

GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 1 (370) Январь 2026

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 ВИНТИ 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 ВИНТИ 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. Корректур авторам не высылаются, 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 საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ 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. რენტგენოგრაფიების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის 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 ფხიხლებში 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.

Yu.V. Dumanskyi, A.V. Bondar, A.A. Patskov, Ye.A. Stolyarchuk. ARM-ICG IN THE PREVENTION OF LYMPHEDEMA AFTER SURGICAL TREATMENT OF BREAST CANCER.....	6-9
Chuan-Min Liu, Jia-Shu Guo. EFFICACY ANALYSIS OF SHENFU INJECTION COMBINED WITH DAPAGLIFLOZIN IN THE TREATMENT OF SEPTIC HEART FAILURE.....	10-15
Lilya Parseghyan, Anna Darbinyan, Sona Poghosyan, Armenuhi Moghrovyan, Armen Voskanyan. DOSE-DEPENDENT PROTECTIVE EFFECTS OF TAURINE IN EXPERIMENTAL ENVENOMATION BY THE BLUNT-NOSED VIPER (MACROVIPERA LEBETINA OBTUSA).....	16-23
Yusup A. Bakaev, Mariya E. Makarova, Zurab S. Khabadze, Nikita A. Dolzhikov, Gor G. Avetisian, Dzhandet F. Rasulova, Anastasya A. Ivina, Ekaterina E. Starodubtseva, Daria A. Pervozvanova, Alisa A. Vavilova, Khalid Yu. Halituev, Oleg S. Mordanov, Anastasiya V. Mordanova. CLOSED HEALING OF THE PALATE MUCOSA: INDEX ASSESSMENT AND CLINICAL SIGNIFICANCE.....	24-29
Mereke Alaidarova, Assem Kazangapova, Ulbossyn Saltabaeva, Gulnar Zhaksylykova, Raushan Baigenzheyeva, Gani Uakkazy, Gudym Yelena, Marlan Basharlanova, Amangali Akanov, Joseph Almazan. NURSES' PERCEIVED PROFESSIONAL PERFORMANCE IN PRIMARY HEALTH CARE: A NATIONAL STUDY OF ORGANIZATIONAL AND WORKFORCE DETERMINANTS.....	30-37
Alaa Mohammed Mahmoud Qasem, Abdelgadir Elamin, Marwan Ismail, Mavlyanova Zilola Farkhadovna, Ahmed L. Osman. EVALUATION OF SERUM GALECTIN-3 LEVELS IN PATIENTS WITH HYPOTHYROIDISM AND HYPERTHYROIDISM IN AJMAN, UNITED ARAB EMIRATES.....	38-44
George Tchumburidze, Lukhum Tchanturia, Irakli Gogokhia. ADVANTAGES OF COMPUTER-NAVIGATED KNEE REPLACEMENT: IMPLICATIONS FOR BIOMECHANICS, PAIN MANAGEMENT, AND RECOVERY.....	45-49
Omar Abdul Jabbar Abdul Qader. GENOTOXIC AND MOLECULAR STRESS EFFECTS OF DENTAL RESIN MONOMERS ON ORAL EPITHELIAL CELLS.....	50-55
Sinan Arllati, Kreshnik Syka. CLINICAL MANAGEMENT OF IMMEDIATE IMPLANT PLACEMENT AND LOADING IN THE ESTHETIC ZONE WITH FINAL PROSTHETIC RESTORATION.....	56-60
Elina (Christian) Manzhali, Yuri Dekhtiar, Valentyn Bannikov, Galyna Girnyk, Ivan Bavykin. ARTIFICIAL INTELLIGENCE IN CLINICAL DIAGNOSTICS FOR EARLY DETECTION OF CHRONIC DISEASES: A SYSTEMATIC REVIEW.....	61-73
Yusup A. Bakaev, Mariya E. Makarova, Zurab S. Khabadze, Nikita A. Dolzhikov, Gor G. Avetisian, Dzhandet F. Rasulova, Anastasya A. Ivina, Ekaterina E. Starodubtseva, Daria A. Pervozvanova, Alisa A. Vavilova, Khalid Yu. Halituev, Nadejda A. Khachatryan, Oleg S. Mordanov. CLINICAL APPLICATION OF THE PALATAL MUCOSAL OPEN HEALING INDEX FOR EVALUATION OF PALATAL DONOR SITE HEALING.....	74-78
Raushan Aibek, Mairash Baimuratova, Zamanbek Sabanbayev, Alma-Gul Rakhimovna Ryskulova, Mariya Laktionova. EPIDEMIOLOGICAL TRENDS OF SALMONELLOSIS IN THE REPUBLIC OF KAZAKHSTAN: ANALYSIS OF NATIONAL DATA (2013–2024).....	79-90
Raghad Albarak, Ibtihaj Abdulmohsen Almutairi, Shatha Shia Alshumaym, Haifa Saleh Alfouzan, Sadeem Sulaiman Alsenidi, Joud Muneer Almotairi, Lamees Fahad Alharbi, Tuqa Rashed Alyahyawi, Rawan Mushwah Alharbi, Ghaida Awadh Alfanoud, Omar Saleh Almisnid. THE PATTERN AND INFLUENCING FACTORS OF OPIOID-PRESCRIBING BEHAVIOR AMONG EMERGENCY PHYSICIANS IN THE QASSIM REGION: A CROSS-SECTIONAL STUDY.....	91-95
Shalva Skhirtladze, George Petriashvili, Nana Nikolaishvili, Ana Apulava. FOLDABLE CAPSULAR VITREOUS BODY IMPLANTATION IN A PRE-PHTHISICAL EYE: A PRELIMINARY SHORT-TERM CASE REPORT.....	96-99
Rehab K. Mohammed, Nuha Mohammed. ENHANCEMENT OF KNOWLEDGE ABOUT DASH DIET AMONG HYPERTENSIVE PATIENTS: DIETARY EDUCATIONAL INTERVENTION.....	100-103
Mohammed Aga, Mohammad Hendawi, Safa Awad, Fatima Aljenaid, Yazid Aldirawi, Hamza Shriedah, Salih Ibrahim, Zarnain Kazi, Rafea Jreidi, Arkan Sam Sayed-Noor. CHARACTERISTICS, CLINICAL PRESENTATION AND MANAGEMENT OF PATIENTS WITH SNAKE BITES TREATED AT AL-DHAID HOSPITAL IN UNITED ARAB EMIRATES: TWELVE YEARS' EXPERIENCE.....	104-109
David Gvarjaladze, Nunu Metreveli. QPA AND HIV-INTEGRASE APTAMER IN THE PRESENCE OF LEAD IONS.....	110-115
Zhao Luting, Fang Qilin, Zhang Haoxu, Mo Pengli, Yu Xiaoxia. OBSERVATION ON THE CURATIVE EFFECT OF FACIAL PNF TECHNOLOGY COMBINED WITH MIRROR THERAPY IN THE TREATMENT OF PERIPHERAL FACIAL PARALYSIS.....	116-122

