# GEORGIAN MEDICAL MEWS

ISSN 1512-0112

NO 7-8 (364-365) Июль-Август 2025

## ТБИЛИСИ - NEW YORK



# ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии საქართველოს სამედიცინო სიახლენი

## **GEORGIAN MEDICAL NEWS**

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

**GMN:** Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

## WEBSITE

www.geomednews.com

## К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

- 1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра. Используемый компьютерный шрифт для текста на русском и английском языках Times New Roman (Кириллица), для текста на грузинском языке следует использовать AcadNusx. Размер шрифта 12. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.
- 2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.
- 3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

- 4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).
- 5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи. Таблицы и графики должны быть озаглавлены.
- 6. Фотографии должны быть контрастными, фотокопии с рентгенограмм в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста в tiff формате.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

- 7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.
- 8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform\_requirements.html В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.
- 9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.
- 10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.
- 11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.
- 12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

## REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

- 1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface Times New Roman (Cyrillic), print size 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.
- 2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.
- 3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

- 4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.
- 5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles. Tables and graphs must be headed.
- 6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

- 7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.
- 8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform\_requirements.html http://www.icmje.org/urm\_full.pdf
- In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).
- 9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.
- 10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.
- 11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.
- 12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

#### ᲐᲕᲢᲝᲠᲗᲐ ᲡᲐᲧᲣᲠᲐᲓᲦᲔᲑᲝᲓ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

- 1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში Times New Roman (Кириллица), ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ AcadNusx. შრიფტის ზომა 12. სტატიას თან უნდა ახლდეს CD სტატიით.
- 2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ,რუსულ და ქართულ ენებზე) ჩათვლით.
- 3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).
- 4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).
- 5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.
- 6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით tiff ფორმატში. მიკროფოტო-სურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სუ-რათის ზედა და ქვედა ნაწილები.
- 7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა უცხოური ტრანსკრიპციით.
- 8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.
- 9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.
- 10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.
- 11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.
- 12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

# GEORGIAN MEDICAL NEWS NO 7-8 (364-365) 2025

# Содержание:

Babry I. Oren, Marina I. Devdariani, Gela V. Beselia, Nino N. Sikharulidze, Manana G. Dashniani, Maia A. Burjanadze, Ia R. Kvachakidze, Marina I. Nebieridze, Lena Sh. Davlianidze, Lali M. Gumberidze, Nodar P. Mitagvaria.  ROLE OF ANTIOXIDANT FOLIUM EXPOSURE ON OXIDATIVE SRESS IN A VALPROIC ACID-INDUCED ANIMAL MODEL OF AUTISM
Hajdi Gorica, Pavllo Djamandi, Gentian Vyshka.  DELAYED ONSET OF MYASTHENIA GRAVIS FOLLOWING COLECTOMY FOR ULCERATIVE COLITIS: A CASE STUDY16-17
Zhadyra Yersariyeva, Bagdad Suleyeva, Botagoz Turdaliyeva, Yeldos Tussipbayev.  HEMOSTASIS GENE POLYMORPHISM IN RETINAL VASCULAR OCCLUSION: A SYSTEMATIC REVIEW
Ilia Nakashidze, Nameera Parveen Shaikh, Shota Nakashidze, Aleena Parveen Shaikh, Sarfraz Ahmad, Irina Nakashidze.  EVALUATION OF TNF-A LEVELS IN MALE PATIENTS WITH STROKE: PROGNOSTIC IMPLICATIONS
Yerbolat Iztleuov, Marat Iztleuov, Altynbek Dushmanov, Gulmira Iztleuova.  PREVENTION IN THE PARENTAL GENERATION OF EXPOSED RATS: CONSEQUENCES OF TOXIC EXPOSURE TO CHROMIUM AND GAMMA IRRADIATION IN AN EXPERIMENTAL MODEL
Rashid Nassar, Nadine Khayyat, Michele Halasa, Fahad Hussain.  TRAUMATIC ANTERIOR SHOULDER INSTABILITY (TUBS): A NARRATIVE REVIEW OF CURRENT LITERATURE46-50
Albadawi Abdelbagi Talha, Mawaheip A. Abdo Jeweser, Abubakr Ali Elamin Mohamed Ahmed, Abdelrahman Eldaw Mohammed, Elhadi Abdalla Ahmed, GadAllah Modawe, Sanaa Elfatih Hussein.  THE HBV AND HCV SEROPREVALENCE AMONG BLOOD DONORS IN Al-DAMAZIN STATE, SUDAN: A THREE-YEAR RETROSPECTIVESTUDY
Hiba Salah Hasan, Teeb Ali, Kadhim Adnan Ali, Al hassan Ali, Hany A. Al-hussaniy.  MODELING DRUG-ORGAN INTERACTIONS AND OPTIMIZING IMMUNOTHERAPY: A QUANTITATIVE SYSTEMS PHARMACOLOGY AND ODRONEXTAMAB DYNAMICS
Zilola Mavlyanova, Davron Ravshanov, Malika Ibragimova, Lola Irbutaeva, Khalimova Fariza, May K. Ismail, Shawgi A. Elsiddig, Marwan Ismail, Salma E R Mohamed, Sara Mohammed Ali.  PROGNOSTIC SIGNIFICANCE OF PROLIFERATION (KI-67) AND ANGIOGENESIS (CD34) MARKERS IN MENINGIOMAS FOR THE DEVELOPMENT OF REHABILITATION STRATEGIES
A.R. Abzaliyeva, K.K. Kurakbayev, A.R. Ryskulova, Z.R. Abzaliyev, E. Tasmagambet, D.Zh. Saussanova.  TURNOVER INTENTIONS AMONG PHYSICIANS AND NURSES IN KAZAKHSTAN DURING THE COVID-19 PANDEMIC: A CROSS- SECTIONAL STUDY OF PSYCHOLOGICAL AND PROFESSIONAL CHALLENGES
A.A. Mammadov, A.N. Mustafayev, A.H. Aliyev. RADIOLOGICAL IMAGING METHODS FOR ACCURATE DIAGNOSIS OF ABDOMINAL POSTOPERATIVE COMPLICATIONS73-76
I.A. Lebedev, E.V. Zakharchuk, Yu.V. Boldyreva, I.A. Aptekar, E.I. Malinina. OSSIFICATION OF THE POSTERIOR LONGITUDINAL LIGAMENT: A CASE REPORT AND LITERATURE REVIEW
Zhanar Balmukhamedova, Gulmira Derbissalina, Aliya Dzholdasbekova, Dariga Blyalova, Luiza Murzakhalova.  SPECKLE-TRACKING ECHOCARDIOGRAPHY FOR EARLY DETECTION OF SUBCLINICAL SYSTOLIC DYSFUNCTION IN PERIMENOPAUSAL WOMEN WITHOUT APPARENT DIASTOLIC DYSFUNCTION
Arkam Thabit Al Neama, Musab Mohammed Khalaf, Ahmed A.J. Mahmood.  PATTERNS OF ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE ACTIVITY IN COMMON CARDIOVASCULAR PHENOTYPES
Argjira Veseli, Shefqet Mrasori, Ivana Čuković-Bagić, Lul Raka, Kaltrina Veseli, Enis Veseli.  PARENTAL QUALITY OF LIFE WHEN RAISING CHILDREN WITH AUTISM SPECTRUM DISORDER: A NARRATIVE REVIEW
Anas Ali Alhur, Daliya T. Sendi, Miad M. AlZahrani, Layla T. Abusharha, Rahaf Y. Abudaak, Rahmah Alsinan, Rama R. Alharbi, Lamia Almadhi, Laila M. Alotaibi, Mona A. Hadadi, Shaima H. Alattas, Fatimah Almisbah, Fathi Almisbah, Abdulrahman Alrashed, Kawkab Alharbi. EVALUATING THE TRUSTWORTHINESS OF CHATGPT-GENERATED HEALTH INFORMATION AMONG FUTURE HEALTH CARE PROFESSIONALS
Ting-Ting Wang, Yan Wang.  HUMANISTIC CARE NURSING FOR PATIENTS IN THE OPERATING ROOM DURING THE PERIOPERATIVE PERIOD: FULL-CYCLE CARE FROM PHYSIOLOGY TO PSYCHOLOGY
Zauresh Barmanasheva, Mariya Laktionova, Anna Onglas, AyauIym Kossetova, Ivan Melnikov.  PREVALENCE AND RISK FACTORS OF UTERINE FIBROIDS IN WOMEN OF REPRODUCTIVE AGE: A FACILITY-BASED STUDY IN A MEGACITY
Bolat Ashirov, Assel Kassymova, Jamilya Mansurova, Andrey Orekhov, Meiramgul Tokbulatova, Mirgul Kapakova, Zhanar Toktarova, Aisulu Zhunuspekova.  PROGNOSTIC MARKERS OF ISCHEMIC AND HEMORRHAGIC COMPLICATIONS IN PATIENTS WITH ATRIAL FIBRILLATION

