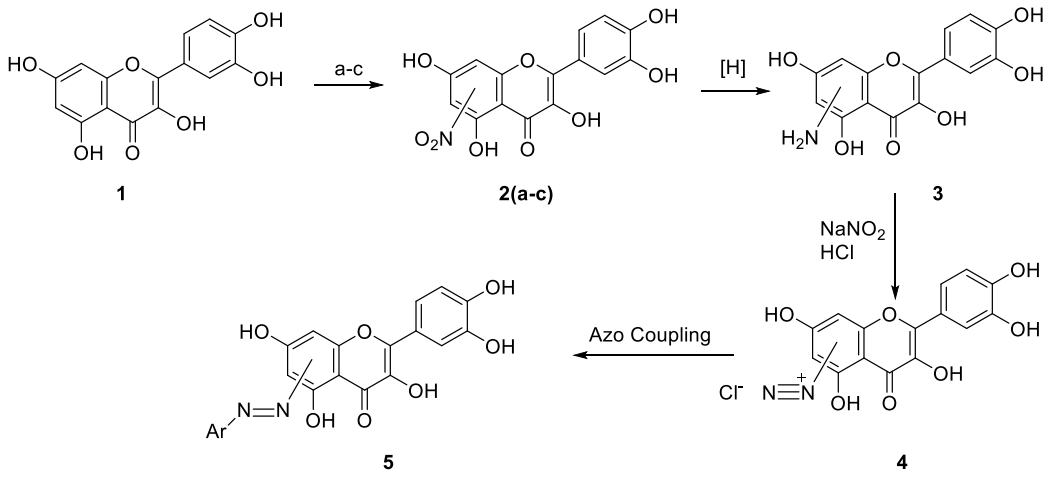
Azo dyes derived from natural products are attractive alternatives to petrochemical chromophores in pharmaceutical and textile applications [1]. Most azo dyes exhibit structure-dependent toxicity: enzymatic or microbial reduction of the azo bond (–N=N–) often cleaves the dye into primary aromatic amines (pAAs) which are genotoxic/carcinogenic species [3]. Researchers have shown that azo dyes made from onion-derived flavonoid extracts form stable pigments expected to be less toxic to the environment than other dyes [4]. Nitration of quercetin (3,3’,4’,5,7-pentahydroxyflavone) is a strategic transformation because nitro substituents can be selectively reduced to amines, diazotized and coupled to form azo derivatives [2].

Overall strategy of the synthesis desired eco-friendly quercetin containing azo dyes is shown on the Scheme 1. Most studies on azo dyes focus on phenolic coupling, which limits structural diversity. By converting quercetin into a diazonium salt, the molecule becomes a versatile intermediate. Selective nitration of polyhydroxylated flavonoids is, however, challenging due to competing oxidation and acid-promoted degradation. In this research we developed three nitration strategies. All reactions were carried out under the conditions shown in Table 1. Reaction execution has been monitored by TLC analysis using AcOEt as the eluent in all cases.

Nitration of quercetin (1) using potassium nitrate in concentrated sulfuric acid resulted in rapid substrate consumption and the formation of highly polar, over-oxidized by-products, consistent with acid-promoted degradation pathways. Replacing the strong acidic nitration system with a milder

combination of ammonium nitrate and trichloroacetic acid (TCA) in acetonitrile led to no detectable conversion, as confirmed by TLC analysis.



where: Ar - moiety of biological active aromatic compound
(a) KNO_3/H_2SO_4; (b) NH_4NO_3/TCA/MeCN; (c) KNO_3/TCA/MeCN.

Scheme 1. Strategy of the synthesis of quercetin containing azo compounds

In contrast, a system comprising potassium nitrate and TCA in acetonitrile afforded isolable nitro derivative of quercetin with limited visible oxidative degradation. Formic acid proved insufficiently acidic to promote nitration under the evaluated conditions.

Improved reproducibility and selectivity were achieved through controlled reagent stoichiometry, defined order of addition, and moderate temperature elevation (~35 °C). Ongoing work focuses on yield optimization, reaction scale-up, and preliminary dyeing evaluations.

Table 1. Experimental conditions

Run	Source of NO_2^+	Acid	Solvent	Temperature (°C)	Yield (%)
2a	KNO_3	H_2SO_4	-	0-5	-
2b	NH_4NO_3	TCA	MeCN	rt-35	-
2c	KNO_3	HCOOH	MeCN	rt-reflux	trace
2d	KNO_3	TCA	MeCN	rt-35	27

References:

[1] Mendes, F. D. P., Fernandes, A. M., Silva, C. J. & Gonçalves, M. S. T.. 2025, 'Application of eugenol-derived azo dyes on natural textile fabrics', Chemistry Proceedings, vol. 18, no. 1, pp. 14.

[2] Tavera-Hernández, R., Jiménez-Estrada, M., Alvarado-Sansininea, J. J., Nieto-Camacho, A., López-Muñoz, H., Sánchez-Sánchez, L. & Escobar, M. L.. 2021, 'Synthesis of Chrysin, Quercetin and Naringin Nitroderivatives: Antiproliferative, Anti-inflammatory and Antioxidant Activity', Letters in Drug Design & Discovery, vol. 18, no. 8, pp. 795–805.

[3] Feng, Jinhui, Cerniglia, Carl E. & Chen, Huizhong. 2012, 'Toxicological significance of azo dye metabolism by human intestinal microbiota', Frontiers in Bioscience (Elite Ed), vol. 4, no. 2, pp. 568–586.

[4] Akaho, A. A., Chukwu, U. J. & Akaranta, O.. 2019, 'Cu (II)-Red Onion Skin Extract-Azo metal Complex - A Potential for Oilfield Applications', Chemical Science International Journal, vol. 26, no. 2, pp. 1–7.

PP–14. SYNTHESIS OF CERTAIN NEW 5A-STEROID HYDRAZONES

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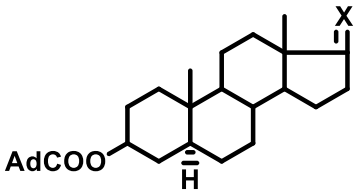
The synthesis of new bioactive steroid compounds remains relevant due to their diverse pharmacological effects. Steroidal oximes and hydrazones are characterized by anticancer, antifungal, antibacterial, antiviral, cytotoxic activity. Moreover, the cytotoxic activities of hydrazones obtained via esterification of steroidal alcohols have been reported to be higher than those of their parent compounds. Given the pronounced biological activity of steroidal hydrazones, the design and synthesis of new derivatives based on this framework remain an important direction in the search for prototype therapeutic agents for the treatment of various diseases [1-5].

Based on the steroid sapogenin-tigogenin isolated from the plant *Yucca gloriosa*, the conversion of the esterified steroid ketone - 3β-(1-adamantoate)-5α-androstan-17-one to hydrazones **1-12** was investigated. The structure of the synthesized 5α-steroidal hydrazones was proved using IR-, ^{1}H-NMR and mass spectra data.



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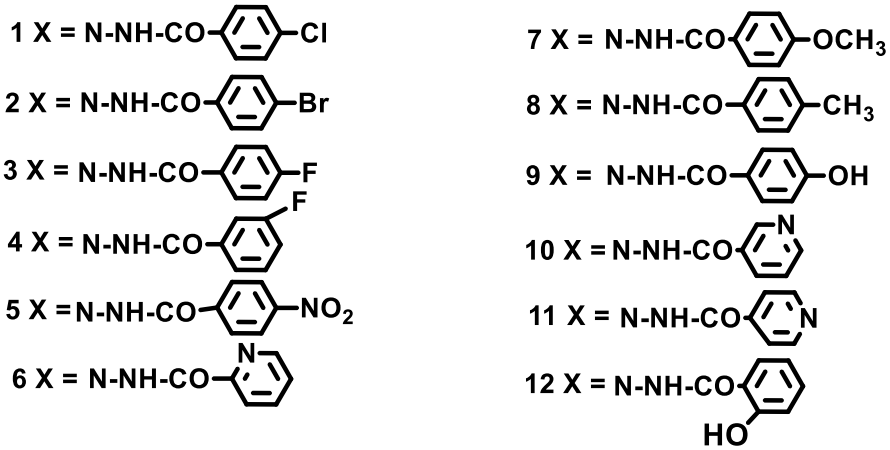

Cytotoxic activity of the synthesized compounds, was evaluated *in vitro* assays against lung carcinoma (A-549) cells, colorectal adenocarcinoma (DLD-1) cells, and normal skin fibroblasts (WS-1). Anti-inflammatory activity was assessed by inhibition of nitric oxide (NO) production in RAW 264.7 murine macrophages, whereas the antioxidant activity was determined by the DPPH radical-scavenging assay.

Among the synthesized steroid hydrazones compound **8** demonstrated the highest cytotoxic potency toward lung carcinoma cells, steroid **1** exhibited a pronounced anti-inflammatory effect and only hydrazone **12** displayed weak radical-scavenging activity.

References

[1] Gaši KMP, Djurendic EA, Szecsi M et al. Microwave assisted synthesis and biomedical potency of salicyloyloxy and 2-methoxybenzoyloxy androstane and stigmastane derivatives. *Steroids*. 2015;94 31-40.

[2] Mistry Sh, Kumar A. Synthesis and in vitro antimicrobial activity of new steroidal hydrazone derivatives. *Future J Pharm Sci*. 2022;8:7.

[3] Merlani M, Nadaraia N, Amiranashvili L et al. Antimicrobial activity of some steroidal hydrazones. *Molecules*. 2023;28 [11]67.
[4] Nadaraia NSh, Barbakadze NN, Kakhabrishvili ML et al. Synthesis and antiviral activity of modified 5α-steroids. *Chem Nat Compd*. 2022;58 [17]8-180.
[5] Nadaraia NSh, Barbakadze NN, Kvaratskhelia TB et al. Transformation of 5α-pregnenolone into some hydrazones: synthesis and biological activity. *Chem Nat Compd*. 2025;61 [30]0-305Lon

PP–15. AI-DRIVEN DESIGN OF PLANT SECONDARY METABOLITES-DERIVED PHARMACEUTICAL FORMULATIONS

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Plant secondary metabolites such as flavonoid glycosides often exhibit potent pharmacological efficacy in *in vitro* antioxidant and anti-inflammatory assays. Despite the therapeutic potential, their pharmacokinetic profile, in particular, low bioavailability, has been perceived as a barrier to further pharmaceutical development. However, for topical formulations, systemic absorbance is neither necessary nor desirable. Instead, low skin permeability, often misinterpreted as a liability, ensures prolonged residence in the stratum corneum and upper epidermis, where antioxidant, anti-inflammatory, and membrane-stabilizing activities can exert localized effects without systemic exposure. Recent advancements in artificial intelligence (AI) methods have enabled breakthroughs in drug design by introducing approaches and platforms that accelerate the early stages of drug development while significantly reducing the time and costs compared to traditional processes.

In the current study, we aimed to apply AI models for biological profiling (PASS platform) [1] and preclinical testing (SwissADME, pkCSM, GUSAR) [2, 3] to reevaluate the pharmacological potency and safety of a plant-derived secondary metabolite, clitorin, a flavonoid glycoside found in various botanicals.

Through integrated *in silico* approach including ADMET profiling and safety assessment, combined with data obtained in *in vitro* experiments [4], we demonstrate that clitorin will function effectively as a localized agent for wound healing and UV protection. We further present AI-suggested four rationally designed, nanocarrier-free topical formulations—ranging from lightweight serums to barrier-repair creams—each optimized for specific clinical scenarios. Finally, cost-per-batch analysis revealed formulations scalable from affordable general-use products to premium medical-grade preparations.

This study provides a comprehensive approach for the AI-driven development of pharmaceuticals, aligning natural product chemistry with modern dermatological needs. Shifting the paradigm from viewing low permeability as a flaw to recognizing it as a feature enabled the rational design of topical formulations for conditions like acute/chronic wounds and UV-induced oxidative stress.

References

[1] Lagunin A, Stepanchikova A, Filimonov D, Poroikov V. (2000). *Bioinformatics, 16(8), 747–748*; DOI 10.1093/bioinformatics/16.8.747
[2] Daina A, Michielin O, & Zoete V. (2017). *Scientific Reports, 7, 42717*; DOI 10.1038/srep42717
[3] Pires DEV, Blundell TL, Ascher DB. (2015). *Journal of Medicinal Chemistry, 58(9), 4066–4072*; DOI 10.1021/acs.jmedchem.5b00104
[4] Sukhishvili N, Mulkijanyan K, Getia M, et al. (2025) *GSC Biological and Pharmaceutical Sciences, 33(02), 253–266*; DOI 10.30574/gscbps.2025.33.2.0455.

PP–16. STUDY OF PHENOLIC COMPOUNDS OF WILD-GROWING DWARF ELDER (SAMBUCUS EBULUS) IN GEORGIA

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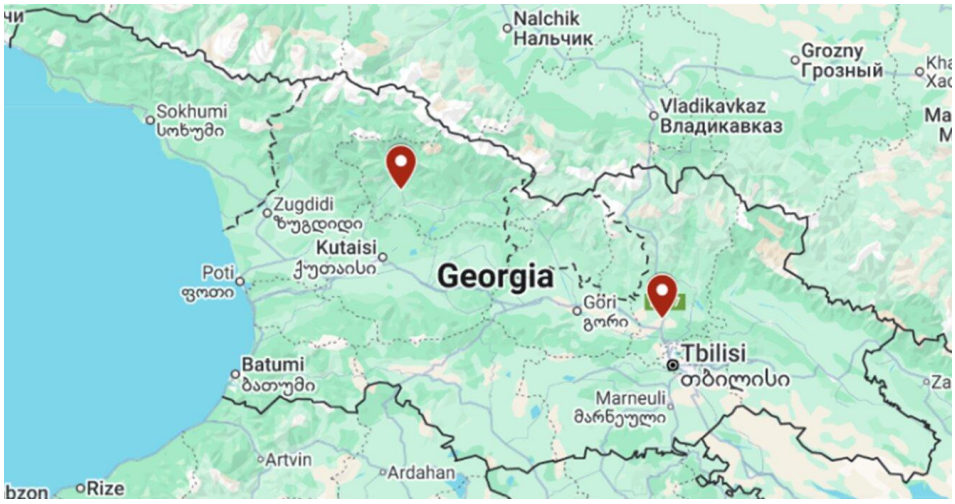
Dwarf elder (*Sambucus ebulus*) is a medicinal plant widely distributed in Georgia and traditionally used in folk medicine for its anti-inflammatory, antimicrobial and antioxidant properties. These biological activities are largely attributed to its rich content of phenolic compounds. The present study aimed to investigate the phenolic profile of wild-growing S. ebulus populations collected from different regions of Georgia. This study evaluated the phenolic profile of berries collected from two different climatic zones of Georgia: Tsageri Municipality (village Orbeli - August harvest, Dfb climate, 569.4 m a.s.l.,) and Mtskheta Municipality (village Misaktsieli - August harvest, Cfa climate, 549.1 m a.s.l.) (Fig.1.).

Fig.1. Locations the Elderberry samples were harvested from



Berries were separated into skins, seeds and juice. Total phenolic content (TPC) was determined using the Folin–Ciocalteu reagent spectrophotometrically (1). Juice samples were further analyzed for total anthocyanins (TAC) using pH differential spectrophotometry (2); total catechins (TCC) with vanillin reagent spectrophotometrically; total flavonols (TFC) using Aluminum chloride solution (3) and color intensity with spectrophotometrical method. Phenolic acids were identified qualitatively by thin-layer chromatography (TLC): system–chloroform: methanol (90 [10]), Developed with diazotized sulfanilic acid. Thermal stability of phenolic compounds was assessed by boiling juice samples at 100°C for 20 minutes (4).

Samples from Orbeli (Dfb climate zone) exhibited consistently higher phenolic accumulation than Misaktsieli samples (Cfa climate zone). TPC in skins reached 7.961 g/L gallic acid equivalent (GAE) (Dfb) compared to 6.373 g/L (Cfa), while seeds contained 7.864 g/L and 5.206 g/L GAE, respectively. Juice showed the highest phenolic concentration, with 10.52 g/L GAE (Dfb) versus 8.04 g/L (Cfa). Total anthocyanins were 3.043 and 2.972 g C3G/L, respectively. Catechin content was markedly higher in the Dfb samples (360 mg/L catechin equivalents) compared to Cfa (240 mg/L). Total flavonol content showed minor difference. The concentrations were 23.2 mg/L (Dfb) and 24.4 mg/L (Cfa) (quercetin equivalents).

