

# GEORGIAN MEDICAL NEWS

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ISSN 1512-0112

NO 12 (345) Декабрь 2023

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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 ბაზებშიდან.

### WEBSITE

[www.geomednews.com](http://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](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.nlm.nih.gov/bsd/uniform_requirements.html)  
[http://www.icmje.org/urm\\_full.pdf](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. რენტგენოგრამების 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.

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## COMPARATIVE ANALYSIS OF THE EFFECTS OF SOME HEPATOPROTECTORS IN EXPERIMENTALLY INDUCED MAFLD IN ADULT WISTAR RATS

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### Abstract.

Metabolic associated fatty liver disease (MAFLD) is one of the most common chronic diseases characterized by increased fat accumulation in the liver and metabolic dysfunction. MAFLD is now taking on the character of a pandemic. In addition to dietary therapy and physical activity, hepatoprotectors are included in the pharmacotherapy of MAFLD. This study was to perform a comparative analysis of the efficacy of some hepatoprotectors in experimentally induced MAFLD in adult Wistar rats.

**Key words.** Hepatoprotectors, MAFLD, metabolic associated fatty liver disease, ademethionine, honey, thioctic acid, Wistar.

### Introduction.

Metabolic associated fatty liver disease (MAFLD) is one of the most common chronic diseases characterized by increased fat accumulation in the liver and metabolic dysfunction [1,2,3]. Due to the increasing number of patients suffering from diabetes mellitus and obesity. MAFLD is now taking on the character of a pandemic [1,3,4]. MAFLD affects a quarter of the population, and has no approved drug therapy [2,3]. It is of concern that MAFLD is increasingly being diagnosed in children and adolescents, and this, when paired with the intimately associated hepatic as well as cardiovascular and oncological sequelae, places an enormous burden on individuals, families, and health care systems [3-8]. MAFLD can progress from simple steatosis to steatohepatitis, and eventually end-stage liver diseases [3-8]. The MAFLD diagnosis, as published in guidelines, requires hepatic steatosis of  $\geq 5\%$  without concurrent liver disease, including "significant" alcohol use with factors of metabolic dysregulation as a prerequisite for diagnosis [5-8]. In addition to dietary therapy and physical activity, hepatoprotectors are included in the pharmacotherapy of MAFLD in order to reduce the degree of liver damage and regress the immunoinflammatory process [4,5,7]. This group of drugs is very heterogeneous and includes substances of different chemical groups, the effect of which is aimed at maintaining the endogenous detoxification system, suppressing lipid peroxidation (LPO) and enhancing the activity of antioxidant systems [9,10]. Today there is a wide and diverse choice of drugs on the market, differing in their pharmacological effect [10]. According to the latest clinical recommendations of the Russian Society for Liver Research and the Russian Gastroenterological Association (2016), ursodeoxycholic acid is an effective hepatoprotector in the treatment of MAFLD [1]. However, studies on the comparative efficacy of other groups of drugs are scarce [9,10]. Therefore, it is relevant and necessary to evaluate the effect of each of them and determine their therapeutic efficacy.

**The aim of the study** was to perform a comparative analysis of the efficacy of hepatotropic drugs: ademethionine (Heptral<sup>®</sup>), honey (Metrop<sup>®</sup> GP) and thioctic acid (Thioctacid<sup>®</sup>), in experimental-induced MAFLD.

### Materials and Methods.

All studies were conducted according to the requirements of the decision of the Council of the Eurasian Economic Union in the Sphere of Circulation of Medicines from 03.11.2016 № 81. The study was conducted on Wistar rats (n=40), white color, bred in vivarium conditions, with an initial body weight of  $256.15 \pm 9.77$  g. The animals underwent a 14-day quarantine before the start of the study. The studies were conducted for a period of 8 months.

### Stages of the studies:

Stage 1 - development of MAFLD model.  
Stage 2 - evaluation of hepatotropic drugs efficacy in conditions of experimentally induced MAFLD.

### Development of the MAFLD model:

A large number of studies have revealed that the predictor of MAFLD development is lifestyle: dietary disorders (high-calorie diet, excessive intake of saturated fats, refined carbohydrates) and sedentary lifestyle [11]. To develop the MAFLD model, we took both of these conditions into account.