Khalilov Sh. Dzh. ELECTROCARDIOGRAPHY CHARACTERISTICS OF THE PATIENTS WITH NON-ST-ELEVATION MYOCARDIAL INFARCTION (NS TEMI)
Salome Kordzaia, Elene Dolmazashvili, Khatuna Tsiklauri, Lasha Khmaladze, Nana Chikhladze. FROM INFUSION REACTION TO IMMUNE CASCADE: A CASE OF SEQUENTIAL TAXANE AND CAPECITABINE TOXICITIES IN TRIPLE-NEGATIVE BREAST CANCER
Yu Zhu, Fandong Zeng, Weiwei Chang, Liying Wen, Lijun Zhu, Yuelong Jin. AN EMPIRICAL STUDY ON THE ASSOCIATION BETWEEN ASPIRATION INDEX AND ACADEMIC PERFORMANCE AMONG PREVENTIVE MEDICINE STUDENTS
Alaa O Ahmed, Mubarak S Karsany, Mohamed Elfatih Abdelwadoud, Mutaz Ali, Osama Mohamed, Amged Gaffer Mostafa, Hussam Ali Osman, Elryah I Ali, Elyasa Elfaki, Tagwa Yousif Elsayed Yousif, Ayman H. Alfeel, Mohammed Ibrahim Saeed.  MOLECULAR DETECTION OF HIGH RISK HUMAN PAPILLOMA VIRUS SUBTYPES IN CERVICAL SMEARS AMONG SUDANESE WOMEN
Tchernev G, Tchernev KG Jr, Krastev DS, Krastev NS, Kordeva S.  DERMATOLOGIC SURGERY ROUNDS: RECONSTRUCTIVE SURGERY EMPLOYING THE SHARK ISLAND FLAP FOR BASAL CELL CARCINOMA AFFECTING THE NASAL ALA
Saltanat Imanalieva, Bayan Sagindykova, Rabiga Anarbayeva, Murat Omirali, Gulnara Ospanova, Murat Ashirov.  CURRENT STATUS AND PROSPECTS FOR THE DEVELOPMENT OF PEDIATRIC DOSAGE FORMS BY THE EXAMPLE OF  COMBINED MELOXICAM AND VITAMIN B12 TABLETS
Ahmed Miri Saadoon. INCIDENCE OF PRESSURE SORE IN THE INTENSIVE CARE UNIT AT AL-DIWANYIA TEACHING HOSPITAL
Isoyan A.S, Danielyan M.H, Antonyan I.V, Azizyan N.H, Mkrtchyan A.A, Karapetyan K.V, Nebogova K.A. MORPHOHISTOCHEMICAL ANALYSIS OF CORTICAL STRUCTURES IN AN EXPERIMENTAL MODEL OF PROLONGED COMPRESSION SYNDROME OF THE HIND LIMB IN RATS
Abdulaziz Alroshodi, Faisal A. Al-Harbi, Rasil Sulaiman Alayed, Fahad M. Alharbi, Khalid A Alkhalifah, Mayadah Assaf Alawaji, Ibrahim S. Alsabhawi.  FACTORS IMPACTING HEMODIALYSIS TREATMENT ADHERENCE IN END-STAGE RENAL DISEASE PATIENTS RECEIVING INCENTER HEMODIALYSIS IN QASSIM REGION
Gulshat Alimkhanova, Marat Syzdykbayev, Rinat Ashzhanov, Kulsara Rustemova, Maksut Kazymov, Rustem Kazangapova, Saule Imangazinova, Yernar Kairkhanov, Bazar Tuleuov, Sanzhar Khalelov, Roman Khripunov, Samatbek Abdrakhmanov, Abay Mijatov.  THE TRANSVERSUS ABDOMINIS PLANE BLOCK AS A METHOD OF MULTIMODAL OPIOID-SPARING POSTOPERATIVE  ANALGESIA: A NARRATIVE REVIEW
Zhengmei Fang, Xiaoling Ran, Lijun Zhu, Yingshui Yao, Yuelong Jin.  THE IMPACT OF BMAL1 GENE POLYMORPHISM ON SLEEP QUALITY IN HEALTHY CHINESE YOUTH: A GENDER-SPECIFIC ANALYSIS
Muwafaq H. Zaya, Ahmed A. J. Mahmood, Musab M. Khalaf. CROSS SECTIONAL EVIDENCE FOR OPPOSING EFFECTS OF HYPERGLYCAEMIA AND HYPERLIPIDAEMIA ON CHOLINESTERASEACTIVITIES
Erleta Muçaj, Erëza Durmishi, Serbeze Kabashi Muçaj, Leart Kuçi, Elza Muçaj, Gerta Durmishi.  CHALLENGES IN RADIOLOGICAL DIAGNOSIS: CRANIOPHARYNGIOMA VS ASTROCYTOMA
Uday Mahajan, Imran Khan, Ria Gupta, Meraj Akhtar, Vibhore Gupta, Edward Spurrier, Mohamed Kabary, Adnan Asif, Salman Shoukat Ali Parpia.
NAMING CONVENTIONS FOR UNIDENTIFIED PATIENTS IN EMERGENCY AND TRAUMA SETTINGS: A NARRATIVE REVIEW
Xuexue Li, Wenjie Wen, Dandan Ren.  MOLECULAR MECHANISMS OF DIABETIC PERIODONTITIS: IDENTIFICATION OF KEY OXIDATIVE STRESS-RELATED GENES AND POTENTIAL THERAPEUTIC ROLE OF METFORMIN THROUGH MMP14 AND PXDN
Davron Ravshanov, Zilola Mavlyanova, Kholmirzayev Bakhtiyor, Malika Tursunovna, Khalimova Fariza. HISTOPATHOLOGICAL PREDICTORS AND FUNCTIONAL RECOVERY IN PATIENTS WITH INTRACRANIAL MENINGIOMAS
Aymuhambetov Y, Khismetova Z A, Iskakova N, Akhmetova K, Serikova-Esengeldina D, Shalgumbayeva G.M.  ASSESSMENT OF QUALITY OF LIFE IN BREAST CANCER PATIENTS BY USING EORTC QLQ-C30 QUESTIONNAIRE IN EAST KAZAKHSTANREGION
Yujing Tao, Long Hua, Liu Zhang, Ying Feng, Liying Wen, Weiwei Chang. THE CORRELATION BETWEEN STRESS, ACADEMIC PERFORMANCE, AND SLEEP DISTURBANCES AMONG HIGH SCHOOL STUDENTS IN ANHUI PROVINCE: A CROSS-SECTIONAL STUDY
Fahad AlAmr, Muhannad Essa S. Alghamdi, Ahmed Saeed A. Alghamdi, Osama Khamis A. Alghamdi, Hassan Mahfouz B. Alghamdi, Osama Mesfer S. Alghamdi, Abdullah Ali A. Almimoni, Abdulmalik Ahmed S. Al-Zahrani.  PREVALENCE AND ASSOCIATED RISK FACTORS OF NOCTURNAL ENURESIS AMONG CHILDREN AGED 5-18 YEARS IN ALBAHA REGION, SAUDI ARABIA

