# 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 ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

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

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

**WEBSITE**

www.geomednews.com

## К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

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

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

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

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

**При нарушении указанных правил статьи не рассматриваются**.

## REQUIREMENTS

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

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

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

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

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

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

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

## ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის 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 ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

*GEORGIAN MEDICAL NEWS*
*NO 1 (370) 2026*

*Содержание:*

*GEORGIAN MEDICAL NEWS*
*No 1 (370) 2026*

# DOSE-DEPENDENT PROTECTIVE EFFECTS OF TAURINE IN EXPERIMENTAL ENVENOMATION BY THE BLUNT-NOSED VIPER (MACROVIPERA LEBETINA OBTUSA)

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## Abstract.

**Background:** Envenomation by viper species remains a clinically relevant medical problem in the Caucasus region and is frequently associated with systemic toxicity, including vascular injury, coagulation disturbances, and inflammatory responses. Although antivenom therapy is the standard treatment, supportive agents capable of reducing systemic complications are of continuing interest. Taurine is a sulfur-containing amino sulfonic acid with well-documented cytoprotective and vasomodulatory properties.

**Objective:** The aim of this study was to evaluate the protective effect of taurine against systemic toxicity induced by *Macrovipera lebetina obtusa* venom in an experimental mouse model.

**Methods:** Male mice were administered *M. lebetina obtusa* venom intraperitoneally at a dose of 2.5 $LD_{50}$. Taurine (1–500 mg/kg) or selected taurine conjugates were injected immediately after envenomation. Survival rate, mean survival time, and changes in venom $LD_{50}$ were determined using the Behrens and Miller–Tainter methods.

**Results:** Taurine administration at a dose of 100 mg/kg resulted in a partial improvement of survival probability (33%) under hemotoxic envenomation conditions and increasing the venom $LD_{50}$ from 1.8 to 2.4 mg/kg. Taurine conjugates, including sodium taurocholate and retinylidene taurine, did not demonstrate protective effects.

**Conclusion:** Taurine demonstrated a dose-dependent protective effect against systemic toxicity caused by *M. lebetina obtusa* venom in mice. These findings suggest that taurine may be considered as a potential supportive agent alongside standard antivenom therapy. Further experimental and clinical studies are required to clarify its mechanisms of action and clinical relevance.

**Key words.** Taurine, viper envenomation, systemic toxicity, experimental model, $LD_{50}$, adjunctive therapy.

## Introduction.

Taurine (2-aminoethanesulfonic acid) is an abundant sulfur-containing amino acid-like compound involved in osmoregulation, bile acid conjugation, membrane stabilization, and calcium signaling. Although endogenous synthesis occurs via cysteine oxidation, it is insufficient under stress conditions, making dietary supplementation critical during toxicity or metabolic imbalance. Beyond its homeostatic role, taurine has been recognized as a potent cytoprotective and antitoxic agent. Studies have shown that taurine can attenuate xenobiotic-induced organ damage, inhibit lipid peroxidation, and modulate inflammatory responses, leading to reduced tissue injury in models of cardiotoxicity, hepatotoxicity, and neurotoxicity [1,2].

Despite this growing body of evidence, the potential of taurine to counteract systemic envenomation remains underexplored. Snakebite envenomation continues to be a major medical problem in many parts of the world, including the Caucasus region, where *Macrovipera lebetina obtusa* (MLO) is responsible for most severe viper envenomation. MLO venom is a complex mixture of enzymes and bioactive peptides, with snake venom metalloproteinases (svMPs) and phospholipases $A_2$ ($PLA_2$s) as key toxic components. These enzymes mediate local hemorrhage, tissue necrosis, and systemic coagulopathy, with svMP-I isoform directly degrading vascular basement membranes, while svMP-III isoform disrupt endothelial cell–matrix adhesion [3].

$PLA_2$ activity generates lysophosphatidylcholine (LPC) and arachidonic acid derivatives, which amplify inflammation and cytotoxicity. Interestingly, LPC has been reported to inhibit taurine uptake in intestinal cells, suggesting that venom-derived LPC may lower local taurine availability at sites of injury [4]. Computational modeling has indicated that taurine aggregates with LPC, potentially reducing its membrane-disruptive effects. These observations suggest that taurine could counteract venom toxicity by stabilizing membranes, neutralizing toxic lipid metabolites, and maintaining vascular integrity [5].