TLC analysis showed that both samples exhibited contents of same phenolic acids with no qualitative differences between locations. TLC analysis revealed the presence of gallic, syringic, protocatechuic, p-coumaric, ferulic, 4-hydroxybenzoic (4-HBA), chlorogenic and synapic acids. Thermal treatment resulted in a decrease in TPC of 33.27% (Dfb) and 30.22% (Cfa) (Fig.2.). Color intensity of Dwarf Elder juice strongly corresponded with anthocyanin concentration.

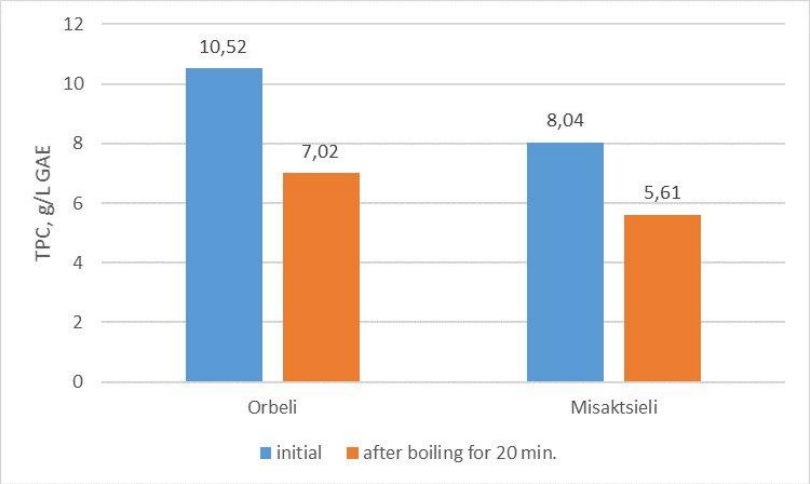


Fig.2. Effect of thermal treatement on Dwarf Elder juice TPC

Overall, berries from the cooler Dfb climatic zone demonstrated enhanced phenolic accumulation compared to those from the Cfa zone. These findings confirm the influence of climatic conditions on phenolic compound biosynthesis and support the potential of Georgian wild-growing S. ebulus as a valuable source of bioactive compounds for functional food and nutraceutical applications.

References

[1] Carolina B Casati, Virginia Sánchez, Rosa Baeza, Natalia Magnani, Pablo Evelson, María C Zamora. 2012, 'Relationships between colour parameters, phenolic content and sensory changes of processed blueberry, elderberry and blackcurrant commercial juices', *International Journal of Food Science and Technology*, vol. 47, no. 8, pp. 1728-1736.

[2] Lee, Jungmin, et al. 2005, 'Determination of Total Monomeric Anthocyanin Pigment Content of Fruit Juices, Beverages, Natural Colorants, and Wines by the PH Differential Method: Collaborative Study', Journal of AOAC International, vol. 88, no. 5, pp. 1269–1278.

[3] Vujanović et al., 2020, 'Elderberry (Sambucus Nigra L.) Juice as a Novel Functional Product Rich in Health-Promoting Compounds', RSC Advances, vol. 10, no. 73, pp. 44805–44814.

[4] Jiménez, Pilar, et al. 2017, 'Lectin Digestibility and Stability of Elderberry Antioxidants to Heat Treatment in Vitro', Molecules, vol. 22, no. 1, p. 95.

PP–17. DEVELOPMENT AND VALIDATION OF AN LC-MS/MS METHOD FOR THE QUANTIFICATION OF AB-CHMINACA AND ITS METABOLITE M4 IN HUMAN BLOOD

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Synthetic cannabinoids constitute an expanding class of new psychoactive substances that act as potent agonists of the cannabinoid CB1 and CB2 receptors, often exhibiting greater receptor affinity than Δ9-tetrahydrocannabinol. [2, 7] Their metabolites may also retain pharmacological activity and interact with additional non-cannabinoid targets, contributing to complex and unpredictable

toxicological effects. [3, 6, 9, 10] Among various structural classes, indazole-3-carboxamides are one of the most prevalent and pharmacologically potent subclasses in forensic casework. [1, 4, 5] AB-CHMINACA, a highly lipophilic indazole-based synthetic cannabinoid classified as a Schedule I controlled substance, undergoes extensive biotransformation, making it difficult to detect the parent compound analytically in biological samples. [5, 8] Therefore, reliable analytical methods capable of targeting both the parent compound and its metabolites are essential for forensic toxicology investigations. This study aimed to develop and validate a sensitive and selective LC-MS/MS method for quantifying AB-CHMINACA and its major metabolite in blood.

In compliance with the study objective, blood samples were prepared using solid-phase extraction (OASIS HLB, 3 cc, 60 mg). Analysis was performed using an Agilent 1290 liquid chromatograph coupled to a 6460 triple quadrupole mass spectrometer with an electrospray ionization (ESI) source. Separation was carried out on a Zorbax Eclipse Plus C18 column (100 × 3.0 mm, 1.8 µm). The mobile phases consisted of 0.1% formic acid in water (A) and 0.1% formic acid in acetonitrile (B), applied under gradient elution conditions. Injection volume was 5.00 µL at a flow rate of 0.8 mL/min. The mass spectrometer was operated in positive ESI mode with multiple reaction monitoring (MRM) acquisition. Method validation was conducted using drug-free human blood samples spiked with the target analytes. The method was evaluated for selectivity, specificity, linearity, limit of detection (LOD), lower limit of quantitation (LLOQ), within- and between-day precision, accuracy, and extraction recovery.

Linearity was established for both analytes over the concentration range of 1-50 ng/mL ($r^2 > 0.995$). The limit of detection (LOD) and the lower limit of quantification (LLOQ) were 0.5 ng/mL and 1 ng/mL for each analyte, meeting predefined accuracy and precision acceptance criteria. Intra and inter-day accuracy ranged from 89.2-104.2% and 90.1-102.1%, with precision ranging from 11.7% to 11.9% across both analytes. Extraction efficiencies were 82.3% and 90.2%, with minimal matrix effects (<15%) and a process efficiency within the range 82- 94%. No significant carryover was observed during the analysis. Both analytes demonstrated adequate stability under all evaluated experimental conditions.

The developed LC–MS/MS method offers a sensitive, robust, and rapid analytical approach for the reliable detection and quantification of AB-CHMINACA and its metabolite M4 in human blood over the validated concentration range of 1–50 ng/mL. The method demonstrated adequate selectivity, precision, and stability, confirming its suitability for routine application in forensic and clinical toxicology investigations.

References

[1] Antonides, LH., Cannaert, A. & Norman, C. 2019, 'Enantiospecific synthesis, chiral separation, and biological activity of four indazole-3-carboxamide-type synthetic cannabinoid receptor agonists and their detection in seized drug samples', *Frontiers in Chemistry*, vol. 7, article 321.

[2] Ayman, A., Fatimah, F. & Khasawneh, R. 2024, 'The synthetic cannabinoids menace: a review of health risk and toxicity', *European Journal of Medical Research*, vol. 29, no. 1.

[3] Cooper, ZD. 2016, 'Adverse effects of synthetic cannabinoids: management of acute toxicity and withdrawal', *Current Psychiatry Reports*, vol. 18, no. 5, pp. 52–60.

[4] European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2018, *Fentanils and synthetic cannabinoids: driving greater complexity into the drug situation — an update from the EU Early Warning System*, EMCDDA Report, Luxembourg.

[5] [5] European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2024, *Synthetic cannabinoids in Europe– updates 2020–2024*, EMCDDA Report, Luxembourg.

[6] [Granja-Galeano, G., Dominguez-Rubio, AP. & Zappia, MP. 2023, 'CB1 receptor expression and signaling are required for dexamethasone-induced aversive memory consolidation', *Neuropharmacology*, vol. 229, art.109674.

[7] Kelkar, AH., Smith, NA. & Martial, A. 2018, 'An outbreak of synthetic cannabinoid–associated coagulopathy in Illinois', *The New England Journal of Medicine*, vol. 379, no. 13, pp. 1216–1223.

[8] Roque-Bravo, R., Silva, RS. & Malheiro, RF. 2022, 'Synthetic cannabinoids: a pharmacological and toxicological overview', *Annual Review of Pharmacology and Toxicology*, vol. 62, pp. 131–154.

[9] Solimini, R., Busardò, FP., Rotolo, MC., Ricci, S., Mastrobatista, L., Mortali, C., Graziano, S., Pellegrini, M., Di Luca, NM. & Palmi, I. 2017, 'Hepatotoxicity associated with synthetic cannabinoid use', *European Review for Medical and Pharmacological Sciences*, vol. 21, no. 1, pp. 1–10.

[10] Walsh, KB. & Andersen, HK. 2020, 'Molecular pharmacology of synthetic cannabinoids: delineating CB1 receptor-mediated cell signaling', International Journal of Molecular Sciences, vol. 21, no. 17, article 6115.

PP–18. SYNTHESIS OF *N*-SUBSTITUTED DERIVATIVES OF FURO(THIENO)[3,2-*D*]PYRIMIDINES

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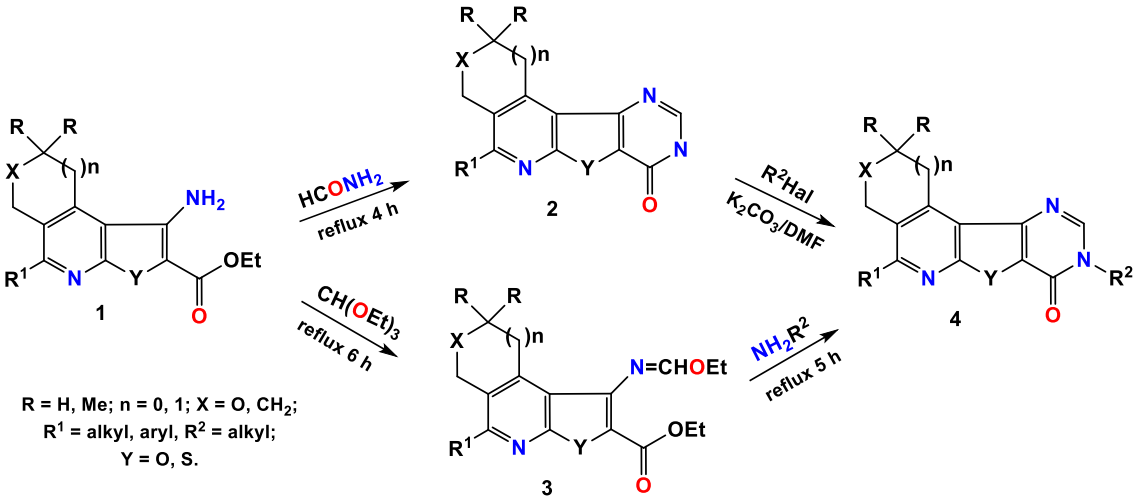
Fused furo(thieno)[3,2-*d*]pyrimidines have attracted significant attention due to their diverse biological activities, including antitumor [1,2], antifungal [3], antibacterial [4] and antiproliferative [5] properties. These compounds are pharmaceutically interesting scaffolds, and identified as a key moiety in the development of various inhibitors [6]. Building on this foundation, our research focused on the synthesis of a series of novel *N*-alkyl derivatives of fused pyrido[3′,2′:4,5]furo(thieno)[3,2-*d*]pyrimidines. For this purpose, aminoesters of furo(thieno)[2,3-*b*]pyridines **1** [7] were used. These compounds were cyclized into furo(thieno)[3,2-*d*]pyrimidin-7(8)-ones **2**, which then were alkylated to give the aimed compounds **4**. *N*-Substituted derivatives of furo(thieno)[3,2-*d*]pyrimidines **4** were also synthesized by reacting compounds **1** with triethyl orthoformate. The resulting ethoxymethylene derivatives **3** were converted into the target *N*-substituted compounds **4** under the action of hydrazine hydrate and amines.



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References

[1] Zhang Y., Shen J., Li JW. Et al. 2023, Design, synthesis, and biological evaluation of novel thieno[3,2-*d*]pyrimidine derivatives as potent antitumor agents, New J. Chem., vol. 47, pp. 21318–21331.

[2] Ye T., Han Y., Wang R. et al. 2020**,** Design, synthesis and biological evaluation of novel 2,4-bismorpholinothieno[3,2-*d*]pyrimidine and 2-morpholinothieno[3,2-*d*]pyrimidinone derivatives as potent antitumor agents, Bioorg. Chem.*,* vol. 99, pp. 103796.

[3] Abuelhassan S., Bakhite EA-G., Abdel-Rahman AE., El-Mahdy AFM. 2021, Synthesis, characterization, and biological activities of some novel thienylpyrido[3',2':4,5]thieno[3,2-*d*]pyrimidines and related heterocycles, J.Heterocycl. Chem., vol. 58, pp. 1784–1801.
[4] Sirakanyan SN., Kartsev VG., Geronikaki A. et al., 2020, Synthesis and evaluation of antimicrobial activity and molecular docking of new n-1,3-thiazol-2-ylacetamides of condensed pyrido[3',2':4,5]furo(thieno)[3,2-*d*]pyrimidines, Curr. Top. Med. Chem., vol. 20, no. 24, pp. 2192–2209.

PP–19. GEORGIAN INDIGENOUS GRAPEVINE (*VITIS VINIFERA* L.) CULTIVARS AS A POTENTIAL SOURCE OF AROMATASE-INHIBITORY POLYPHENOLS

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Grapevine (*Vitis vinifera* L.) by-products are rich sources of structurally diverse polyphenolic compounds, including flavanols, flavonols and stilbenes [1, 2]. Plant-derived polyphenols have attracted considerable attention due to their multitarget biological activities, including the modulation of enzymes involved in hormone biosynthesis. Among these, aromatase (CYP19A1), a cytochrome P450 enzyme responsible for the conversion of androgens into estrogens, plays a central role in estrogen-dependent pathologies [3, 4]. Excessive aromatase activity contributes to the progression of hormone receptor-positive breast cancer, the most prevalent molecular subtype of the disease. Although synthetic aromatase inhibitors such as letrozole and anastrozole are clinically effective, their long-term use may be associated with adverse effects and resistance [5, 6]. Consequently, the identification of natural aromatase modulators remains of scientific interest. The present study investigated viticultural residues from two indigenous Georgian white cultivars - Mtsvane Kakhuri and Khikhvi - with the aim of determining the content of individual polyphenolic constituents and evaluating their *in vitro* aromatase inhibitory potential.

Grapevine shoots (collected post-flowering, July 2025) and grape pomace (harvested after completion of alcoholic fermentation, October 2025) were obtained from *Vitis vinifera* L. cv. Mtsvane Kakhuri and cv. Khikhvi cultivated in the Kakheti wine-growing region (Georgia). Pomace samples were dried at 40-45 °C in a ventilated oven, while shoots were air-dried at room temperature. The dried materials were ground to uniform particle sizes.

Polyphenol-rich extracts were prepared using ultrasound-assisted extraction with 70% ethanol (1 ^{20} w/v). Sonication was performed at 60 °C for 30 min (40 kHz), in two sequential extraction cycles to maximize recovery. Combined filtrates were used for phytochemical profiling and bioactivity assessment. Individual phenolic compounds were identified and quantified using LC–MS/MS and HPLC-DAD analysis. Aromatase inhibitory activity of the prepared extracts was evaluated *in vitro* using a fluorometric Aromatase (CYP19A1) Inhibitor Screening Kit (ab284522, Abcam, Cambridge, UK) based on the enzymatic conversion of a fluorogenic substrate (Ex/Em 488/527 nm). Extracts were tested at multiple concentrations. Letrozole served as the reference inhibitor. IC_{50} values were calculated from concentration-response curves.

