GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 7-8 (352-353) Июль-Август 2024

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 7-8 (352-353) 2024

Содержание:

GEORGIAN MEDICAL NEWS
No 7-8 (352-353) 2024

ASSESSMENT OF CIPROFLOXACIN EFFECTS ON SOME CHICKS' ORGANS: A COMPREHENSIVE BIOCHEMICAL AND HISTOLOGICAL STUDY

Sana A. Abdulmawjood[1], Eman S. Mahmoud[2], Rana T Altaee[3].

[1]*College of Sciences, University of Mosul, Mosul, Iraq.*
[2]*College of Dentistry, University of Mosul, Mosul, Iraq.*
[3]*College of Education for Pure Sciences, University of Mosul, Iraq.*

Abstract.

The aim is to evaluate ciprofloxacin toxicity in the liver and kidneys by assessing their functioning, histological alterations, and GFAP expression in chicks. In the acute trial, the chicks were divided into 3 groups of six. The 1st was the control. The 2nd and 3rd received injections of 250 and 500 mg/kg cipro. In the subchronic experiment, the animals were separated into two groups: the 1st group was control and 2nd groups were administered 125 mg/kg cipro for two weeks. The acute treatment at a dose of 500 mg/kg resulted in a significant increase in AST (alanine aminotransferase), ALT (aspartate aminotransferase), Mg (magnesium), and Ca (calcium), as did the subchronic trial at a level of 125 mg/kg. Acetylcholinesterase inhibition was measured at ciprofloxacin dosages of 250 and 500 mg/kg in the acute trial, as well as 125 mg/kg in the subchronic study. Histological examination revealed mild to severe lesions in the liver and kidneys treated with 250-500 mg/kg. The dose of 125 mg/kg resulted in significant coagulative necrosis of liver cells, sinusoidal enlargement, and severe inflammatory cell infiltration. Severe coagulative necrosis of the epithelial cells lining the renal tubules, and glomerular atrophy were all observed. Immunohistochemistry for GFAP in brain tissue showed a high positive result. We concluded that high doses of ciprofloxacin caused obvious biochemical and histological abnormalities in the liver and kidneys, cholinesterase inhibition in response to kidney and liver injuries, and increased glial fibrillary acidic protein (GFAP) expression in the brain.

Key words. Ciprofloxacin, biochemical, histological, liver, kidneys, GFAP.

Introduction.

Ciprofloxacin is one of the fluorinated quinolone derivatives it is a primary metabolite of enrofloxacin [1]. Ciprofloxacin is characterized by its broad spectrum and is used against a large number of negative and positive bacteria, it is also used in the treatment of most bacterial infections in chickens as well as in animals [2]. The most important of these infections in the urinary system are those caused by *Escherichia coli* (*E-coli*) and infections of the respiratory system, bones, joints, and skin [3]. The pharmacokinetics of ciprofloxacin, which was studied in Laboratory animals are significantly different from what is observed in humans and animals, and the reason, is due to the difference in the physiological and biochemical nature of each group [4]. The distribution of ciprofloxacin in the target organs is at a higher concentration than in the rest of the organs, as its concentration in the liver, kidneys, and bones is relatively high [5]. Given Chickens ciprofloxacin at a dose of 10 mg/kg for 5 consecutive days recorded levels of 1.6 mg/kg in the kidney and 0.18 mg/kg in the liver [6]. Ciprofloxacin is excreted through the kidneys by glomerular filtration and tubular secretion [7].