Ahmed Mohammed Ibrahim, Arwa Riyadh Khalil Albarhawi, Samar Saleh Saadi. ASSOCIATION PROPERTIES OF COMPLETE BLOOD COUNT FOR LEVELS OF THYROID STIMULATING HORMONE.....	123-129
Tuleubayev B.E, Makhatov B.K, Vinokurov V.A, Kamyshanskiy Ye.K, Kossilova Ye.Y. OSTEOREGENERATIVE POTENTIAL AND REMODELING OF A COMPOSITE BASED ON NANOFIBRILLATED CELLULOSE, XENOGRAFT, AND BUTVAR-PHENOLIC ADHESIVE: A HISTOLOGICAL STUDY UNDER NORMAL AND INFECTED BONE WOUND CONDITIONS.....	130-143
Zhanat Toxanbayeva, Nyshanbay Konash, Muhabbat Urunova, Zhamila Dustanova, Sveta Nurbayeva, Sabina Seidaliyeva. GC-MS PROFILING OF THE LIPOPHILIC FRACTION AND ACUTE SAFETY ASSESSMENT OF THE AQUEOUS EXTRACT OF <i>SCUTELLARIASUBCAESPITOSA</i>	144-152
Karen Martik Hambarzumyan, Rafael Levon Manvelyan. CHANGES IN LOWER LIMB FUNCTIONAL ACTIVITY AND TREATMENT OUTCOMES IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE FOLLOWING THE APPLICATION OF STANDARD AND MODIFIED TREATMENT PROTOCOLS. A COMPARATIVE ANALYSIS.....	153-159
Asmaa Abdulrazaq Al-Sanjary. SALINE INFUSION SONOGRAPHY IN EVALUATION OF SUBFERTILE WOMEN AND ITS EFFECT ON REPRODUCTIVE OUTCOME.....	160-166
Nino Buadze, Maia Turmanidze, Paata Imnadze, Nata Kazakashvili. IMPACT OF THE COVID-19 PANDEMIC ON THE SURVEILLANCE OF INFECTIOUS DISEASES: ASSESSMENT OF THE LEPTOSPIROSIS SURVEILLANCE SYSTEM IN THE ADJARA REGION (2020–2024).....	167-174
Nurlan Urazbayev, Ruslan Badyrov, Nurkassi Abatov, Alyona Lavrinenko, Yevgeniy Kamyshanskiy, Ilya Azizov. EXPERIMENTAL EVALUATION OF TISSUE RESPONSE TO IMPLANT MATERIALS UNDER <i>ESCHERICHIA COLI</i> CONTAMINATION.....	175-184
Abdulaev M-T.R, Kachikaeva L.T, Murtuzaliev Z.R, Khokhlova M.S, Badalian M.A, Tskaev T.A, Abdulkhalikov A.E, Arutiunian N.A, Rustamov M.T, Yakhyaev R.S, Chuenkova T.S, Zolfaghari Yousef. THE ROLE OF SURGICAL INTERVENTION IN THE MULTIMODAL TREATMENT OF BREAST CANCER IN OLDER WOMEN.....	185-187
Ahmed Abdulraheem Ibrahim Dahy, Mohanad Luay Jawhar, Baraa Ahmed Saeed, Noor Yahya Muneer, Anwer Jaber Faisal. IMPACT OF GINGER SUPPLEMENTATION ON BLOOD PRESSURE AND GLUCOSE LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND CARDIOVASCULAR DISEASE.....	188-192