Table 1. Aromatase (CYP19A1) Inhibitory Activity of Shoot and Pomace Extracts of Mtsvane Kakhuri and Khikhvi

Sample/Control	Relative inhibition (%)	IC_{50} (µg/mL)
Letrozole (nmol)	97.5 ± 0.5	7.0 ± 0.001
Shoots - Mtsvane	32.13 ± 0.2	1.08 ± 0.05
Shoots - Khikhvi	36.58 ± 0.3	0.94 ± 0.05
Pomace - Mtsvane	41.59 ± 0.5	0.87 ± 0.04
Pomace - Khikhvi	47.97 ± 0.5	0.73 ± 0.03

LC-MS/MS analysis revealed the presence of 23 individual phenolic compounds in grapevine shoots and 29 compounds in grape pomace of the investigated cultivars (Mtsvane Kakhuri and Khikhvi). Both shoots and pomace extracts contained flavanols (catechin, epicatechin, epicatechin gallate), flavonols (kaempferol and quercetin derivatives), stilbenes (trans-resveratrol, viniferin) and phenolic acids (gallic and ellagic acids). Pomace samples exhibited comparatively higher concentrations of flavanols and stilbenes than shoots. All investigated extracts demonstrated *in vitro* aromatase (CYP19A1) inhibitory activity. Relative inhibition ranged from 32.13% to 47.97%, with IC_{50} values between 0.73 and 1.08 µg/mL. Khikhvi pomace showed the lowest IC_{50} value (0.73 ± 0.03 µg/mL), while the remaining samples exhibited comparable inhibitory effects within a similar concentration range. Letrozole, used as a reference inhibitor.

The present study demonstrated that grapevine shoots and pomace from the indigenous Georgian cultivars Mtsvane Kakhuri and Khikhvi are characterized by a diverse and quantitatively defined phenolic composition, including flavanols, flavonols, stilbenes, and phenolic acids. Both raw materials exhibited measurable *in vitro* aromatase (CYP19A1) inhibitory activity within a comparable concentration range. Given the complexity of the identified phytochemical profile, the observed enzyme inhibition is unlikely to be attributed to a single dominant compound. Rather, the activity may result from additive or synergistic interactions among multiple phenolic subclasses, particularly flavanols and stilbene derivatives, which have been previously associated with modulation of estrogen biosynthesis pathways. These findings highlight the relevance of indigenous Georgian grapevine cultivars as sources of structurally diverse polyphenols with aromatase-modulating potential and support further investigation of their bioactive constituents in the context of hormone-dependent pathologies.

References

[1] Constantin, O.E., Stoica, F., Rațu, R.N., Stănciuc, N., Bahrim, G.E. & Râpeanu, G. 2024, 'Bioactive components, applications, extractions, and health benefits of winery by-products from a circular bioeconomy perspective: A review', Antioxidants, vol. 13, no. 1, pp. 100.

[2] Di Lorenzo, C., Bani, C., Mercogliano, F., Bosso, A. & Restani, P. 2023, 'Valorization of wine industry by-products: Characterization of phenolic profile and investigation of potential healthy properties', BIO Web of Conferences, vol. 68, pp. 04016.

[3] Burguin, A., Diorio, C. & Durocher, F. 2021, 'Breast cancer treatments: Updates and new challenges', Journal of Personalized Medicine, vol. 11, no. 8, pp. 808.

[4] Poschner, S., Maier-Salamon, A., Thalhammer, T. & Jäger, W. 2019, 'Resveratrol and other dietary polyphenols are inhibitors of estrogen metabolism in human breast cancer cells', The Journal of Steroid Biochemistry and Molecular Biology, vol. 190, pp. 11–18.

[5] Kim, Y.J. & Cohen, P.R. 2020, 'Anastrozole-induced dermatitis: Report of a woman with an anastrozole-associated dermatosis and a review of aromatase inhibitor-related cutaneous adverse events', Dermatology and Therapy, vol. 10, no. 1, pp. 221–229.

[6] Zuffo, G.R., Ricardo, K.A., Comnisky, H. & Czepula, A.D.S. 2023, 'Most prevalent side effects of aromatase inhibitors in the treatment of hormone-positive breast cancer: A scoping review', Mastology, vol. 33.

PP–20. STEROIDAL GLYCOSIDES FROM *EUPHORBIA IBERICA* BOISS. GROWING IN GEORGIA

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The plants of the family Euphorbiaceae are widely distributed worldwide, comprising more than 10 000 species [1]. Forty-five species are recorded in the flora of Georgia. Members of this family exhibit a wide range of pharmacological activities, including cardiotonic, antioxidant, androgenic, and leukopoietic effects. Steroidal glycosides have been reported to possess antiviral and antiproliferative activities. The genus Euphorbia is particularly rich in biologically active compounds and represents an important source for the development of plant-based medicines.

The aim of this research was to investigate the underground parts of Euphorbia iberica Boiss. Air-dried plant material was extracted with 70% aqueous ethanol. After concentration, the resulting extract was dried, and the powder was subjected to silica gel column chromatography to isolate individual compounds. The major compound was obtained in 0.1% yield from the air-dried material. It gave a positive Salkowski color reaction and exhibited IR absorption bands characteristic of a spiroketal group, indicating that it is a 25R-spirostanol.

Acid hydrolysis of this steroidal glycoside yielded the aglycone, identified as (25R)-5α-spirostane-3β-ol-6-one (laxogenin) based on physico-chemical constants and spectral data (IR, mass spectrometry, and NMR) [2]. Gas chromatography (GC) analysis [3] indicated that the sugar moiety consisted of quinovose and glucose in a 2:1 ratio.

Comprehensive methylation of the saponin using the Hakomori method, followed by methanolysis, enabled detailed analysis of the sugar chain branching points and linkage positions.

The FAB mass spectrum of isolated saponin showed key peaks at m/z 921[M+Na]+, 907[M+Na-Me]+, 761[M+Na-Me-deoxyhexose]+, 599[M+Na-Me-deoxyhexose-hexose]+, 453[M+Na- Me-deoxyhexose-hexose-deoxyhexose]+. As a result, a steroidal glycoside was identified as (25R)-5α-spirostane-3β-ol-6-one-3-O-[β-D-(3’’’-O-methyl)-quinovopyranosyl-(1→3)-β-D-glucopyranosyl-(1→4)-β-D-quinovopyranosyl].

A steroidal glycoside containing laxogenin as the aglycone was isolated from the underground parts of Euphorbia iberica Boiss. The compound was identified as a trisaccharide saponin composed of two quinovose units and one glucose residue.

References

[1] Silva, L. M. B., Oliveira, R. C., Formoso, D. D. and Loureiro, M. B. 2025, Properties and medical applications of the Euphorbiaceae family and their bioproducts: a patent review, *Naunyn-Schmiedebergs Archives of Pharmacology*, vol. 398, no. 1, pp. 147-163.

[2] Kikuchi, T., Akihisa, T., Tokuda, H., Ukiya, M., Watanabe, K. and Nishino, H. 2007, Cancer chemopreventive effects of cycloartane-type and related triterpenoids in *in vitro* and *in vivo* models, *Journal of Natural Products*, vol. 70, no. 6, pp. 918-922.

[3] Goroviz, T.G. 1970, Gas-chromatographic determination of sugars and glucuronic acid. Chemistry of Natural Compounds, vol. 6, no. 2, pp. 263-264.

PP–21. DEVELOPMENT OF CREAM CONTAINING BIOLOGICALLY ACTIVE COMPOUNDS FROM *ARMENIACA VULGARIS* MILL. KERNELS GROWN IN GEORGIA

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The development of novel, modern technologies and biotechnological approaches, based on the utilization of plant-derived raw materials, is the focus of global pharmaceutical science. The development and implementation of new technologies must meet the requirements of increasing productivity and efficiency in pharmaceutical enterprises, reducing waste generation, minimizing environmental impact, and decreasing energy and raw material consumption. The pharmaceutical industry has largely embraced the trend of incorporating natural products of plant and animal origin into the production of medicinal preparations, driven by the “green wave” and the growing demand for natural alternatives.

The present study describes the processing of oil-containing raw materials, specifically apricot seeds (Armeniaca vulgaris Mill.) cultivated in Georgia. The oil content of the seeds reaches 50–55%. In addition to lipids, they contain polyphenols (including tocopherols), anthocyanins, flavonoids, carotenoids, vitamin E, proteins, essential amino acids, and other biologically active compounds. During conventional processing of the raw material, the residual by-products may retain up to 15% oil and 30–50% associated substances. Although these components are widely used in cosmetology, such residual materials are rarely utilized in practice. Modification of equipment or replacement of extractants is associated with substantial financial costs. These challenges necessitate the development of new technological approaches.

One possible solution is the application of a native extraction methodology, a field in which we have been conducting research for several years [1,2]. In processing apricot seeds by the native extraction method for the production of cosmetic creams and ointments, the following technological stages were employed:

- Preliminary preparation of raw material (removal of mechanical impurities, disinfection, sterilization);
- Comminution of the raw material using a rotary mill to obtain a finely dispersed powder-like mass;
- Separation of the finely dispersed fraction using a sieve; re-milling of the coarser fraction and subsequent mixing with the primary fraction;
- Preparation of an appropriate cosmetic base with high solubilizing capacity for the intended cosmetic formulation;
- Mixing of the obtained fine-dispersed fraction with the base under intensive stirring conditions;
- Conditioning of the resulting cosmetic formulation at room temperature for 72 hours;
- Packaging of the finished product.

The obtained creams were evaluated according to the following physicochemical parameters: stability, organoleptic characteristics, pH value, drying and film-forming test (time determination), spreadability, occlusivity, osmotic activity, and the potential ability of biologically active substances in the cream to penetrate the skin [3,4]. The results met the established requirements.

References

[1] Yavich P. A., Kakhetelidze M. B ., Kikalishvili B.Yu. On the possibility of using natural plant substances in their native form in cosmetics. Georgian Scientists, 2025, Vol. 7 Issue 2, pp.242-254.

[2] Chelidze N. A., Yavich P. A., Churadze L. I., Kakhetelidze M. B. The development of a technology of a medicinal cream, containing rhizomes of a White Cinquefoil Plant (Potentilla Alba L.) World Journal of Pharmacy and Pharmaceutical Sciences, 2020, Vol 9, Issue 5, pp. 35- 41.
[3] Dave, P, Patel, G., Patel, D., Patel, B., & Jani, R. Herbal face pack containing Coffea arabica Linn, Myristica Fragrans and Lens Culinaris as an antioxidant and antiseptic activity. International Journal of Ayurvedic Medicine, 2022, 13(3), p. 640–646.
[4] Yogesh A. Chaudhari, Anuja G. Patil, Umesh A. Mahajan, Mr. Bhushan P. Patil Formulation And Evaluation Of Herbal Scrub Soap. African Journal of Biomedical Research.2024 Vol. 27, p. 12389-1239.

PP–22. DEVELOPMENT AND ELABORATION OF AN ALTERNATIVE ENVIRONMENTALLY SUSTAINABLE SORPTION METHOD FOR THE NEUTRALIZATION OF PHARMACEUTICAL WASTE

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Waste management has become one of the most critical environmental challenges worldwide. In recent years, scientists, regulatory authorities, and the EU Water Framework Directive 2000/60/EC of the European Commission have recognized pharmaceutical compounds as an emerging global environmental concern [1, 2]. These substances are often classified as Persistent Organic Pollutants, whose presence is typically not monitored in routine water quality assessments. The increasing occurrence of pandemics, the necessary or uncontrolled consumption of pharmaceuticals, and the lack of adequate infrastructure for the proper management and recycling of pharmaceutical waste have contributed to the growing accumulation of these contaminants in aquatic systems and soils [3 - 5].

Conventional wastewater treatment processes do not ensure a sufficient level of removal of pharmaceutical contaminants. As a result, pharmaceutical residues often persist in treated wastewater and are subsequently discharged into aquatic ecosystems, including lakes, rivers, reservoirs, groundwater, and even sources of drinking water. The presence of these compounds poses a significant environmental and public health risk, particularly due to their potential to promote the development and spread of antibiotic-resistant pathogens. Consequently, it is essential to minimize the release of pharmaceutical substances into the environment through all possible means. In response to this challenge, research efforts are being conducted both to improve the efficiency of existing wastewater treatment facilities and to develop fundamentally new approaches for the removal of pharmaceutical pollutants [6].

The main goal of the presented work is to provide information on the sorption properties of carbon materials obtained from hazelnut/walnut shells and nectarine kernel using the technology developed at the R. Agladze Institute of Inorganic Chemistry and Electrochemistry of Ivane Javakhishvili Tbilisi State University [7], as well as to demonstrate the possibility of their use for the purification of water contaminated with pharmaceuticals (paracetamol) from model solutions.

The adsorption properties of the obtained carbonaceous materials were investigated under static conditions using model solutions of Paracetamol. The study evaluated the influence of several parameters on the adsorption process, including the initial concentration of paracetamol, the amount of adsorbent, particle fraction size, contact time, and pH.

The experimental results demonstrated the following:

The optimal conditions for paracetamol removal were determined to be a contact time of 30 minutes, an adsorbent dosage of 0.01 g, and an initial paracetamol concentration of 50 mg/L;

The highest selectivity toward paracetamol was observed for carbon materials produced from walnut shells and walnut shell–derived materials, with removal efficiencies (R, %) of 97% and 98.55%, respectively;

An increase in the adsorbent dosage combined with a decrease in the pollutant concentration resulted in an increased removal efficiency, reaching up to 100%.

Isothermal adsorption studies indicated that the adsorption of paracetamol on the prepared carbon materials can be adequately described by both the Langmuir Adsorption Isotherm and the Freundlich Adsorption Isotherm models.

References

[1] Fatta-Kassinos D., Meric S., Nikolaou A. (2011) Pharmaceutical residues in environmental waters and wastewater: current state of knowledge and future research; Anal Bioanal Chem, vol. 399, pp. 251-275

[2] Küster, Adler N., 2014, Pharmaceuticals in the environment: scientific evidence of risks and its regulation. Phil. Trans. R. Soc. B. 369 (1656), 20130587

[3] Kadam P.S., Rajagopal N.K., Yadav A.K., et al. (2023) Biomedical waste management during pandemics; AIP Conf. Proc. 2603, 050004

[4] Ferreira A.P, Baldo A.P., Silva A.S., et al. (2025) Enhancing single and multi-component adsorption efficiency of pharmaceutical emerging contaminants using bio waste-derived carbon materials and geopolymers,, Journal of Water Process Engineering, v.75, 107914,

[5] Chen H., Zhang Y. (2026). Chapter 2 - Adsorption of pharmaceuticals and personal care products in soils and water. In B. Gao & J. Lu (Eds.), Adsorption and degradation of emerging contaminants in soils and water (pp. 9–44). Elsevier. https://doi.org/10.1016/B978-0-443-33046-9.00004-4

[6] Chowdhury A., Sajid M., Jahan N. et al. (2021) A secondary approach with conventional medicines and supplements to recuperate current COVID-19 status, Biomedecine & pharmacotherapie, 142, 111956. https://doi.org/10.1016/j.biopha.2021.111956

[7] Ananiashvili N., Tatishvili G., Marsagishvili T. et al. (2021). Method for receiving sorbents from waste of plastics and cellulose (Patent No. P 2021 7309 B). SAKPATENTI–National Intellectual Property Center of Georgia.

PP–23. PHARMACEUTICAL PROSPECTS OF ARSENIC DERIVATIVES FROM SECONDARY RAW MATERIALS OF GEORGIA

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The search of novel and cost-effective raw materials, derived either from secondary resources or natural deposits, has become increasingly significant in addressing contemporary environmental and industrial challenges. Such efforts not only foster sustainable innovation but also mitigate ecological risks associated with industrial waste pollution. Within this framework, Georgia demonstrates significant potential.

Arsenic-containing industrial waste or natural deposits of Georgia may serve as a valuable starting material for the production of and synthesis of diverse compounds, including gold, barium hydrous arsenate, strontium hydrous arsenate, magnesium-ammonium arsenate, sodium monoselenoarsenate, and cyclic esters of arsenic acid. Considering the context of resource scarcity, the synthesis of novel bioactive polyelement coordination compounds produced based on transformation of arsenic-containing industrial by-products, which exhibit a diverse array of distinctive properties offer

substantial prospects for the development of commercially significant materials for further broad and impactful practical applications including materials science and pharmaceuticals [1-4]. This approach would facilitate also could be addresses a critical environmental challenge to reduce an arsenic-related pollution.

Based on transformation products derived from arsenic-containing industrial waste and natural resources of Georgia, coordination compounds of the type [M(Py)n]3(AsS4)2, involving certain transition d-metals, were successfully synthesized. Pyridine, one of the most promising and readily available nitrogen-containing heterocyclic ligands, was selected for this purpose. As the initial precursor, sodium tetrathioarsenate (Na3AsS4·8H2O), obtained through the processing of arsenic production residues, was employed.