Differences in the functions of liver enzymes occur in 2-3% of patients who take quinolones, in addition to differences in the function of the liver itself in 0.3-0.9% of patients. High doses of it cause a significant decrease in enzyme activity. Alkaline phosphatase in the blood plasma of rats [8]. There is few information on the effect of using the drug in high doses in poultry. Ciprofloxacin has a genitourinary side effect that appeared in patients taking treatment with ciprofloxacin, and the epidemic of loss of kidney function was 3-7 days after treatment. Treatment in some patients over the age of 50 [9]. Studies have shown that ciprofloxacin is related to the appearance of hematuria and the formation of crystals in the basal urine of laboratory animals [10]. Rare cases of hematuria, interstitial nephritis, and acute kidney failure have also been recorded, as the kidney usually returns to its function several weeks after stopping treatment. [11]

In this study, we sought to know the pathological toxicological effect of ciprofloxacin on the liver and kidneys of chickens, in terms of pathological and histological changes, as well as measuring the level of the ALT and AST enzymes. To determine the extent to which liver function is affected, as well as measuring the level of Ca and Mg, and percentage of cholinesterase inhibition and GFAP # in relation to the damage to the kidneys and liver.

Materials and Methods.

Animals: This experiment used chicks old 2-3 week that were raised in the animal house and fed with concentrated feed throughout the experiment, the animals were put in standard condition in dark and light 12/12 hr [12].

Ethical approval: This study received ethical approval from the College of Science, Chemistry Department, University of Mosul.

Drugs: Ciprofloxacin was used as powder obtained from the General Company for Pharmaceuticals and Medical Supplies, pioneer-Iraq. It was dissolved in distilled water.

Experimental design.

Acute Experiment:

The chicks in this experiment were randomly divided into three groups, each group consisting of 6 chicks.

- The first group was considered a control group was given distilled water only.
- The second group was given ciprofloxacin at a dose of 250 mg/kg.
- The third group of 500 mg/kg, all doses given as single i.p dose. After 24 hours had passed since the start of giving the treatment, the chicks were sacrifice by cutting the jugular vein for the purpose of collecting blood and separating the serum.

Sub chronic Experiment.

The study involved splitting the chicks into two groups with each group comprising six chicks:

- The first group considered a control given only distilled water.
- The second group was given ciprofloxacin on a daily dose of 125 mg/kg i.p.

The treatment lasted for two weeks. Following the completion of administering the medication the young birds were euthanized by severing the vein to gather blood and organs (kidney, liver and brain) for examination. The organs were then preserved in a buffered formalin solution to prepare sections using the method to investigate any histopathological alterations [13].

Histopathological Method

The histopathological technique includes extracting liver and kidney tissue samples from both the treated and control groups, followed by preserving them with formalin. These samples are then sliced thinly using a microtome and dyed with stains, of hematoxylin and eosin. Afterward the slices are scrutinized under a microscope to evaluate any alterations [14].

GFAP Measurement in the Brain Using Immunohistochemistry

This procedure involves collecting brain tissue samples from the groups that received treatment and those, in the control group. The samples are preserved using formalin. Then sliced into sections, with a microtome. These sections undergo preparation through deparaffinization and antigen retrieval. Primary antibodies targeting GFAP are applied to the sections followed by the introduction of antibodies attached to an enzyme or fluorescent dye. After a period of incubation, the sections are. The presence and distribution of GFAP are assessed using either a microscope or a fluorescence microscope.

Kits for measuring parameter

- ALT (Alanine aminotransferase) and AST (Aspartate aminotransferase) Kits from Elabscience American Company.
- Calcium and Magnesium, Biolabo France company kits.
- Cholinesterase was measured using a modified electrometric method was used to measure modified cholinesterase [12].

Statistical analysis:

The findings were examined utilizing the SPSS software, ANOVA test, for analysis of variance and subsequently the results underwent, LSD testing. The outcomes were assessed with a t-test, $p \leq 0.05$.

Results.

The data presented in Table 1, recorded statistical analysis of the biochemical parameters individually. ALT Levels, a significant increase is observed in both treatment groups compared to the control. AST Levels also show a significant increase with ciprofloxacin treatment, particularly at the higher dose.

Mg (Magnesium) Levels significantly increase in both ciprofloxacin-treated groups compared to control, with the highest increase in the 500 mg/kg group. Ca (Calcium) Levels show a significant rise in both treatment groups.