### Feed selection:

- 1) free access to water.
- 2) hypercaloric diet created by adding 20% melted beef fat to the standard feed (animal fats are more effective than vegetable fats in forming metabolic disorders, with beef fat being steatosis), 5% d-fructose (its consumption rather quickly causes liver obesity with the development of resistance to leptin in both animals and humans), 5% isolated soy protein, 2% choline, 0.5% cholesterol, sodium glutamate (to enhance nutritional appeal).

Hypodynamic conditions were created by restricting the motor activity of the animals by placing them in narrow individual cages.

Animal selection. Male rodents are the most optimal test system for modeling MAFLD and are more susceptible to alimentary disturbances, due to which they develop this pathology more quickly and easily by analogy with humans.

### Evaluation of the efficacy of hepatotropic drugs in experimental-induced MAFLD:

Animals were divided into 5 groups (n=8 in each group):  
Group 1 - "Intact" - intact animals, standard diet, no restriction in motor activity.



Group 2 - "MAFLD" - high-calorie diet, hypodynamia.

Group 3 - "Heptral" - high-calorie diet, hypodynamia followed by administration of the drug Heptral®.

Group 4 - "Metrop GP" - high-calorie diet, hypodynamia followed by administration of the drug Metrop® GP.

Group 5 - "Thioctacid" - high-calorie diet, hypodynamia followed by administration of the drug Thioctacid®.

The light day was 12/12. Throughout the study (8 months), rats of groups №2-5 received a high-calorie diet, were put away in individual cages, however, starting from the 6th month, the third group additionally received Heptral®; (214 mg/kg), the fourth group received Metrop® GP (12 mg/kg), and the fifth group received Thioctacid®. (42 mg/kg). During the study, all animals had their body weight measured monthly. At the 6th and 8th month of the study, all animals underwent blood sampling from tail veins (with preliminary 8-hour fasting) for further biochemical analysis for ALAT, ASAT, alkaline phosphatase, triacylglycerides (TAG), and glucose. The material was examined on a Sapphire 400 biochemical analyzer using Randox system reagents (RANDOX Laboratories Ltd., United Kingdom). HOMA-IR index was also calculated at month 8 of the study. Statistical processing of the data was performed using the t-criterion of Student's t-test. The criterion of statistical reliability of the obtained conclusions was considered to be the value of  $p < 0.05$ , which is generally accepted in medicine.

## Results.

In the course of analyzing the dynamics of changes in body weight of rats, a statistically significant increase in body weight was revealed in groups 2-5 (Figure 1).

Body weight in animals of "MAFLD" group at the end of 5 months of the study increased 1,5 times compared to the initial body weight (1 month - 255,5±9,35 g, at the end of 5 months - 394,5±12,44 g), by the end of the experiment - 1,76 times compared to the initial body weight, 1,37 times compared to the group of intact animals ( $p < 0,05$ ).

Body weight in animals of "Heptral" group at the end of 5 months of the study increased in 1,48 times in comparison with the initial body weight (1 month - 254,38±9,13 g, at the end of 5 months - 376,88±13,35 g), but by the end of the experiment the body weight gain in animals was lower than in "MAFLD" group - in 1,5 times in comparison with the initial body weight, in 1,2 times in comparison with the group of intact animals ( $p < 0,05$ ).

Dynamics of body weight changes in animals in the "Metrop GP" group was completely comparable with that in the "MAFLD"

group; statistically significant changes were not revealed.

Body weight in animals of "Thioctacid" group at the end of 5 months of the study increased by 1.46 times compared to the initial body weight (1 month – 256,88±11,44 g, at the end of 5 months - 376,13±5,99), but by the end of the experiment the body weight gain was also lower than in "MAFLD" group - 1.6 times compared to the initial body weight, 1.26 times compared to the group of intact animals ( $p < 0,05$ ).

Body weight gain in the study was noted gradually - by the end of the experiment the difference between the groups "MAFLD", "Heptral", "Metrop GP", "Thioctacid" averaged 27%, 17.9%, 27%, 20% respectively compared to the body weight of animals of the group "Intact" at the end of the experiment.

Analysis of selected biochemical indices of blood serum of the studied groups revealed different disorders of carbohydrate, lipid metabolism. In the group of intact animals no significant fluctuations of indicators were observed (Table 1). In the groups "Heptral" and "Thioctacid" the changes were less pronounced in comparison with the groups "MAFLD" and "Metrop GP", which may indicate an effective therapeutic effect on liver function of the first two drugs.