The composition and structure of the synthesized compounds were determined using a range of physicochemical analyses methods, including elemental analysis, infrared spectroscopy, X-ray phase analysis, and thermographic studies. Furthermore, density functional theory (DFT) calculations were employed to evaluate the total energy of tetrahedral complex ions [M(Py)4]2+ and to analyze the sequence of metal–nitrogen bond interactions within these systems. For these estimations, a basis set incorporating pseudopotentials—accounting only for valence electrons—was applied, thereby incorporating relativistic corrections into the computational framework.

Theoretical assessments of the bioactivity of metal-pyridine fragments of tetrathio-arsenates(V) of selected d-metals were conducted using the computer program PASS C&T. According to the calculations, the conjugation of metal-pyridine and tetrathioarsenate fragments appears to be a promising strategy for the synthesis of coordination compounds exhibiting a broad spectrum of biological activities (Pa = 0.570–0.900). The predicted activities include potential applications in the treatment of atherosclerosis, antineoplastic effects, antiseborrheic properties, antiviral activity against Picornaviruses, and cytoprotective functions, among others.

References:

[1] Paul, N.P., Galván, A.E., Yoshinaga-Sakurai, K., Rosen, B.P. 2023, Arsenic in medicine: past, present and future, Biometals, 36, pp. 283-301. https://doi.org/10.1007/s10534-022-00371-y

[2] Yang, Y., Li Y., Li, R., Wang, Z. 2024, Research progress on arsenic, arsenic-containing medicinal materials, and arsenic-containing preparations: clinical application, pharmacological effects, and toxicity, Front. Pharmacol., 15, 1338725. doi: 10.3389/fphar.2024.1338725

[3] Liu, J., Lu, Y., Wu, Q., Goyer, R. A., Waalkes, M.P. 2008, Mineral Arsenicals in Traditional Medicines: Orpiment, Realgar, and Arsenolite, The Journal of Pharmacology and Experimental Therapeutics, vol. 326, no. 2, pp. 363-368.

[4] Avakyan, L. A., Avakyan, A. L. 2022, The technological basis for extraction of arsenic from various raw materials, Theoretical Foundations of Chemical Engineering, vol. 56, no. 4, pp. 703-710. Springer Nature. https://doi.org/10.1134/S004057952204002X

PP–24. QUALITATIVE AND QUANTITATIVE CHARACTERIZATION OF PHENOLIC COMPOUNDS IN WINE LEES FROM GEORGIAN INDIGENOUS GRAPE VARIETIES (QISI, RKATSITELI AND SAPERAVI)

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In recent years, global interest in natural bioactive compounds has increased significantly, particularly those exhibiting antioxidant, anti-inflammatory, and antimicrobial properties. Polyphenols are well recognized for their biological activity, and grape-derived products, including wine, represent one of the richest dietary sources of these compounds. Consequently, winery by-products such as wine lees have attracted attention as potential sources of valuable phenolics.

Wine production generates substantial quantities of by-products, including grape pomace, seeds, and wine lees. The present study aimed to qualitatively and quantitatively characterize phenolic compounds in wine lees obtained from commonly cultivated Georgian grape varieties (Saperavi, Rkatsiteli, and Qisi), produced using two different winemaking technologies (Traditional Kakhetian method and factory conditions). Georgia, one of the oldest wine-producing regions in the world with approximately 8,000 years of documented viticulture and nearly 500 indigenous grape varieties, provides a unique context for investigating grape-derived bioactive compounds. These varieties offer an opportunity to evaluate the influence of grape genotype and winemaking technology on phenolic composition [1-3].

Phenolic compounds were analyzed using LC–MS/MS, while total phenolic content (TPC) was determined spectrophotometrically using the Folin–Ciocalteu method. In total, 21 phenolic compounds were identified and quantified in five wine lees samples: Quercetin-3-Orutinoside, Quercetin, Apigenine, catechin, Ferulic acid, Gallocatechin, Kaempferol-3-O-galactoside, Kaempferol-3- O-glucoside, p-Coumaric acid, Protocatechuic acid, Delphinidin-3-O-glucoside, Quercetin-3-O-glucoside, Caffeic acid, Malvidin- 3-O-glucoside, Petunidin-3-Oglucoside, Cyanidin-3-O-glucoside, Gallic acid, Kaempferol, Epicatechin gallate, Luteolin-7-O-glucoside, Ellagic acid. The representative LC–MS/MS chromatogram of traditionally produced Rkatsiteli wine lees demonstrates the qualitative phenolic profile corresponding to the identified compounds.

Traditionally produced Saperavi wine lees exhibited the richest qualitative phenolic profile, with 13 identified compounds among the analyzed samples. Total phenolic content (TPC), expressed as µg GAE/mL, is summarized in Table 1. Traditionally produced Saperavi wine lees showed the highest TPC value (256.68 µg GAE/mL). Comparative analysis of samples derived from the same grape variety but processed using different technologies confirmed the significant influence of winemaking technique on total phenolic content.

Table 1. Total Phenolic Content (TPC) of Wine Lees Samples

Sample	Total Phenolic Content (µg GAE/mL)
Qisi (T)	142.53
Rkatsiteli (T)	121.64
Saperavi (T)	256.68
Rkatsiteli (F)	102.32
Saperavi (F)	160.80

T –traditional Kakhetian method, F - Factory conditions.

The present study provides a comprehensive qualitative and quantitative characterization of phenolic compounds in Georgian wine lees and highlights their significant bioactive potential. In total, twenty-one phenolic compounds were identified across all analyzed samples, with traditionally produced

Saperavi wine lees exhibiting the richest qualitative profile and the highest total phenolic content. The observed variability among grape varieties and winemaking technologies confirms the influence of both grape genotype and production method on phenolic composition.

Overall, the findings indicate that Georgian wine lees, currently regarded as a by-product of the wine industry, represent a promising and sustainable source of biologically active compounds. These results support further investigation into the biological properties and potential applications of wine lees-derived phenolics.

References

[1] Commission of the European Communities 2011, 'A resource-efficient Europe–flagship initiative under the Europe 2020 Strategy', Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee, and the Committee of the Regions, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX[52]011DC0021

[2] McGovern, P., Jalabadze, M., Batiuk, S., Callahan, M.P., Smith, K.E., Hall, G.R., et al. 2017, 'Early Neolithic wine of Georgia in the South Caucasus', Proceedings of the National Academy of Sciences of the United States of America, vol. 114, no. 48, pp. E10309–E10318.

[3] Santos-Buelga, C., González-Manzano, S., González-Paramás, A.M. 2021, 'Wine, Polyphenols, and Mediterranean Diets. What Else Is There to Say?', Molecules, vol. 26, no. 18, pp. 5537.

PP–25. ACTORS AFFECTING THE SEQUENTIAL EXTRACTION PROCESS OF VALUABLE PRODUCTS FROM AGRO-INDUSTRIAL WASTE

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Agricultural plant residues are a source of various bioactive compounds and can be used for the production of different products such as essential oils, natural food colorants, polyphenols, and other valuable chemicals. The use of agricultural waste as a raw material can help reduce production costs and decrease environmental pollution [1].

Sequential, stepwise extraction of valuable products from agricultural residues is a method that we have developed over recent years. Examples include the utilization of grape pomace and seeds, tangerine and orange peels, tomato paste waste, onion peel, and almond hulls using a sequential extraction approach [2-5].

The main advantage of this method is that it enables the recovery of more than one valuable product from a single agro-industrial waste material. Factors affecting successful sequential extraction include the shelf life of the waste material and the correct sequence of extraction steps, which ensures ease of extraction and high purity of the selected products. Conventional, ultrasonic, and supercritical fluid extraction methods are commonly used as tools in sequential extraction processes.

The use of supercritical CO_2 extraction for the recovery of valuable compounds from different wastes has several advantages over other extraction techniques. The solvent can be easily removed from the mixture by pressure reduction. Supercritical fluid extraction is irreplaceable for sequential extraction when one of the target products is oil. Pure CO_2 is used as the solvent in the first extraction step. The second and subsequent steps require the selection of co-solvents with increasing polarity to extract more polar compounds. Examples include sequential supercritical CO_2 extraction used to obtain oil and different polyphenols from grape seeds, as well as essential oil, β-carotene, and hesperidin from tangerine and orange juice processing waste.

Ultrasound-assisted extraction offers high reproducibility in a shorter time, higher product yields, simplified operation, reduced processing temperatures, and lower energy consumption. This method

has been used for the sequential extraction of quercetin and natural colorants from red onion skin; lycopene and β-carotene from tomato paste waste; and polyphenols, pentacyclic triterpenoids, and pectin from apple peel and almond hulls.

Some conventional stepwise extraction methods represent low-cost alternatives to supercritical and ultrasonic techniques. For example, conventional extraction has been applied to obtain essential oil, β-carotene, pectin, and hesperidin from tangerine and orange juice processing waste. This method is fast and simple but highly specific and cannot be easily generalized to other agricultural wastes.

In some cases, it is preferable to use solvents with decreasing polarity, in sequential ultrasound extraction method, especially when the raw material contains a large amount of simple water-soluble carbohydrates. An example is the extraction of carbohydrates, pectin, and pentacyclic triterpenoids—ursolic, oleanolic, and betulinic acids, from almond hulls.

References

[1] Taurisano, V., Anzelmo, G., Poli, A.,Nicolaus,B., Di Donato,P. 2014, 'Re-use of Agro-industrial Waste: Recovery of Valuable Compounds by Eco-friendly Techniques', International Journal of Performability Engineering, vol. 10, no. 4, pp. 419-425.

[2] Oboladze, Sh., Tsitsagi, M., Rubashvili, I., Chkhaidze, M., Khachidze, M., Ebralidze, K. 2024, 'Development and Feasibility Evaluation of the Extraction Methods for Obtaining Quercetin from Onion Peel', The Chemist-Journal of the American Institute of Chemist, vol. 95, no. 1.

[3] Tsitsagi, M., Chkhaidze, M., Ebralidze, K., Rubashvili, I., Tsitsishvili, V. 2018, 'Sequential Extraction of Bioactive Compounds from Tangerine (Citrus Unshiu) Peel', Annals of Agrarian Science, vol. 16, no. 2, pp. 236-241.

[4] Rubashvili, I., Tsitsagi, M., Zautashvili, M., Chkhaidze, M., Ebralidze, K., Tsitsishvili, V. 2020, 'Four Valuable Bioactive Compounds Obtained from Citrus Waste Using Sequential Two-Step Ultrasound Assisted Extraction Method', Revue Roumaine de Chimie, vol. 65, no. 10, pp. 919-928.

[5] Tsitsagi, M., Rubashvili, I., Chkhaidze, M., Khachidze, M., Ebralidze, K. 2021, 'Extraction and analysis of oleanolic acid and ursolic acid from apple processing waste materials using ultrasound-assisted extraction technique combined with high performance liquid chromatography', Bulletin of the Georgian National Academy of Sciences, vol. 15, no. 4, pp. 50-56.

PP–26. POLYVINYL ALCOHOL-BASED FILMS FOR THE TRANSDERMAL DELIVERY OF ENDOGENOUS GROWTH-INHIBITING PROTEINS

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The feasibility of transdermal delivery of a thermostable protein complex (TPC) from adult rat liver was assessed using polyvinyl alcohol (PVA)-based films. TPC immobilized in PVA–vinyltriethoxysilane (VTES) films significantly reduced the mitotic index in liver (–46%) and kidney (–30%) cells, whereas PVA-only films had no effect. The incorporation of starch as a third component did not enhance film solubility, hence it did not alter the growth-inhibitory effect of the immobilized TPC. It is well known that various routes of drug administration exist, including oral, intravenous, intramuscular, and subcutaneous delivery; however, each of these routes is associated with specific limitations. These include the low stability of the drug in the gastrointestinal tract and its susceptibility to first-pass metabolism. In addition, drugs may undergo degradation due to enzymatic activity or the acidic environment of the stomach [1]. These and other limitations are particularly pronounced when administering peptide- or protein-based drugs [2]. Therefore, the search for alternative routes for delivering protein compounds into the body is highly relevant. One suh route is the transdermal delivery of bioactive substances. Transdermal drug delivery (TDD) is a noninvasive or minimally invasive method that allows a certain amount of drug to pass through the epidermal layer of the skin by free diffusion or other means and

continues to enter the systemic circulation at a controlled rate [3]. When substances are delivered via this route, the aforementioned limitations are largely avoided.

Among transdermal delivery systems, films are the most common and widely used form. The film-forming polymers can be applied alone or in combination with other polymers to produce films with the desired properties [4]. Accordingly, the aim of the present study was to evaluate the feasibility of delivering a thermostable protein complex (TPC), which inhibits cell growth, immobilized in polyvinyl alcohol-based films of varying composition, into the body.

We have previously demonstrated that TPC inhibits cell proliferation through transcriptional suppression.In the present study, we sought to determine whether this endogenous protein complex retains its biological activity in vivo when administered noninvasively via the transdermal route. For this purpose, PVA-based films were used.

To exclude any potential negative (toxic) effects of the polymer films on the morpho-functional activity of cells, we evaluated their impact on liver histoarchitecture in white rats. The results demonstrated that film application did not induce any histoarchitectural changes in the liver or kidney tissues of experi mental animals, indicating that the observed reduction in mitotic activity was due to the specific biological action of the protein complex rather than polymer toxicity.

Compared to intact controls, treatment with TPC immobilized in PVA/VTES films resulted in a significant decrease in mitotic activity in both liver and kidney, suggesting that TPC is absorbed through the skin and reaches these organs, retaining its ability to suppress mitotic activity in juvenile rat tissues. In contrast, TPC immobilized in PVA-only films showed no effect on proliferative activity in liver or kidney, indicating that the presence of a crosslinker, in this case VTES, is essential for protein release from the film.

Furthermore, the addition of starch to PVA-only films did not confer antiproliferative activity of immobilized TPC, confirming that VTES is necessary for protein release. In PVA/VTES films, starch addition did not increase the antiproliferative effect of immobilized TPC, which may be due to the limited absorption rate through the skin despite enhanced release from the film.

Interestingly, in tissues of experimental animals, while the mitotic index decreased under TPC treatment, the number of Ki-67-positive cells increased, likely reflecting compensatory accelerated entry of cells into the cell cycle in the juvenile organism.

Based on the results of the present study, we can conclude that the feasibility of using a polyvinyl alcohol/vinyltriethoxysilane (PVA/VTES) film for non-invasive delivery of biologically active substances is directly dependent on the presence of vinyltriethoxysilane. Moreover, The use of starch as an additional component in a film based on polyvinyl alcohol cannot ensure an increase in the penetration rate of the thermostable protein complex through the film, and consequently, does not enhance its inhibitory effect.

References

[1] Dahan A, Miller JM, Amidon GL. Prediction of solubility and permeability class membership: provisional BCS classification of the world's top oral drugs. AAPS J. 2009;11 740–6.

[2] Wen NX, Venkatraman S. Protein delivery options: how well have we succeeded? Ther Deliv. 2015;6 537–539. doi: 10.4155/tde.15.11.

[3] Long, L., Zhang, J., Yang, Z., Guo, Y., Hu, X., & Wang, Y. (2020). Transdermal delivery of peptide and protein drugs: Strategies, advantages and disadvantages. Journal of Drug Delivery Science and Technology, 60, 102007.

[4] Pünnel LC, Lunter DJ. Film-Forming Systems for Dermal Drug Delivery. Pharmaceutics. 2021 Jun 23;13(7) 932. doi: 10.3390/pharmaceutics13070932. PMID: 34201668; PMCID: PMC8308977

PP–27. MORPHO-ANATOMICAL STUDIES FOR DETERMINING THE PHARMACOGNOSTIC POTENTIAL OF GEORGIAN ENDEMIC PLANTS

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The flora of Georgia is distinguished by a high degree of endemism, which grants it particular importance both in terms of biodiversity and in the study of medicinal plants [1,4]. The investigation of the morpho-anatomical structure of endemic plants of the local flora has been driven by the need to determine their pharmacognostic potential, thereby establishing a foundation for pharmacognostic analysis and the evaluation of medicinal potential based on the identification and standardization of endemic species [3,5,7]. Determining the microstructural diagnostic characteristics of phylogenetically related endemic species of officinal medicinal plants carries special significance in pharmacognostic research, since these very features serve as the basis for the identification and quality control of medicinal and potentially medicinal plants.