Table 1. *Biochemical parameters concentrations in blood of chicks treated with ciprofloxacin.*

Groups	ALT u/l	AST u/l	Mg µg/dl	Ca µg/dl
Control	12±0.5	18±0.2	6.4±0.1	4.7±0.5
Ciprofloxacin 250 mg\kg	16±0.5	25±0.3	8.7±0.3	9.97±0.1*
Ciprofloxacin 500 mg\kg	35±0.3*	30±0.7*	10.19±0.2*	10.18±0.2*
Values represent the mean ± standard error for six chicks/group *The values are significantly different from the control group at the probability level p≤0.0 5.				

Table 2. *Biochemical concentrations in the blood serum of chickens treated with a dose of 125 mg/kg for two weeks.*

Groups	ALT u/l	AST u/l	Mg µg/dl	Ca µg/dl
Control	11.1±0.5	15±1.2	7.5±2.5	5.5±0.6
Ciprofloxacin 125 mg\kg	19.8±0.2*	18±0.3*	12.7±3.1*	9.5±5.1*
Values represent the mean ± standard error for six chicks/group *The values are significantly different from the control group at the probability level p≤0.0 5.				

Table 3. *Values of inhibition of acetylcholine esterase in a dose of 250 and 500 mg/kg of ciprofloxacin.*

Groups	Inhibition of Acetyl choline esterase\serum	Inhibition of Acetyl choline esterase\brain
Control	1.6 ± 0.02	0.37±0.06
Ciprofloxacin 250 mg\kg	1.55±0.1	0.19 ±0.08*
Ciprofloxacin 500 mg\kg	1.5±0.08	0.20 ±0.1 *
Values represent the mean ± standard error for six chicks/group *The values are significantly different from the control group at the probability level p≤0.0 5		

Table 4. *The acetylcholine esterase in serum of chicks treated with a dose of 125 mg/kg for two weeks.*

Groups	Inhibition of acetyl choline esterase
Control	1.8 ±0.06
Ciprofloxacin 125 mg\kg	0.5±0.04*

To analyse data presented in Table 2, the ALT levels show a significant increase in the ciprofloxacin-treated group compared to the control. AST levels also increase significantly with ciprofloxacin treatment, indicating possible hepatocellular damage. The rise, though less pronounced than ALT, still indicates a stress response or liver involvement. Magnesium levels are significantly higher in the ciprofloxacin-treated group. Calcium levels show a significant increase in the ciprofloxacin-treated group.

To analyse Table 3, the changes in serum acetylcholine esterase a slight decrease with ciprofloxacin treatment at both 250 mg/kg and 500 mg/kg doses compared to the control. The changes in brain acetylcholine esterase show a significant decrease in both ciprofloxacin-treated groups compared to the control.

Table 4 show the acetylcholine esterase in serum of group treated with 125 mg\kg in sub chronic study shows no significant deference in the group treated with 125 mg/kg of ciprofloxacin compared to the control group.

Histopathological Study Observations.

Acute Experiment (Figure 1):

- **Control Group (A&D)**: **Liver (A)**: Intact hepatocytes and central vein. **Kidney (D)**: Intact glomeruli and renal tubules.
- **Ciprofloxacin 250 mg/kg Group (B&E)**: **Liver (B)**: Vacuolar degeneration of hepatocytes and congestion of the central vein. **Kidney (E)**: Vacuolar degeneration of the epithelial cells lining the renal tubules.

Ciprofloxacin 500 mg/kg Group (C&F): **Liver (C)**: Vacuolar degeneration and coagulative necrosis of hepatocytes, along with proliferation of inflammatory cells. **Kidney (F)**: Severe vacuolar degeneration and coagulative necrosis of the epithelial cells lining the renal tubules. **Staining**: H&E stain, 400X magnification (Upper panel: liver; lower panel: kidney).