Another rationale for taurine supplementation lies in its high physiological concentration in platelets and leukocytes, where it contributes to coagulation regulation and immune function. Taurine deficiency leads to impaired leukocyte activity and weakened immune responses, which may worsen venom-induced inflammatory cascades. Considering that envenomation can reduce taurine levels in blood and tissues, exogenous taurine could restore immune competence and modulate the systemic inflammatory response [6].

Taken together, these data support the hypothesis that taurine administration after envenomation may to reduce mortality by mitigating venom-induced circulatory damage, to protect the neurovascular unit and renal capillaries from svMP-mediated degradation, to stabilize coagulation dynamics by promoting the formation of smaller, more easily cleared fibrin clots, and to accelerate clearance of cytotoxic phospholipid metabolites [7].

The present study systematically investigated taurine's antitoxic potential in a murine model of MLO envenomation. We determined the optimal therapeutic dose range and aimed to highlight its possible use as an adjunct therapy in the management of viperid envenomation.

## Materials and Methods.

**Animals:** Male outbred albino mice (20 ± 2 g) were used throughout the experiments and sourced from the animal breeding facility of the L. A. Orbeli Institute of Physiology of National Academy of Sciences of the Republic of Armenia

(OIPH). The study was conducted according to the "Principles of Laboratory Animal Care" and complied with the European Communities Council Directive 2010/63/EU of September 22, 2010. Experimental procedures were approved by the IACUC of the OIPH, protocol № 05.06.2025/1). The total of 90 mice were used in this study.

**Reagents:** taurine, sodium taurocholate, retinylidene taurine (tauret)

**Venoms:** Venoms from *Macrovipera lebetina obtusa* (vMLO) and *Naja naja oxiana* (vNNO), were used in this study. The venoms were obtained from the snakes of OIPH animal breeding facility and Yerevan State Zoological Garden.

**Preparation of Injectable Solutions:** The injected venoms and reagents were dissolved in saline. The injection solutions were prepared so that the required doses were in 0.1 ml aliquots. All injections were provided intraperitoneally (IP).

**Assessment of taurine's antitoxic activity against vMLO and vNNO:**

Two groups of mice (n=6 per group) received 2.5 $LD_{50}$ doses of either vMLO (5mg/kg or 100μg per mouse in 0.1ml, IP) or vNNO (3.0 mg/kg or 60μg per mouse in 0.1ml, IP). Immediately after venoms injection, the taurine at 100 mg/kg (2mg per mouse in 0.1ml, IP) dose was injected contralaterally. Survival was assessed after 24 hours.

The taurine antitoxic effective dose determination against vMLO toxicity:

Six groups of mice (n=6 in each) were administered 2.5 $LD_{50}$ of vMLO [8]. Each group then received the following different taurine doses (in 0.1 ml, IP), except control group where the saline was injected (Control group, not included in table 1). This experimental group results are available from previous experiments [8]. Control group data were derived from experiments conducted under identical experimental conditions (same animal strain, age, weight range, venom batch, injection route, and laboratory environment). No protocol deviations occurred between experiments. This approach was applied strictly in accordance with the 3R principle to minimize animal use.

Time of death was recorded for each animal within a 24-hour observation window. Two approaches were used for data analysis:

1. a qualitative analysis based on survival percentages and
2. a quantitative analysis using survival time (in minutes), with 1440 minutes assigned to animals that survived the full 24 hours (according to established methods, such as the Behrens method, an animal that survives 24 hours after venom injection is considered to have overcome).

**The protective effects of taurine against vMLO toxicity ($LD_{50}$) in mice:**

5 groups of mice (n = 6 per group) were conducted. In both experimental series, mice were injected intraperitoneally with 5 different doses of *vMLO*. Immediately after the *vMLO* injection, mice in the treatment groups received a contralateral intraperitoneal injection of taurine. Taurine was administered at a dose of 100 mg/kg (2 mg per mouse in 0.1 ml) (Table 2). Mortality was estimated 24 hours after injection, and the $LD_{50}$ was calculated using the methods of Behrens and Miller-Tainter to determine any change in venom toxicity under the influence of taurine.