Common sage, *Salvia officinalis* L., is widely used in the pharmaceutical industry of many countries. The genus *Salvia* L. is represented in Georgia by 13 species, among which *Salvia garedji* Troitzk. (Labiatae) belongs to the local endemics of the native flora [1,2,6]. With the aim of revealing its biological characteristics, the morpho-anatomical structure of Garedji sage has been studied and established.

Garedji sage is a perennial, light-loving, densely pubescent, xerophilous plant. It is characterized by both simple, uni- and multicellular, conical trichomes (often curved hook-like) as well as glandular trichomes with spherical heads. The covering tissue of all organs of Garedji sage is coated with a thick, often unevenly undulating cuticle. Its axial organs are distinguished by the differentiation of mechanical tissues - lamellar and mixed-type collenchyma, xylem and phloem fibers. The conducting system in the internodes of the shoot is monocyclic, represented by a continuous cylinder of phloem and xylem; the phloem is perixylary, while the xylem is dominated by tracheids and vessels with spiral thickenings of uneven caliber (rarely annular). Homogeneous radial rays of one or two rows and fibrous xylem cells are also observed. In the petiole zone, the leaf stalk, and the main vein of the lamina, collateral-type primary and lateral vascular bundles are differentiated. The leaf lamina of Garedji sage is bifacial in form, with amphistomatic, dorsiventral mesophyll structure. The basal cells of the adaxial and abaxial epidermis are irregular, curved, and wavy-walled. The leaf's ventilatory system is represented by a diacytic type of stomatal apparatus. The parenchymal tissue of the vegetative organs of Garedji sage is rich in starch grains, large oval plastids, fatty (essential oil) droplets, and crystals (raphides), which indicate the species' secretory activity.

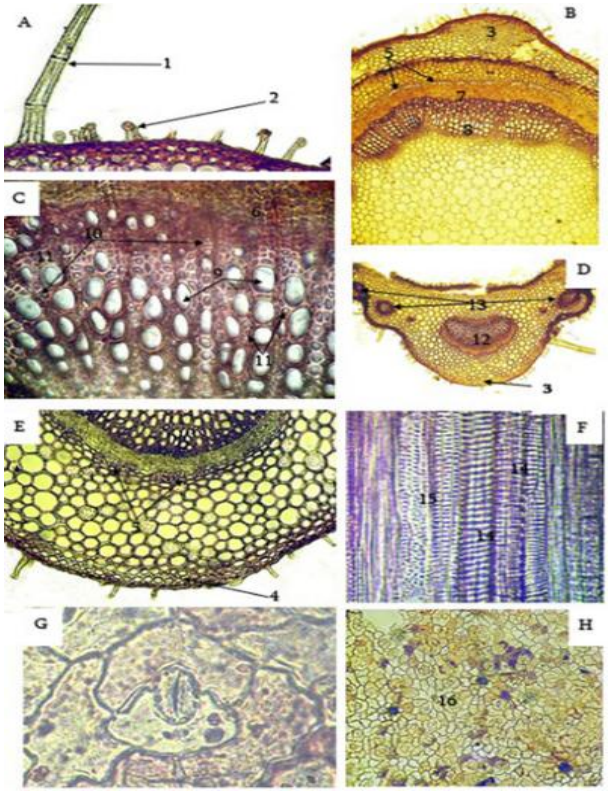

Figure. Macro- and microstructural features of *S. garedji* Troitzk. Trichomes (A), shoot internode (B), xylem tracheary tissue (C), leaf petiole or mesopetiole (D), main vein of the leaf lamina (E), tracheary vessels in longitudinal section (F), diacytic stomatal apparatus (G), and leaf epidermis (H). The structures comprise conical multicellular and glandular spherical-headed trichomes (1–2), lamellar and mixed-type collenchyma (3–4), phloem fibers (5), cambium (6), phloem (7), xylem (8), lumina of conducting vessels and tracheids (9–10), xylem fibers (11), median and lateral collateral vascular bundles (12–13), spiral and pitted tracheary elements (14–15), and non-stitched, curved, wavy-walled basal cells (16).

References:

[1] Flora Georgiae, edition secunda,v.XI, Tbilisi,1987; Pp.150-170;
[2] Gagnidze R. - Vascular plants of Georgia a nomenclatural checklist; Tbilisi 2005, p. 137-138
[3] Gergauli N., Mchedlidze K., Aneli J. 2024, Blackberry species endemic to the flora of Georgia - *Rubus cyri* Juz. Microstructural features of above-ground vegetative organs, Georgian Scientists, vol. 6 no. 1, https://doi.org/10.52340/gs.2024.06.01.29;
[4] Kuchukhidze J., Gagnidze R., Gviniashvili TS., Jokhadze M. 2006, Endemic flowering plants of Georgian flora, pp.-213;
[5] Korkotadze T., Berashvili D., Getia M., Mchedlidze K., Legault J., Mshvildadze V. 2024, Pharmacognostical study of aerial Parts of *Thymus collinus* Bieb. growing in Georgia, Georgian Scientists, vol. 6 no. 1, https://doi.org/10.52340/gs.2024.06.01.11;
[6] Nomenclatural checklist of flora of Georgia, Tbilisi 2018, p. 170;
[7] Sukhishvili N., Mchedlidze K., Mulkijanyan K., Mskhiladze L. 2023, Microstructural Features of *Primula woronowii* Losinsk., *Primula macrocalyx* Bunge. and *Primula saguramica* Gavr. from Georgian Flora, Georgian Biomedical News, vol.1, no.2, DOI: 10.52340/GBMN.2023.01.01.17

PP–28. TIKHA ASCANE–REINFORCED BIODEGRADABLE POLYMER BLENDS FOR THERAPEUTIC DELIVERY APPLICATIONS

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In response to the growing demand for multifunctional biomaterials in biomedical and cosmetic applications [1, 2], this study focuses on the development and physicochemical characterization of hybrid matrices composed of Georgian natural bentonite (Tikha-Ascane, TA) [3, 4], sodium alginate (SA), and polyvinylpyrrolidone (PVP), formulated with and without polyethylene glycol (PEG). Rutin (Rut) incorporated at two concentrations (0.5% and 4%, w/w), was selected as a model bioactive agent [5] to assess the potential of these blends as drug delivery systems.

Poly-blends were composed by initially preparing separate aqueous solutions of polymers and hydrated clay dispersion. The SA and PVP solutions were combined and stirred at 40–60 °C for 30 min to obtain a homogeneous polymer blend. This mixture was then gradually added to the pre-hydrated TA dispersion under continuous stirring until a uniform hybrid matrix was formed. In PEG-containing systems, the plasticizer was introduced slowly to the clay suspension under steady agitation prior to polymer incorporation, ensuring its uniform distribution within the matrix. Drug-loaded systems were obtained by introducing RUT into the hydrated TA prior to polymer blending, ensuring its homogeneous distribution within the composite network.

The incorporation of PEG resulted in changes to the physicochemical and functional characteristics of the formulations. Specifically, PEG addition resulted in a substantial increase in viscosity, with values rising by 1.5-fold in the PEG-containing base formulation and by 3.3-fold and 12.7-fold in formulations loaded with 0.5% and 4% rutin, respectively, compared with PEG-free systems. This effect was more pronounced at higher RUT concentration, indicating a synergistic contribution of PEG and active compound loading to the structural reinforcement of the gel matrix.

Moisture loss studies demonstrated a reduction in water evaporation of approximately 7 to 9% following PEG incorporation, indicating improved water-retention capacity and potentially enhanced formulation stability during storage and application.

Textural analysis revealed a PEG-dependent decrease in spreadability (Fig.1). Compared to PEG-free formulations, spreadability was reduced by 9.7% in the PEG-containing base formulation, by 22.1% in the 0.5% rutin-loaded formulation, and by 37.6% in the 4% rutin-loaded formulation, in accordance with the observed viscosity enhancement.

Microscopic analyses confirmed the homogeneity of the formulations revealing the formation of dense and uniform systems (Fig.2) compared to PEG-free samples.

Chromatographic evaluation demonstrated that RUT was efficiently incorporated into the gel formulations without detectable degradation or loss during formulation.

Therefore, the developed hybrid matrices containing Georgian bentonite, SA, and PVP, optionally modified with PEG reveal favorable physicochemical properties, and suitability for biomedical and cosmetic use.

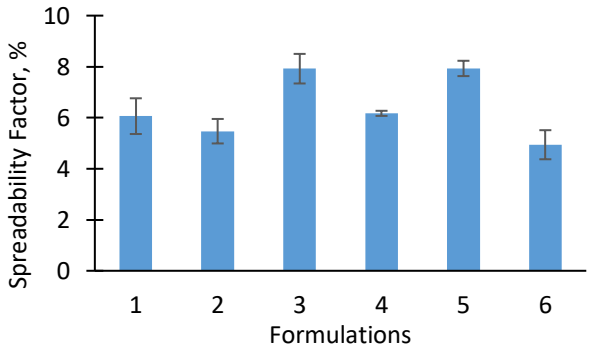

Fig. 1. Effect of PEG on the spreadability of the formulations: 1-base, 2-base+PEG, 3-base+0.5% RUT, 4 - base+PEG +0.5% RUT, 5-base+4% RUT, 6- base+PEG +4% RUT .

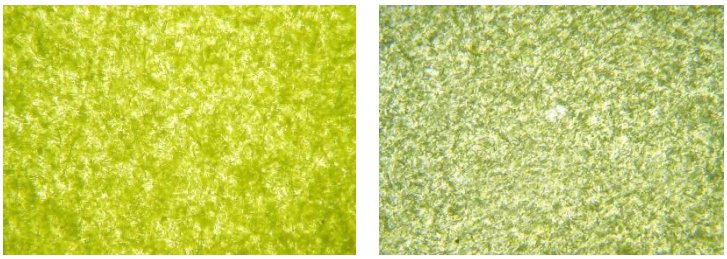

Fig. 2. RUT loaded formulations with (A) and without (B) PEG.

References

[1] Morariu, S., Brunchi, CE., Honciuc, et all. 2023, Development of hybrid materials based on chitosan, poly(ethylene glycol) and Laponite® RD: effect of clay concentration. *Polymers,* vol. 15, no. 4, pp. 841.
[2] Ali, M., Mir, S., Atanase, LI., et all. 2024, Chitosan–PVA–PVP/nano-clay composite: a promising tool for controlled drug delivery. *RSC Advances*, vol. 14, no. 22, pp. 14157–14177.
[3] Kutateladze I.G. (1955), Tikha-ascane for medical purpose. Tbilisi, "*Gruzmedgiz*", 39 p (in Russian).
[4] Tsiklauri, L., Tsagareishvili G. 2011, Gastroenterological and dermatological soft drug formulations containing Georgian bentonite clay preparation–Thikha-ascanae. Tbilisi, *"Universal"*, 89 p (in Georgian)
[5] Kalita, B., Das, MK. 2018, Rutin–phospholipid complex in polymer matrix for long-term delivery of rutin via skin for the treatment of inflammatory diseases. *Artificial Cells, Nanomedicine, and Biotechnology*, vol. 46, no. 1, pp. 41–56.

PP–29. FORMULATION AND TECHNOLOGY OF ROSEHIP (*ROSA CANINA* L.) CREAM.

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Modern pharmacies offer a wide range of cosmetics, most of which are synthetic in origin and can cause allergic reactions (skin itching, redness, swelling, peeling, rash) [6]. Safe and effective cosmetics for dry skin include creams, formulated with natural ingredients and free of preservatives, corrigents (dyes, fragrances, or glitter) [2,3]. Plant-based ingredients are successfully used in cosmetology, including rosehip oil and extract, which contain a rich complex of biologically active substances: flavonoids, vitamins, fatty acids, and microelements. Rosehip (*Rosa canina* L.) products are used in ointments, creams, gels, shampoos, and more. Its chemical composition ensures skin regeneration, hydration, nutrition, protection, and regulation of metabolic processes. Therefore, in the studied cream formulations, rosehip fruit oil extract has been included as anactive pharmaceutical ingredient

(API). This extract contains a large amount of carotenoids and vitamins C and E, which help prevent the formation of free radicals and protect the skin from dryness and aging[1,7].

The aim of the research was to define the optimal formulation and develop a technology ofa cosmetic cream for dry skin care based on rosehip (*R. canina* L.) oil extract [4].

The research used physico–chemical, biopharmaceutical and technological methods [5]. The research objects were research formulations of an cream for dry skin care.

Table 1. Cream Formulations**.**

№	Ingredients (g)	F1	F2	F3	F4	F5	F6	F7
1	Wax	1.0	1.0	1.0	1.0	1.0	1.0	1.0
2	Spermaceti	4.0	4.0	4.0	4.0	4.0	2.0	2.0
3	Olive oil				25.0	25.0		
4	Corn oil	25.0						
5	Peach oil		25.0				10.0	
6	Almond oil			25.0				
7	Cocoa butter		2.0	2.0				
8	Coconut butter	2			2.0	2.0		
9	Shea butter						1.0	1.0
10	Aromatic rose water	14.0					14.0	14.0
11	Aromatic mint water		14.0	14.0				
11	Aromatic tea tree water					14.0		
12	Distilled water				14.0			
13	Tween-60 (polysorbate 60)						5.0	5.0
14	Peg-400						2.0	
15	Rosehip oil extract	4.0	4.0	4.0	4.0	4.0	10.0	17.0
16	Glycerin						5.0	2.0
17	Propylene glycol							5.0
18	Isopropyl myristate							2.0
19	Monostearate glycerin							1.0
Total amount of cream		50.0	50.0	50.0	50.0	50.0	50.0	50.0

On the basis of physical-chemical, biopharmaceutical and technological studies, the optimal composition was selected from seven research recipes of cream for dry skin care - F7: 1 g of wax, 2.0 g of spermaceti, 17.0 g of rosehip oil extract (*R. canina* L.), 1.0 g of shea butter, 11 ml of aromatic rose water, 5.0 g of emulsifier Tween-60, 5.0 g Glycerin, 1.0 g of monostearate glycerin, 5.0 g of propylene glycol, 2.0 g of isopropyl myristate.

A technological scheme for the preparation of rosehip cream (*R. canina* L.) of the emulsion (water/oil) type and the technological process of its preparation were developed, the material balance was drawn up and the technical and economic indicators were calculated: technological yield ɳ= 96.6%; technological costs E = 4.4%; cost factor K = 1.04; The studied indicators of the quality of rosehip cream for dry skin care: Organoleptic indicators (uniformity, odor, color), ability to distribute and absorb on the skin; hydrogen indicator pH; rheological indicators viscosity, colloidal stability, thermal stability.The dynamics of carotenoid release from a cosmetic cream was studied using Franz diffusion cells. The study found that 56% of the active pharmaceutical ingredient (carotenoid) was released from a rosehip cream for dry skin care within 3 hours.

Based on physicochemical, biopharmaceutical, and technological studies, the formulation of an emulsion cream (w/o) containing rosehip oil extract for the cosmetic care of dry skin was established, and the technology for its preparation was developed. The cream qualityindicators were evaluated and the release dynamics of the active pharmaceutical ingredientfrom the cream were determined.

References:

[1] Amin Selahvarzian1, Abuzar Alizadeh1, Peyman Amanolahi Baharvand and others. 2018; „Medicinal Properties of *Rosa canina* L.“ Journal . Herbal Medicines. Vol.3, No1,Pages:1-8;

[2] Katya Hutova, Velichka Andonova, Natalina Panova and others.2025.Design and „Characterization of Cosmetic Creams Based on Natural Oils from the Rosaceae Family“. Journal „Cosmetics“.12(6),p.248;

[3] Muggu SankaraBhavani, CH.Naveena, P.Nagamani, B. Sowmya. 2023. „Formulation and Evaluation of Herbal Face Cream“. International Journal of Pharmaceutical Sciences Review and Research. November–December. Article No. 11, Pages: 74-78;

[4] Pooja Babasaheb Ligade, Sayli Sagar Jadhav, Arti Ingole, Dr.P.N. Sable. 2025. „Formulation and Evaluation of Herbal Moisturizer Containing Cucumber, Rosehip Oil and Lavender Oil: A Topical Approach for Skin Wellness“. International Journal of „Pharmaceutical Research and Applications“. Volume 10, Issue 6 Nov - Dec, pp: 424-433;

[5] Sabitov Askhat Sultanovich. 2022. „Development and conformity assessment of perfumery and cosmetic products based on broad-thorn rose (Rosa platyacantha Schrenk)“. 6D074800–Pharmaceutical Production Technology. Dissertation.;

[6] Satyapriya Roy, Shilpi Saha, 2025.„Potential Health Risks Associated with Cosmetics and Personal Care Products: An Overview“. AJMCRR, 2025, Volume 4 (7). p.1-19.