Sub-Chronic Experiment (Figure 2):

- **Control Group (A&C)**: **Liver (A)**: Intact hepatocytes and central vein. **Kidney (C)**: Intact glomeruli and renal tubules.
- **Ciprofloxacin 125 mg/kg Group (B&D)**: **Liver (B)**: Severe coagulative necrosis of hepatocytes, expansion of sinusoids, and severe infiltration of inflammatory cells. **Kidney (D)**: Severe coagulative necrosis of the epithelial cells lining the renal tubules, detachment of renal tubules from the basal membrane, and atrophy of glomeruli. **Staining**: H&E stain, 400X magnification (Upper panel: liver; lower panel: kidney).

Immunohistochemistry of GFAP in Brain (Figure 3):

- **Control Group (A)**: Mild positive reaction.
- **Ciprofloxacin 125 mg/kg Group (B)**: Strong positive reaction.

Discussion.

Medications, given to humans or animals in high doses, cause the body to deal with them differently, with the liver and kidneys being most effective in excreting and reducing toxic effects, leading to side effects and illnesses [3,15]. This study discovered that administering a single dosage of ciprofloxacin shows significant increase in ALT and AST levels in ciprofloxacin-treated chicks suggests hepatotoxicity induced by the antibiotic. ALT and AST are liver enzymes, and their elevated levels are indicative of liver damage or stress [16]. The dose-dependent rise, particularly marked at 500 mg/kg, indicates a correlation between ciprofloxacin dosage and liver enzyme levels. This aligns with the known side effects of ciprofloxacin, which include potential liver toxicity. The increase is more pronounced in the 500 mg/kg group, indicating a dose-dependent effect. As the growth the activity of liver enzymes shows the breakdown of liver cells in hens, but it does not provide information regarding hepatocyte function [17]. This finding differed from [8], which showed a decrease in ALT when mice were administered a dosage of 250 mg/kg body weight in the paw.

The difference is attributable to the type of animal and the biochemical makeup of each type, or the absence of damage to the mice's livers, as well as a possible difference in dose size. The significant increase in ALT and AST levels in ciprofloxacin-treated for 14 days, suggests hepatotoxic effects of the antibiotic. ALT is more sensitive to liver injury, which is reflected in the more substantial increase in its levels compared to AST. The significant elevation of these enzymes indicates liver stress or damage, which is a known side effect of ciprofloxacin [18].

Magnesium plays a role, in biochemical reactions. The rise in magnesium levels seen during ciprofloxacin treatment could be linked to kidney issues or changes in how the body absorbs and gets rid of magnesium. The increase in magnesium levels based on dosage indicates how ciprofloxacin affects the balance of magnesium in the body, which could affect cell functions and enzyme activities [19].

During the research project, it was noted that the chicks administered with ciprofloxacin showed levels of calcium