Marwan Ismail, Mutaz Ibrahim Hassan, Mosab Khalid, Jaborova Mehroba Salomudinovna, Assiya Gherdaoui, Majid Alnaimi, Raghda Altamimi, Mahir Khalil Jallo, Iriskulov Bakhtiyar Uktamovich, Shukurov Firuz Abdufattoevich, Shawgi A. Elsiddig, Ramprasad Muthukrishnan, Kandakurthi Praveen Kumar, Elryah I Ali, Asaad Babker, Abdelgadir Elamin, Srija Manimaran. DIFFERENTIAL ASSOCIATIONS BETWEEN PHYSICAL ACTIVITY AND GLYCEMIC CONTROL ACROSS BODY MASS INDEX IN TYPE 2 DIABETES: A COMPARATIVE ANALYSIS OF HBA1C AND FRUCTOSAMINE.....	193-199
Ketevan Tsanova, Malvina Javakhadze, Ekaterine Tcholdadze, Lia Trapaidze, Tamar Sokolova, Gvantsa Kvariani. SEVERE TOXIC EPIDERMAL NECROLYSIS COMPLICATED BY ACUTE KIDNEY INJURY: DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS.....	200-204
Torgyn Ibrayeva, Assel Iskakova, Togzhan Algazina, Gulnar Batpenova, Dinara Azanbayeva, Gulnaz Tourir, Issa Emir Ardakuly, Aizhan Shakhanova. ECZEMA AND TRANSEPIDERMAL MOISTURE LOSS: A SYSTEMATIC REVIEW AND META-ANALYSIS (REVIEW).....	205-212
Kalashnik-Vakulenko Yu, Kostrovskiy O, Aleksandruk N, Makaruk O, Kudriavtseva T.O, Lytovska O, Leliuk O, Alekseeva V. ANATOMICAL FEATURES OF THE CAROTID ARTERIES, OPHTHALMIC NERVES, MANDIBULAR NERVE AND EXTRAOCULAR ARTERY BASED ON MULTISLICE COMPUTED TOMOGRAPHY (MSCT) DATA.....	213-218
Rigvava Sophio, Kusradze Ia, Karumidze Natia, Kharebava Shorena, Tchgonia Irina, Tatrishvili Nino, Goderdzishvili Marina. PREVALENCE, PHYLOGENETIC DIVERSITY, AND ANTIMICROBIAL RESISTANCE OF UROPATHOGENIC <i>ESCHERICHIA COLI</i> IN GEORGIA.....	219-227
Babchuk O.G, Gulbs O.A, Lantukh I.V, Kobets O.V, Ponomarenko V.V, Lytvynova I.L, Lukashevych N.M, Minin M.O, Rogozhan P.Y, Pustova N.O. PECULIARITIES OF THE DEVELOPMENT OF THE PSYCHOLOGICAL STATE OF MEDICAL STUDENTS AND LAW ENFORCEMENT UNIVERSITY CADETS.....	228-233
Kirill I. Seurko, Roman A. Sokolov, Alexandr N. Kosenkov, Elena V. Stolarchuk, Kseniya I. Seurko, Elena N. Belykh, Mikhail I. Bokarev, Magomed E. Shakhbanov, Alexandr I. Mamykin, Andrew I. Demyanov, Omari V. Kanadashvili. LEFT HEMICOLECTOMY IN PATIENTS WITH COLORECTAL CANCER: SURGICAL VIEW ON INFERIOR MESENTERIC ARTERY ANATOMY VARIABILITY.....	234-242
Pere Sanz-Gallen, Inmaculada Herrera-Mozo, Beatriz Calvo-Cerrada, Albert Sanz-Ribas, Gabriel Martí-Amengual. OCCUPATIONAL ALLERGIC DERMATITIS IN METALWORKERS.....	243-249
Erkin Pekmezci, Songül Kılıç, Hakan Sevinç, Murat Türkoğlu. THE EFFECTS OF <i>ROSMARINUS OFFICINALIS</i> ON VEGF AND IL-1 α GENE EXPRESSIONS IN HACAT CELLS: UNRAVELING ITS MECHANISM OF ACTION IN WOUND HEALING AND HAIR LOSS.....	250-254