[7] Somnath S Davkhar, Aarti S Bhandari, Sanjivani A Akolkar. 2023. „Formulation and Evaluation of Multipurpose Herbal Cream“. Journal Sys Rev Pharm .14 (1). p.23-28.

PP–30. STANDARDIZED ENDODONTIC IRRIGANT BASED ON LEAVES' POLYPHENOLS FROM COTINUS COGGYGRIA GEORGIAN CULTIVAR: INTEGRATED ASSESSMENT

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Persistent intraradicular infection remains a principal cause of endodontic treatment failure. Resistant microorganisms, particularly Enterococcus faecalis, demonstrate survival following conventional chemomechanical preparation and irrigation protocols. Moreover, commonly used irrigants may induce cytotoxicity, dentinal alteration, discoloration, and hazardous precipitate formation during sequential application. These limitations justify the investigation of standardized phytochemical alternatives capable of providing effective and biologically safe canal disinfection.

A hydrolysable tannin–rich extract derived from cultivated Cotinus coggygria leaves (Georgia) was investigated. Phytochemical characterization by HPLC/UV and HPLC/MS confirmed the presence of 22 phenolic constituents, predominantly galloyl glucose derivatives. Purification yielded a tannin-dominant fraction demonstrating structural stability after microwave sterilization and improved antimicrobial consistency compared to crude extract preparations. In vitro antimicrobial assessment revealed that the 5% crude extract exhibited no activity, and only limited activity at 10% and 15%. In contrast, similar concentrations of purified fraction demonstrated concentration-dependent efficacy (Table.1)

The clinical phase included 30 patients (35 infected teeth). Root canal samples were obtained prior to instrumentation and analyzed at the Eliava Bacteriophage Analytical Diagnostic Center. Bacterial identification was performed using the automated VITEK® 2 Compact system. Clinical isolates included Enterococcus faecalis, Streptococcus sanguinis, Streptococcus oralis, Staphylococcus aureus, Staphylococcus epidermidis, and Leuconostoc mesenteroides ssp. cremoris. Antimicrobial susceptibility testing was conducted according to EUCAST standards. [1]

Table 1. Susceptibility of clinical isolates to extract preparations

Formulation	5%	10%	15%
Crude extract	R	Low susceptibility	Low susceptibility
Purified fraction	S (partial)	S (majority)	S (all isolates)

* R–Resistant; S - Susceptible

The 10% purified formulation demonstrated marked antimicrobial efficacy in the majority of isolates, whereas the 15% purified fraction showed maximal antimicrobial effect against all clinically derived strains (Tab. 1). Acute toxicity assessment (OECD guidelines) demonstrated wide safety margins relative to projected clinical exposure levels, with no irritative or sensitizing effects observed. Chemical compatibility testing confirmed absence of cytotoxic precipitate formation when combined with commonly used endodontic irrigants.

The integration of phytochemical standardization, antimicrobial validation, chemical compatibility assessment, toxicological safety evaluation, and clinical microbiological confirmation provides a strong translational framework for this preparation. Ongoing investigations aim to further evaluate its long-term clinical performance and therapeutic integration into contemporary irrigation protocols. Based on the currently available experimental and patient-derived data, it can be confidently stated that the standardized Cotinus coggygria polyphenol extract represents a biologically safe, highly effective, natural alternative or adjunctive irrigant for the management of endodontic infections.

References:

[1] European Committee on Antimicrobial Susceptibility Testing. (n.d.). *EUCAST*. https://www.eucast.org

PP–31. ANTIOXIDANT PROPERTIES OF HUMIC ACID-DERIVED NANOCOMPOSITES WITH METAL NANOPARTICLES

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The development of multifunctional antioxidant agents based on biocompatible and environmentally benign matrices represents a critical direction in contemporary pharmacology. In this context, humic acids, as naturally occurring macromolecular systems, have attracted increasing attention due to their intrinsic redox activity. The present study aims to evaluate the antioxidant potential of novel noble metal-containing bionanocomposites synthesized using humic acids as stabilizing and functional matrices. Humic acids are complex macromolecular systems with a cross-linked network structure containing a wide variety of functional groups, including phenolic hydroxyl, quinone, alcoholic hydroxyl, methoxyl, and carboxyl groups. These functionalities confer pronounced electron-donating and electron-accepting properties, enabling humic substances to participate in redox cycling, metal ion chelation, and radical scavenging processes. Moreover, their amphiphilic nature and buffering capacity allow them to regulate protolytic equilibria in biological systems, further contributing to their antioxidant behavior.

The presence of multiple coordination-active sites facilitates the formation of stable interactions between humic acids and metal nanoparticles, including noble metals. As a result, humic acids serve as efficient stabilizing agents, promoting the formation of metal-containing bionanocomposites with enhanced stability and resistance to aggregation. The incorporation of metal nanoparticles into the humic matrix leads to synergistic effects, combining the antioxidant activity of humic acids with the redox properties of metal nanostructures, thereby expanding their functional potential for ensuring pharmaceutical applicability.

The antioxidant activity of the synthesized bionanocomposites was evaluated using the DPPH radical scavenging assay and electrochemical methods, with ascorbic acid as a reference standard. The obtained results demonstrate that all synthesized nanocomposites exhibit antioxidant activity, which independent of the metal content in the humic matrix. Electrochemical analysis also confirms their ability to participate in redox processes, indicating efficient electron transfer capabilities. In conclusion, the resulting bionanocomposites retain the antioxidant properties of the humic matrix while benefiting from the additional functional contributions of metal nanoparticles. These findings highlight their potential as promising multifunctional antioxidant agents with prospective applications in pharmacology, particularly in the development of anti-inflammatory formulations.

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PP–32. THE IMPACT OF GMP AND GDP STANDARDS ON THE REGULATORY ENVIRONMENT AND QUALITY ASSURANCE OF THE PHARMACEUTICAL SECTOR

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Quality management of medicinal products remains a paramount priority within contemporary healthcare systems. To ensure the delivery of efficacious, safe, and high-quality pharmaceutical products to the end-user, the manufacturing and distribution cohorts must be governed by rigorous and transparent regulatory frameworks. In Georgia, the mandatory implementation of international benchmarks Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP) was enacted on January 1, 2022 (Government Decree No. 349). These standards delineate the comprehensive pharmaceutical quality assurance continuum:

- Raw Material Oversight: Selection of validated, certified precursors.
- Manufacturing (GMP): Utilization of cleanrooms, calibrated instrumentation, and stringent personnel hygiene protocols.
- Quality Control (QC): Systematic laboratory testing and batch release authorization.
- Warehousing and Logistics (GDP): Strict adherence to thermolabile requirements and "Cold Chain" integrity.
- Pharmacy and Patient: Ensuring the provision of non-compromised therapeutic interventions.

To evaluate the impact of these regulations on local manufacturing and the supply chain by comparing the pre- and post-implementation landscapes of GMP/GDP standards the following qualitative research instruments were used:

- Regulatory framework analysis: Assessment of the alignment between Georgian legislation and the EU directives.
- Structural market review: Analysis of the transformation of domestic pharmaceutical enterprises resulting from the integration of these standards.
- Comparative assessment: Identification of regulatory dividends (enhanced quality, export potential) versus systemic challenges (capital expenditure, market concentration).

The study revealed the two major effects:

1. Standardization efficacy: The integration of GMP/GDP standards has harmonized product quality throughout the lifecycle, from the synthesis phase to the point of consumption.

2. Data integrity: Pharmaceutical information has transitioned into a managed, structured, and audited resource. Comparative metrics indicate a significant longitudinal increase in quality indicators.

Table 1: Comparative Analysis of Information Quality and Regulatory Indicators

Indicator	Pre-Implementation	Post-Implementation	Growth Dynamics
SOP–Standardization	40%	90%	+50%
Record Accuracy and Reliability	35%	95%	+60%
Data Traceability	25%	90%	+65%
Regulatory Compliance	30%	85%	+55%

3. Infrastructural and structural paradigm shifts: The escalation of regulatory rigor catalyzed market optimization, necessitating the replacement of sub-standard units with high-technology facilities.

- Pre-Implementation: Approximately 51 pharmaceutical manufacturers and 750 wholesale distributors operated in Georgia.
- Post-Implementation: Only 4 manufacturers and 85 wholesale distributors achieved full compliance with the updated GMP/GDP mandates.

The tightening of the regulatory net has yielded a dual-faceted impact:

- Positive externalities: Augmented trust in domestic production, expanded export horizons within international markets, and the mitigation of risks associated with counterfeit or sub-standard medicines.
- Evidence-based challenges: Exorbitant financial outlays for re-inventarization, the exit of small-scale enterprises (leading to market concentration), and a palpable deficit in highly specialized human capital.

The strategic prospect of import substitution and the expansion of domestic manufacturing indices necessitate robust state intervention. During this critical adaptation phase, the government should consider targeted subsidies or concessional credit lines for smaller enterprises to ensure market diversity and resilience.

References

[1] Ismail, M., & Zaki, N. M. (2021). Impact of GMP and GDP on Pharmaceutical Quality Systems. *J. Pharm. Sci.*
[2] Vogel, D. (2012). *The Politics of Precaution: Regulating Health in Europe*. Princeton University Press.
[3] WHO (2022). *Technical Report Series 1044: Good Manufacturing Practices*.
[4] Law of Georgia "On Medicines and Pharmaceutical Activities."
[5] World Health Organization (2022). *WHO TRS 1044 - Annex 2: Good Manufacturing Practices for Pharmaceutical Products*.
[6] Tskhakaia, L., et al. (2023). Development of the Pharmaceutical Market and Regulatory Challenges in Georgia.

PP–33. COUPLING ANTIOXIDANT SCREENING WITH HEMOLYSIS ASSAY FOR RAPID SAFETY EVALUATION OF PLANT-DERIVED BIOACTIVE MIXTURES

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Oxidative stress arising from excessive production of reactive oxygen species (ROS) contributes to the development of numerous pathological conditions, including inflammatory, cardiovascular, metabolic, and neurodegenerative diseases due to the imbalance between ROS production and antioxidant defence mechanisms [1]. The interest in plant-derived secondary metabolites as potential therapeutic candidates, fosters search for safer and more effective antioxidant agents.

Plants synthesize diverse bioactive compounds, particularly flavonoids and other phenolic compounds, which exhibit antioxidant and anti-inflammatory activities [2]. Nevertheless, the distribution of these compounds among different extract fractions and their corresponding biological activity and safety profiles often remains insufficiently characterized. This highlights the need for targeted studies aimed at identifying the fractions that combine strong antioxidant activity with acceptable safety characteristics, especially when systemic application is considered.

Using a modified DPPH dot blot assay [3] as a rapid screening method for antioxidant activity, while simultaneously assessing preliminary safety through an in vitro hemolysis assay [4] the current study aimed to comparatively evaluate the fractions obtained from three Primula species growing in Georgia (*Primula macrocalyx, P.woronowii*, and *P. saguramica*).

The study revealed no direct correlation between the antioxidant and hemolytic activities of the fractions; however, it enabled the identification of those that may be potentially unsuitable for systemic application.

Overall, integrating rapid antioxidant screening with a hemolysis assay provides a practical approach to early safety evaluation of bioactive plant mixtures and may facilitate the more rational design of subsequent preclinical investigations, including both in vitro and in vivo studies.

References

[1] Martindah, E., Khairullah, A. R., Widiastuti, R. et al. (2025). Oxidative stress: Molecular mechanisms, role in pathology, and therapeutic implications. *Trends in Sciences*, 22(12), 11462. https://doi.org/10.48048/tis.2025.11462

[2] Ragusa, A. (2023). Secondary Metabolites for the Reduction of Oxidative Stress. *Molecules*, 28(22), 7555. https://doi.org/10.3390/molecules28227555

[3] Sirivibulkovit, K., Nouanthavong, S., Sameenoi, Y. Paper-based DPPH Assay for Antioxidant Activity Analysis. *Anal. Sci.* 34, 795–800 (2018). https://doi.org/10.2116/analsci.18P014

[4] Evans, B. C., Nelson, C. E., Yu, et al. (2013). Ex vivo red blood cell hemolysis assay for the evaluation of pH-responsive endosomolytic agents for cytosolic delivery of biomacromolecular drugs. *Journal of visualized experiments* : JoVE, (73), e50166. https://doi.org/10.3791/50166

PP–34. BIOLOGICALLY ACTIVE COMPOUNDS OF ENDEMIC SPECIES OF CAUCASUS – *SALVIA GAREDJI*

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The phytochemical study of the aerial part of the Caucasus endemic plant *Salvia garedji* Troitz. (Lamiaceae Lindl.) collected during flowering (east Georgia, near to the monastery complex David Garedji), revealed the presence of phenolic compounds. 22 substances were isolated and identified from ethyl ether, chloroform, acetone, water extracts: n-nonacosanone, a stereoisomeric mixture of ursolic and oleanolic acids, rosmarinic acid, salvigenin, condensed tannin, danshensu (salvianic acid A), yunnaneic acid F, salvianolic acid A and its isomer, luteolin-7-*O*-glucuronide, apigenin-7-*O*-glucuronide, sagerinic acid, nepetin, cirsimaritin, methyl gallate, carnosic acid, hispidulin, rosmadial, epigallocatechin, methyl rosmarinate, carnosol [1].

The aqueous extract of the aerial parts of *S. garedji* is characterized by an abundant content of phenolic compounds - 49.8% tannin by permanganometry titration method [2]. To determine the nature of polyphenols, acidic hydrolysis of the aqueous extract was performed.

HPLC-MS analysis of the hydrolysate revealed the presence of phenolic acids, their derivatives, terpene phenols, and flavonoids (in total 32 compounds). 13 of them - carnosol, carnosic acid, yunnaneic acid F, sagerinic acid, salvianolic acid A, salvianolic acid A isomer, luteolin-7-0-glucuronide, apigenin-7-0-glucuronide, rosmarinic acid, methyl gallate, cirsimaritin, epigallocatechin, danshensu (salvianic acid A) - were previously identified in the native aqueous extract [1]. 19 compounds–rosmanol **(1)**, $C_{20}H_{26}O_5$, UV (λ_{max}, nm): 212, 286, ESI-MS *m/z* 345 $[M-H]^-$; salvianolic acid F **(2)**, $C_{17}H_{14}O_6$, UV (λ_{max},nm): 286, 320, ESI-MS *m/z* 313 $[M-H]^-$; rosmaridiphenol **(3)**, $C_{20}H_{28}O_3$, UV (λ_{max}, nm): 220, 275, ESI-MS *m/z* 315 $[M-H]^-$; caffeoyl threonic acid **(4)**, $C_{13}H_{14}O_8$, UV (λ_{max}, nm): 220, 250, 290, ESI-MS m/z 297 $[M-H]^-$; p-hydroxybenzoyl glucose **(5)**, $C_{13}H_{16}O_8$, UV (λ_{max}, nm): 267, 275, ESI-MS *m/z* 299 $[M-H]^-$; caftaric acid **(6)**, $C_{13}H_{12}O_9$, UV (λ_{max}, nm): 328, ESI-MS *m/z* 311 $[M-H]^-$; miltirone **(7),** $C_{19}H_{22}O_2$, UV (λ_{max}, nm): 224, 265 (пл.), ESI-MS *m/z* 281 $[M-H]^-$; ethyl rosmarinate **(8)**, $C_{20}H_{20}O_8$, UV (λ_{max}, nm): 230, 275, ESI-MS *m/z* 387 $[M-H]^-$; yunnaneic acid E **(9)**, $C_{27}H_{24}O_{14}$, UV (λ_{max}, nm): 266, ESI-MS *m/z* 571 $[M-H]^-$; yunnaneic acid D **(10)**, $C_{27}H_{24}O_{12}$, UV (λ_{max}, nm): 326, ESI-MS *m/z* 539 $[M-H]^-$; eriodictyol-di-glucoside **(11)**, $C_{27}H_{32}O_{16}$, UV (λ_{max}, nm): 283, ESI-MS *m/z* 611 $[M-H]^-$; rosmarinic acid isomer **(12)**, $C_{18}H_{16}O_8$, UV (λ_{max}, nm): 267, 325, ESI-MS *m/z* 359 $[M-H]^-$; yunnaneic acid H**(13)**, $C_{36}H_{26}O_{16}$, UV (λ_{max}, nm): 278, 396, ESI-MS *m/z* 713 $[M-H]^-$; cirsilineol **(14)**, $C_{18}H_{16}O_7$, UV (λ_{max}, nm): 252, 274, 345, ESI-MS *m/z* 343$[M-H]^-$; feruloyl tartrate (fertaric acid) **(15)**, $C_{14}H_{14}O_9$, ESI-MS *m/z* 325$[M-H]^-$; 6-hydroxy-luteolin-7-O-glucuronide **(16)**, $C_{21}H_{18}O_{13}$, UV (λ_{max}, nm): 281, 342, ESI-MS *m/z* 477 $[M-H]^-$; chrysin-7-glucuronide **(17)**, $C_{21}H_{18}O_{10}$, UV (λ_{max}, nm): 270, 306 (пл.), ESI-MS *m/z* 429 $[M-H]^-$; 5-hydroxy-6,7,3',4'-tetramethoxyflavone **(18)**, $C_{19}H_{18}O_7$, UV (λ_{max}, nm): 270, 340 ESI-MS *m/z* 357 $[M-H]^-$; 3-O-feruloylquinic acid **(19)** $C_{17}H_{20}O_9$, UV (λ_{max}, nm): 287 (пл.), 324, ESI-MS *m/z* 367 $[M-H]^-$ - present the products of hydrolysis. These compounds were characterized for the first time from the hydrolysate of *S. garedji* aerial part aqueous extract.