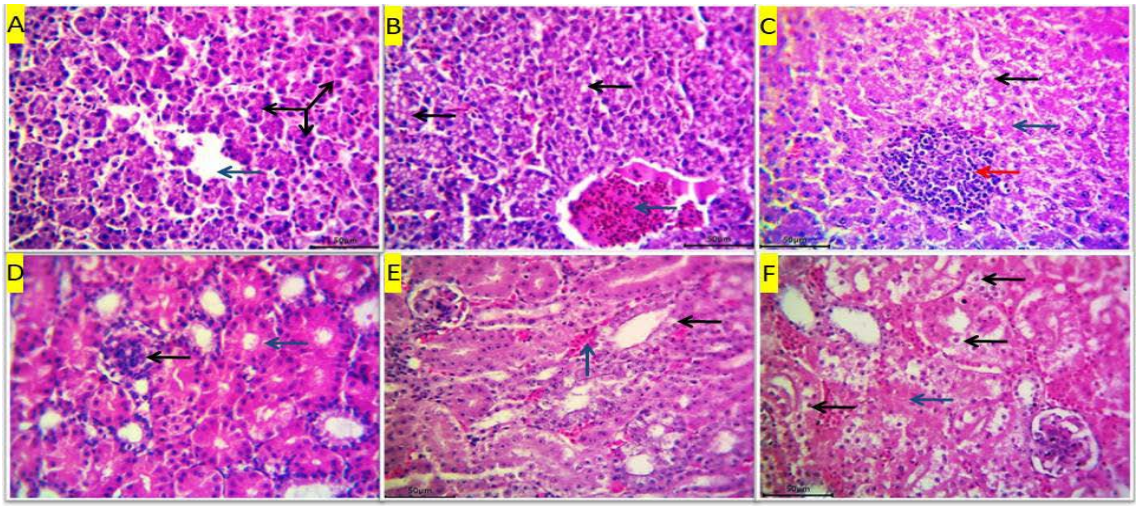

Figure 1. *Histological sections of the chick's liver and kidney in the acute experiment. (A&D): Control group; (A, Liver): intact hepatocytes (black arrow) and central vein (blue arrow); (D, kidney): intact glomeruli (black arrow), and renal tubules (blue arrow). (B&E): Ciprofloxacin 250 mg/kg group; (B, Liver): vacuolar degeneration of hepatocytes (black arrow) and congestion of central vein (blue arrow); (E, kidney): vacuolar degeneration of the epithelial cells lining renal tubules (blue arrow); (C&F): Ciprofloxacin 500 mg/kg group; (C, Liver): vacuolar degeneration (black arrow) and coagulative necrosis of hepatocytes (blue arrow) and proliferation of inflammatory cells (red arrow); (F, kidney): severe vacuolar degeneration (black arrow) and coagulative necrosis of the epithelial cells lining renal tubules (blue arrow). H&E stain, 400X. (Upper panel: liver; lower panel: kidney).*

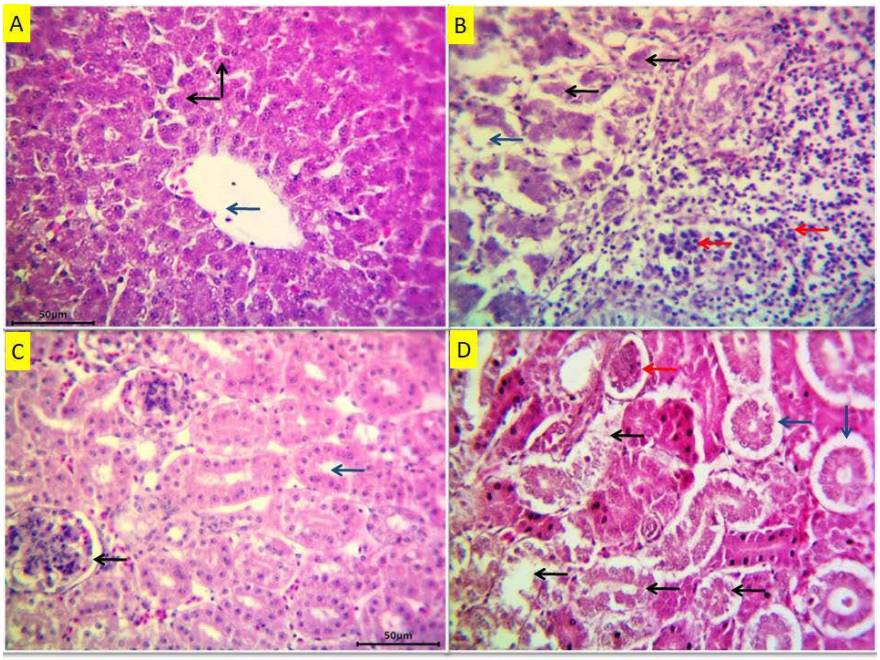

Figure 2. *Histological sections of the chick's liver and kidney in the Sub-Chronic experiment. (A&C): Control group; (A, Liver): intact hepatocytes (black arrow) and central vein (blue arrow); (B, kidney): intact glomeruli (black arrow), and renal tubules (blue arrow). (B&D): Ciprofloxacin 125 mg/kg group; (B, Liver): severe coagulative necrosis of hepatocytes (black arrow), expansion of sunusoids (blue arrow) and sever infiltration of inflammatory cells (red arrow); (D, kidney): severe coagulative necrosis of the epithelial cells lining renal tubules (black arrow), detachment of renal tubules to basal membrane (blue arrow) and atrophy of glomeruli (red arrow). H&E stain, 400X. (Upper panel: liver; lower panel: kidney).*

