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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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საქართველოს სამედიცინო სიახლენი

**GEORGIAN MEDICAL NEWS**

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**GMN: Georgian Medical News** is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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.

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# COQ10 PROVIDES CARDIOPROTECTION AGAINST THE TOXIC EFFECTS OF TRASTUZUMAB AND DOXORUBICIN IN RAT MODEL

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## Abstract.

The study was aimed at investigating the effect of coenzyme Q10 (CoQ10) on reducing the cardiotoxic effects of trastuzumab (TRZ) and doxorubicin (DOX) in a rat model. The experiment duration was 20 days and involved sixteen healthy albino rats, subdivided into four groups: the negative control group, in which rats received a daily dose of a placebo vehicle; the positive control group, receiving a daily placebo vehicle and a single dose of a combination of TRZ+DOX; the third group, pretreated with CoQ10 (10 mg/kg orally daily for 10 days), followed by 10 days of placebo vehicle and a single dose of a combination of TRZ+DOX at day 10; and finally, the fourth group pretreated with 10 days of placebo vehicle then followed by CoQ10 (10 mg/kg orally daily for 10 days) and a single dose of a combination of TRZ+DOX at day 10. Histological analysis of cardiac tissues was conducted, and the serum levels of cardiac troponin and redox markers were evaluated. The results showed that there were several histopathological changes like necrosis, edema, inflammation, and others in Group 2, which did not receive CoQ10, with high serum levels of cTnI. However, a high degree of improvement was achieved in Groups 3 and 4 in which rats were administered CoQ10 either before or after TRZ and DOX administration. The improvement was expressed by the disappearance of histopathological changes and a significant decrease in the serum level of cardiac troponin compared with Group 2. The findings of the study suggest that the administration of CoQ10 could be beneficial in minimizing the cardiac side effects caused by TRZ and DOX. This study provides a basis for further research and development of CoQ10 as a potential cardioprotective agent against the cardiac side effects of chemotherapy.

**Key words.** CoQ10, Trastuzumab, Doxorubicin, Cardiac toxicity, Troponin, Oxidative stress.

## Introduction.

Chemotherapy resistance is a significant challenge in cancer treatment, as not all patients respond [1,2]. It occurs when cancer cells become less sensitive or resistant to the drugs used in chemotherapy, leading to treatment failure and disease progression [3]. Many factors contribute to chemotherapy resistance, including genetic mutations, changes in the tumor microenvironment, and the presence of cancer stem cells [4]. Researchers are working hard to develop strategies to overcome chemotherapy resistance [5]. One approach is identifying and targeting specific molecular pathways contributing to drug resistance [6]. Another strategy is combining therapies that simultaneously target multiple pathways [6]. Additionally, advances in precision medicine have led to the development of personalized treatment options based on a patient's specific genetic profile [7]. Combination chemotherapy is a treatment method that involves the use of multiple drugs to combat cancer. Trastuzumab (TRZ) and doxorubicin (DOX) are two commonly used drugs in combination chemotherapy [8]. These drugs have several side effects in addition to their ability to effectively treat cancer. One of the most severe side effects of these drugs is cardiotoxicity, which is damage to the heart muscle [9].

Trastuzumab, also known as Herceptin, is a monoclonal antibody that is used to treat breast cancer [10]. It works by targeting a protein called HER2 that is found on the surface of cancer cells. Although TRZ is generally well-tolerated by patients, it can cause cardiotoxicity in some cases [11]. Studies have shown that TRZ can cause a reduction in left ventricular ejection fraction (LVEF), which is a measure of how much blood the heart pumps out with each beat [12]. This reduction can lead to heart failure, arrhythmias, and other cardiac complications [11]. Doxorubicin, also known as Adriamycin, is a chemotherapy drug that is used to treat a variety of cancers, including breast cancer, lymphoma, and leukemia [12,13]. Like TRZ, DOX can also cause cardiotoxicity [13]. It works by interfering with the DNA of cancer cells, but it can also damage the DNA of healthy cells, including heart cells [14]. This damage can reduce LVEF, which can cause heart failure and other cardiac complications [12]. When TRZ and DOX are used together in combination chemotherapy, the risk of cardiotoxicity is even higher [8]. Patients who are receiving this treatment should be closely monitored for signs of cardiotoxicity, such as shortness of breath, swelling, and fatigue [10]. If cardiotoxicity is detected, treatment may need to be adjusted or discontinued altogether [12]. CoQ10 is a naturally occurring antioxidant that can help protect cells from damage caused by free radicals [15]. To reduce these negative side effects, many trials have been conducted over the years. This study is an extension of these efforts and CoQ10 was used as an exogenous protectant substance to counteract the harmful effects of these anti-cancer drugs on the heart.