THE EFFECTS OF *ROSMARINUS OFFICINALIS* ON VEGF AND IL-1A GENE EXPRESSIONS IN HACAT CELLS: UNRAVELING ITS MECHANISM OF ACTION IN WOUND HEALING AND HAIR LOSS

Erkin Pekmezci^{1*}, Songül Kılıç², Hakan Sevinç², Murat Türkoğlu².

¹Istanbul Medipol University, International Faculty of Medicine, Department of Dermatology, İstanbul, Turkey.

²Biota Laboratories, R&D Department, 34785 Sancaktepe, İstanbul, Turkey.

Abstract.

Background and Objective: *Rosmarinus officinalis* (*Ro*), popularly known as rosemary, is an aromatic perennial shrub originated from Mediterranean region and belongs to family Lamiaceae. Although the health promoting effects of *Ro* in dermatology, especially in wound healing and hair loss were documented to a certain extent, specific studies in this field are lacking. In this study it is investigated the molecular bases of these cutaneous effects, by determining gene expression levels of VEGF and IL-1 α , in a human keratinocyte cell line (HaCaT) treated with *Ro* extract.

Methods: After the preparation of *Ro* leaf extract and determination of non-cytotoxic concentration, HaCaT cells were treated with the extract. RNA isolations were carried out from both non-treated and treated cell groups. Gene expressions were determined by real time RT-qPCR analysis.

Results: Results were represented as Target/Control Fold Change, and the treatment ended up with 7.45 ± 1.87 and 0.80 ± 0.17 fold changes for VEGF and IL-1 α respectively. Results of gene expression analyses showed that, although the plant extract caused statistically significant upregulation of VEGF ($P = 0.0258$), downregulation of IL-1 α was not significant ($P = 0.2821$) compared to gene expressions of untreated control cells.

Conclusions: Although the modulation of IL-1 α found non-significant, the significant upregulation of VEGF may partially explain the mechanism of the beneficiary effects of *Ro* in wound healing and hair loss. Further *in-vitro* and *in-vivo* studies are needed to discover the molecular bases of the therapeutic effects of this plant, and to reveal its potential applications in various skin disorders.

Key words. *Rosmarinus officinalis*, VEGF, IL-1 α , wound healing, hair loss.

Introduction.

Rosmarinus officinalis (*Ro*) popularly known as rosemary, is an aromatic perennial shrub which belongs to family Lamiaceae. It is originated from Mediterranean region but it can be found all over the World [1]. *Ro* has therapeutic properties and has been used in the folk medicine, pharmaceutical, and cosmetic industries; mainly for its antioxidant and anti-inflammatory properties [2]. Several medicinal applications of *Ro* have been identified, such as treatment of disorders associated with the nervous, cardiovascular, gastrointestinal, hepatic, genitourinary, reproductive, respiratory and integumentary systems [3]. The molecules responsible from the biological activities of *Ro* are primarily phenolic compounds [4]. The main phytochemicals

present in the extracts of *Ro* are rosmarinic acid, caffeic acid, ursolic acid, betulinic acid, carnosic acid and carnosol in proportions that vary according to the vegetative stage and bioclimatic conditions [3-5]. However, specific and solitary compounds causing these effects have rarely been identified due to the synergistic actions of several metabolites present in the plant [2].

Rosemary has been shown to have beneficial roles in the treatment of various skin disorders such as, ultraviolet (UV) damage, skin cancer, aging, alopecia and wound healing as well as promoting the survival of skin flaps [2,6]. The photoprotective role of a water-soluble extract of *Ro* was identified by showing its ability to downregulate both the basal levels of matrix metalloproteinase-1 (MMP-1) and the transcription of UVA/UVB-induced MMP-1 in dermal fibroblasts [7]. A study exploring the healing potential of *Ro* performed on rats showed that wound healing in the 4% *Ro* cream group was faster than 2% *Ro* cream and control groups [8]. In a study performed on rats aiming to determine whether the use of systemic *Ro* extract can prevent flap necrosis and improve skin flap recovery, the mean percentage of viable surface area and mean vessel diameter were significantly greater in the groups which had given oral or parenteral *Ro*, compared to control group. It was concluded that in addition to its anti-inflammatory and anti-oxidant effects, *Ro* has vasodilatory effects that contribute to increased skin flap survival [9]. Alopecia areata is an autoimmune and inflammatory disease [10]. In a clinical study performed on patients with alopecia areata to assess the therapeutic potential of a mixture of essential oils including *Ro*, it was shown significant improvement against the control group [11]. Mice with testosterone-induced alopecia were treated topically with hydroalcoholic extracts of rosemary, and the results showed a significant increase in hair growth after the 16th day of treatment compared to control group [12]. In a clinical study which compared the efficacy of rosemary essential oil to 2% minoxidil solution for the treatment of androgenetic alopecia (AGA), a significant increase in hair count reported for both treatments with no difference between the two study groups, confirming the therapeutic effectiveness of *Ro* [6]. Given the inflammatory component, shown as perifollicular inflammatory infiltrate in the pathogenesis of AGA, anti-inflammatory activity of *Ro* is desirable in treatment of this disorder [13]. *Ro* was shown to have positive effects even in healthy follicles: 1% methanolic extract of *Ro* displayed a potent hair growth promoting activity on healthy mice, compared to standard 2% minoxidil hair lotion [14]. Rosemary acts by improving blood circulation and improving vascularity helping the regeneration of follicles with

a similar effect that is provided by minoxidil [15].

In the light of the previous studies, we investigated probable molecular bases in dermo-therapeutic effects of *Ro*. Therefore, we treated human keratinocyte cells (HaCaT) with *Ro* leaf extract, in order to determine the gene expression levels of vascular endothelial growth factor (VEGF) and interleukin-1 α (IL-1 α), which were previously reported as having positive and negative impacts respectively both in chronic cutaneous wounds and non-cicatricial hair loss.