The absence of gallic and ellagic acid residues in the hydrolysate, exclude the predominant content of hydrolysable tannins in aqueous extract.

Therefore, the result (49.8 %) obtained by the permanganometric titration method for the quantitative determination of tannins in plant raw materials given in the State Pharmacopoeia [2] is actually due to the oxidation of polyphenols of another groups.

The aqueous extract showed high antioxidant activity in various *in vitro* experiments (Table 1).

Table 1. Antioxidant activity of the aqueous extract of *Salvia garedji*

Object	Cell culture (WS1)	ORAC test	Thiobarbituric acid test
	IC_{50} μ/ml	μmol Trolox/mg	Relative activity in %
Extract	0.42 ± 0.06	8 ± 2	100
Quercetin	0.027 ± 0.004	23 ± 4	
EDTA			90
α - Tocopherol			97

References:

[1] Sagareishvili TG, Getia MZ. 2024, Chemical composition of *Salvia garedji*, an endemic plant of the Caucasus, Chem. Nat. Compd., vol. 60, no. 4, pp. 766-767.

[2] State Pharmacopoeia of the Russian Federation, 2018, 14th ed. vol. II,, Moscow, 3262 p.

PP–35. THE ROLE OF A CLINICAL PHARMACIST IN THE TREATMENT OF OSTEOARTHRITIS

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Osteoarthritis is a fairly common disease today. It occurs in both elderly and young patients.

It requires complex and long-term treatment, taking into account the etiological factor. The simultaneous appointment of several medications may have undesirable effects. It is the duty of the clinical pharmacist to participate in the pharmacotherapeutic process together with the doctor, analyze the mechanism of action and interaction of drugs and make necessary adjustments.

The aim of the study was to analyze the prescription of a patients with osteoarthritis based on the study of histology in order to avoid undesirable drug interactions. We selected patients with osteoarthritis, whose prescription included more than 5 medications. At the next stage, their condition was monitored, and the compatibility of the prescribed drugs was checked.

In all cases, the patients were prescribed a nonsteroidal anti-inflammatory drug, a muscle relaxant, a stomach protectant. In two cases had diuretic prescription, and in one patient was ordered to also take statin and an antidepressant. Interaction schemes were created separately for all patients in order to identify noteworthy and dangerous interactions.

Interactions to watch out for included: The gastroprotector pantoprazole and the diuretic hydrochlorothiazide. Chronic use of proton pump inhibitors, including pantoprazole, can sometimes cause hypomagnesemia, and the risk may be further increased when combined with other drugs that have this effect, such as hydrochlorothiazide. In severe cases, hypomagnesemia can cause irregular heartbeat, muscle spasms, tremors, and seizures. Dosage adjustments or more frequent monitoring by a doctor may be necessary to safely use both medications; Naproxen (a nonsteroidal anti-inflammatory drug) and hydrochlorothiazide increase each other's toxicity through pharmacodynamic antagonism. Nonsteroidal anti-inflammatory drugs reduce the synthesis of vasodilating renal prostaglandins and, therefore, affect fluid homeostasis and may reduce antihypertensive activity.

The use of the antidepressant duloxetine with acetaminophen increases the toxicity of the latter. The combination of perindopril + metformin is also noteworthy, perindopril increases the toxicity of metformin, increases the risk of hypoglycemia and acidosis. Several corrections were made to the prescription by the doctor and clinical pharmacist.

In conclusion, it can be clearly stated that the cooperation of the clinical pharmacist and the doctor will make the pharmacotherapeutic process even more effective, save its time and help minimize unwanted risks.

References

[1] Glyn-Joines S., Palmer A.J.R., Agricola R. et al. (2015). Osteoarthritis. The Lancet, 386(9991), 376–387. https://doi.org/10.1016/S0140-6736(14)60802-3.
[2] Kennedy J., Roll J.M., Schraudner T. et al. (2014). Prevalence of persistent pain in the US adult population. The Journal of Pain, 15(10), 979–984. https://doi.org/10.1016/j.jpain.2014.05.009.
[3] Gvantseladze, V., & Kalandrishvili, G. (2010). Diagnosis and therapy of internal diseases: Osteoarthrosis. Tbilisi.
[4] Katz, J. N., Arant, K. R., & Loeser, R. F. (2021). Diagnosis and treatment of hip and knee osteoarthritis. JAMA, 325(6), 568–578. https://doi.org/10.1001/jama.2020.22171.

PP–36. INVESTIGATION OF COMPLEX FORMATION PROCESSES OF SELECTED HEAVY METALS WITH FULVIC ACIDS BY THE GEL CHROMATOGRAPHIC METHOD

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Supramolecular organic substances, fulvic acids, due to functional groups, actively participate in stable compounds with complex formation and sorption processes occurring in natural waters, bottom sediments, and soils. They form heavy metals and radioactive elements and stipulate their migration forms in natural objects. Literature data on the stability constants of metal–fulvic acid complexes are heterogeneous and differ from each other by several ranges. This condition is mainly stipulated by the ignoring the changes of ionization degree of fulvic acids and average molecular weights of fulvic acids associates according to pH in complex formation process, which ultimately leads to inaccurate results. The aim of the present study was to isolate pure samples of fulvic acids from natural waters of Georgia and to determine the composition of Mn(II), Ni(II), Cu(II), and Zn(II) fulvate complexes at pH 5, as well as to calculate their stability constants using the gel chromatographic method. It was demonstrated that, in calculating the stability constants of fulvates, the using of the average molecular weight of the oligomer of fulvic acids is optimal, rather than the use of their associated forms [1–3].

References:

[1] Makharadze, G, et al. New Version of Calculation of Stability Constant of Metal-fulvate Complexes on the Example of Zinc Fulvate. Int. J. Environ. Sci. Technol. 2018. 15, 2165-2168.
[2] Makharadze, T., Makharadze, G. Investigation of The Complex Formation Process Of Lead (II) With Natural Macromolecular Organic Substances (Fulvic Acids) By The Solubility And Gel Chromatographic Methods. Chem. Chem. Technol. 2023. 17, 740–747.
[3] Makharadze, T.; Makharadze. G. Investigation of Complex Formation Process of Copper with Macromolecular Organic Substances. Org. Chem. Plus. 2020, 1, 1-5.

PP–37. FORMULATION AND BIOPHARMACEUTICAL EVALUATION OF SUPPOSITORIES CONTAINING SEA BUCKTHORN OIL AND THYMOL

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Inflammatory and infectious diseases often necessitate prolonged therapeutic intervention. Vaginitis remains one of the most prevalent gynecological conditions, affecting approximately one in three women of reproductive age. To expand the range of effective, high-quality, and mild-acting phytopreparations for its treatment, it was considered to develop a new combined therapeutic agent. The proposed formulation integrates the nutrient-rich fruit oil of sea buckthorn (*Hippophae rhamnoides* L.)—abundant in carotenoids, tocopherols, vitamins, and minerals—with thymol, the primary bioactive constituent of essential oils derived from the *Thymus* species.

The model suppositories were prepared using the molding (fusion) method. Quality parameters of the suppositories were determined in accordance with pharmacopeial standards. Qualitative and quantitative assessments of the active substances—carotenoids—were conducted spectrophotometrically. The fatty acid content was determined through the esterification of triglycerides in an acetyl chloride medium in the presence of a small amount of ethanol. The release and solubility profile of the active substance were evaluated using *in vitro* dissolution test.

Out of the three investigated formulations (based on cocoa butter, Witepsol W-35, and a PEG 400 / PEG 1500 blend), only the the Witepsol W-35 based suppositories complied with pharmacopeial standards (regarding uniformity, color, shape, and mechanical strength). The formulation constituents were thymol 0.1 g, sea buckthorn oil 0.5 g, and Witepsol W-35 2.4 g per suppository.

The physicochemical parameters of the suppositories were established, including the acid value, peroxide value, and melting and solidification temperatures. The quantitative analysis of carotenoids yielded 1.00–1.25 mg per suppository. Within the fatty acid profile of the suppository extract, the predominant components were identified as the triglycerides of oleic (31.41%), palmitic (28.61%), and stearic (27.3%) acids.

In vitro study of the release and solubility of the active substance revealed that 50–55% of carotenoids are released within one hour. Dissolution test results indicated that suppositories disintegrate within 5–10 minutes in a 30% ethanol medium, with 60–65% of the carotenoids released into the solvent.

Based on the conducted research, it can be concluded that the sea buckthorn oil and thymol suppositories formulated on a Witepsol W-35 base are physicochemically stable. Anti-inflammatory, antibacterial, and regenerative properties of the developed formulation should be investigated prior recommending it as a therapeutic agent.

PP–38. PRELIMINARY STUDY OF SOME PLANTS DISTRIBUTED AND CULTIVATED IN GEORGIA ON THE CONTENT OF BIOLOGICALLY ACTIVE SUBSTANCES

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Preliminary studies were conducted on the content of biologically active compounds - flavonoids and triterpene secondary metabolites in 20 species of the Georgian flora (Tab.1)[1].

The analysis revealed that most of them contain flavonoids in the above-ground organs. *Datisca cannabina* L. was a rare exception, the presence of flavonols was confirmed in its underground parts.

Table 1. Content of biologically active secondary metabolites

	Flavonoids	Triterpenes
Argyrolobium biebersteinii	+	-*
Astragalus brachycarpus	+	+*
Cercis siliquastrum	+	+
Cerinthe minor	+	+*
Clematis orientalis	+	+
Cytisus caucasicus	+	+
Cytisus hirsutissimus	+	+
Datisca cannabina	+	+*
Echium vulgare	+	+*
Genista patula	+	- *
Hypericum perforatum	+	-
Onobrychis kachetica	+	+
Polygonatum glaberrimum	+	+*
Rhododendron brachycarpum	+	+*
Rhododendron delavayi	+	+*
Rhododendron ungernii	+	+*
Satureja laxiflora	+	-*
Spartium junceum	+	+*
Stachys iberica	+	-
Vaccaria segetalis	+	+*

* - detected for the first time in Georgian species

The flavonol glycoside, datin-3-rutinoside or datinoside (Fig. 1) has been isolated and identified from the roots of *Datisca cannabina*.

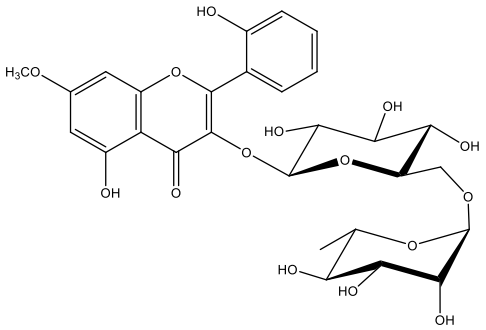

Figure 1. 2´,3,5-tri-hydroxy-7-methoxy-flavone-3-O-[O-α-L-rhamnopyranosyl-(1→6)-β -D-glucopyranoside

From the analysed species, the following 14 ones, common in Georgia were studied for the first time on the content of triterpene compounds: *Argyrolobium biebersteinii, Astragalus brachycarpus, Datisca cannabina, Cerinthe minor, Echium vulgare, Polygonatum glaberrimum, Rhododendron brachycarpum, Rhododendron delavayi, Spartium junceum, Vaccaria segetalis, Rhododendron ungernii, Genista patula*, and *Clematis orientalis*.

References

[1] Alania, M. Shalashvili, K., Sagareishvili, T. Kavtaradze, N., Sutiashvili, M., Aneli, J. 2023, *Phenolic compounds of some plants spread and cultivated in Georgia* [in Georgian], Tbilisi, 334 p.

[2] Pangarova, TT. Zapesochnaya, GG. Structure of the flavonoids from *Datisca cannabina*, II, 1974, *Chemistry of Natural compounds*, vol. 10, no.6, pp. 810-811.

PP–39. RHEOLOGICAL PROPERTIES OF PAPAIN CONTAINING GELS

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The rheological characteristics of a soft pharmaceutical formulation determine its quality, efficacy, optimal consistency, technological and consumer properties, ease of application, and accurate dosing [1]. Viscosity influences the bioavailability of ointments and gels and ensures the stability of the dosage form during storage [2].

The objects of the study were model samples of a 2% papain-containing gel with various gelling agent (Carbopol 940) concentration. The study was conducted using the rotational viscometry method.

Research samples of papain-containing gels were prepared using base with the following concentrations: 0.6%; 0.8%; 1.0% and 1.2%. The proteolytic activity of papain gels was determined using a modified Anson method. In all four formulations, the active substance and all excipients were included in identical quantities. Study conditions: Temperature of 24,5^{0}C (room temperature), spindles S3 and S4, and a sample size of 50 g.

During the experiment, the rotation speed of the coaxial cylinder was consistently increased within a specific range for each trial and then consistently decreased after reaching the maximum shear stress value. Based on the obtained data, relevant graphs were plottted.

Hysteresis loops are prominent on the rheograms, indicating the thixotropy of the systems. The arrangement of the ascending curves of the system's breakdown process and the descending curves of the recovery process on the flow rheogram shows that the degree of recovery is different for all samples. According to the results, all the studied samples represent structured dispersion systems: with increasing shear rate, the dynamic viscosity decreases and the shear stress increases. In addition, prepared on 0.6 and 0.8% Carbopol 940 samples are characterized by outstanding rheological properties (Fig. 1 and 2).

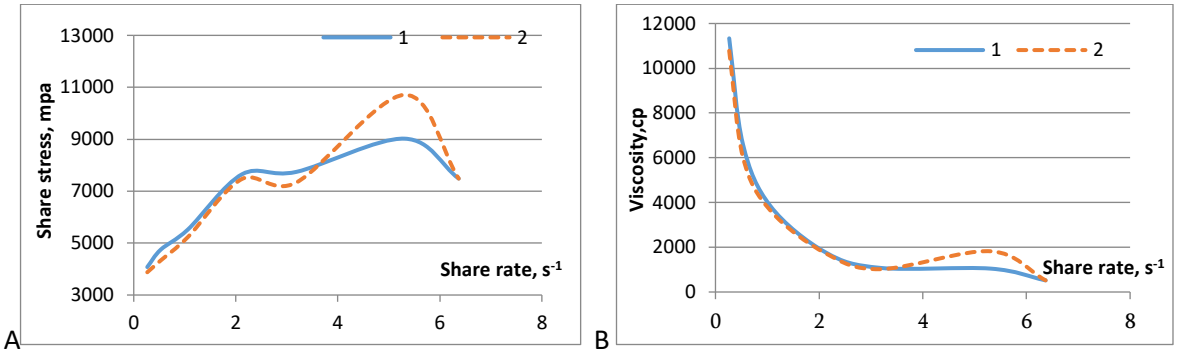

Figure 1. 2% Papain gel prepared on a 0.6% Carbopol 940 base: A–Graph of shear stress versus shear rate (viscosity curve); B–Graph of dynamic viscosity versus shear rate–flow curve (1–descending, 2–ascending).