The present study was conducted to investigate the effect of CoQ10 administration on reducing the cardiotoxicity caused by TRZ and DOX.

## Materials and Methods.

### Sources of experimental animals:

Experimental animals are often used in research studies to understand the biological mechanisms involved in various diseases and to develop new treatments. In this particular study, sixteen healthy white albino adult male rats (aged 2-3 months), kindly provided by animal house College of Veterinary Medicine, University of Mosul, were used. These rats were carefully selected to ensure they were in good health and did not

carry any pre-existing conditions that could affect the results of the study. The rats were weighed at the start of the experiment, and their weights were found to range from 260–380 g. This weight range was deemed appropriate for the study, as it ensured that the rats were of a similar size and weight, which would help to minimize any variations in the results that could be attributed to differences in the rats' size or weight. To ensure the welfare of the rats, they were placed in an animal house under standard conditions. This included providing them with appropriate food and water, maintaining a constant temperature and humidity, and ensuring that they were not exposed to any harmful substances or conditions [16,17].

**Experimental groupings and treatments:**

The study was designed to run for a period of 20 days, during which the rats were observed and monitored closely. The study involved four groups of rats (4 rats per group), each of which received different treatments throughout the experiment, as illustrated in Figure 1. Group 1 (negative control) was administered pure corn oil orally at a dose of 1 ml/kg from the first day until the end of the experiment. For Group 2 (positive control), the rats received pure corn oil orally at a dose of 1 mg/kg daily for twenty days; On the 10$^{th}$ day of the experiment, the rats were given a single dose of TRZ (10 mg/kg) and DOX (10 mg/kg) intraperitoneally. Group 3 (pretreated group) was administered Co-Q10 orally at a dose of 10 mg/kg daily from the first day until the 10th day of the experiment; On the 10th day, the rats were given a single dose of TRZ and DOX intraperitoneally. From day 10 to day 20 of the experiment, the rats were administered pure corn oil orally at a dose of 1 ml/kg. The rats in Group 4 (post-treated group) were given pure corn oil orally at a dose of 1 ml/kg from day 1 to day 10 of the experiment; On the 10$^{th}$ day, the rats were given a single dose of TRZ and DOX intraperitoneally. From day 10 to day 20, the rats were given CoQ10 orally at a dose of 10 mg/kg. The administration of pure corn oil was necessary to eliminate the effect of corn oil, which was the solvent used for CoQ10 in the experiment.

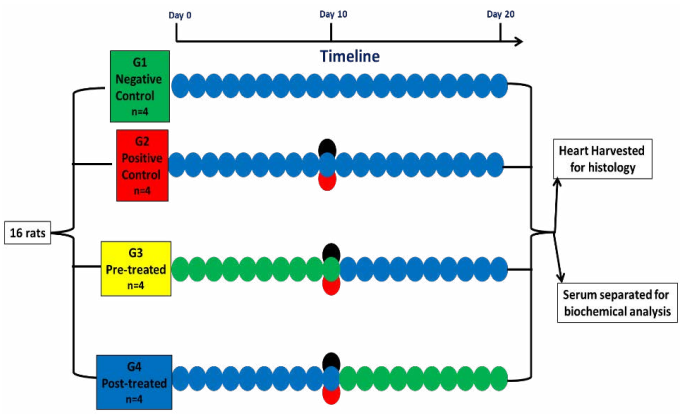


***Figure 1.*** *Schematic diagram describing workflow of the study design involving 16 rats (4 in each group). Group 1 represented the negative control group; Group 2 represented the positive control group; Group 3 represented the pre-treated group; Group 4 represented the post-treated group; Each circle represents a day in the study period; Blue circle: Pure corn oil; Green circle: CoQ10; Red circle: Trastuzumab; Black circle: Doxorubicin.*

