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Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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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.

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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.

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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.

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GC–MS PROFILING OF THE LIPOPHILIC FRACTION AND ACUTE SAFETY ASSESSMENT OF THE AQUEOUS EXTRACT OF *SCUTELLARIA SUBCAESPITOSA*

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Abstract.

Objectives: This study aimed to characterize the lipophilic (petroleum ether) fraction of *Scutellaria subcaespitosa* using gas chromatography–mass spectrometry (GC–MS) and to evaluate the acute toxicity and sub-chronic dermal and mucosal tolerability of an aqueous infusion prepared from the aerial parts of the plant in experimental animals.

Materials and Methods: Lipophilic constituents were analysed by GC–MS following ultrasonic extraction with petroleum ether. Acute toxicity of the aqueous preparation (10%, w/v) was evaluated in albino mice and albino rats after oral (intra-gastric) and intraperitoneal administration. In rats, intra-gastric doses ranged from 5 to 5000 mg/kg body weight, with a 15-day observation period. Clinical signs, behaviour, body weight, and mortality were recorded. Sub-chronic dermal and mucosal exposure to the aqueous infusion (1:10, w/v) was assessed over a three-month period in rats and rabbits.

Results: GC–MS analysis of the petroleum ether extract revealed 43 chromatographic peaks in the total ion chromatogram. Two peaks corresponded to phthalate esters (dibutyl phthalate and diisooctyl phthalate), which were considered probable laboratory contaminants and therefore excluded from compositional interpretation; 41 plant-derived components are presented in Table 1. The most abundant constituents included nonacosane and tetriacontane, along with eugenol, palmitic acid, phytol, camphor, and γ -sitosterol. Acute toxicity testing demonstrated no mortality in rats following intra-gastric administration at doses up to 5000 mg/kg and no clinically significant signs of intoxication. In mice, mortality occurred only at the highest intraperitoneal dose tested. Sub-chronic dermal and mucosal exposure over three months produced no observable local adverse reactions.

Conclusion: The aqueous preparation of *S. subcaespitosa* demonstrated no observable acute toxicity in rats within the tested dose range and did not produce adverse local effects under sub-chronic exposure conditions. These safety findings apply exclusively to the aqueous preparation. The toxicological profile of the lipophilic petroleum ether fraction requires independent evaluation before conclusions regarding the safety of fat-soluble constituents can be drawn.

Key words. Acute toxicity, aqueous infusion, fat-soluble compounds, GC–MS analysis, *Scutellaria subcaespitosa*,

medicinal plants, sub-chronic dermal and mucosal exposure assessment.

Introduction.

The arsenal of folk medicine is still the main source of the search for new medicinal plants. Therefore, it is very important to study the plants used in indigenous medicine for the treatment of various diseases. For this purpose, it is relevant to study *Scutellaria subcaespitosa* Pavl., one of the promising medicinal plants which have been widely used in folk medicine and grown in the southern regions of Kazakhstan.

There are about 15 species of *Scutellaria* in Turkestan region of Kazakhstan (Table 1) [1,2].

1. *Scutellaria galericulata* L.
2. *Scutellaria ramosissima* M.Pop.
3. *Scutellaria flabellulata* Juz.
4. *Scutellaria microdasys* Juz.
5. *Scutellaria androssovii* Juz.
6. *Scutellaria mesostegia* Juz.
7. *Scutellaria cordifrons* Juz.
8. *Scutellaria adsurgens* M.Pop.
9. *Scutellaria talassica* Juz.
10. *Scutellaria linczewskii* Juz.
11. *Scutellaria immaculata* Nevski ex Juz.
12. *Scutellaria karatavica* Juz.
13. *Scutellaria subcaespitosa* Pavl.
14. *Scutellaria kurssanovii* Pavl.
15. *Scutellaria haematochlora* Juz.

The chemical composition of representatives of the *Scutellaria* L. family has been studied to varying degrees. The composition of biologically active compounds of 5 species was studied in detail (*S.baicalensis*, *S.galericulata*, *S.scordiifolia*, *S.creticola*, *S.orientalis*). Phenolic compounds, steroids, iridoid glycosides were found in all studied species. The chemical composition of *Scutellaria* L. related plants is diverse and represented by phenolic acids, iridoids, di- and triterpene compounds, cardenolides, coumarins, tannins and flavonoids [3].

According to the literature review, the flavonoid composition was studied to a certain extent from 10 representatives of the *Scutellaria* genus growing in the territory of the Russian Federation. The highest number of components was determined in 5 species of *Scutellaria* (*S.baicalensis*, *S.galericulata*, *S.scordiifolia*, *S.creticola*, *S.orientalis*). In *S.albida* L.,

Table 1. GC–MS-identified lipophilic constituents of the petroleum ether extract of the aerial parts of *Scutellaria subcaespitosa*.