Antitoxic potential of taurine conjugates:

To explore the protective potential of taurine conjugates, three groups of mice (n=6 in each) were injected with 2.5 $LD_{50}$ of vMLO (100 μg per mouse in 0.1ml, IP). In addition to venom,

***Table 1.*** *Experimental groups and doses of Taurine with fixed MLO dose.*

| **Groups of mice** | | | | | |
|---|---|---|---|---|---|
| **Group I** | **Group II** | **Group III** | **Group IV** | **Group V** | **Group VI** |
| vMLO 5.0 mg/kg (100.0 μg per mouse) | | | | | |
| Taurine | | | | | |
| 1.0 mg/kg (0.02 mg per mouse) | 5.0 mg/kg (0.1 mg per mouse) | 50.0 mg/kg (1.0 mg per mouse) | 100.0 mg/kg (2.0 mg per mouse) | 200.0 mg/kg (4.0 mg per mouse) | 500.0 mg/kg (10 mg per mouse) |

***Table 2.*** *Experimental groups and doses of MLO with fixed Taurine dose.*

| **Groups of mice** | | | | |
|---|---|---|---|---|
| **Group I** | **Group II** | **Group III** | **Group IV** | **Group V** |
| Taurine 100.0 mg/kg (2.0 mg per mouse) | | | | |
| vMLO | | | | |
| 1.0 mg/kg (20.0 μg per mouse) | 2.0 mg/kg (40.0 μg per mouse) | 3.0 mg/kg (60.0 μg per mouse) | 4.0 mg/kg (80.0 μg per mouse) | 5.0 mg/kg (100.0 μg per mouse) |

***Table 3.*** *Experimental groups and doses of Taurine Conjugates with fixed MLO dose.*

| **Groups of mice** | | |
|---|---|---|
| **Group I** | **Group II** | **Group III** |
| vMLO 5.0 mg/kg (100.0 μg per mouse) | | |
| TauC 430.0 mg/kg (8.6 mg per mouse) | Tauret | |
| | 0.2 mg/kg (4.0 μg per mouse) | 2.0 mg/kg (40.0 μg per mouse) |

*Survival outcomes were recorded for 24 hours.*

each group received one of the following substances (Sodium taurocholate (TauC) and Tauret in 0.1 ml, IP. Saline data of previous groups was used. TauC was administered at a dose equimolar to 100 mg/kg taurine (Table 3).

**Statistical Analysis**

The long-rank Kaplan–Meier survival test was used to compare the survival distribution of the different doses and treatment groups. Differences between groups were evaluated using the log-rank (Mantel–Cox) test. Animals surviving the 24-hour observation period were treated as censored observations. The p value less than 0.05 was considered statistically significant. Graph Pad Prism® (GraphPad Software, USA) version 8.0.1 software was used for all statistical analysis.

## Results.

**Evaluation of taurine's antitoxic activity against vMLO and vNNO venoms:**

In the preliminary assessment of taurine protective effects against the lethality of two snake venom (vMLO as hemotropic and vNNO as neurotropic) with differing biological actions, distinct survival outcomes were observed. Administration of taurine at a dose of 100 mg/kg with vNNO venom (2.5 $LD_{50}$, 60 µg/mouse) resulted in 100% mortality within 24 hours (0/6 survivors). In contrast, taurine administered with vMLO venom (2.5 $LD_{50}$, 100 µg/mouse) yielded a 33% survival rate (2/6 animals survived at 24 hours), indicating visible protective efficacy against this venom type.

**Preliminary dose determination in experiments of taurine antitoxic effect:**

To further explore the dose-dependent antitoxic potential of taurine, two doses were tested against a fixed dose of vMLO (2.5 $LD_{50}$). After 24 hours, survival rates were 33% (2 out of 6) in the 100 mg/kg taurine group and 17% (1 out of 6) in the 500 mg/kg group.

The taurine antitoxic effect dose optimization against vMLO:

To determine the optimal protective dose of taurine against vMLO, the survival times for each animal within a 24-hour observation period were recorded and analyzed using both qualitative and quantitative methods. The survival time of all mice after injections in minutes, the average survival time of animals in the groups (assessment of the trend of increasing survival time), and the percentage of non-surviving/surviving animals in groups are given in Table 4.