**Sample collection, preparation, and histopathological analysis:**

Cardiac tissue specimens from rats were used to investigate the changes in the heart tissue. The first step in the preparation of the cardiac tissue samples was to fix them to preserve their structure and prevent any further changes. This was followed by dehydration, clearing, impregnation, and embedding, which involved the removal of water and its replacement with a suitable medium. The medium used was paraffin wax, which provided a solid matrix for sectioning. The next step was sectioning, which involved cutting the tissue samples into thin slices of about 4-5 microns. To facilitate this process, the samples were embedded in paraffin blocks, which helped in obtaining uniform sections. The sections were then dewaxed, rehydrated, and stained with hematoxylin and eosin stains (H&E). Hematoxylin stains the nuclei of the cells blue, while eosin stains the cytoplasm and extracellular matrix pink. The staining of the cardiac tissue sections helped identify the structural changes in the heart tissue. Finally, the sections were mounted on glass slides and examined under a microscope (18,19). The histopathological examination of the cardiac tissue samples provided valuable insights into the changes in the heart tissue, which could be used to diagnose and study various cardiac diseases. The histopathological changes were classified as scores by pathologists according to the degrees of toxicities and their pathologic descriptive severity (Table 1).

***Table 1.*** *Severity scoring system of histopathological cardiac abnormalities in rats.*

| Histopathological changes | Description | Score |
|---|---|---|
| -Cell injury<br>1-Degeneration<br>2- Necrosis | No lesions | 0 |
| -Circulatory disturbances<br>1- Edema<br>2- Congestion of blood vessels<br>3- Hemorrhage | Mild lesions | 1 |
| - Cell adaptation<br>1- Atrophy<br>2- Hyperplasia<br>3- Metaplasia | Moderate lesions | 2 |
| - Inflammation: infiltration of inflammatory cells | Severe lesions | 3 |

**Blood sample collection and biochemical analysis:**

The blood samples were collected at the end of the experiment. The rats were euthanized using ether, and the blood samples were collected directly from the retro-orbital venous plexus. After the samples were collected, the rats were sacrificed. The collected blood samples were then centrifuged at 3000 RPM to separate the serum, which was then stored at -20°C. To determine the serum level of rat cardiac troponin-I (cTn-I) [20], a chemiluminescence immunoassay analyzer (CLIA) was used along with a kit from Elabscience Biotechnology, China. The CLIA kit uses the CLIA-sandwich principle, which involves a microplate that is pre-coated with an antibody specific to rat cTn-I. This method allows for the quantitative determination

of the serum level of cTn-I with high accuracy and precision. In addition to cTn-I, serum levels of malondialdehyde (MDA) and T-AOC were also measured in the same samples using a quantitative colorimetric assay kit and a spectrophotometer (Elabscience Biotechnology, China) [18,19]. The MDA assay kit detects the level of lipid peroxidation, which is an important biomarker of oxidative stress. The T-AOC assay kit determines the total antioxidant capacity of the serum, which is crucial in evaluating the overall health status of the rats.

## Statistical analysis.

Statistical tests were used to analyze the data at the level of $p<0.05$ value and for comparison among groups. The Kruskal-Wallis test was employed to evaluate the scores of histopathological changes using the statistical package for social sciences (SPSS) program. The analysis of variance (ANOVA), on the other hand, was used to analyze the variance among the groups. The Duncan test is a post hoc test that was used to compare the means of different groups. Finally, post hoc tests were used to determine which groups are significantly different from each other after the ANOVA test was performed.

## Results.

The intensity of collagen fibers in the heart, the architecture of the tissue, endocardium endothelial cells, myocardium muscle fibers of blood vessels, and infiltration of inflammatory cells were investigated in the present study. The goal of the study was to examine the effects of TRZ and DOX on the heart tissue of rats and determine whether Co-Q10 could help alleviate the negative effects of chemotherapy on the heart. The results of the microscopy on Group 2 tissues, in which rats received TRZ and DOX only, showed several abnormalities compared with the control group (Group 1). These abnormalities included circulatory disturbances such as haemorrhage and oedema between myocardial muscle fibers and congestion of the blood vessels. Cell adaptation, such as the conversion of endothelial cells to cuboidal shapes, was also observed, as was the infiltration of inflammatory cells. Moreover, cell injuries such as hyaline degeneration and necrosis of myocardial muscle fibers were also observed in Group 2. In contrast to Group 2, the histopathological changes of rats' hearts in Groups 3 and 4, in which CoQ10 was administered either pre-or post-TRZ and DOX, revealed high degrees of improvement of heart tissue against chemotherapy (TRZ+DOX). These results suggest that CoQ10 may be a promising candidate for reducing the negative effects of chemotherapy on the heart tissue (Table 2 and Figure 2).