Aya Saad Aldewachi, Mohammed I Aladul.  APPETITIVE TRAITS AND QUALITY OF LIFE IN WOMEN WITH OBESITY USING GLUCAGON-LIKE PEPTIDE-1 RECEPTOR  AGONISTS: INSIGHTS FROM A PCOS-ENRICHED SAMPLE
George Shaburishvili, Nikoloz Shaburishvili, Georg Becker, Solomon Zeikidze, Bacho Tsiklauri. INCIDENCE OF ADVERSE EVENTS RESULTING FROM BETA-BLOCKER TITRATION IN PATIENTS WITH HEART FAILURE
Blushinova A.N, Orazalina A.S, Shalgumbayeva G.M. INDUCED ABORTION IN KAZAKHSTAN: WOMEN'S PERCEPTIONS AND EXPERIENCES BASED ON CROSS-SECTIONAL STU DY
Qunru Hu, Liying Wen, Jingqi Zhang, Weiwei Chang, Yuelong Jin, Anshi Wang, Lijun Zhu.  IS CORE SELF-EVALUATION A PROTECTIVE FACTOR FOR COLLEGE STUDENTS'MARITAL ATTITUDES? THE MODERATING ROLE OF PSYCHOLOGICAL STATUS
Gulfariza Gani, Ubaidilla Datkhayev, Kairat Zhakipbekov, Serzhan Mombekov, Murat Ashirov, Nurgali Rakhymbayev, Zhanerke Seitova. STUDY OF THE CHEMICAL COMPOSITION AND ANTIMICROBIAL ACTIVITY OF SUBCRITICAL CO <sub>2</sub> EXTRACT FROM <i>EUPHORBIA HUMIFUSA</i> WILLD
Maysoon Mohammed Hassan, Mohammed Abdulwahab Ati Al-askeri, Naseer Kadhim Jawad.  PROGNOSTIC IMPACT OF EGFR2 AND KI-67 OVEREXPRESSION WITH DOWNREGULATION OF <i>miR-17</i> AND <i>miR-1307</i> IN FEMALE BREAST CANCER PATIENTS
Imzharov Talgat Abatovich, Zhakiev Bazylbek Sagidollievich, Sarkulov Marat Nukinovich, Pavlov Valentin Nikolaevich, Kurmangaliev Oleg Maratovich.
THE EFFECTIVENESS OF METAPHYLAXIS OF NEPHROLITHIASIS DURING PERCUTANEOUS NEPHROLITHOTRIPSY: A SYSTEMATIC REVIEW AND META-ANALYSIS
Yan Wang, Ting-Ting Wang, Chang-Sheng He. PROGRESS IN T-CELL IMMUNE RESEARCH ON HYPERLIPIDEMIC PANCREATITIS
Marwan I Abdullah. MINING THE CELLMINER DATABASE TO IDENTIFY SHARED BIOMARKERS OF 5-FU AND OXALIPLATIN RESPONSE327-341
Shyngys Adilgazyuly, Tolkyn Bulegenov, Akmaral Mussakhanova, Tasbolat Adylkhanov, Kanat Abdilov, Zhannur Altybayeva, Gulmira Bazarova, Malike Kudaibergenova, Makpal Alchimbayeva, Aigul Utegenova, Gulnara Otepova.  ASSESSING THE INFLUENCE OF MEDICAL EDUCATION REFORMS ON ONCOLOGIST WORKFORCE AND LUNG CANCER MORTALITY IN KAZAKH-STAN: AN INTERRUPTED TIME SERIES ANALYSIS WITH PREDICTIVE MOD-ELING OF NATIONWIDE DATA FROM 1998 TO 2023
Wen-Wen Liu, Zhi-Juan Xu, Fang Xu.  NEW INSIGHTS INTO THE PATHOGENESIS AND TREATMENT ADVANCES OF AGE - RELATED MACULAR  DEGENERATION
Zhamilya Zholdybay, Zhanar Zhakenova, Madina Gabdullina, Yevgeniya Filippenko, Suria Yessentayeva, Galymzhan Alisherov, Aigerim Mustapaeva, Jandos Amankulov, Ildar Fakhradiyev.  68GA-FAPI PET/CT IN DIAGNOSIS OF THE BREAST CANCER DEPENDING ON THE MOLECULAR SUBTYPES AND EXPRESSION STATUS OF HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 (HER2/NEU)
A.I. Rybin, V.E. Maksymovskyi, O.V. Kuznetsova, V.V. Osyk, A.S. Bohdan. THE RESULTS OF LIFE QUALITY ASSESSMENT IN PATIENTS WITH PRIMARY OVARIAN CANCER DURING TREATMENT: EFFECT OF DIFFERENT TACTICS AND HIPEC
Miranda Sejdiu Abazi, Arbër Prokshaj, Shpëtim Prokshaj, Fitim Alidema, Nora Leci, Linda Abazi Morina.  ASSESSMENT OF PRACTICAL PERFORMANCE IN ORTHODONTIC CLASP FABRICATION AMONG DENTAL TECHNICIAN STUDENTS AT UBT: A REAL-TIME ANALYSIS OF WORKING TIME AND PERCEIVED STRESS
Abylay Baimakhanov, Ainash Oshibayeva, Temirkhan Kozhakhmetov, Nazarbek Omarov, Dinara Akhmetzhanova, Berikuly Duman. RESULTS OF MEDICAL CARE FOR PERSONS WITH POLYTRAUMA IN ALMATY AND CORRECTION OF THE ORGANIZATIONAL APPROACH
Khatia Mikeladze, Nino Chikadze, Nino Gachechiladze, Marina Tediashvili, Irina Datikashvili-David, Peter Lydyard, Nina Porakishvili. SERUM IL-6, IL-12, AND IL-10 LEVELS IN EARLY-STAGE, UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS: INSIGHTSFROMGEORGIA
Musayeva H.H. FREQUENCY OF COMPLICATIONS IN PATIENTS WITH ADENTIA (BASED ON ARCHIVAL DATA)
Hong-Xia Wang, Xiao-Xia Hou, Jie Xu.  NURSING RESEARCH ON EMERGENCY GASTROSCOPIC TREATMENT OF UPPER GASTROINTESTINAL FOREIGN BODIES
Tolegenova Z.Zh, Tokanova Sh.E, Baibussinova A.Zh, Kalikhanova K, Iskakova A.M, Shalgumbayeva G.M. ASSESSMENT OF INFECTIOUS DISEASE RISK FACTORS, INCLUDING COVID-19, AMONG HEALTHCARE WORKERS IN EAST KAZAKHSTAN REGION