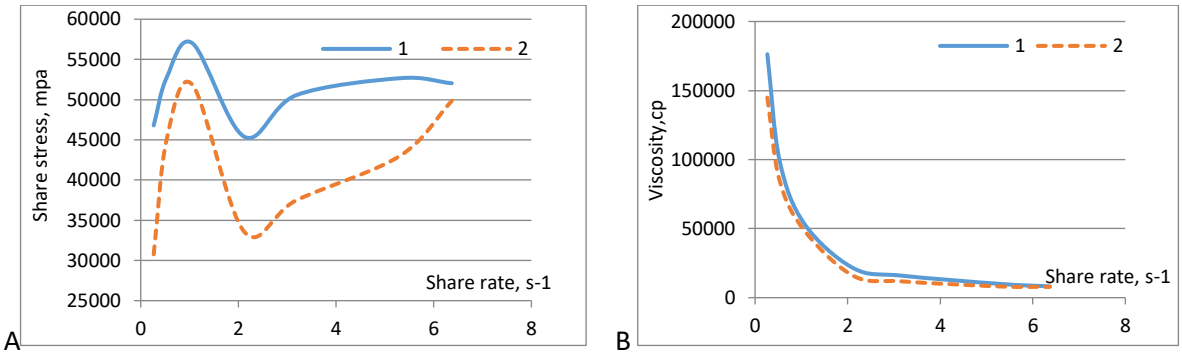

Figure 2. 2% Papain gel prepared on a 0.8% Carbopol 940 base: A–Graph of shear stress versus shear rate (viscosity curve); B–Graph of dynamic viscosity versus shear rate–flow curve (1–descending, 2–ascending).

The rheological properties of 2% papain gel model samples prepared on Carbopol 940 bases of various concentrations have been studied, and effective viscosity ranges at different shear rates have been determined. Optimal rheological characteristics are obtained with 2% papain gels prepared on 0.6 and 0.8% Carbopol 940 bases. The obtained results allow us to assume that the gels' consistency will remain stable during long-term storage.

References

[1] Ozon E.A., Anastasescu M., Musuc A.M. et al. 2025, Formulation and Characterization of Carbopol-Based Porphyrin Gels for Targeted Dermato-Oncological Therapy: Physicochemical and Pharmacotechnical Insights. Int. J. Mol. Sci. 26, 3641. https://doi.org/10.3390/ijms26083641.

[2] Mustafin R.A., Nasibullina N.M., Potselueva L.A. 2010, Examination of rheological properties of meloxicam dosages forms for outward application, Success of modern art. No. 1. pp. 11-14.

PP–40. REGULATORY CHALLENGES FOR REGISTRATION OF THE NEW FORMULATIONS IN GEORGIA

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Today the pharmaceutical industry has made number of innovations in the area of targeted drug delivery and optimization of pharmacokinetics for existing drugs to try to maximize therapeutic effect while simultaneously minimizing adverse consequences of medication side effects. The sample of such new development is new pharmaceutical form of suspension of well-established combination of Ibuprofen/Phenylephrine HCL. [1,2]

This presentation relates to the challenges arisen during the registration of a new developed liquid pharmaceutical composition for oral administration in the form of suspension of ibuprofen and phenylephrine hydrochloride, in a pharmaceutically acceptable salt thereof, as active substances, and relatively low allergic excipients. The idea of such combination drugs can ease the patient's condition and help shorten the duration of the illness provided that they are administered in due time. In addition, solid oral dosage forms may not be suitable for some patient populations who may have difficulties for swallowing whole tablets or capsules, including the pediatric, geriatric or disabled patients. For those patient populations, the use of liquid formulations is generally regarded as advantageous. Therefore, a liquid formulation may be more suitable for adjusting the dose of the active substances according to the age of the patients and for having a greater control over the amount of medicine administered, especially in children [3] (see table I).

Table I - Comparative use in children of suspension, tablets and other pharmaceutical forms

Form	Approximate Use in Pediatrics	Reasons for Preference
Suspensions (liquid)	60–70% of prescriptions in infants and preschool children	Easier to swallow, flexible dosing by weight/age, taste masking possible
Tablets (solid)	20–30% in older children (school age and above)	More stable, portable, precise dosing, longer shelf life
Other forms (chewables, dispersibles, powders)	10–20%	Bridge between liquids and tablets, useful for transition

The discussed drug formulation is stable, has good organoleptic properties and shows excellent pharmacokinetic profile, providing quick absorption of the drugs. The present development also relates to the use of the composition for treating the symptoms of flu and common cold, particularly in adults and in children over 7 years old. [4]

Even, surprising quicker absorption and quicker therapeutic effect, thus making the current composition a fast-acting medicine that provides a favorable environment for early and potent therapeutic effect; but the evidence of the product safety still was very complicate issue. Even, surprising quicker absorption and quicker therapeutic effect, thus making the current composition a fast-acting medicine that provides a favorable environment for early and potent therapeutic effect; but the evidence of the product safety still was very complicate issue and main challenge to prove the safety of the product, due to lacks of similarities of understandings with international regulations, during the registration in Georgia [5,6].

The Pharmaceutical Company operating in Georgia as a license holder of the product, envisaged to do the registration of this new development in the country, faced the regulatory issues associated with a regulation text's dual understanding or interpretations and lacks of the terminology or definitions. In same time the regulation mainly is not harmonized with EU regulation, as the main reference, and that sometimes causes the milestones on the way of registration.

Based on the done evaluation and comparison of the Georgian regulation with international regulations, can be concluded the following:

1. Drug regulation law needs the refresh to answer the challenges of today, and regulation should consider the registration of the dugs classified as “well established drug”.

2. Regulation should have more detailed explanations and definitions and precised formulation of the terminology and especially it is related to a subject “the batch releaser”.

3. Regulation should avoid the general statements, that after could be interpreted in different modes. Should be enlarged the list of variations of Ia and Ib line, to avoid it automatically transfer into II line variation.

References:

[1] https://cima.aemps.es/cima/pdfs/ipe/90049/IPE_90049.pdf
[2] De Sutter AI, Eriksson L, van Driel ML. Oral antihistamine-decongestant-analgesic combinations for the common cold. Cochrane Database Syst Rev. 2022 Jan 21;1
[3] Van Riet-Nales DA, et al. Arch Dis Child 2013;98:725–731. doi:10.1136/archdischild-2012-303303
[4] Marta Vicario De La Torre, Nuria SANZ MENÉNDEZ, José Ángel SÁNCHEZ GARCÍA, José Carlos IGLESIAS SÁNCHEZ, Luis SANTE SERNA. Liquid composition comprising ibuprofen and phenylephrine. International Publication Number WO 2021/130126 A. Publication Date: 01 July 2021 (01.07.2021) p 34.
[5] LAW OF GEORGIA ON MEDICINES AND PHARMACEUTICAL ACTIVITIES. https://matsne.gov.ge/ka/document/download/29836/22/en/pdf
[6] EMEA Guideline on the Investigation of Bioequivalence, CPMP/EWP/QWP/1401/98 Rev. 1/Corr **, London, January 20, 2010.

PP–41. ALBENDAZOLE-BASED NANOCOMPOSITE: STRUCTURE AND BIOLOGICAL ACTIVITY

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The synthesized nanocomposite material (Fig.1), based on albendazole ($C_{12}H_{15}N_3O_2S$) and copper sulfate ($CuSO_4$), was investigated for its potential anthelmintic activity. Albendazole is a well-established benzimidazole derivative used against helminths [1,2], while copper ions are known to possess antimicrobial properties. The rationale for combining these components was to explore possible synergistic effects in parasite inhibition.

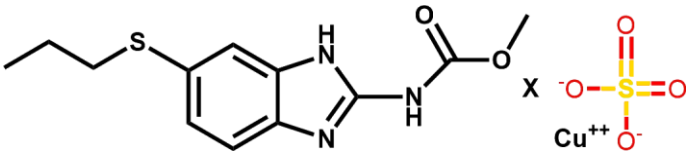

Figure 1. Structural formula of anthelmintic nanocomposite**.**

Structural characterization using X-ray diffraction confirmed that the crystalline structure of albendazole remained intact within the composite. Transmission electron microscopy revealed particle sizes averaging 270 nm, placing the material at the upper boundary of the nanoscale range.

Figure 2. Neurobehavioral evaluation of test composite materials in rodents

Biological activity has been studied on inbred mice, focused on general physiological parameters. Prelminary results reveal that the synthesized composite minimizes toxicity to host organisms and completely eliminates helminths, reducing their resistance to albendazole. Our future goal is to offer farmers the composites we have developed, which have been positively evaluated due to their decreased toxicity in animals and fewer contraindications. In the future, we plan to synthesize three more albendazole-based composites.

References

[1] Gigauri R., Khvichia L., Arabuli L. (2023) Role of anthelmintic compounds in zoological medicine. In: Mukbaniani O., Tatrishvili T., & Abadie M.J.M. (Eds.). (2023). Advanced Polymer Structures: Chemistry for Engineering Applications (1sted.). Apple Academic Press. https://doi.org/10.1201/9781003352181

[2] Gaikwad NM, Chaudhari PD, Shaikh KS, Chaudhari SY, Saleem RM, Algahtani M, et al. (2023) Albendazole repurposing on VEGFR-2 for possible anticancer application: In-silico analysis. PLoS ONE18(8): e0287198. https://doi.org/10.1371/journal.pone.0287198

PP–42. ELECTROCHEMICAL SYNTHESIS OF NANOMAGNETITE FROM A WATER/ETHANOL MEDIA CONTAINING NaCl ELECTROLYTE

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Magnetite nanoparticles Due to their good biocompatibility, are used in the biomedical field, in particular in the diagnostics and treatment of tumour cells, in the fields of regenerative medicine, gene therapy, dentistry, oncology, the aesthetics industry, targeted delivery of medicinal products and therapy. Nanocrystals, liposomes, micelles, biomolecules and nanoparticles of metal oxides are used in nano preparations. In theranostics (theranostics - a new approach to creating a pharmaceutical composition, it provides for the development of a drug that provides early diagnosis and at the same time therapeutic treatment) nanoparticles of metal oxides are often used, more often iron oxide coated with polymers (sucrose, dextran, carbon) is used.

Due to their large specific surface area and high reactivity, they are used as a catalyst in ammonia production, in the process of alcohol oxidation, for the purification of natural and wastewater, in optics and electronics, etc. Many methods are used to obtain nanomaterials. By using an environmentally friendly, simple electrochemical synthesis method - by changing the electrolysis parameters and using various surfactants, it is possible to obtain nanoparticles with controlled size and shape.

The properties of nanoparticles also depend on the synthesis method. More often used are co-precipitation, thermal decomposition, micellar synthesis, hydrothermal synthesis, sol-gel method, green synthesis, wet chemical recovery and electrochemistry.

Electrochemical synthesis makes it possible to obtain metals, metal oxides, alloys, and quantum dots[1,2].

In the direction of electrochemical engineering, a method for synthesizing nanoparticles of metals and their oxides in a double-layer bath was developed. Nanoparticles were obtained in a double-layer bath, which contained immiscible electrolyte and organic solutions (two layers). The organic solution was a solution of oleic acid dispersed in hexane or toluene [3,4]. The organic solution was replaced with a mixture of water/alcohol in various ratios (a single-layer bath), and the process became more environmentally friendly and economically justified.

At a cathode speed of 600 rpm, the dependence of particle size on current density, water/ethanol ratio, temperature, electrolyte concentration, and oleic acid concentration was studied.

Particle size and zeta potential were estimated using the Zeta Sizer Malvern method, while X-ray diffraction and infrared spectroscopy methods were used to characterize the composition and structure of magnetite nanoparticles.

Oleic acid-modified nanomagnetite is biocompatible, the optimal conditions when using a water/ethanol mixture are as follows: water/alcohol ratio 30/70; 40/60; 50/50 vol.%, current density 10, 20 A/dm^2, temperature 45 ° C, oleic acid concentration 1 vol.%, electrolyte concentration 0.08 mol/L.

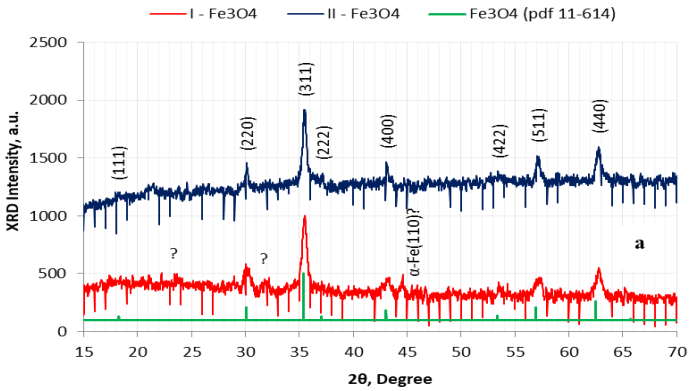

Fig.1. X-ray diffraction pattern of nanomagnetite: a) dried, b) calcined at 300 °C

As can be seen from the X-ray phase analysis, the sample, after drying at 120°C for 5 hours, has a protective layer of oleic acid, which prevents the crystal structure from being fixed, while the X-ray phase analysis of the magnetite sample fired at 300°C (Fig. 1,a,b) shows that the main phase is only magnetite.

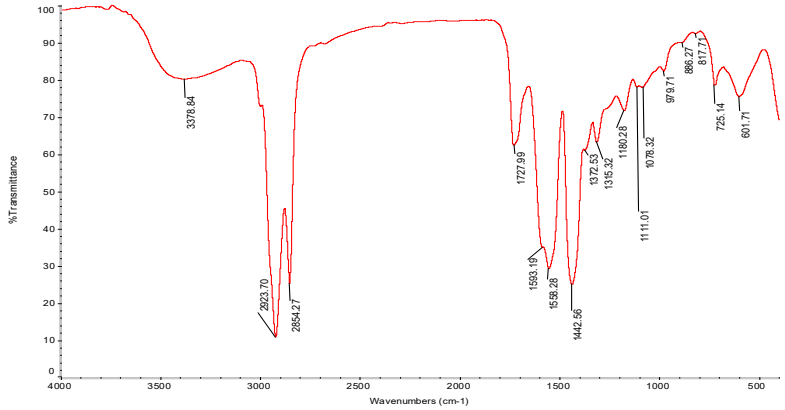

Fig.2. Infrared spectrum: magnetite modified with oleic acid

In the FT-IR spectrum of magnetite modified with oleic acid (Fig. 2), a peak characteristic of the vibration of the C=O bond is observed at 1727 cm-1, the peaks obtained at 1593 and 1558 cm-1

correspond to the symmetrical and asymmetric vibrations of the carboxyl group (COO-). 2923 cm-1 and 2854 cm-1 correspond to the asymmetrical and symmetric vibrations of the CH2 group, while 601 cm-1 and 510 cm-1 show peaks characteristic of the Fe-O bond, the 1079.99 cm-1 vibration indicates the chemisorption of Fe_3O_4 with the CO group of oleic acid.

References

[1] Lozano I., Casillas N., de León C. P., Walsh F. C., Herrasti P., 2017, New Insights into the Electrochemical Formation of Magnetite Nanoparticles*, J. Electrochemist. Soc.* 164, 184−191.

[2] Cabrera L., Gutierrez S., Menendez, N., Morales M.P., Herrasti P.,2008, Magnetite Nanoparticles: Electrochemical Synthesis and Characterization, *Electrochim. Acta* 53, 3436−3441.

[3] Donadze M., Makhaldiani N., 2024, Electrosinthesis of Nanomagnetite and Application for Purification of Phenol Previously Contaminated Water, *Advanced Polymer Structures Chemistry for Engineering Applications*, Appl Academic Press.25.

[4] Agladze T., Donadze M., Gabrichidze M., Toidze P., Shengelia J., Boshkov N., Tsvetkova N., 2013, Synthesis and Size Tuning of Metal Nanoparticles, *Zeitschrift für Physikalische Chemie*, 227,1187-1198.

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