Peak No.	Retention Time (min)	Compound Name	Match Quality (%)	Relative Area (%)
	8.88	Eucalyptol (1,8-cineole)	70	0.62
	13.74	Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-, (1S)-	94	2.97
	20.19	Eugenol	92	6.69
	22.22	Nonadecane	66	0.27
	24.56	Nonadecane	75	0.61
	24.85	Hexadecyl trichloroacetate	68	0.46
	25.03	Caryophyllene oxide	84	2.71
	25.64	7-epi-Sesquisabinene hydrate	73	1.31
	25.83	Isoaromadendrene epoxide	66	0.71
	26.17	5,6,7,7a-Tetrahydro-4,4,7a-trimethylbenzofuranone (R)	85	2.11
	26.28	Phosphonofluoridic acid, isopropyl heptyl ester	60	0.48
	26.78	Octadecane	72	0.58
	27.75	Cis-1,4a,7-tetramethyl-octahydrobenzocyclohepten-7-ol	63	0.41
	28.78	5 β ,7 β H,10 α -Eudesmen-1-en-4-ol	79	4.15
	28.90	Nonadecane	82	0.70
	29.23	6,10,14-Trimethyl-2-pentadecanone	91	3.08
	29.73	Acetic acid derivative (oxepane ester)	67	1.36
	29.90	Corymbolone	71	1.29
	30.92	Eicosane	81	0.74
	31.01	Heptyl benzoate	76	0.72
	31.34	trans-Longipinocarveol	71	0.86
	32.14	Phthalic acid, hept-4-yl isobutyl ester	88	1.51
	32.28	Ethyl hexadecanoate	68	3.58
	32.41	n-Hexadecanoic acid (palmitic acid)	90	6.26
	34.55	Phytol	77	1.35
	35.83	Octadecyl hexadecanoate	60	0.68
	36.00	Octadecanoic acid (stearic acid)	70	1.74
	36.41	9,12,15-Octadecatrienoic acid (α -linolenic acid)	61	0.53
	36.51	Heneicosane	87	1.67
	36.57	5-Dodecyldihydro-2(3H)-furanone	70	0.40
	38.21	Tetracosane	80	0.79
	39.87	Hexacosane	90	3.46
	40.00	4,8,12,16-Tetramethylheptadecan-4-olide	71	0.48
	43.00	Octacosane	92	4.89
	44.29	1-Tetracosanol	84	1.81
	45.98	Nonacosane	92	20.40
	46.37	17-Pentatriacontene	66	0.38
	47.27	Tetratetracontane	79	1.22
	48.67	Tetriacontane	91	11.49
	54.25	Stigmasterol	64	0.81
	55.26	γ -Sitosterol	73	0.80

S.polyodon Juz., *S.altissima*, *S.granulosa*, *S.oreophila* Grossh, few components (from two to four flavone aglycones and one to four glycoside derivatives) were identified. Analysis of published data shows that species of the *Scutellaria* genus contain a complex of flavonoid aglycones and glycosides in above-ground and below-ground organs. The most common are flavone aglycones: chrysin (13), baicalein (1), scutellarein (4), apigenin (5), luteolin (6), wogonin (7), oroxylin A (8), dynatin (9) (table. 2). Identified aglycones in plants are mainly in the form of 7-O glycosides (7-O-glucuronides and 7-O-glucosides) [3-6].

The phenolic compounds of skullcap are flavones, flavanones, flavonols, phenylpropanoids, chalcones, isoflavones, biflavones, and lignoflavonoids. The biological activity of the phenolic

compounds of *Scutellaria* has attracted constant interest in this research [7]. In the world literature, a large amount of material has been collected on the isolation, identification, structure and biological activity of phenolic compounds of different species of *Scutellaria* L. V.M. Malikov and M. P. According to Yuldashev, phenolic compounds of 65 species of *Scutellaria* L. have been studied, and more than two hundred compounds have been isolated and identified from them [3].

Flavones take the leading place among phenols in terms of distribution in *Scutellaria* L., among which baicalin, chrysin, wogonin, scutellarein, oroxylin, apigenin, luteolin are often found [7,8].

Baikal skullcap is a widely known medicinal plant, which contains valuable biologically active compounds - flavonoids,

Table 2. Acute toxicity of the aqueous preparation (10% suspension; 1:10, w/v) of crushed aerial parts of *Scutellaria subcaespitosa* in mice and rats after oral and intraperitoneal administration.