Bassam A. Al- jabery, Majid R. Al-bahrani.	
ENVIRONMENTALLY SAFE CsPbBr3/MXene/MWCNTs HYBRID NANOCOMPOSITES: OPTOELECTRONIC AND STRUCTURAL	
CHARACTERISTICS FOR POSSIBLE BIOMEDICAL AND HEALTH APPLICATIONS	414
Hasan AlAidarous.	
PIGMENTED VILLONODULAR SYNOVITIS IN THE ANKLE OF A PEDIATRIC PATIENT: A CASE REPORT415	419
Kuat Zhussupov, Nazarbek Omarov, Sagit Imangazinov, Saule Imangazinova, Yernar Kairkhanov, Olga Tashtemirova, Rustem Kazangapov,	
Aldiyar Masalov, Darkhan Otkenov.	
ENDOSCOPIC INJECTION HEMOSTASIS AND LOCAL TREATMENT OF GASTRODUODENAL BLEEDING. LITERATURE REVIEW	W
AND OWN DEVELOPMENTS420-4	424

# STUDY OF THE CHEMICAL COMPOSITION AND ANTIMICROBIAL ACTIVITY OF SUBCRITICAL CO<sub>2</sub> EXTRACT FROM *EUPHORBIA HUMIFUSA* WILLD

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#### Abstract.

**Introduction:** One of the priority areas of development in pharmacy is the study of local plants possessing antimicrobial activity. In this regard, determining the chemical composition of the CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. with the aim of identifying new promising compounds with antimicrobial and antifungal activity is a pressing issue.

**Materials and methods:** Using subcritical carbon dioxide extraction, 23 g of CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. was obtained. To determine the potential use of *Euphorbia humifusa* Willd., we analysed the composition of the extract using GC-MS and the antimicrobial activity obtained by CO<sub>2</sub> extraction.

**Results:** For the first time, a comprehensive study of the CO<sub>2</sub> extract from the aerial parts of *Euphorbia humifusa* Willd., collected during the flowering phase in the Bostandyk district of Almaty Region, was conducted. Using gas chromatographymass spectrometry (GC/MS) with Wiley 7th edition and NIST'02 libraries, 47 components were identified.

**Conclusions:** The obtained CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. can be used in pharmaceutical technology as a substance. **Key words.** *Euphorbia humifusa* Willd, GC-MS analysis, CO<sub>2</sub> extraction, antimicrobial activity.