The data obtained show that mortality in the first three groups was 100%. Starting from the fourth group, which received 50 mg/kg of taurine, mortality decreased to 83.3%. In the groups receiving 100 mg/kg and 200 mg/kg of taurine, mortality was 66.6%, corresponding to a survival rate of 33.3%. Higher doses (300–400 mg/kg) were not tested, as previous data indicated that 500 mg/kg had no beneficial effect and in case of 200 mg/kg there was not obtained better result compared to 100 mg/kg. Since 100 mg/kg and 200 mg/kg produced comparable results, the use of higher doses was deemed unnecessary. The survival curves in each group are shown in Figure 1.

Kaplan–Meier analysis demonstrated a trend toward increased survival in the taurine-treated groups compared to control; however, the difference did not reach statistical significance in all groups.

**Comparative data on the probability of mouse mortality ($LD_{50}$) are presented in Figure 2.**

***Table 4.*** *Survival time of mice exposed to vMLO after administration of taurine (in min).*

| | Group I | Group II | Group III | Group IV | Group V | Group VI | Group VII |
|---|---|---|---|---|---|---|---|
| | 5mg/kg vMLO + saline | 5mg/kg vMLO + 1mg/kg Taurine | 5mg/kg vMLO + 5mg/kg Taurine | 5mg/kg vMLO + 50mg/kg Taurine | 5mg/kg vMLO + 100mg/kg Taurine | 5mg/kg vMLO + 200mg/kg Taurine | 5mg/kg vMLO + 500mg/kg Taurine |
| **Mouse 1** | 84.0 | 85.0 | 111.0 | 95.0 | 68.0 | 115.0 | 85.0 |
| **Mouse 2** | 89.0 | 100.0 | 128.0 | 145.0 | 119.0 | 128.0 | 89.0 |
| **Mouse 3** | 102.0 | 102.0 | 183.0 | 149.0 | 124.0 | 134.0 | 107.0 |
| **Mouse 4** | 154.0 | 123.0 | 184.0 | 166.0 | 147.0 | 145.0 | 128.0 |
| **Mouse 5** | 174.0 | 174.0 | 600.0 | 420.0 | 1440.0 | 1440.0 | 140.0 |
| **Mouse 6** | 177.0 | 230.0 | 802.0 | 1440.0 | 1440.0 | 1440.0 | 1440 |
| **Median survival time** | 128.0 | 112.5 | 183.5 | 157.5 | 135.5 | 139.5 | 117.0 |
| **Dead/survival, %** | 100/0 | 100/0 | 100/0 | 83.3/16.7 | 66.6/33.4 | 66.6/33.4 | 16.6/83.4 |

***Table 5.*** *Survival time of mice (in min) exposed to vMLO after administration of taurine conjugates.*

| | Group I | Group II | Group III |
|---|---|---|---|
| | Sodium taurocholate | 4 µg tauret | 40 µg tauret |
| **Mouse 1** | 10.0 | 108.0 | 23.0 |
| **Mouse 2** | 14.0 | 112.0 | 38.0 |
| **Mouse 3** | 15.0 | 112.0 | 41.0 |
| **Mouse 4** | 15.0 | 122.0 | 42.0 |
| **Mouse 5** | 75.0 | 127.0 | 45.0 |
| **Mouse 6** | 1440.0 | 145.0 | 54.0 |
| **Median survival time** | 15 | 117 | 41.5 |
| **Dead/surviving, %** | 83.3/16.7 | 100/0 | 100/0 |