The comparison indicated that Group 2 had a higher level of measured parameters compared to the other groups, and this difference was significant at a value of $p<0.05$. Moreover, the results indicated that the administration of CoQ10 had a positive impact on the experimental animals. In groups where CoQ10 was given either pre-or post-TRZ and DOX, high degrees of improvement were observed, which is a promising result that supports the use of CoQ10 as a therapeutic agent. Interestingly, the highest degree of improvement was observed in Group 3, where the rats were administered CoQ10 before TRZ and DOX. This suggests that the timing of the CoQ10 administration might play a crucial role in its effectiveness (Figure 3).

***Table 2.*** *Histopathological results of the studied parameters.*

| **Features** | G2 (TRZ+DOX) | **Sequential CoQ10 treatment** | |
|---|---|---|---|
| | | G3 CoQ10 pretreated+ (TRZ+Dox) | G4 CoQ10 posttreatment (TRZ+Dox) |
| General appearance | Haemorrhage and oedema | mild changes | mild changes |
| Endothelial cells | Conversion to cuboidal shape | Normal | Normal |
| Blood vessels | Congestion with inflammatory cell infiltration | Intact with no infiltration | Intact with no infiltration |
| Myocardium | Hyaline degeneration and necrosis | Mild haemorrhage and no necrosis | Mild haemorrhage and no necrosis |

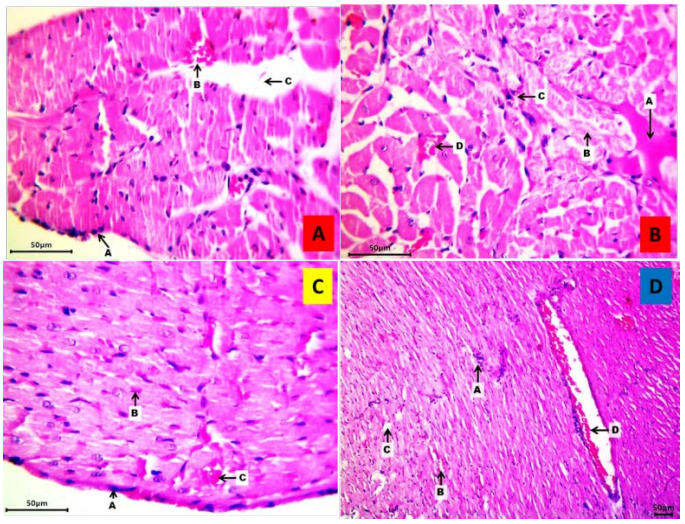


***Figure 2.*** *CoQ10 restored near-normal tissue architectural features of rats' cardiac histology following exposure to TRZ+DOX. A: Control group (400x); B: TRZ+DOX-treated group (400x); C: CoQ10 pre-treated+TRZ+DOX group (400x); D: Co-Q10 post-treated+TRZ+DOX group (100x); The tissues were stained with eosin-hematoxylin stain.*

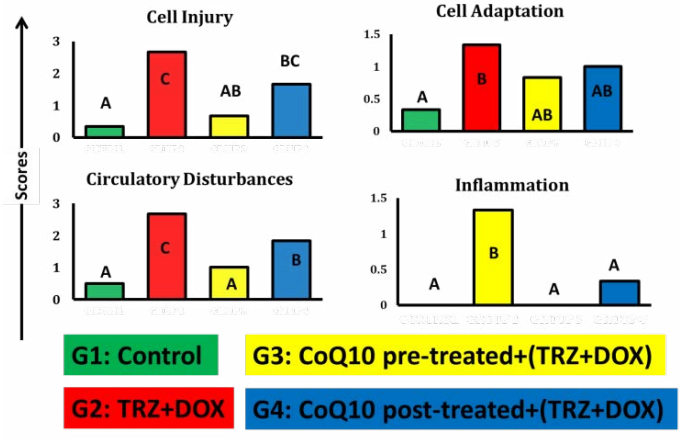


***Figure 3.*** *Histological scores of measured parameters of the studied group. The same letters represent non-significant differences in Chi-square. Different letters represent significant differences in Chi-square.*