## Introduction.

In Kazakhstan, ensuring the population's access to affordable medical and pharmaceutical services is one of the most important areas of state policy, in accordance with the objectives of the National Medical Policy [1,2], which represents a complex integrative structure [3]. Implementing this policy requires a comprehensive approach that includes not only effective personnel management [4]—such as planning for seasonal workforce needs [5], developing communication skills [6], or forming pharmaceutical clusters [7]—but also the strategic development of the pharmaceutical industry itself as a high-profit and rapidly growing economic sector, serving as a driver for the country's socio-economic development [8,9].

A key challenge in achieving these goals is the high dependence of Kazakhstan's pharmaceutical market on imported products. In this regard, a priority task is the development of the national pharmaceutical industry [10] by increasing the volume of domestic production. One of the most promising and strategically important directions in this context is the development and manufacture of medicines based on domestic plant materials.

Thus, the scientific assessment of the potential of local flora and the screening of Kazakhstan's biodiversity for the presence of biologically active compounds become practical tools for addressing national tasks. This line of work directly contributes to import substitution, the formation of economic independence and national security [11,12], as well as opens new opportunities for the development of evidence-based phytotherapy and the creation of effective medicines [13,14].

Currently, many promising plant species native to Kazakhstan are already in focus of scientific interest, such as *Nicotiana Tabacum L.* [15], *Echinops Ritro* [16], *Portulaca Oleracea L.* [17], *Brassica Napus L.* [18], *Plantago Major L.* [19], representatives of the *Apiaceae* family [20], *Ferula Asafoetida L.* [21,22] and others. Within this strategic direction and with the aim of further expanding the raw material base of the domestic pharmaceutical industry, this study focuses on the species *Euphorbia humifusa* Willd. This species was selected as the main object of scientific analysis due to its rich content of biologically active compounds and diverse pharmacological potential, making it a promising source for the development of new medicines.

The studied plant, Euphorbia humifusa Willd., belongs to the genus Euphorbia of the family Euphorbiaceae. The Euphorbiaceae family is very diverse in terms of range, distribution and morphology and consists of a variety of species that grow on the mainland as shrubs, weeds, trees or climbing vines. Euphorbia is one of the largest genera of flowering plants with more than 2,000 species [23]. One of the species of the genus Euphorbia is the annual herbaceous plant Euphorbia humifusa Willd. (Figure 1).

Research of herbarium specimens confirmed the wide distribution of *Euphorbia humifusa* Willd. in the flora of Kazakhstan. Analysis of the herbarium specimens showed the widespread distribution of *Euphorbia humifusa* Willd. in the territories of Almaty Region, Zhambyl Region, Mangistau Region, and Central Kazakhstan Region (Figure 2).

Scientific studies have revealed that the key components of *Euphorbia humifusa* Willd. are flavonoids, triterpenes, coumarins, sterols, tannins and phenolic acid derivatives [24].

A literature review demonstrated that various extracts and isolated compounds from *Euphorbia humifusa* Willd. possess a broad spectrum of pharmacological activities, such as antimicrobial activity [25], anti-vitiligo effects [26], anti-tumor effects [27], antidiabetic effect [28], anti-influenza activity [29] and hepatoprotective effects [30].

The aim of this study is to analyse the chemical components and evaluate the antimicrobial properties of CO<sub>2</sub> extract from *Euphorbia humifusa* Willd. with a view to using, it in the future to create medicinal products that demonstrate antimicrobial and antifungal efficacy.

To achieve the stated objective of the study, we have defined the following tasks:

1. Obtain a CO<sub>2</sub> extract from the plant *Euphorbia humifusa* Willd.

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Figure 1. Picture of Euphorbia humifusa Willd.

#### A - Collected plant; B - Plant flowers; C - Plant stem.



Figure 2. Distribution area of Euphorbia humifusa Willd. within the Republic of Kazakhstan.

- 2. Perform a comprehensive chemical analysis of the CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. to identify the main bioactive compounds using gas chromatography-mass spectrometry (GC/MS) and to quantify the key components of the extract.
- 3. Evaluate the antimicrobial activity of the studied extract against Gram-positive bacteria (*Staphylococcus aureus*), Gramnegative bacteria (*Escherichia coli*), and Fungal microorganism (*Candida albicans*).

#### Materials and Methods.

#### Plant raw material:

Euphorbia humifusa Willd. was collected in autumn (August-September) 2024 in Almaty, Kazakhstan, in accordance with the requirements of Good Agricultural and Collection Practice (GACP). The plant material was identified at the Republican State Enterprise 'Institute of Botany and Phytointroduction' of the Committee for Forestry and Wildlife of the Ministry of Ecology, Geology and Natural Resources of the Republic of Kazakhstan (Reference registration number No. 01-05 / 490).

# CO, extraction procedure:

For our research, we chose subcritical  $\mathrm{CO}_2$  extraction to obtain extract.

Traditional extraction methods have demonstrated limited efficiency, and the resulting extracts contained impurities and residues of organic solvents, which significantly reduced their potential for practical application [31]. As an alternative, subcritical CO<sub>2</sub> extraction technology was chosen, which complies with the principles of green chemistry and modern environmental requirements [32]. This method, being thermosensitive, ensures the gentle extraction of thermolabile and easily oxidisable biologically active components [33].

The extraction was carried out on a carbon dioxide extraction unit (CO<sub>2</sub>-5L flow extraction system) at the production facility of "Zhanapharm" Company (a pharmaceutical enterprise, Almaty, Kazakhstan). The process was conducted in a subcritical mode in accordance with the requirements of the National Standard 27658-1910 – LLP-02-2011. Liquefied carbon dioxide (GOST 8050-85) was used as the extractant.

#### Chemical detection of biologically active compounds:

After obtaining the CO<sub>2</sub> extract, its component composition was analysed using gas chromatography with mass spectrometric detection.

The chemical analysis of the component composition was performed at the Al-Farabi Kazakh National University in the Centre for Analytical, Colloid Chemistry and Rare Element Technology. The study was conducted using gas chromatography with mass spectrometric detection (GC-MS) using an Agilent 7890A/5975C chromatographic system [34].