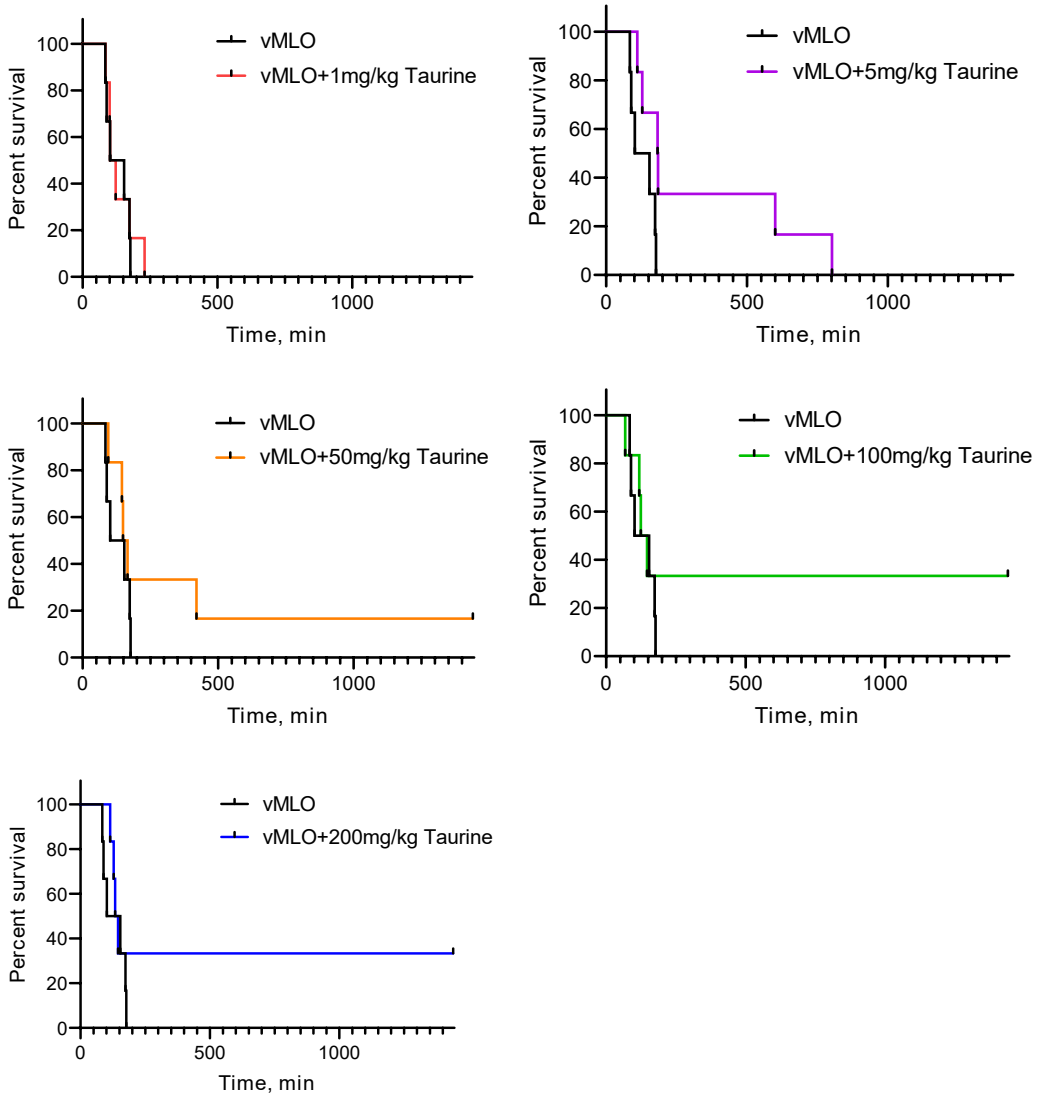


***Figure 1.*** *Survival of mice with a fixed dose of vMLO and different doses of Taurine.*

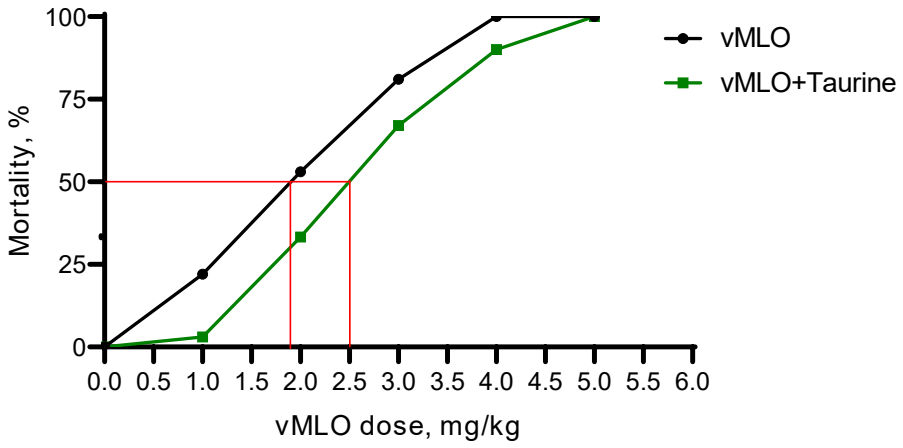


***Figure 2.*** *$LD_{50}$ of group of mice, where vMLO only was injected and in group additionally treated with Taurine 100mg/kg.*