Materials and Methods.

Plant material and preparation of the extract:

The plant, *Ro*, was collected locally, and identified using a stereomicroscope and a guidebook in Biota Laboratories, İstanbul-Turkey. Dried leaves of the plant were used for extraction. Forty grams of fine-cut leaves were extracted with 500 mL (70% Alcohol + 30% distilled water) mixture using a Soxhlet extractor at the boiling point of the solvent, completing two full cycles. The extract was filtered through a 0.45 μ m filter into a glass vial.

HaCaT cells and cell culture:

HaCaT cells are the spontaneously immortalized human keratinocyte cell line that has been used for studies of the epidermal homeostasis and its pathophysiology [16]. HaCaT cell line has a high differentiation potential in cell culture, based on the expression of various epidermal differentiation markers [17]. Additionally, keratinocytes can both synthesize and react (by receptors) to both VEGF [18] and IL-1 α [19].

HaCaT cells were maintained in New Brunswick incubator (Eppendorf) at 37°C in a humidified atmosphere at 5% carbon dioxide, in Dulbecco's Modified Eagle's Medium with high glucose, supplemented with 10% heat-inactivated fetal bovine serum and 100 U/ml gentamicin. All supplements and media were purchased commercially.

Cell proliferation assay and cytotoxicity analysis:

The cellular toxicity of *Ro* extract was investigated using 2,3-bis (2-methoxy-4-nitro-5-sulphophenyl) S-[(phenylamino) carbonyl]-2-tetrazolium hydroxide (XTT) cell proliferation assay (Roche Diagnostics) according to scientific principles [20] and manufacturer's instructions. HaCaT cells were seeded into 96-well plates at a density of 1×10^4 cells / well. Plant extract was diluted with culture medium and cells were subjected to various concentrations (100%, 3%, 1%, 0.5% and 0%) of the plant extract. After 72 h incubation period, cells were exposed to XTT and activator reagents for 4 h as described by the manufacturer. The viability of the cells was reflected in the activity of mitochondrial hydrogenases of the cells converting XTT into color-dense formazan compound. The optical density (OD) of soluble formazan compound was measured at 495 nm by microplate reader (Bio-Rad). The cell viability, which was compared to the control group as percent value, was calculated by using the formula below:

$$\text{Cell Viability (\%)} = [\text{Mean OD of test group} / \text{Mean OD of control group}] \times 100$$

The concentration of extract at the value which corresponds to nearest 80% cell proliferation ratio was chosen. Otherwise, to take this ratio higher makes the study to be performed with

a very low concentration, which may be inappropriate for the experiment. Cell proliferation (%) / Extract concentration (%) data are depicted in Figure 1.

RNA isolation and reverse transcription:

Total RNA was extracted from the cells treated with *Ro* extract solution and from untreated cells, using the TRI reagent (Sigma Aldrich) according to the scientific principles [21,22] and the manufacturer's instructions. RNA quantity and purity were determined spectrophotometrically using BioSpec-nano. Transcriptor First Strand Complementary DNA (cDNA) Synthesis Kit (Roche Diagnostics) was used for reverse transcription. cDNA synthesis was carried out using 500 ng total RNA, 2 μ M each final concentration of gene specific primers of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as reference gene, IL-1 α and VEGF as study materials (Integrated DNA Technologies), 10 U of Transcriptor Reverse Transcriptase, 20 U of Protector RNase Inhibitor, 1 mM each of dNTP mix, and Transcriptor Reverse Transcription Buffer (5X) according to the manufacturer's (Roche Diagnostics) instructions. Primer sequences (5'-3') are given in Table 1.

Gene expression analysis:

Real-time reverse transcription quantitative polymerase chain reaction (RT-qPCR) was carried out in Light Cycler 96 (Roche Diagnostics). The analysis was performed according to the

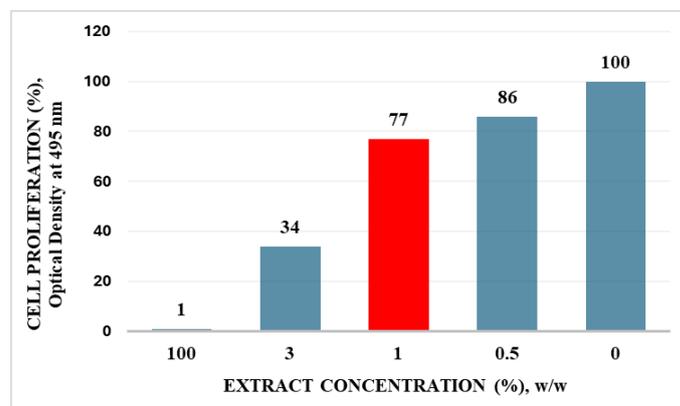


Figure 1. Cytotoxicity analysis result of *Rosmarinus officinalis* leaf extract. The red bar represents the extract concentration chosen for incubation.