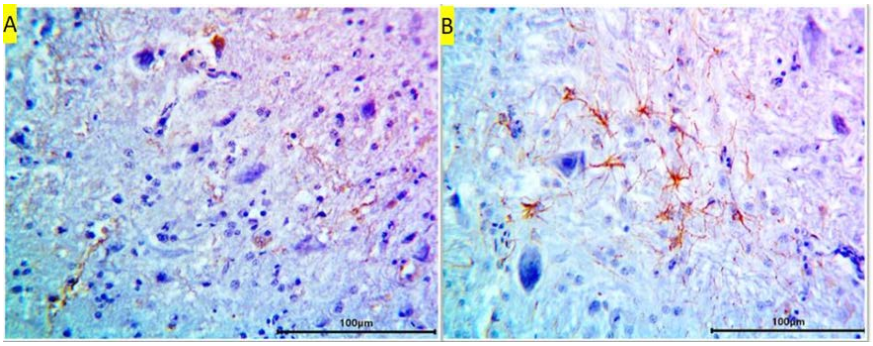

Figure 3. *Immunohistochemistry expression of the GFAP of the chick's brain from (A): control group reveals mild positive reaction. (B): Ciprofloxacin 125 mg/kg group reveals strong positive reaction. (Scale-bar=100µm), 400X.*

and magnesium in their blood when compared to the control group. Various reasons were proposed for this change including how the drug might affect the absorption or management of minerals in their bodies [20,21]. In addition to the drug could be facilitating an intake of calcium and magnesium, from their system or altering how these minerals are spread in their bloodstream [22].

The use of ciprofloxacin could affect the functioning of the kidneys. A factor, in controlling the levels of calcium and magnesium in the bloodstream. Changes, in kidney function may result in the buildup of these minerals [23].

The results demonstrate that giving chickens a 125 mg/kg dose of ciprofloxacin for two weeks leads to shifts in biochemical markers. Higher ALT and AST levels hint at liver issues while changes in magnesium and calcium levels point to disruptions in mineral balance. These findings underscore the importance of monitoring these parameters when using ciprofloxacin to safeguard the well-being of the subjects.

The result was Inhibition of the activity of acetyl cholinesterase in brain when given at a subchronic dose for two weeks. This could be due to ciprofloxacin's ability to penetrate the blood-brain barrier and its potential neurotoxic effects, which may lead to altered brain metabolism [24]. It has been demonstrated that the function of the liver and kidneys has an effective role in the level of cholinesterase in the body. As it is produced in the liver and any change in liver function results in a change in its activity, and the kidneys also play an effective role in removing it from the blood and filtering it into urine [25].

Cholinesterase is a neurotransmitter that transmits nerve impulses throughout the body [26]. It has been proven that the function of the liver and kidneys. It has an effective role in influencing cholinesterase in the body, because it is produced in the liver, and any change in the functions of the liver leads to a change in its activity, and the kidneys also play an effective role in removing it from the blood and filtering it in the urine [27].

The histopathological study in the acute experiment showed

clear changes in liver and kidney tissues as a result of ciprofloxacin treatment. In the control group, liver cells and kidney tubules were intact without any noticeable changes. When young birds were given a dose of 250 mg/kg of ciprofloxacin they showed signs of liver cell damage, like degeneration and vein congestion. Additionally vacuolar degeneration was seen in the cells lining the kidney tubes suggesting effects on liver and kidney tissues. In another group receiving 500 mg/kg of ciprofloxacin the liver cells displayed changes including vacuolar degeneration, coagulative necrosis and an increase in inflammatory cells. The kidney cells also exhibited damage with degeneration and coagulative necrosis in the tubules lining cells. These findings indicate that higher doses of ciprofloxacin lead to toxicity levels emphasizing the importance of using caution when administering this drug at high concentrations.