A series of experiments and doses in ml/kg		number of animals in series	survived	death	
				Quantity	%
White mice					
I. Orally in a dose	5	10	10	0	
	10	10	10	0	
	15	10	10	0	
	20	10	10	0	
	30	10	10	0	
II. Intraperitoneally	5	10	10	0	
	10	10	10	0	
	15	10	10	0	
	20	10	10	0	
	25	10	9	1	10
White rats					
III. Orally	5,0	10	10	0	
	10,0	10	10	0	
	50,0	10	10	0	
	100,0	10	10	0	
	250,0	10	10	0	
	500,0	10	10	0	
	1000,0	10	10	0	
	2000,0	10	10	0	
	3000,0	10	10	0	
	4000,0	10	10	0	
IV. Intraperitoneally	10	10	10	0	
	15	10	10	0	
	20	10	10	0	

Note: In this table, dose levels are presented as administered volumes (mL/kg) for the aqueous suspension. Rats were evaluated in oral (intragastric gavage) and intraperitoneal series; mice were evaluated in oral and intraperitoneal series. Animals were monitored for clinical signs and mortality and followed for up to 15 days after administration.

Table 3. Comparative assessment of body weight changes in albino rats before dosing and on day 15 after oral administration of the aqueous preparation (10% suspension) of crushed aerial parts of *Scutellaria subcaespitosa* ($X \pm m$).

Doses tested, mg/kg body weight	Animal weight before drug administration		Weight of animals on the 15th day of observation		Weight gain			
	male	female	male	female	male		female	
	g	g	g	g	g	%	g	%
Control	210.0 ± 4.5	212.0 ± 4.9	249.0 ± 5.3	246 ± 6.7	39	19	34	16
5000	207.0 ± 2.8	218.0 ± 5.8	245.0 ± 5.5	252 ± 7.1	38	18	34	16
1000	215.0 ± 4.7	205.0 ± 6.2	247.0 ± 6.2	241 ± 5.3	32	15	36	18

Note: Body-weight dynamics are presented for the control group and two representative dose groups (1000 and 5000 mg/kg BW) selected to reflect a mid-range and the highest tested oral dose. Intermediate dose groups demonstrated comparable physiological weight gain without clinically meaningful deviations from controls; therefore, for clarity and compact presentation, detailed weight data are summarized here for the representative groups.

the most important of which are scutellarein and baicalin. The roots contain waggonin, pyrocatechins, minerals, resins, tannins, starch, and fatty essential oils are found in the glands and glandular fibers of the stems. Chrysin, apigenin, scutellarein, isoscutellarein and luteolin derivatives were found in the aerial parts of *S.baicalensis* [9]. The history of *S.baicalensis* flavonoid research dates back to 1923, when Shibata and his co-authors first isolated and characterized baicalin from the roots of this plant [10]. Scientific information analysis shows

that 125 phenolic compounds have been found in this form to date. Flavones in *S.baicalensis*, like the entire genus and family Lamiaceae, are distinguished by the presence of 2-methylated and glycosidated derivatives, which belong to the group of rare flavone derivatives. According to O. M. Andersen and K. R. Markham, these compounds are chemotaxonomic characters for those at the level of *Scutellaria* L. and Lamiaceae. The presence of 2,6-hydroxylated, methoxylated and glycosidated flavones, as well as rare 3- and 5-substituted compounds in *S.baicalensis* should be highlighted [11].

Table 4. Sub-chronic dermal and mucosal exposure assessment of the aqueous infusion of *Scutellaria subcaespitosa*, growing in Kazakhstan, in an experiment on albino rats and rabbits.

The condition of the skin and mucous membranes after 3 months of use	The degree of severity of indicators	
	rats (80)	rabbits (30)
Application on the skin for 3 months		
Color of the skin	normal	normal
Turgor	unchanged	unchanged
Hyperemia	not observed	not observed
Edema	not observed	not observed
Abrasions	not observed	not observed
Blisters	absent	absent
Erythema	not observed	not observed
The presence of bubbles	absent	absent
Application to the conjunctiva of the eyes for 3 months		
Pupil condition	unchanged	unchanged
Conjunctival hyperemia	absent	absent
Edema of the eyelids	absent	absent
Lacrimation	absent	absent
Purulent discharge	absent	absent
Ptosis	absent	absent
Application in the nasal cavity for 3 months		
Runny nose	absent	absent
Sneezing	absent	absent
Edema	absent	absent
Purulent discharge	absent	absent