Chromatographic analysis conditions: sample volume 0.5 µl, sample injection temperature 260°C, no split flow. Separation was performed using a DB-17ms capillary column 30 m long, with an internal diameter of 0.25 mm and a film thickness of 0.25 µm at a constant carrier gas (helium) flow rate of 1 ml/ min. The chromatography temperature was programmed from 60°C with a heating rate of 20°C/min to 120°C, then with a heating rate of 10°C/min to 270°C (holding time 10 min) and with a heating rate of 5°C/min to 300°C (holding time 10 min). The analysis time was 44 minutes. Detection was performed in SCAN m/z 34-750 mode. Agilent MSD ChemStation software (version 1701EA) was used to control the gas chromatography system and to record and process the results and data obtained. Data processing included determining retention times, peak areas, and processing spectral information obtained using a mass spectrometric detector. The Wiley 7th edition and NIST'02 libraries (total number of spectra in the libraries – over 550,000) were used to decipher the obtained mass spectra.

#### Antimicrobial activity determination:

The antimicrobial activity of the extract was tested by the microbiological laboratory of the Scientific Centre for Anti-Infective Drugs JSC, Almaty, Kazakhstan, accredited by the accreditation system of the Republic of Kazakhstan for compliance with the requirements of GOST ISO/IEC 17025-2019 'General requirements for the competence of testing and calibration laboratories (IK)' (No. KZ. T.02.1395 dated 2 October 2018).

The following culture media were selected: Mueller-Hinton broth M 391 (Himedia, India), Mueller-Hinton agar M 173 (Himedia, India), sodium chloride (Mikhailovsky Chemical Reagents Plant, Russia), 96% ethanol (Talgar Alcohol, Kazakhstan), and purified water.

As test strains, microorganisms obtained from the Republican Collection of Microorganisms (RCM, Astana, Kazakhstan) and the American Type Culture Collection (ATCC, USA) were used: the Gram-positive bacterium *Staphylococcus aureus* ATCC 6538-P (ATCC, Kazakhstan); the Gram-negative bacterium *Escherichia coli* ATCC 8739 (ATCC, USA) and the fungus *Candida albicans* ATCC 10231 (ATCC, USA).

The assessment of the antimicrobial activity of the extract was conducted in accordance with the internal methodological guidelines MI-LM-02 "Determination of the Bactericidal Action of Antimicrobial Agents by the Method of Double Serial Dilutions" (Methodological Instructions of Microbiology Laboratories) [35]. The study employed the method of double serial dilutions in liquid nutrient medium and the disk-diffusion method.

The diameters of the inhibition zones were measured using a caliper with an accuracy of 0.5 mm. The data are presented as mean value  $\pm$  standard deviation (SD).

All methodologies complied with the standards of the Clinical and Laboratory Standards Institute (CLSI, USA) [36].

#### Results.

# Preparation of plant raw materials *Euphorbia humifusa* Willd. for extraction:

The plant material was dried at room temperature  $(25\pm5^{\circ}\text{C})$  in a ventilated room at the «Institute of Botany and Phytointroduction». After drying, the raw material was ground to a size of 1-3 mm using an IKA M20 laboratory mill.

# Technological parameters of CO<sub>2</sub> extraction and storage of the finished *Euphorbia humifusa* Willd. Extract:

The extraction of the aerial parts of *Euphorbia humifusa* Willd. with carbon dioxide was carried out under the following conditions: the extraction temperature was +18+23°C, the operating pressure was maintained at 57-65 atmospheres, and the process duration was 8 hours. The extract yield reached 23 grams.

The CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. must be stored in a dark, cool place in an airtight glass container at a temperature not exceeding +25°C, protected from direct sunlight. The shelf life under these conditions is two years.

# Biologically active compounds of the *Euphorbia humifusa* Willd. CO<sub>2</sub> extract:

An analysis of the chemical composition of the *Euphorbia humifusa* Willd. CO<sub>2</sub> extract using gas chromatography-mass spectrometry (GC-MS) revealed 47 chemical compounds. The chromatogram and the list of identified compounds are presented in Figure 3 and Table 1.

GC-MS analysis of the CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. revealed the presence of fatty acids and their derivatives, terpenes and isoprenoids, steroids and triterpene compounds, tocopherols and vitamins, hydrocarbons (alkanes and alkenes), lactones, and other organic components. The following compounds were identified during the study: among fatty acids and their derivatives, Hexadecanoic acid (9.57%), Octadecanoic acid (3.99%), 9,12-Octadecadienoic acid (5.55%) and 9,12,15-Octadecatrienoic acid, (Z,Z,Z)- (linolenic acid) (17.78%); in the group of hydrocarbons, Tetratriacontane (6.45%) was identified; Among steroids and triterpenoids,  $\gamma$ -Sitosterol (8.25%),  $\beta$ -Amyrin (2.46%), Lupeol (11.08%) and Lanosterol (2.28%) were identified; in the group of terpenes and isoprenoids, Phytol (4.26%) was identified.

# Results of antimicrobial activity of CO2 extract of *Euphorbia humifusa* Willd.

The aim of this study was to evaluate the antimicrobial activity of CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. The testing was carried out using double serial dilutions in broth and agar diffusion against Gram-positive (*Staphylococcus aureus* ATCC 6538-P) and Gram-negative (*Escherichia coli* ATCC 8739) microorganisms and yeast-like fungi (*Candida albicans* ATCC 10231). The results of the study are presented in Table 2 and Figure 4.

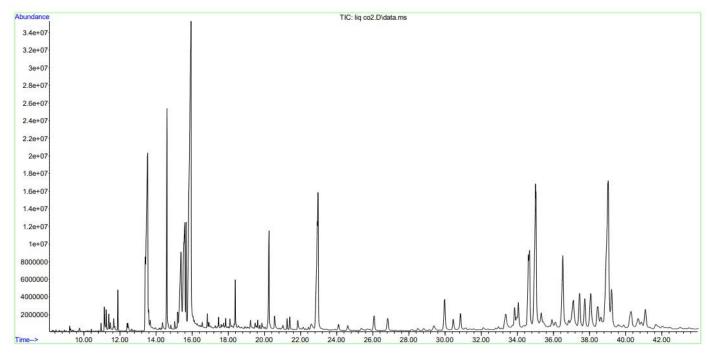
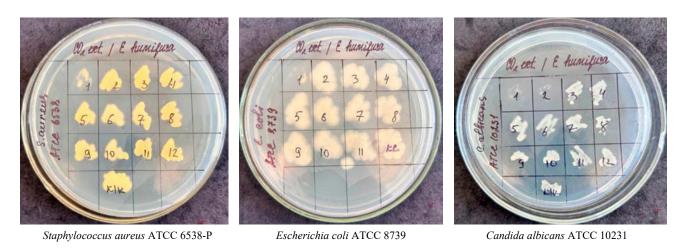


Figure 3. Chromatogram of CO<sub>2</sub> extract of Euphorbia humifusa Willd.