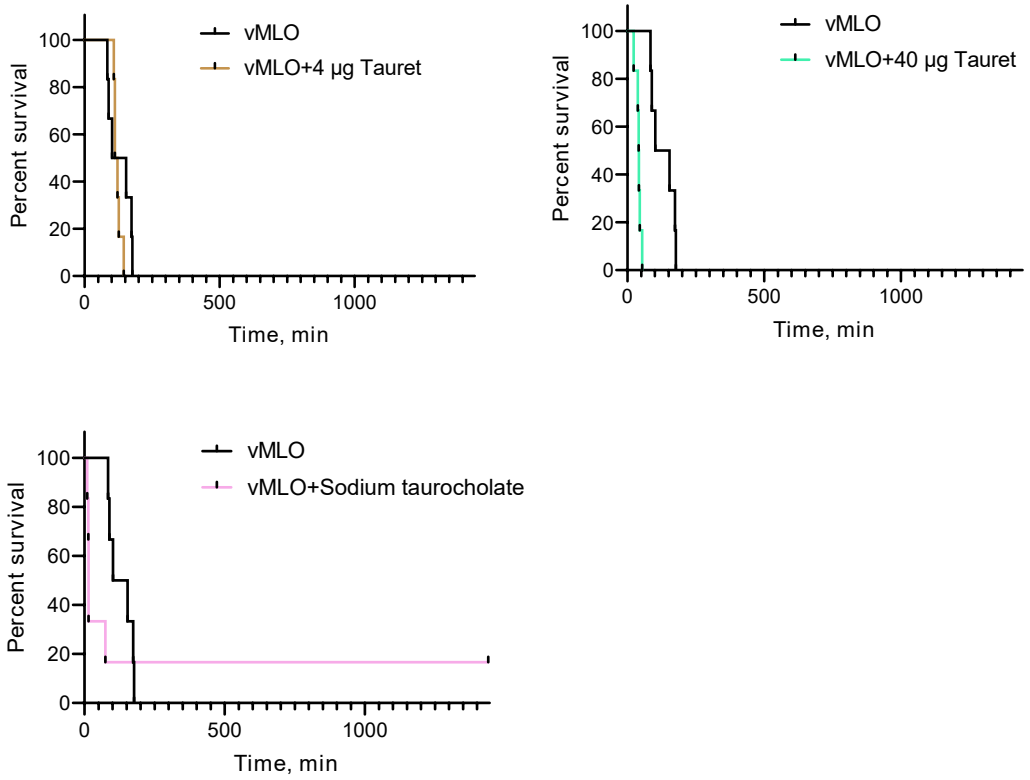


***Figure 3.*** *Survival with a fixed dose of vMLO (2.5LD$_{50}$) and taurine conjugates.*

According to the Miller–Tainter method [8], the $LD_{50}$ of vMLO was 1.86 ± 0.21 (mean ± SE), whereas the $LD_{50}$ of vMLO + taurine (100 mg/kg) was 2.39 ± 0.16.

**The determination of antitoxic effect of taurine conjugates:**

The results of studies on the possible antitoxic effect of taurine in the conjugated state are presented in the table 5, and the comparative survival curves are shown in Figure 3.

Kaplan–Meier analysis demonstrated a trend toward increased survival in the taurine conjugates-treated groups compared to control; the difference did not reach statistical significance in all groups (log-rank test).

## Discussion.

It is well established that snake venoms exert their toxic action predominantly through two major physiological systems: the circulatory and the nervous, and are therefore generally classified as hemotropic or neurotropic, respectively [9]. Guided by this distinction, we conducted preliminary experiments employing the venom of the blunt-nosed viper (Macrovipera lebetina obtusa) and the Central Asian cobra (Naja naja oxiana) in order to evaluate the potential antitoxic activity of taurine and to delineate the system-specific direction of its protective effects.

Our findings demonstrated a marked difference in the outcomes of taurine administration depending on the type of envenomation. In the cobra venom–treated group, mortality reached 100%, whereas in the vMLO–treated group the mortality was reduced to 66.6%. The clear divergence in taurine's efficacy between the two models provided a rationale for selecting hemotoxic venoms for subsequent investigations. Specifically, the protective influence of taurine against viperid venom, in contrast to its negligible effect against elapid venom, suggests that taurine exerts a modulatory role on the vascular and hematological disturbances characteristic of hemotoxic envenomation.