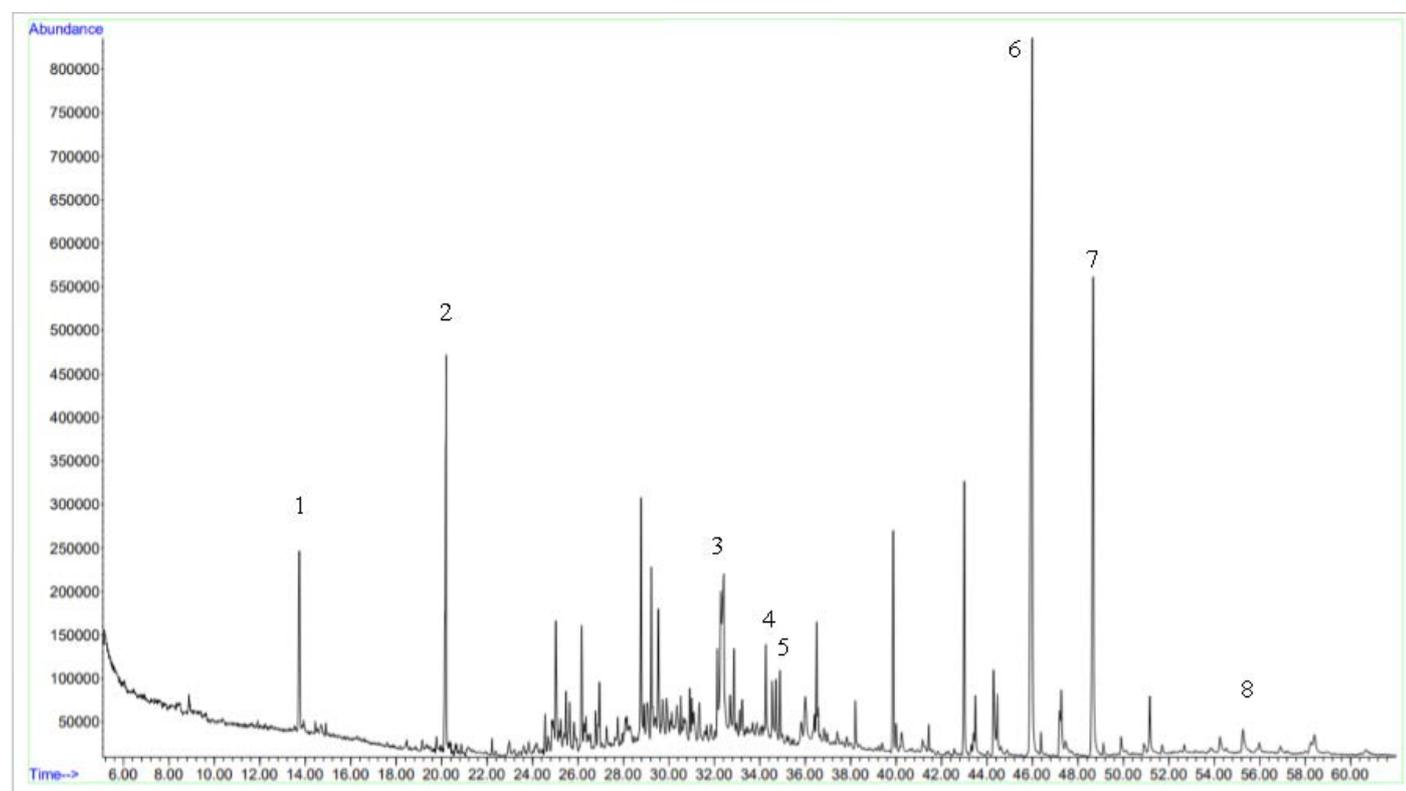


Figure 1. Chromatogram of petroleum ether extract of *Scutellaria subcaespitosa*. Conventional signs: 1-eugenol, 2-camphor, 3-n-hexadecanoic acid, 4- γ -sitosterol, 5-nonacosane, 6-phytol, 7-tetratriacontane.

Based on the analysis of data on the qualitative composition of flavonoids, the flora of Kazakhstan was not fully studied, so the data of the flora of Russia were taken into account. During the analysis of 10 studied species of *Scutellaria* genus of Russian flora, it was found that flavone derivatives were mainly found in many representatives. In addition, the presence of baicalein is observed for all these species. This component, as well as chrysin, scutellarein and their glycoside derivatives, are flavonoid compounds of many representatives of the genus *Scutellaria* [12].

The aerial parts of *Scutellaria subcaespitosa* Pavl. have been pharmacognostically analysed in previous works of authors. Due to the lack of knowledge about safety and therapeutic properties of *Scutellaria subcaespitosa* grown in Turkestan region it is important to chemically profile the extract of the plant by gas chromatography-mass spectrometric (GC-MS) analytic method. Plant extracts exhibit chemical profiles that are profoundly influenced by the polarity of the solvent used. Extraction with petroleum ether preferentially isolates non-polar, lipophilic constituents such as terpenoids, alkanes, sterols, and fatty acids. These compounds, which may be poorly represented in aqueous extracts, are essential for a comprehensive phytochemical profile. Conversely, an aqueous preparation (infusion or suspension) mirrors the traditional mode of administration in folk medicine. Therefore, this preparation is the most relevant for a preliminary safety assessment, as it reflects a realistic scenario of human exposure.