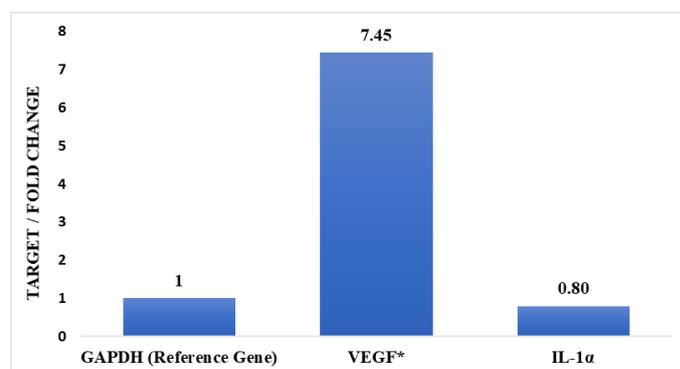


Figure 2. Gene expression levels and P values of VEGF and IL-1 α in *Rosmarinus officinalis* leaf extract treated cells, compared to untreated control cells. *P < 0.05.

Table 1. Primers (5'-3') of the genes studied.

Primers	Forward Primer	Reverse Primer
GADPH*	ATGGGTGTGAACCATGAGAA	GTGCTAAGCAGTTGGTGGTG
IL-1 α	ACCAGTGCTGCTGAAGGAGAT	GTGCCGTGAGTTTCCCAGAA
VEGF	ATGCGGATCAAACCTCACCA	CCACAGGGACGGGATTTCTTG

*GADPH is the reference gene.

scientific principles [21,22] and the manufacturer's instructions. Amplification of products was detected via Fast Start DNA Green Master Kit (Roche Diagnostics). Each 20 μ L reaction contained 10 μ L SYBR Green Master Mix (2X), 0.5 μ M of forward and reverse primers, 2.5 ng cDNA and appropriate amount of nuclease free water. All samples were run as triplicates in each run including a non-template control and four standards (1:1, 1:10, 1:100 and 1:1000). All reactions subjected to initial denaturation step at 95°C for 10 min and 45 cycle of 3-step amplification. Melting curve analysis was performed to confirm the specificity of the amplified products. The $\Delta\Delta$ Ct method of relative quantification was used to determine the fold change in expression. Fold change was calculated by the equation below:

$$\text{Fold change} = 2^{-\Delta\Delta C_t}$$

Statistical analysis:

All data are representatives of three repeats and expressed as mean and standard error of the means. Statistical evaluation was performed by t-test, using 'Graph Pad Prism 5' software and the results with $p < 0.05$ were accepted as significant.

Results.

Cell proliferation assay and cytotoxicity analysis:

Based on cell proliferation ratios of treated cells with respect to the control cells, cytotoxicity levels of the plant extract were determined. Higher concentrations were found to be cytotoxic for HaCaT cells. For the subsequent analysis, the possible highest concentration was determined as 1% and HaCaT cells were incubated with 1% concentration of plant extract (Figure 1).

Gene expression analysis:

Results were represented as Target/GAPDH Fold Change. Results of gene expression analyses via real time RT-qPCR showed that plant extract caused statistically significant upregulation of VEGF ($P = 0.0258$) and non-significant downregulation of IL-1 α ($P = 0.2821$) gene expressions, compared to untreated control cells. Plant extract treatment ended up with 7.45 ± 1.87 and 0.80 ± 0.17 fold changes for VEGF and IL-1 α respectively (Figure 2).

Discussion.

VEGF, is one of the most widely expressed pro-angiogenic mediators in the skin. It can be produced by diverse cell types, but mainly by keratinocytes [18]. VEGF released by follicular keratinocytes, boosts perifollicular angiogenesis which expands follicle size. Numerous disorders characterized by hair loss, including AGA, display changes in skin vasculature [23]. VEGF stimulates hair growth by easing the supply of nutrients to the hair follicle, which leads to an increase in the base of follicle diameter [24]. Although the mesenchyme-derived papilla regulates the epithelial follicle in various aspects, intrinsic

dermal-epidermal interactions are central to the development and growth of hair. Besides the inductive powers of dermal papilla cells, germinative epidermal cells (i.e. keratinocytes) of the lower follicle also have androgenic receptors and stimulate hair growth [25,26]. In a study performed to reveal VEGF expression in cultured human follicular cells, dermal papilla cells, fibrous sheath fibroblasts, dermal fibroblasts, and follicular and interfollicular keratinocytes; all expressed VEGF in various amounts at mRNA level [27]. Minoxidil was revealed to increase human hair follicle vascularization by upregulating the expression of VEGF in dermal papilla cells [28]. VEGF demonstrated a significant proliferation in perifollicular vascularization during the anagen phase of murine hair follicle [29]. Angiogenesis also has an essential role in wound repair. VEGF is a unique factor in the migration process of fibroblasts and has a pleiotropic role in tissue repair via neovascularization, reepithelialization, and regulation of extracellular matrix [30,31]. It is upregulated during the early days of healing, when capillary growth is maximal [32]. In chronic wounds as in diabetes, VEGF synthesis was found decreased, indicating that the lack of this factor can be related to insufficient wound healing. It is interesting that, keratinocytes which are the major sources for VEGF production in skin, also express VEGF receptors. These non-angiogenic targets for VEGF, causing keratinocyte growth and migration may supply new therapeutic opportunities in wound healing [18]. The keratinocytes also both synthesize IL-1 α , a proinflammatory polypeptide mediator, and react to it by relevant receptors [19]. IL-1 α is a direct growth inhibitory factor which has antiproliferative effects in hair follicles, and it is a salient agent in the pathogenesis of AGA, and alopecia areata [33,34]. Besides hair growth, IL-1 α has negative effects on wound healing also [35].