Taken together, these results support the hypothesis that taurine may function as a vasculoprotective or hemoprotective agent, attenuating the microvascular damage induced by viper venoms, while lacking efficacy against neurotoxic mechanisms typical of elapid venoms. This system-specific activity highlights the importance of considering the toxicodynamic profile of different snake venoms when evaluating candidate antitoxic agents.

As previously reported, the optimal physiological dose of taurine for rats ranges between 100–500 mg/kg body weight [10]. In the present study, we attempted to delineate the effective range of taurine capable of exerting antitoxic activity against vMLO. Our results indicate that taurine at 100 mg/kg provided a measurable protective effect and may be considered a potential adjunct therapy.

This finding is in agreement with earlier toxicological and pharmacological studies, which have also documented beneficial actions of taurine at comparable dosing levels [11,12].

**Dose-dependent effects of taurine.**

It was therefore essential to establish the optimal dose of taurine capable of providing maximal protection against the toxic effects of vMLO venom and to clarify the nature of this protective action. In our study, mean survival time in the untreated control

group was 130 ± 17.8 minutes. In our experimental groups, mortality in the first three cohorts was 100%. A notable shift was observed beginning with the group that received 50 mg/kg of taurine, in which mortality decreased to 83.3%. Further reduction was observed in the 100 mg/kg and 200 mg/kg taurine groups, where mortality reached 66.6%, corresponding to a survival rate of 33.3%. These findings indicate a dose-related protective trend, with 100 mg/kg representing the most consistent beneficial effect. Doses exceeding 200 mg/kg were not tested, as preliminary data and previous reports suggested that 500 mg/kg lacks therapeutic efficacy and may even exert adverse effects. Thus, administration of higher doses (≥300 mg/kg) was considered unnecessary, given that 100–200 mg/kg demonstrated comparable protective outcomes.

**Mechanistic considerations.**

Given the pleiotropic functions of taurine in the organism [13], defining a single mechanism responsible for its antivenom activity against vMLO is inherently challenging. This complexity is further underscored by the fact that several known antidotes contain sulfur or sulfosulfate moieties. Additionally, many highly sulfonated polyanionic glycans, such as heparin and heparan sulfate, which are abundant in the extracellular matrix, are known substrates for enzymatic degradation by snake venom components [14]. Interestingly, heparin itself has been reported to suppress the activity of certain venom enzymes, including hyaluronidases from both snake and scorpion venoms [15]. However, the anticoagulant activity of heparin is strictly dependent on its sulfate groups, and even partial desulfation results in a loss of activity [16]. Although structurally distinct, heparin and taurine share a notable chemical feature: both contain sulfonated groups that are critical for their biological effects. Heparin is a large macromolecular polymer integrated into vascular walls, whereas taurine is a small, free sulfonamino acid. From this perspective, it is plausible to hypothesize that taurine could act as a donor of sulfonate groups, providing negatively charged moieties that might substitute or complement the role of polyanions during venom-induced vascular injury. Taken together, these findings indicate that the protective effect of taurine cannot be solely attributed to the presence of a sulfonate group. The observed protective effects may plausibly be related to taurine's well-documented antioxidant capacity [12], membrane-stabilizing properties [5], calcium homeostasis modulation, and sulfate donor function, all of which have been shown in independent models to attenuate venom-induced systemic injury.

**Microvascular and biochemical protective role of taurine.**

Taurine is a multifunctional amino acid involved in lipid metabolism, energy regulation, and the formation of bile acid conjugates [17]. Within hepatocyte microsomes, taurine participates in the formation of numerous taurine conjugates through the action of acyl-CoA:amino acid N-acyltransferase (ACNAT), an enzyme involved in bile acid conjugation and xenobiotic detoxification pathways. The amino group of taurine serves as an anchoring site for conjugation with a variety of bioactive molecules, while its sulfonic group remains fully ionized at physiological pH (≈7.4), conferring high hydrophilicity and chemical stability to taurine and its conjugates [18]. Consequently, under physiological conditions, taurine predominantly exists as a zwitterion, with nearly complete ionization of both its amino and sulfonic groups.