To bridge the gap between comprehensive chemical characterization and practical toxicological relevance, the present study integrates two complementary approaches: (i) GC-MS profiling of the petroleum ether fraction to fully characterize the lipophilic constituents, and (ii) toxicological evaluation of an aqueous preparation to assess the safety profile of the extract most likely used in traditional practice. It is important to note that safety conclusions drawn from aqueous testing cannot be directly extrapolated to the petroleum ether fraction without separate, targeted evaluation.

Therefore, the aim of this study was twofold: to characterize the lipophilic constituents of *S. subcaespitosa* via GC-MS profiling of a petroleum ether extract, and to assess its safety profile by performing an acute toxicity study and a dermal irritation test using an aqueous preparation of the crushed aerial plant materials.

Materials and Methods.

Plant material:

Aerial parts of *S. subcaespitosa* were collected in June 2021 (flowering period) near Kaskasu settlement, Turkestan region, Kazakhstan.

Determination of fat-soluble compounds (petroleum ether extract) and GC-MS analysis:

Five grams of crushed plant material were placed in a 100-mL flask and extracted with 40 mL petroleum ether (1:8, w/v) in an ultrasonic bath (KQ5200B, 40 kHz) for 3 × 1 h. The extract was filtered through paper filter and concentrated using an EYELA N-1300 rotary evaporator at 35°C. The yield of dry extract was 0.089 g from 5 g of raw material.

GC-MS analysis was performed using an Agilent 7890A GC system coupled to a 5975C mass selective detector. One microliter of sample was injected at an inlet temperature of 250°C in splitless mode. Separation was carried out on a DB-35MS capillary column (30 m × 0.25 mm i.d., 0.25 µm film thickness) with helium as the carrier gas at 1 mL/min. The oven temperature program was: 40°C (0 min), ramp 5°C/min to 150°C (3 min), then ramp 5°C/min to 280°C (1 min). Mass spectra were acquired in SCAN mode (m/z 34–750). Data acquisition and processing were performed using Agilent MSD ChemStation (version 1701EA). Compound identification was performed by comparison with Wiley (7th edition) and NIST'02 mass spectral libraries.

Acute toxicity study:

The general toxic effects of the aqueous preparation of crushed aerial plant material were assessed in accordance with the “Methodological recommendations for the study of the general toxic effect of pharmacological agents” [7] and the “Guidelines for the experimental (preclinical) study of new pharmacological substances” [13]. All procedures involving animals were carried out in compliance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes [14].

The acute toxicity of an aqueous preparation of *Scutellaria subcaespitosa* was evaluated using a freshly prepared aqueous infusion/suspension (1:10, w/v) obtained from the crushed aerial parts. The test substance consisted of dry crushed powder derived from the aerial part of the plant. Immediately prior to administration, the powder was diluted with distilled water to obtain a 10% (w/v) aqueous suspension. Because the test material was administered as a suspension, dose levels can be expressed either as an equivalent mass dose (mg/kg BW) or as an administered volume (mL/kg) depending on the reporting format; in the present manuscript, Table 2 summarizes the dosing scheme as administered volumes (mL/kg), whereas the descriptive text provides the corresponding planned dose levels (mg/kg BW) used for rat gavage dosing. The study was conducted using 60 white albino mice (body weight 18–20 g) and 220 outbred white albino rats (males and females; body weight 160–200 g). Rats were maintained under standard vivarium conditions and quarantined for 15 days prior to the experiment. At the beginning of the study, the mean rat body weight ranged from 195.0 ± 5.3 g to 210.0 ± 3.7 g.

Toxicological assessment in rats:

In rats, the aqueous suspension was administered by intragastric gavage (oral route) at planned dose levels of 5, 10, 50, 100, 250, 500, 1000, 2000, 3000, 4000, and 5000 mg/kg BW. Control animals received an equivalent volume of distilled water. To achieve administration of high total doses while maintaining safe single-gavage volumes, the preparation was administered either as a single dose or as fractionated doses at 3–5 h intervals during the first 6–8 h. According to preclinical study guidance, the maximum recommended volume for a single intragastric administration in rats weighing 200–240 g is 4–5 mL [15].

In addition to the oral (intragastric) series, a separate set of rat experiments was performed using the intraperitoneal (i.p.) route, in accordance with the experimental design summarized

in Table 2. The i.p. groups were monitored under the same observation schedule and endpoints as the oral groups. Animals were observed for 15 days following administration. During the observation period, the following parameters were recorded systematically: general clinical condition; behavioral responses (with particular attention to the early post-administration period); locomotor activity; food and water intake; and mortality. Animals were also examined for visible pathological changes throughout the observation period.