Furthermore, in a chronic study even a lower dose of ciprofloxacin (125 mg/kg) resulted in significant pathological changes. While liver and kidney cells remained healthy in the control group, those treated with ciprofloxacin showed necrosis, in liver cells expansion of hepatic sinusoids and substantial infiltration of inflammatory cells. In the kidneys significant tissue damage was observed, including necrosis, in the epithelial cells lining the renal tubules, detachment of renal tubules from the basement membrane and glomerular atrophy. These findings suggest that when ciprofloxacin is administered in doses for extended periods it can lead to notable harm [28].

Analysis of immunohistochemistry results in the brain revealed a positive reaction in GFAP in the group treated with ciprofloxacin (125 mg/kg) compared to a milder positive reaction in the control group. This implies that ciprofloxacin affects the expression of proteins in astrocytes within the brain potentially affecting function and central nervous system integrity. The elevated expression of GFAP in the brain suggests that ciprofloxacin at high doses induces neuroinflammation or glial activation, which could lead to neuronal damage These discoveries highlight effects of ciprofloxacin on liver, kidney and brain tissues in chicks [29] particularly with high doses or prolonged use. Further research is needed to establish dosage levels and understand the mechanisms behind these effects for ensuring safe and efficient utilization of this medication in avian species.

Conclusion.

In conclusion, our study indicates that administering toxic amounts of ciprofloxacin leads to biochemical and histological abnormalities, in both liver and kidney tissues. Identified by measuring the levels of the ALT and AST enzymes to determine the extent to which liver function is affected, as well as measuring the levels of Ca and Mg, and the percentage of cholinesterase inhibition in relation to the kidney and liver injury and, GFAP expression.

REFERENCES

1. Badawy S, Yang Y, Liu Y, et al. Toxicity induced by ciprofloxacin and enrofloxacin: oxidative stress and metabolism. Critical Reviews in Toxicology. 2021;51:754-787.

2. Millanao AR, Mora AY, Villagra NA, et al. Biological effects of quinolones: a family of broad-spectrum antimicrobial agents. Molecules. 2021;26:7153.

3. Moustafa A, Kheireldine R, Khan Z, et al. Cervical spinal osteomyelitis with epidural abscess following an Escherichia coli urinary tract infection in an immunocompetent host. Case Reports in Infectious Diseases. 2019;2019.

4. Xu N, Sun W, Zhang H, et al. Plasma and tissue kinetics of enrofloxacin and its metabolite, ciprofloxacin, in yellow catfish (Pelteobagrus fulvidraco) after a single oral administration at different temperatures. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology. 2023;266:109554.

5. Tomas A, Stilinović N, Sabo A, et al. Use of microdialysis for the assessment of fluoroquinolone pharmacokinetics in the clinical practice. European Journal of Pharmaceutical Sciences. 2019;131:230-42.

6. Al-Snafi AE. A review on chemical constituents and pharmacological activities of Coriandrum sativum. IOSR Journal of Pharmacy. 2016;6:17-42.

7. Landersdorfer CB, Kirkpatrick CM, Kinzig M, et al. Competitive inhibition of renal tubular secretion of ciprofloxacin and metabolite by probenecid. British journal of clinical pharmacology. 2010;69:167-78.

8. Van Bambeke F, Michot JM, Van Eldere J, et al. Quinolones in 2005: an update. Clinical Microbiology and infection. 2005;11:256-280.

9. Ten Doesschate T, Kuiper S, van Nieuwkoop C, et al. Fosfomycin vs ciprofloxacin as oral step-down treatment for Escherichia coli febrile urinary tract infections in women: a randomized, placebo-controlled, double-blind, multicenter trial. Clinical Infectious Diseases. 2022;75:221-9.