To elucidate whether conjugated forms of taurine possess antitoxic properties akin to free taurine, we tested taurine in combination with lipophilic compounds such as bile acids or retinal (taurates). Taurets, for example, play an established antitoxic role in the retina [19]. Our experimental results indicate that taurine conjugates do not replicate the protective effects observed with free taurine. Mortality in groups receiving venom alone, venom plus tauret at 0.2 mg/kg (4 μg per mouse), and venom plus tauret at 2 mg/kg (40 μg per mouse) was 100%, while survival time was only modestly increased in the 2 mg/kg taurret group. Conversely, sodium taurocholate and tauret at 2 mg/kg appeared to potentiate vMLO venom toxicity, whereas tauret at 0.2 mg/kg showed only a marginal, non-significant attenuation.

Collectively, these findings indicate that the antitoxic efficacy of taurine is specific to its free form, and conjugation with bile acids or other lipophilic molecules does not enhance, and may even reduce, its protective action against hemotoxic envenomation. This underscores the importance of taurine's unbound biochemical state in mediating vascular and systemic protective effects during viper envenomation.

**Limitations, mechanistic interpretation, and optimal dose considerations.**

The cumulative data from this study indicate that taurine, in its free zwitterionic form, exerts a markedly more favorable antitoxic effect against vMLO than its bound conjugates, which, although physiologically important as lipid signaling molecules, are ineffective in the context of viper envenomation. Our results suggest that vMLO venom rapidly depletes taurine reserves within leukocytes and platelets, implying that taurine is consumed in neutralizing reactive derivatives generated by venom activity.

Specifically, hemolysis of erythrocytes induced by viper venom produces arachidonic acid and lysolecithin. Taurine conjugates with arachidonic acid to form arachidonoyl taurine, a water-soluble compound that can be efficiently cleared via blood and lymphatic flow [20]. Concurrently, taurine aggregates with free lysolecithin molecules, mitigating their membrane-damaging effects Additionally, exposure to vMLO venom induces disseminated intravascular coagulation, increasing vitamin K activity. Since taurine is essential for vitamin K–dependent processes, its consumption is further amplified [21]. These mechanisms collectively contribute to endogenous taurine depletion during envenomation.

Our experiments demonstrate that exogenous taurine supplementation can restore systemic taurine levels, thereby supporting these protective processes. In contrast, taurine conjugates are ineffective because they cannot participate in these critical neutralization and aggregation pathways, and in some cases, may even facilitate venom dissemination. Similar to bile and other surface-active substances, high concentrations of conjugates can increase vascular and tissue permeability, promoting toxin spread [22]. Consequently, administration of excessive taurine doses can paradoxically invert the antitoxic

effect, likely due to overproduction of conjugates and enhanced venom distribution.

Taken together, these findings confirm that the optimal antitoxic dose of taurine against vMLO venom lies between 100–200 mg/kg. Doses below this range are insufficient to achieve significant protection, whereas doses above this range may exacerbate venom toxicity through the mechanisms outlined above. This underscores the critical importance of precise dose selection in developing taurine-based therapeutic strategies for hemotoxic envenomation.

From the Elapidae family, the Central Asian cobra (Naja naja oxiana) was included as a representative neurotoxic venom, since our experiments confirmed that taurine shows little protective effect in the context of neurotoxicity.

This design allowed us to evaluate whether taurine's vasoprotective effect is specific to hemorrhagic and hemolytic mechanisms, or if it could also attenuate the broader range of pathological actions associated with other venom types. Studies have demonstrated that even following oral administration of taurine, peak plasma taurine concentrations are reached approximately 1.5 hours after ingestion [23]. The toxicodynamics of MLO venom demonstrate that systemic toxicity generally develops within 30–60 minutes, as venom components enter the circulation. Peak systemic and inflammatory effects occur approximately 1.5–3 hours after the bite [24]. This indicates that, if taurine is taken immediately after a snakebite, it should attain systemic levels rapidly enough to exert its potential antitoxic effects. Therefore, taurine should not be regarded as a substitute for antivenom therapy, but rather as a potential early adjunctive measure that could be administered immediately after a blunt-nosed viper bite, pending definitive medical treatment; however, its efficacy under delayed post-envenomation conditions remains to be established and requires further investigation.

## Conclusion.

Taurine demonstrated a dose-dependent protective effect against systemic toxicity caused by *M. lebetina obtusa* venom in mice. These findings suggest that taurine may be considered as a potential supportive agent alongside standard antivenom therapy. Further experimental and clinical studies are required to clarify its mechanisms of action and clinical relevance.

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