Toxicological assessment in mice:

In mice, acute toxicity was evaluated using both oral and intraperitoneal administration routes in accordance with the dosing scheme presented in Table 2. Briefly, mice received the aqueous preparation orally at the planned dosing/volume levels (mL/kg) shown for the oral series, and separately received intraperitoneal administration at the planned dosing/volume levels shown for the i.p. series. Following administration, animals were monitored for immediate clinical signs (particularly within the first hours after dosing), for mortality during the acute phase, and then continuously during the remainder of the observation period in accordance with the study protocol.

Sub-chronic dermal and mucosal exposure study (3 months):

Sub-chronic dermal and mucosal exposure of the aqueous infusion (1:10, w/v) was evaluated in 80 albino rats and 30 rabbits. A freshly prepared infusion was filtered two to three times through filter paper and applied to shaved/cleaned skin areas and to the conjunctival and nasal mucosa under repeated-exposure conditions for 3 months. After completion of the exposure period, animals were examined for local adverse reactions including erythema, edema, abrasions, vesicle formation, conjunctival hyperemia, lacrimation, eyelid swelling, nasal discharge, and other pathological changes.

Results and Discussion.

Species of the genus *Scutellaria* are known to contain a wide spectrum of phytochemical constituents, many of which possess significant biological activity and diverse pharmacological properties [16]. Numerous secondary metabolites isolated from representatives of this genus have demonstrated the ability to induce apoptosis in tumor cells, inhibit influenza virus replication, and exert anti-inflammatory effects [17-20]. The investigation of fat-soluble components of plant raw materials represents an important physicochemical characteristic for the evaluation of medicinal plant quality and potential pharmacological relevance. Since traditional medicine remains a major source in the search for new therapeutic agents, the systematic study of medicinal plants used in folk practice is of considerable importance. One of the current priorities of the domestic pharmaceutical industry is to increase the utilization of herbal medicinal resources native to the Republic of Kazakhstan, thereby ensuring the availability of effective, safe, and affordable phytotherapeutic agents. In this context, the study of *Scutellaria subcaespitosa* Pavl., growing in the southern regions of Kazakhstan, is of particular scientific and practical interest.

Gas chromatography–mass spectrometry (GC–MS) analysis of the petroleum ether extract revealed 43 chromatographic peaks in the total ion chromatogram (Figure 1). Two peaks matched

phthalate esters (dibutyl phthalate and diisooctyl phthalate), which are frequently reported as laboratory contaminants originating from plasticware and solvents; therefore, these signals were excluded from phytochemical interpretation. After this exclusion, 41 plant-derived components are presented in Table 1. The predominant constituents by relative peak area were nonacosane (20.40%) and tetriacontane (11.49%), followed by eugenol (6.69%), n-hexadecanoic acid (palmitic acid; 6.26%), octacosane (4.89%), 5 β ,7 β H,10 α -eudesmen-1-en-4-ol (4.15%), ethyl hexadecanoate (3.58%), hexacosane (3.46%), and 6,10,14-trimethyl-2-pentadecanone (3.08%). The remaining compounds occurred at lower relative abundances and included terpenoid-derived constituents, fatty acid derivatives, sterols, and long-chain hydrocarbons typical of non-polar plant fractions.

Acute toxicity testing demonstrated that administration of the aqueous preparation (10% suspension) of crushed aerial parts of *Scutellaria subcaespitosa* did not produce significant mortality or deterioration of general condition in experimental animals at the tested dose and volume levels (Table 2).

In albino rats, intragastric (oral gavage) administration at dose levels ranging from 5.0 to 5000 mg/kg body weight was not associated with mortality or clinically significant signs of intoxication during the 15-day observation period. Animals remained active, maintained normal feeding and drinking behavior, and demonstrated appropriate responses to external stimuli. A mild and transient increase in locomotor activity was occasionally observed shortly after administration; however, this effect resolved within the first hour and was not followed by delayed adverse manifestations. Intraperitoneal administration in rats, performed according to the experimental scheme summarized in Table 2, likewise did not result in mortality or pronounced systemic toxic effects. In albino mice, oral administration of the aqueous preparation did not result in mortality at the tested dose levels. Following intraperitoneal administration, mortality was observed only at the highest tested dose level, where 1 of 10 animals (10%) died, whereas lower dose levels were not associated with lethal outcomes. No persistent clinical signs of systemic toxicity were observed in surviving animals.