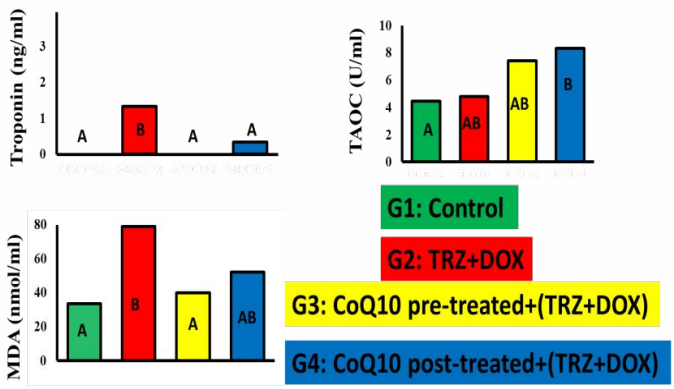


***Figure 4.*** *Biochemical analysis of the studied groups at the end of the study after 20 days. The same letters represent non-significant differences in Chi-square; Different letters represent significant differences in Chi-square; MDA: Malondialdehyde; TAOC: Total antioxidant capacity.*

The results (Figure 4) revealed that Group 2 showed a significant effect for both cTnI and MDA as compared to the other groups. The statistical analysis of T-AOC was significant in Group 1 as compared to Group 4, with little variation between Group 2 and Group 3. Cardiac troponin (cTnI) is a biomarker that is used to detect heart damage. The results of this study show that Group 2 had significant results for cTnI as compared to the other groups. This suggests that Group 2 may have experienced some sort of cardiac damage or injury. Malondialdehyde (MDA) is a biomarker that is used to detect oxidative stress. The results of this study show that Group 2 had significant results for MDA as compared to Groups 1 and 3, with little variation in Group 4. This indicates that Group 2 may have experienced more oxidative stress than the other groups. Total antioxidant capacity (T-AOC) is a biomarker that is used to detect the overall antioxidant capacity of an individual. The results of this study show that Group 1 had significant results for T-AOC as compared to Group 4, with little variation between Groups 2 and 3. This suggests that Group 1 might have had a higher antioxidant capacity compared to Group 4, which may have helped in protecting against oxidative stress.

## Discussion.

The study examined the heart tissue of rats that were treated with TRZ+DOX, and the results were revealing. Under a light microscope, various histopathological structures were observed. Group 2, which consisted of rats that were treated with TRZ+DOX, showed numerous abnormal elements, including cellular necrosis and degeneration, oedema, haemorrhage and congestion of blood vessels, endothelial metaplasia, hyperplasia, atrophy, and infiltration of inflammatory cells from blood vessels to the cardiac interstitial tissue. These findings suggest that TRZ+DOX has cardiotoxic effects on rats, which can lead to a range of pathological conditions in the heart tissue. However, the study also found that Group 3 (CoQ10 pretreated with TRZ and DOX) and Group 4 (CoQ10 post-treated with TRZ and DOX) showed a high degree of improvement compared to Group 2, which did not receive CoQ10. The improvement observed in Groups 3 and 4 demonstrated the beneficial effect of CoQ10, which counteracted the cardiotoxic effects of TRZ and DOX. CoQ10, a potent antioxidant, has been shown to have a protective effect on the heart tissue by preventing oxidative stress and reducing inflammation.

Several studies have been conducted to investigate the effects of CoQ10 on the heart, and many of them have demonstrated its cardioprotective properties [21-25]. In one study, rats were given CoQ10 before being subjected to ischemia-reperfusion injury, a condition that occurs when blood flow to the heart is temporarily blocked and then restored. The results showed that CoQ10 was able to reduce the size of the infarct (the area of tissue damage caused by a lack of oxygen) and improve heart function [26]. Another study found that CoQ10 supplementation was able to improve cardiac function in rats with heart failure [27]. The rats were given CoQ10 for weeks, and the results showed that it was able to improve left ventricular function and reduce oxidative stress in the heart. In addition to its cardioprotective effects, CoQ10 has also been shown to have other health benefits. It has been found to have antioxidant properties, which can help protect cells from damage caused by free radicals [28]. It has also been shown to have anti-inflammatory properties, which can help reduce inflammation in the body [29]. While these studies have been conducted in rats, there is evidence to suggest that CoQ10 may also have cardioprotective effects in humans [21-25]. Several clinical trials have been conducted to investigate the effects of CoQ10 on various cardiovascular conditions, including heart failure and hypertension, and many of them have reported positive results.