**Figure 4.** Results of antimicrobial activity of CO<sub>2</sub> extract of Euphorbia humifusa Willd.

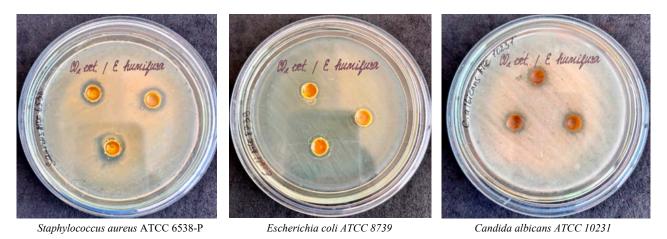


Figure 5. Results of antimicrobial activity of CO<sub>2</sub> extract of Euphorbia humifusa Willd. against Staphylococcus aureus ATCC 6538-P, Escherichia coli ATCC 8739 and Candida albicans ATCC 10231.

 $\textbf{\textit{Table 1.}} \ \textit{Results of GC-MS analysis of CO}_{2} \ \textit{extract of Euphorbia humifusa Willd}.$ 

No.	Retention time,	Compounds	Probability of identification,	Percentage content,
1	9.22	Dodecanoic acid	88	0.08
2	9.27	3-Buten-2-one, 4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-	83	0.05
3	9.77	Vanillin	80	0.11
4	10.42	Caryophyllene oxide	73	0.03
5	10.96	Fumaric acid, ethyl 2-methylallyl ester	74	0.12
6	11.14	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	87	0.46
7	11.24	2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro-4,4,7a-trimethyl-, (R)-	90	0.40
8	11.38	Tetradecanoic acid	90	0.31
9	11.89	2-Pentadecanone, 6,10,14-trimethyl-	93	0.52
10	12.40	Pentadecanoic acid	82	0.11
11	13.53	Hexadecanoic acid	94	9.57
12	13.67	Oleic Acid	80	0.36
13	14.36	Heptadecanoic acid	79	0.39
14	14.60	Phytol	91	4.26
15	15.38	Octadecanoic acid	82	3.99
16	15.59	9,12-Octadecadienoic acid (Z,Z)-	92	5.55
17	15.67	9,12,15-Octadecatrienoic acid, ethyl ester, (Z,Z,Z)-	96	1.57
18	15.93	9,12,15-Octadecatrienoic acid, (Z,Z,Z)	93	17.78
19	16.84	Pentacosane	89	0.37
20	17.46	4,8,12,16-Tetramethylheptadecan-4-olide	84	0.32
21	18.39	Heptacosane	91	1.08
22	19.49	17-Pentatriacontene	75	0.19
23	20.25	Nonacosane	83	2.77
24	21.26	Squalene	92	0.23
25	21.40	Triacontane	90	0.30
26	22.97	Tetratriacontane	90	6.45
27	24.11	1-Pentatriacontanol	77	0.20
28	25.37	Dotriacontane	85	0.09
29	26.07	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	78	0.59
30	28.50	γ-Tocopherol	72	0.09
31	28.82	1,30-Triacontanediol	67	0.11
32	29.98	α-Tocopherolquinone	75	1.40
33	30.46	Vitamin E	91	0.46
34	33.36	Campesterol	86	1.16
35	33.86	Stigmasterol	82	0.89
36	34.68	4α,14-Dimethyl-5α-ergosta-8,24(28)-dien-3β-ol	87	2.79
37	35.01	y-Sitosterol	90	8.25
38	35.33	Phytonadione	76	0.99
39	37.11	β-Amyrin	87	2.46
40	37.45	9,19-Cyclolanost-24-en-3-ol, (3β)-	90	1.88
41	37.74	6a,14a-Methanopicene, perhydro-1,2,4a,6b,9,9,12a-heptamethyl-10-hydroxy-	78	1.55
42	38.07	Lanosterol	85	2.28
43	38.45	9,19-Cyclolanostan-3-ol, 24-methylene-, (3β)-	80	1.44
44	39.03	Lupeol	91	11.08
45	39.22	D:B-Friedo-B':A'-neogammacer-5-en-3-ol, (3β)-	81	2.13
46	40.29	Stigmasta-4,24(28)-dien-3-one, (24E)-	84	1.48
47	41.10	Lanosterol	80	1.28

Table 2. Results of testing the antimicrobial activity of the Euphorbia humifusa Willd. CO2 extract.

Test strains	MIC values, mg/mL	Result (growth inhibition)
Staphylococcus aureus ATCC 6538-P	1 000	+
Escherichia coli ATCC 8739	1 000	+
Candida albicans ATCC 10231	1 000	+

<sup>\*</sup>MIC values are expressed in mg/mL. The initial extract concentration was 1000 mg/mL.

Table 3. Antimicrobial activity zones of CO, extract of Euphorbia humifusa Willd.

Test strains	Zone of inhibition, mm	
	Average value	
Staphylococcus aureus ATCC 6538-P	$15.33 \pm 1.15$	
Escherichia coli ATCC 8739	$14.0 \pm 0.5$	
Candida albicans ATCC 10231	$11.67 \pm 0.58$	

The data obtained show that the CO<sub>2</sub> extract of *Euphorbia humifusa* Willd. has the same antimicrobial and antifungal activity, with a MIC value of 1000 mg/mL against all test strains: *Staphylococcus aureus* ATCC 6538-P, *Escherichia coli* ATCC 8739 and *Candida albicans* ATCC 10231.

The results of testing the antimicrobial activity of the test sample using the agar diffusion method are presented in Figure 5 and Table 3.

The results of the study of the antimicrobial activity of the CO<sub>2</sub> extract of *Euphorbia humifusa* Willd., presented in Table 3 and Figure 5, demonstrate the following indicators:

- 1. Against *Staphylococcus aureus* ATCC 6538-P an inhibition zone of  $15.33 \pm 1.15$  mm was recorded.
- 2. Against *Escherichia coli* an inhibition zone of  $14.0 \pm 0.5$  mm was observed.
- 3. Antifungal activity against *Candida albicans* ATCC 10231 is demonstrated by an inhibition zone of  $11.67 \pm 0.58$  mm.