10. Krishnan N, Moledina DG, Perazella MA. Toxic Nephropathies of the Tubulointerstitium: Core Curriculum 2024. American Journal of Kidney Diseases. 2024.

11. Esteras R, Fox JG, Geddes CC, et al. Hematuria is associated with more severe acute tubulointerstitial nephritis. Journal of Clinical Medicine. 2020;9:2135.

12. Qasim HO, Jabber IM, Ahmed SM, et al. Aripiprazole cognitive effects on attention deficit hyperactivity disorder (ADHD) in experimental mouse model. Review of clinical pharmacology and pharmacokinetics, international edition. 2024;38:197-204.

13. Younis MA, Hamid OA, Dhaher R, et al. Characterization of the renal safety profiles of coumacines. Pharmakeftiki. 2023;35.

14. Al-Shakarchi W, Saber Y, Merkhan M, et al. Acute toxicity of coumacines: an in vivo study. Georgian Medical News. 2023;338:126-31.

15. Mostafa MS. A modified method for measurement of true acetylcholinesterase activity. Egy J Pure Appl Sci. 2017;55:33-8.

16. Garcia-Cortes M, Robles-Diaz M, Stephens C, et al. Drug induced liver injury: an update. Archives of Toxicology. 2020;94:3381-407.

17. Wang X, Xing C, Yang F, et al. Abnormal expression of liver autophagy and apoptosis-related mRNA in fatty

liver haemorrhagic syndrome and improvement function of resveratrol in laying hens. Avian Pathology. 2020;49:171-178.
18. Zhang K, Shi Y, Huang C, et al. Activation of AMP-activated protein kinase signaling pathway ameliorates steatosis in laying hen hepatocytes. Poultry science. 2021;100:100805.
19. Badawy S, Yang Y, Liu Y, et al. Toxicity induced by ciprofloxacin and enrofloxacin: oxidative stress and metabolism. Critical Reviews in Toxicology. 2021;51:754-87.
20. Fujita T, Palmieri GM. Calcium paradox disease: calcium deficiency prompting secondary hyperparathyroidism and cellular calcium overload. Journal of bone and mineral metabolism. 2000;18:109.
21. Shapses SA, Schlussel YR, Cifuentes M. That Impact Mineral Status. Handbook of Drug–Nutrient Interactions. 2004:301.
22. Chouhan N, Hait M, Roymahapatra G, et al. Complexation of antibiotics with transition metal ions: a review. ES Food & Agroforestry. 2022;8:1-1.
23. D'Alessandro C, Benedetti A, Di Paolo A, et al. Interactions between food and drugs, and nutritional status in renal patients: a narrative review. Nutrients. 2022;14:212.
24. Chesler M. Regulation and modulation of pH in the brain. Physiological reviews. 2003;83:1183-221.
25. Badawy S, Yang Y, Liu Y, et al. Toxicity induced by ciprofloxacin and enrofloxacin: oxidative stress and metabolism. Critical Reviews in Toxic. 2021;51:754-87.
26. Elizalde-Velázquez GA, Rosas-Ramírez JR, Raldua D, et al. Low concentrations of ciprofloxacin alone and in combination with paracetamol induce oxidative stress, upregulation of apoptotic-related genes, histological alterations in the liver, and genotoxicity in Danio rerio. Chemosphere. 2022;294:133667.
27. Zhang K, Shi Y, Huang C, et al. Activation of AMP-activated protein kinase signaling pathway ameliorates steatosis in laying hen hepatocytes. Poul science. 2021;100:100805.
28. Winiarska A, Filipska I, Knysak M, et al. Dietary phosphorus as a marker of mineral metabolism and progression of diabetic kidney disease. Nutrients. 2021;13:789.
29. Rajagopalan V, Venkataraman S, Rajendran DS, et al. Acetylcholinesterase biosensors for electrochemical detection of neurotoxic pesticides and acetylcholine neurotransmitter: A literature review. Enviro Rese. 2023:115724.