Considering the abovementioned reports, it can be suggested that, while VEGF exerts positive effects in hair loss and wound healing, IL-1 α has negative effects in both. Our results given as significant upregulation of VEGF with a fold change of 7.45 in HaCaT cells by *Ro* leaf extract, may partially explain the molecular bases of the beneficiary effects of this plant on skin disorders, which were mentioned in previous ethnobotanical and clinical reports. Of course, natural products are not pharmaceuticals and the complexity of chemical composition of extracts suggests involvement of various mechanisms leading to difficulties in identifying just one pathway of molecular action [36,37]. It is highly plausible that the compounds of an extract act in synergistic ways [36]. In this preliminary study which was aimed to find whether *Ro* could modulate VEGF and IL-1 α at mRNA level, we did not perform phytochemical analyses, both because it would not have any consequence on the outcome of the experiment, and it would not impact our way of interpretation of the results. Although this may seem

as a limitation, the important point here is to establish a solid connection between the chemical features of the plant and the results of the study. Indeed, to establish a cause-effect relationship in this manner, will be quite complicated and will need additional studies for each revealed constituent separately, and then collectively to uncover probable synergistic effects. Lack of protein level validations and lack of comparisons with positive controls may be considered as the other limitations of this study. Through additional *in-vitro* and *in-vivo* studies, and by way of understanding its constituents and mechanisms of therapeutic effects further, *Ro* may be utilized in producing supportive medicinal products against both non-cicatricial hair loss and chronic cutaneous wounds.

Conclusion.

The significant upregulation of VEGF gene expression revealed in HaCaT cells by *Ro* leaf extract provide preliminary evidence that *Ro* can modulate gene expressions in keratinocytes. This result may partially explain the molecular bases of the beneficiary effects of this plant in hair loss and wound healing. Further *in-vitro* and *in-vivo* studies are needed to confirm the mechanisms of action extensively and to find out potential applications of *Ro* in various skin disorders.

Conflict of interest statement.

The authors declare no conflicts of interest.

Ethics statement.

This is an *in-vitro* study and the authors have nothing to report.