The average level of triacylglycerides (TAG) of rats in animals on a high-calorie diet under hypodynamic conditions (groups 2-5) was found to be increased at the 6th month of the study compared to intact animals ( $p < 0,05$ ).

However, there was a significant decrease in the level of TAG in rats after using the drugs "Heptral" and "Thioctacid", and in the group "Heptral" the decrease was more pronounced ( $p < 0,05$ ).

The study of transaminases revealed a tendency to increase serum ASAT and ALAT, but the differences between the groups were not statistically significant.

The development of hyperglycemia against the background of concomitant obesity and lipid metabolism disorders was noted in all studied groups at the 6th month of the experiment, but the glucose level at the 8th month decreased in the groups "Heptral" and "Thioctacid" in comparison with its level at the 6th month ( $p < 0,05$ ). The obtained data on the correlation between MAFLD and fluctuations in glucose level are in full compliance with the literature data.

We also calculated the HOMA-IR insulin resistance index (Figure 2).

Insulin resistance (IR) is a condition in which the body's cells stop responding to insulin and become resistant to it. In this case, insulin cannot transport glucose inside the cells, and it

**Table 1.** Indicators of biochemical blood analysis of the studied groups.

Group	Intact		MAFLD		"Heptral"		"Metrop GP"		"Thioctacid"	
	6	8	6	8	6	8	6	8	6	8
Glucose (mmol/L)	4,56±0,14	4,14±0,15	5,47±0,08	5,9±0,31	5,52±0,12	5,01±0,09	5,61±0,10	5,80±0,21	5,54±0,15	5,12±0,08
ALAT (IU/L)	71,4±0,87	72,3±0,93	75,0±0,86	82,3±0,95	75,2±0,75	71,0±0,84	75,2±0,78	83,6±1,08	74,98±1,12	72,0±0,76
ASAT (IU/L)	68,2±0,96	70,1±1,08	73,0±1,54	79,6±0,82	72,96±1,24	71,2±1,14	73,4±1,47	79,8±0,9	73,2±1,6	71,4±1,25
Alkaline phosphatase (IU/L) (ME/π)	326,2±4,87	324,1±5,03	338,9±3,87	366,8±3,94	340,1±3,65	321,4±4,47	340,1±3,24	368,4±4,02	339,4±3,9	328,5±3,97
TAG (mmol/L)	1,05 ±0,1	1,1 ±0,15	2,15 ±0,12	2,26 ±0,31	2,1 6±0,07	1,74 ±0,12	2,16 ±0,09	2,24 ±0,27	2,18 ±0,14	1,85 ±0,14