Body weight measurements in rats were performed prior to administration and on day 15 of observation. Both experimental and control groups demonstrated a slight physiological increase in body weight without pronounced intergroup differences (Table 3). For clarity and representative comparison, detailed analysis is presented for the medium (1000 mg/kg) and high (5000 mg/kg) oral dose groups, as intermediate dose groups exhibited comparable trends without clinically meaningful deviations. Body weight gain ranged from 3 to 7 g (approximately 2.0–4.0%), indicating the absence of detectable systemic toxic effects. Since no mortality occurred in rats within the tested intragastric dose range, the median lethal dose (LD₅₀) could not be determined under the conditions of this study. Based on these findings, the aqueous preparation may be considered to exhibit low acute toxicity within the investigated dose range.

Sub-chronic dermal and mucosal exposure of the aqueous infusion (1:10, w/v) over a three-month period did not produce

observable adverse local reactions (Table 4). No erythema, edema, abrasions, vesicle formation, peeling, or other pathological alterations of the skin were detected. Similarly, repeated application to the conjunctival and nasal mucosa of experimental animals did not result in hyperemia, lacrimation, edema, discharge, or other signs of irritation.

The obtained results therefore indicate the absence of observable acute and sub chronic toxicity for the aqueous preparation of this species. It should be emphasized that the toxicological evaluation was performed exclusively using the aqueous extract, whereas chemical profiling was conducted on the lipophilic petroleum ether fraction. Consequently, the safety conclusions derived in this study apply only to the aqueous preparation and cannot be extrapolated to the lipophilic extract without separate targeted toxicological investigation.

Study limitations

The absence of detailed in vitro and in vivo pharmacological studies is the limitation of our study.

Conclusion.

The present study demonstrated no observable acute toxicity or adverse local effects of the aqueous infusion of crushed aerial parts of *Scutellaria subcaespitosa* under the experimental conditions used. These findings suggest that the tested preparation may be relatively safe at doses up to 5000 mg/kg body weight in experimental animals. Further studies, including the isolation and characterization of active phytoconstituents and evaluation of pharmacological activity (e.g., antioxidant and anti-inflammatory assays), are required to substantiate its potential therapeutic applications. The study does not claim safety of the lipophilic extract and further dedicated toxicological investigation is required.

Ethics Committee Approval.

The Medical Ethics Committee of State Educational Institution "Tajik State Medical University named after Abuali Ibni Sino".

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Author contributions.

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Conflict of interest statement.

The authors declared no conflict of interest.

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Аннотация.

Цели: Целью данного исследования было охарактеризовать липофильную (петролейный эфир) фракцию *Scutellaria subcaespitosa* с помощью газовой хроматографии-масс-спектрометрии (ГХ-МС) и оценить острую токсичность и субхроническую переносимость на коже и слизистых оболочках водного настоя, приготовленного из надземных частей растения, у экспериментальных животных.

Материалы и методы: Липофильные компоненты анализировали методом ГХ-МС после ультразвуковой экстракции петролейным эфиром. Острую токсичность водного препарата (10%, масс./об.) оценивали на мышах и крысах-альбиносах после перорального (внутрижелудочного) и внутрибрюшинного введения. У крыс внутрижелудочные дозы варьировались от 5 до 5000 мг/кг массы тела, период наблюдения составлял 15 дней. Регистрировали клинические признаки, поведение, массу тела и смертность. Субхроническое воздействие водного раствора (1:10, масс./об.) на кожу и слизистые оболочки крыс и кроликов оценивалось в течение трех месяцев.

Результаты: Анализ экстракта петролейного эфира методом ГХ-МС выявил 43 хроматографических пика на хроматограмме общего ионного тока. Два пика соответствовали фталатным эфирам (дибутилфталату и диизооктилфталату), которые были признаны вероятными лабораторными примесями и поэтому исключены из анализа состава; 41 компонент растительного происхождения представлен в таблице 1. Наиболее распространенными компонентами были наонакозан и тетрааконтан, а также эвгенол, пальмитиновая кислота, фитол, камфора и γ -ситостерол. Тестирование на острую токсичность показало отсутствие смертности у крыс после внутрижелудочного введения в дозах до 5000 мг/кг и отсутствие клинически значимых признаков интоксикации. У мышей смертность наблюдалась только при самой высокой исследованной внутрибрюшинной дозе. Субхроническое кожное и слизистое воздействие в течение трех месяцев не вызывало наблюдаемых местных побочных реакций.

Заключение: Водный препарат *S. subcaespitosa* не продемонстрировал наблюдаемой острой токсичности у крыс в исследованном диапазоне доз и не вызвал неблагоприятных местных эффектов в условиях субхронического воздействия. Эти данные о безопасности относятся исключительно к водному препарату. Токсикологический профиль липофильной фракции петролейного эфира требует независимой оценки, прежде чем можно будет сделать выводы о безопасности жирорастворимых компонентов.