REFERENCES

1. de Oliveira JR, Camargo SEA, de Oliveira LD. Rosmarinus officinalis L. (rosemary) as therapeutic and prophylactic agent. J Biomed Sci. 2019;26:5.
2. de Macedo LM, Santos ÉMD, Militão L, et al. Rosemary (Rosmarinus officinalis L., syn Salvia rosmarinus Spenn.) and its topical applications: A review. Plants (Basel). 2020;9:651.
3. Begum A, Sandhya S, Shaffath Ali S, et al. An in-depth review on the medicinal flora Rosmarinus officinalis (Lamiaceae). Acta Sci Pol Technol Aliment. 2013;12:61-73.
4. Andrade JM, Faustino C, Garcia C, et al. Rosmarinus officinalis L.: an update review of its phytochemistry and biological activity. Future Sci OA. 2018;4:FSO283.
5. Ulbricht C, Abrams TR, Brigham A, et al. An evidence-based systematic review of rosemary (Rosmarinus officinalis) by the Natural Standard Research Collaboration. J Diet Suppl. 2010;7:351-413.
6. Li Pomi F, Papa V, Borgia F, et al. Rosmarinus officinalis and skin: Antioxidant activity and possible therapeutical role in cutaneous diseases. Antioxidants (Basel). 2023;12:680.
7. Martin R, Pierrard C, Lejeune F, et al. Photoprotective effect of a water-soluble extract of Rosmarinus officinalis L. against UV-induced matrix metalloproteinase-1 in human dermal fibroblasts and reconstructed skin. Eur J Dermatol. 2008;18:128-135.
8. Nejati H, Farahpour M, Nagadehi MN. Topical Rosemary officinalis essential oil improves wound healing against disseminated Candida albicans infection in rat model. Comp Clin Pathol. 2015;24:1377-1383.
9. İnce B, Bilgen F, Gündeşlioğlu AÖ, et al. Use of systemic Rosmarinus officinalis to enhance the survival of random-pattern skin flaps. Balkan Med J. 2016;33:645-651.
10. Ito T, Kageyama R, Nakazawa S, et al. Understanding the significance of cytokines and chemokines in the pathogenesis of alopecia areata. Exp Dermatol. 2020;29:726-732.
11. Hay IC, Jamieson M, Ormerod AD. Randomized trial of aromatherapy. Successful treatment for alopecia areata. Arch Dermatol. 1998;134:1349-1352.
12. Murata K, Noguchi K, Kondo M, et al. Promotion of hair growth by Rosmarinus officinalis leaf extract. Phytother Res. 2013;27:212-217.
13. Bin Rubaian NF, Alzamami HFA, Amir BA. An overview of commonly used natural alternatives for the treatment of androgenetic alopecia, with special emphasis on rosemary oil. Clin Cosmet Investig Dermatol. 2024;17:2495-2503.
14. Begum A, S S, N AK, Ali SS. Evaluation of herbal hair lotion loaded with rosemary for possible hair growth in C57BL/6 mice. Adv Biomed Res. 2023;12:60.
15. Dhariwala MY, Ravikumar P. An overview of herbal alternatives in androgenetic alopecia. J Cosmet Dermatol. 2019;18:966-975.
16. Seo MD, Kang TJ, Lee CH, et al. HaCaT keratinocytes and primary epidermal keratinocytes have different transcriptional profiles of cornified envelope associated genes to T helper cell cytokines. Biomol Ther (Seoul). 2012;20:171-176.
17. Wilson VG. Growth and differentiation of HaCaT keratinocytes. Methods Mol Biol. 2014;1195:33-41.
18. Ong HT, Dilley RJ. Novel non-angiogenic role for mesenchymal stem cell-derived vascular endothelial growth factor on keratinocytes during wound healing. Cytokine Growth Factor Rev. 2018;44:69-79.
19. Growes RW, Sherman L, Mizutani H, et al. Detection of interleukin-1 receptors in human epidermis. Am J Pathol. 1994;145:1048-1056.
20. Goodwin CJ, Holt SJ, Downes S, et al. Microculture tetrazolium assays: A comparison between two new tetrazolium salts, XTT and MTS. J Immunol Methods. 1995;179:95-103.
21. Van Peer G, Mestdagh P, Vandesompele J. Accurate RT-qPCR gene expression analysis on cell culture lysates. Sci Rep. 2012;2:222.
22. Jensen EC. Real-time reverse transcription polymerase chain reaction to measure mRNA: Use, limitations, and presentation of results. Anat Rec (Hoboken). 2012;295:1-3.
23. Bassino E, Gasparri F, Giannini V, et al. Paracrine crosstalk between human hair follicle dermal papilla cells and microvascular endothelial cells. Exp Dermatol. 2015;24:388-390.
24. Herman A, Herman AP. Mechanism of action of herbs and their active constituents used in hair loss treatment. Fitoterapia. 2016;114:18-25.
25. Jahoda CA, Reynolds AJ. Dermal epidermal interactions. Adult follicle derived cell populations and hair growth. Dermatol Clin. 1996;14:573-583.
26. Itami S, Inui S. Role of androgen in mesenchymal epithelial interactions in human hair follicle. J Invest Dermatol Symp Proc. 2005;10:209-211.

27. Kozłowska U, Blume-Peytavi U, Kodelja V, et al. Expression of vascular endothelial growth factor (VEGF) in various compartments of the human hair follicle. *Arch Dermatol Res.* 1998;290:661-668.
28. Lachgar S, Charveron M, Gall Y, et al. Minoxidil upregulates the expression of vascular endothelial growth factor in human hair dermal papilla cells. *Br J Dermatol.* 1998;138:407-411.
29. Yano K, Brown LF, Detmar M, Control of hair growth and follicle size by VEGF-mediated angiogenesis. *J Clin Invest.* 2001;107:409-417.
30. Keswani SG, Balaji S, Le LD, et al. Role of salivary vascular endothelial growth factor (VEGF) in palatal mucosal wound healing. *Wound Repair Regen.* 2013;21:554-562.
31. Shams F, Moravvej H, Hosseinzadeh S, et al. Overexpression of VEGF in dermal fibroblast cells accelerates the angiogenesis and wound healing function: in vitro and in vivo studies. *Sci Rep.* 2022;12:18529.
32. Bao P, Kodra A, Tomic-Canic M, et al. The role of vascular endothelial growth factor in wound healing. *J Surg Res.* 2009;153:347-358.
33. Mahe YF, Buan B, Billoni N, et al. Pro-inflammatory cytokine cascade in human plucked hair. *Skin Pharmacol.* 1996;9:366-375.
34. Philpott MP, Sanders DA, Bowen J, et al. Effects of interleukins, colony stimulating factor and tumour necrosis factor on human hair follicle growth in vitro: a possible role for interleukin-1 and tumour necrosis factor-alpha in alopecia areata. *Br J Dermatol.* 1996;135:942-948.
35. Lukens JR, Kanneganti TD. SHP-1 and IL-1 α conspire to provoke neutrophilic dermatoses. *Rare Dis.* 2014;2:e27742.
36. Aleksic V, Knezevic P. Antimicrobial and antioxidative activity of extracts and essential oils of *Myrtus communis* L. *Microbiol Res.* 2014;169:240-254.
37. Ajao AA-n, Sadgrove NJ. Cosmetopoeia of African plants in hair treatment and care: Topical nutrition and the antidiabetic connection? *Diversity.* 2024;16:96.