Trastuzumab and doxorubicin are both commonly used chemotherapy drugs that have been shown to cause cardiotoxicity or damage to the heart muscle. While these drugs can be highly effective in treating cancer, they can also have serious side effects on the cardiovascular system, including heart failure. Fortunately, there is growing evidence to suggest that CoQ10 may be able to protect against these cardiotoxic effects. In animal studies, researchers found that supplementation with CoQ10 was able to significantly reduce the cardiotoxic effects of both trastuzumab and doxorubicin [30-32]. CoQ10 supplementation was able to improve cardiac function and reduce oxidative stress and inflammation in the heart muscle [30-32]. This suggests that CoQ10 may be a promising option for protecting the heart during cancer treatment, particularly for patients who are at high risk for cardiotoxicity. In addition to its potential cardioprotective effects during cancer treatment, CoQ10 has also been shown to have numerous other health benefits. It has been shown to improve energy levels, boost immune function, and even improve symptoms of chronic fatigue syndrome [32].

Studies have shown that supplementation with CoQ10 can reduce oxidative stress caused by chemotherapy drugs like trastuzumab and doxorubicin. In a study conducted on rats, it was found that CoQ10 supplementation reduced oxidative stress levels in rats treated with these drugs [33]. Moreover, other studies have also demonstrated the effectiveness of CoQ10 in reducing oxidative stress in human patients undergoing chemotherapy. One study found that CoQ10 supplementation reduced oxidative stress markers in breast cancer patients undergoing chemotherapy [34,35]. In addition to reducing oxidative stress, CoQ10 has other potential benefits for cancer patients. It has been shown to improve heart function, which

can be important for cancer patients who may be at risk of heart damage from chemotherapy drugs [36].

The present study, which was conducted on rats exposed to Trastuzumab and doxorubicin found that CoQ10 supplementation reduced the levels of troponin in the rats. Troponin is a protein that is released by damaged heart muscle cells, and high levels of troponin in the blood are a sign of heart damage. Therefore, the reduction in troponin levels observed in the rats that were given CoQ10 indicates that CoQ10 was able to protect the heart from damage caused by Trastuzumab and doxorubicin. This finding is significant because it suggests that CoQ10 could be used to protect cancer patients' hearts from damage caused by chemotherapy drugs. This could improve the quality of life for cancer patients by reducing the risk of heart failure and other heart-related complications. Additionally, CoQ10 is a natural compound that is generally safe and well-tolerated, making it an attractive option for cancer patients who are already undergoing chemotherapy. CoQ10 has been shown to reduce MDA levels by neutralizing free radicals and preventing lipid peroxidation. Several studies have confirmed that supplementation with CoQ10 can significantly reduce MDA levels in both healthy individuals and those with various medical conditions. Furthermore, CoQ10 also increases antioxidant activity in the body. Antioxidants are substances that protect cells from damage caused by free radicals. Studies have shown that supplementation with CoQ10 can significantly increase antioxidant activities in both healthy individuals and those with various medical conditions.

In this study, the researchers aimed at minimizing the cardiotoxic effects of TRZ+DOX, a combination of drugs that can lead to heart damage, by administering CoQ10 to rats. The antioxidant capacity of the rats' biological system was raised in two ways. The first method was by administering CoQ10 before the rats received TRZ+DOX, represented by Group 3. The second was by administering CoQ10 with TRZ and DOX, represented by Group 4. The results of the study showed a high degree of improvement in cardiotoxicity in both groups, as observed through microscopical examination of cardiac tissues of rats that received CoQ10. The histological examinations revealed reduced cell necrosis, oedema, congestion, and haemorrhage, as well as less inflammation and cellular adaptation. However, the results of Group 3 were better than those of Group 4. The findings suggest that the administration of CoQ10 before giving TRZ+DOX was more effective in minimizing cardiotoxic effects. In general, this study highlights the potential of CoQ10 as a protective agent against the cardiotoxic effects of certain drug combinations, and further research may be needed to explore its potential clinical applications.

Cardiac troponin is a protein that is found in heart muscle cells and is released into the bloodstream when there is damage to these cells. It is commonly used as an indicator of cardiac cell damage resulting from cellular necrosis. In a recent study, rats were treated with TRZ+DOX, a combination of drugs known to have cardiotoxic effects. In Group 2, which received the drugs without any protection, a high serum level of cTnI was observed, indicating cardiac cell damage. However, in Groups 3 and 4, where CoQ10 was used as a protectant against the cardiotoxic effects of the drugs, there was a significant decline in cTnI serum levels compared to Group 2. Group 3, which was pretreated with CoQ10 before receiving TRZ+DOX, showed better results than Group 4, which was post-treated with CoQ10. These findings suggest that CoQ10 may be an effective protectant against the cardiotoxic effects of TRZ+DOX, with pretreatment being more effective than post-treatment. Further research is needed to better understand the mechanisms behind this protective effect and to determine the optimal dosing regimen for CoQ10 in this context.