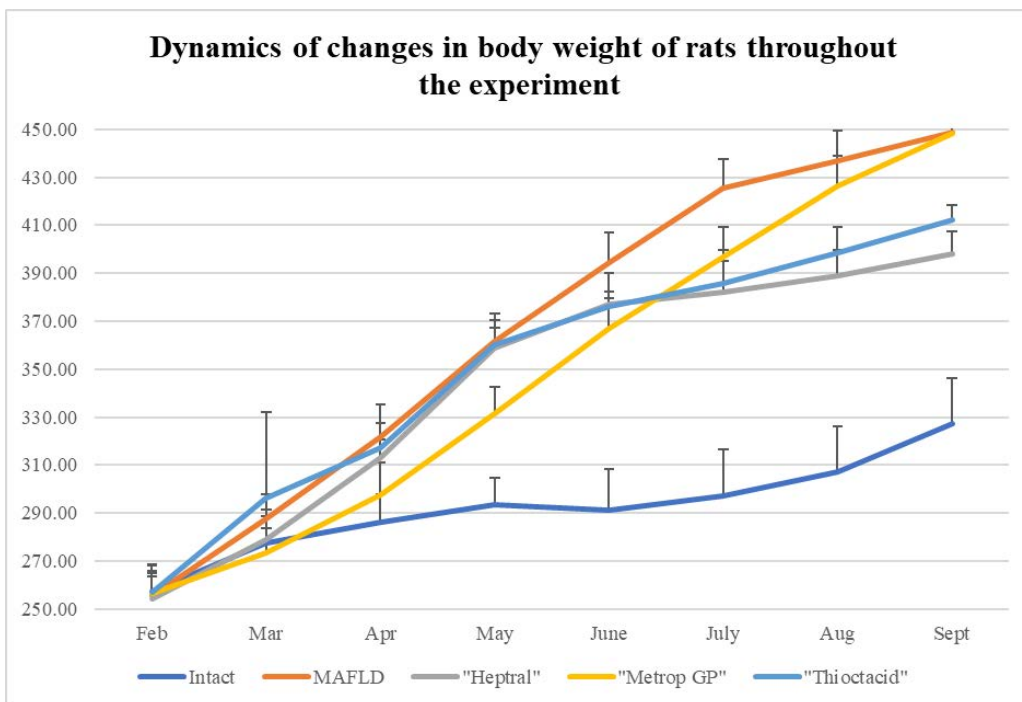


Figure 1. Dynamics of changes in body weight of rats throughout the experiment.

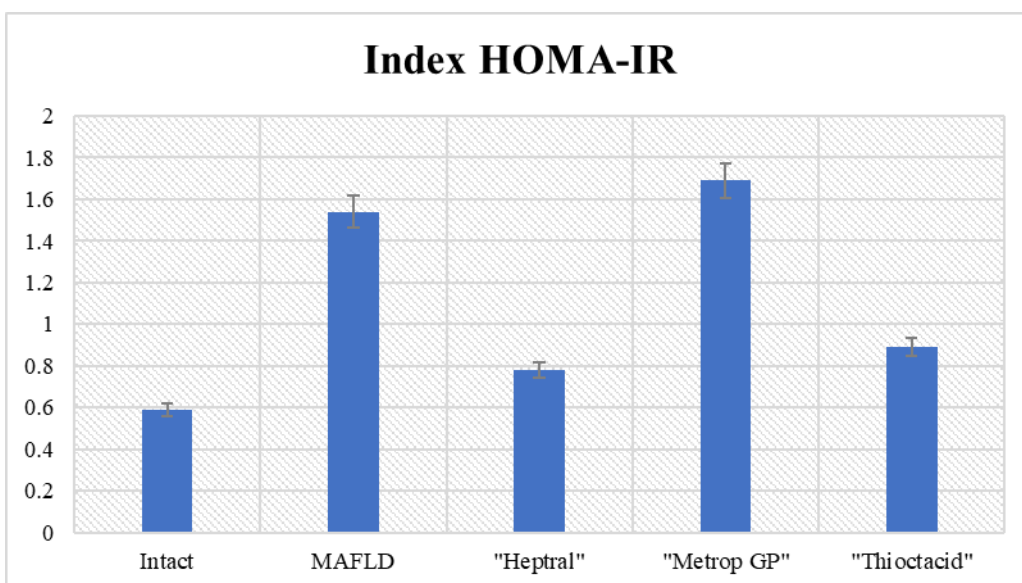


Figure 2. HOMA-IR index value in the study groups at the end of the study.

accumulates in the blood. Insulin resistance is associated with the development of type II diabetes.

The HOMA-IR index (Homeostasis model assessment of insulin resistance) is a formula that takes into account glucose and insulin levels. It is calculated using the formula:  $HOMA\ IR = \text{fasting insulin } (\mu\text{ME/mL}) * \text{fasting glucose (mmol/L)} / 22.5$ . When glucose or insulin levels increase, the HOMA-IR index increases.

A statistically significant increase in HOMA-IR index was found in "MAFLD" and "Metrop GP" groups compared to "Heptral", "Thioctacid" groups ( $p < 0,05$ ).

### Conclusion.

In the course of our study, we created a model of metabolic associated fatty liver disease (MAFLD) and evaluated the effectiveness of the therapeutic effect of three hepatotropic drugs: ademethionine (Heptral®), honey (Metrop® GP) and thioctic acid (Thioctacid®). Administration of preparations with ademethionine and thioctic acid contributed to the reduction of metabolic indices in experimental animals. The honey-based preparation did not show any significant changes. Thus, considering the obtained data, it is possible to assume the effectiveness of ademethionine and thioctic acid in the therapy of

MAFLD. However, it is necessary to repeat additional studies with mandatory inclusion in their plan of liver biopsy with subsequent histologic examination.

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