Ключевые слова: Острая токсичность, водный настой, жирорастворимые соединения, анализ ГХ-МС, *Scutellaria subcaespitosa*, лекарственные растения, оценка субхронического воздействия на кожу и слизистые оболочки

რეზიუმე.

მიზნები: კვლევის მიზანი იყო *Scutellaria subcaespitosa*-ს ლიპოფილური (ნავთობის ეთერი) ფრაქციის დახასიათება გაზის ქრომატოგრაფიულ-მას-სპექტრომეტრიის (GC-MS) გამოყენებით და მცენარის მიწისზედა ნაწილებიდან მომზადებული წყლიანი ნაყენის მწვავე ტოქსიკურობისა და სუბქრონიკული კანისა და ლორწოვანი გარსის ტოლერანტობის შეფასება ექსპერიმენტულ ცხოველებში.

მასალები და მეთოდები: ლიპოფილური შემადგენელი ნაწილები გაანალიზდა GC-MS-ით, ნავთობის ეთერით ულტრაბგერითი ექსტრაქციის შემდეგ. წყლიანი პრეპარატის მწვავე ტოქსიკურობა (10%, w/v) შეფასდა ალბინოს თაგვებსა და ალბინოს ვირთხებში პერორალური (კუჭშიდა) და ინტრაპერიტონეალური მიღების შემდეგ. ვირთხებში, კუჭშიდა დოზები მერყეობდა 5-დან 5000 მგ/კგ სხეულის წონაზე, 15-დღიანი დაკვირვების პერიოდით. დაფიქსირდა კლინიკური ნიშნები, ქცევა, სხეულის წონა და სიკვდილიანობა. წყლიანი ნაყენის (1:10, w/v) სუბქრონიკული კანისა და ლორწოვანი გარსის ზემოქმედება შეფასდა სამთვიანი პერიოდის განმავლობაში ვირთხებსა და კურდღლებში.

შედეგები: ნავთობის ეთერის ექსტრაქტის GC-MS ანალიზმა საერთო იონურ ქრომატოგრამაში 43 ქრომატოგრაფიული პიკი გამოავლინა. ორი პიკი შესაბამებოდა ფტალატის ეთერებს (დიბუტილ ფტალატი და დიიზოქტილ ფტალატი), რომლებიც სავარაუდოდ ლაბორატორიულ დამაბინძურებლებად ითვლებოდა და შესაბამისად, შემადგენლობის ინტერპრეტაციისგან გამოირიცხა; ცხრილში 1 წარმოდგენილია მცენარეული წარმოშობის 41 კომპონენტი. ყველაზე გავრცელებულ შემადგენელ ნაწილებს შორის იყო ნონაკოზანი და ტეტრაკონტანი, ევგენოლთან, პალმიტინის მჟავასთან, ფიტოლთან, კამფორასთან და γ -სიტოსტეროლთან ერთად. მწვავე ტოქსიკურობის ტესტირებამ აჩვენა, რომ ვირთხებში 5000 მგ/კგ-მდე დოზით კუჭში მიღების შემდეგ სიკვდილიანობა არ დაფიქსირებულა და ინტოქსიკაციის კლინიკურად მნიშვნელოვანი ნიშნები არ დაფიქსირებულა. თაგვებში სიკვდილიანობა დაფიქსირდა მხოლოდ ყველაზე მაღალი ინტრაპერიტონეალური დოზის მიღებისას. სამ თვეზე მეტი ხნის განმავლობაში კანისა და ლორწოვანი გარსის სუბქრონიკულმა ზემოქმედებამ არ გამოიწვია ადგილობრივი გვერდითი რეაქციების შესამჩნევი გამოვლინება.

დასკვნა: *S. subcaespitosa*-ს წყლიანმა პრეპარატმა არ აჩვენა შესამჩნევი მწვავე ტოქსიკურობა ვირთხებში შემოწმებული დოზის დიაპაზონში და არ გამოიწვია გვერდითი მოვლენები სუბქრონიკული ზემოქმედების პირობებში. ეს უსაფრთხოების დასკვნები ვრცელდება მხოლოდ წყლიან პრეპარატზე. ლიპოფილური ნავთობის ეთერის ფრაქციის ტოქსიკოლოგიური პროფილი დამოუკიდებელ შეფასებას საჭიროებს, სანამ ცხიშში ხსნადი შემადგენელი ნაწილების უსაფრთხოებასთან დაკავშირებით დასკვნების გამოტანა შესაძლებელი იქნება.

საკვანძო სიტყვები: მწვავე ტოქსიკურობა, წყალხსნარი ინფუზია, ლიპიდებში ხსნადი ნაერთები, GC-MS ანალიზი, *Scutellaria subcaespitosa*, სამკურნალო

მცენარეები, კანსა და ლორწოვან გარსებზე სუბქრონიკული ეფექტების შეფასება.