#### Discussion.

Our results confirm that the composition of biologically active substances in *Euphorbia humifusa* Willd. extract varies significantly depending on ecological growth conditions, the phenological phase at the time of raw material collection and technological extraction parameters. This variability directly affects the severity of the antimicrobial effect, highlighting the need to standardise both the raw materials and the extraction processes to ensure consistent pharmacological action. Our data on antimicrobial activity are consistent with reports from several authors [25,37-39].

Previous studies have shown that triterpenoids play a key role in the formation of antimicrobial properties and are among the main secondary metabolites of the species [40]. As part of our ongoing search for natural compounds with antimicrobial activity in the CO<sub>2</sub> extract of *E. humifusa's* aerial parts, we isolated nine triterpenoid compounds. This correlates well with the data of Jianbo Lin et al. [23], who identified two active triterpenoid components in the methanol fraction of petroleum ether – cycloart-23E-en-3β-25-diol and 24-methylene cycloartanone — with pronounced antimicrobial activity, as well as with the results of Xia R. F. et al. [41], who demonstrated the antimicrobial effect of isolated triterpenoids against several of clinically significant strains (*Staphylococcus aureus*, *S. epidermidis*, *Bacillus cereus*, *Listeria monocytogenes*,

Escherichia coli, Enterobacter sakazakii). Reports by Li Z. J. et al. [42] on the antifungal activity of ellagic acid (EA) from E. humifusa against Candida and Trichophyton rubrum strains, both in vitro and in vivo, expand the range of potential targets for extracts of this species. Additionally, fractionated extracts (petroleum ether, chloroform, ethyl acetate, butanol, and residual methanol) demonstrated activity against Staphylococcus aureus, Escherichia coli and Candida albicans [43], confirming the contribution of several chemical classes to the cumulative effect.

Our extract was found to contain Lupeol (11.08%) and β-amyrin (2.46%), which have been previously described as possessing antimicrobial activity [44]. A significant proportion of the components were also fatty acids, including Hexadecanoic acid (9.57%) and 9,12,15-Octadecatrienoic acid, (Z,Z,Z)- (linolenic acid) (17.78%). Such acids are known to disrupt the integrity of microbial cell membranes, causing a pronounced antimicrobial effect [45]. The biological effect we observed is likely the result of the combined action of triterpenoids and lipophilic acids, including possible synergism.

Methodological aspects also proved critical for interpreting the activity. In the serial dilution test, the extract exhibited a bacteriostatic effect only in its undiluted form inhibitory concentration (MIC) of 1000 mg/mL, whereas no activity was observed at 500 mg/mL. It is important to directly note the key methodological limitation identified in our study: significant antimicrobial activity of the extract was observed only at very high concentrations (MIC = 1000 mg/mL). We interpret the sharp loss of effect upon dilution not as an absence of potentially active compounds, but rather as a direct indication of their extremely low solubility, stability, or bioavailability in the aqueous environment of the test system used. This fundamental limitation of the current experimental model implies that revealing the full therapeutic potential of the extract requires further research. On the other hand, the disk-diffusion method revealed significant antimicrobial activity for the CO2 extract, which may reflect locally high concentrations near the agar surface and/or other specific diffusion patterns of lipophilic molecules in a solid phase. A comparison of our data with reports on ethanolic extracts [25,46] and fractions of varying polarity [47] suggests that optimizing the composition (enrichment with active triterpenoid fractions) and the physicochemical parameters of the carrier formulation could enhance its in vitro efficacy and reproducibility.

The practical significance of the obtained results lies in substantiating the rationale for the targeted standardization of *E. humifusa* extracts based on triterpenoid markers (e.g., lupeol, β-amyrin, cycloartane derivatives) while controlling the content of fatty acids. To overcome the limitation associated with the requirement for high concentrations in broth tests, further purification and fractionation of the extract, as well as the development of pharmaceutical formulations enhancing the solubility and bioavailability of lipophilic components (including solubilization approaches), appear promising. At the next stage, it would be advisable to determine quantitative activity parameters (MIC/MBC, MFC), investigate potential synergy between the isolated triterpenoids and fatty acids, and evaluate the activity against an expanded panel of clinically significant bacterial and fungal pathogens.

Overall, our results are consistent with existing literature data [23,25,37-46] and confirm the potential of *E. humifusa* as a source of antimicrobial compounds. The variable phytochemical profile remains a key factor determining the severity of the effect and requires attention to raw material standards and extraction technology, which is important for subsequent translation into applied developments.

#### Conclusion.

For the first time, a subcritical CO<sub>2</sub> extract (yield 23 g) was obtained from the aerial parts of *Euphorbia humifusa* Willd. harvested in the Almaty Region, using gentle extraction parameters (18-23°C, 57-65 atm, 8 h). This approach ensures the extraction of thermolabile lipophilic metabolites and guarantees a reproducible and scalable process.

According to GC-MS data, 47 compounds were identified, with fatty acids and their derivatives (including 9,12,15-Octadecatrienoic acid, (Z,Z,Z)- (linolenic acid) 17.78 %; Hexadecanoic acid, 9.57 %), triterpenoids (Lupeol, 11.08 %), phytosterols ( $\gamma$ -sitosterol, 8.25 %), and isoprenoids (Phytol, 4.26 %) being the dominant components, collectively forming the characteristic lipophilic profile of the extract.

Antimicrobial testing confirmed the extract's activity against clinically relevant test strains: inhibition zones measured 15.33  $\pm$  1.15 mm (*Staphylococcus aureus* ATCC 6538-P), 14.0  $\pm$  0.5 mm (*Escherichia coli* ATCC 8739) and 11.67  $\pm$  0.58 mm (*Candida albicans* ATCC 10231) in the disk-diffusion test; in serial dilution tests, an antimicrobial/antifungal effect was observed only at the minimum inhibitory concentration (MIC) of 1000 mg/mL.

The combination of data indicates that the biological activity is due to the combined contribution of triterpenoids and fatty acids, and the obtained metabolite profile can serve as a basis for standardizing the extract using marker compounds (e.g., Lupeol,  $\gamma$ -sitosterol) while controlling the content of key acids.

The practical significance of the results lies in demonstrating the potential of CO<sub>2</sub> extract of *E. humifusa* as a pharmaceutical substance for the development of plant-derived antimicrobial agents and in defining the key technological parameters for its production.

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