In a recent study, cardiomyocyte necrosis was found to be associated with a high serum level of MDA in Group 2, which received only TRZ+DOX without CoQ10. However, the administration of CoQ10 resulted in a decline in MDA levels in both Group 3 and Group 4. Notably, Group 3 demonstrated a greater reduction in MDA levels compared to Group 4, indicating that CoQ10 may play a significant role in reducing MDA levels and minimizing cardiotoxicity. Previous research has also suggested that CoQ10 may be effective in reducing MDA levels, and these findings further support the potential benefits of CoQ10 in mitigating cellular damage and promoting overall health and wellness. In general, these findings highlight the importance of identifying reliable markers for cellular damage and exploring potential interventions, such as CoQ10, for minimizing the negative impacts of cellular injury [15-18].

Total antioxidant capacity (T-AOC) is an important biological system that plays a vital role in balancing the production of reactive oxygen species (ROS) and neutralizing the oxidative reactions that can cause tissue damage. It is well known that anti-cancer drugs can significantly reduce the serum level of T-AOC, which is a serious concern for cancer patients undergoing chemotherapy. However, the body has a natural ability to counter this effect by attempting to increase its endogenous antioxidant capacity. This adaptive response was observed in a study where rats were treated with TRZ+DOX, a combination of anticancer drugs, and the serum level of T-AOC was assessed. The results showed that the rats treated with TRZ+DOX alone (Group 2) showed a slight increase in T-AOC levels, which is consistent with the hypothesis of cell adaptation to cell damage mechanisms. Interestingly, the study also found that administering CoQ10, a potent antioxidant, either before or after TRZ+DOX treatment resulted in a significant increase in the serum level of T-AOC. This was observed in Groups 3 and 4, where CoQ10 was administered to rats either before or after TRZ+DOX treatment. Moreover, the results showed that the T-AOC level was higher in Group 4 than in Group 3, indicating that administering CoQ10 after the TRZ+DOX treatment was more effective than administering it before. These findings are significant as they suggest that administering CoQ10 can help cancer patients undergoing chemotherapy maintain their T-AOC levels and reduce the risk of tissue damage. This is particularly important since chemotherapy-induced tissue damage can cause serious long-term health problems for cancer survivors. Therefore, the use of CoQ10 as an adjuvant therapy in cancer treatment has the potential to enhance the effectiveness of chemotherapy while reducing its adverse effects. Therefore, T-AOC is an essential biological system that plays a critical role

in maintaining cellular health, and administering CoQ10 can help cancer patients undergoing chemotherapy maintain their T-AOC levels, which is crucial for their recovery [25-32].

CoQ10, also known as ubiquinone, is a coenzyme found in every cell of the human body. It plays a crucial role in energy production and is particularly important for the proper functioning of the heart. Recent research has shown that CoQ10 has an important role in the prevention and treatment of some heart problems. This effect is obtained through its free radical scavenging and vasodilator effect, which might help in the previous conditions. CoQ10 can protect cells from oxidative damage by neutralizing harmful free radicals that can cause damage to the heart. It also inhibits LDL oxidation, which reduces the progression of atherosclerosis [37]. In addition to its antioxidant properties, CoQ10 has anti-inflammatory effects that can be beneficial to patients with heart failure and coronary artery disease [30]. It decreases proinflammatory cytokines and decreases blood viscosity, which improves patients' conditions [34]. This coenzyme also improves ischemia by reperfusion and revascularization of the injured coronary arteries. Research on CoQ10 and its effects on cardiovascular diseases is ongoing, and there is growing evidence to support its use in therapy. Several studies have shown that CoQ10 supplementation can improve heart function and reduce symptoms in patients with heart disease. Other studies have suggested that CoQ10 may be effective in preventing heart disease in individuals who are at high risk [36].

## Conclusion.

CoQ10 is an important coenzyme with a crucial role in the prevention and treatment of heart problems. Its antioxidant and anti-inflammatory effects, along with its ability to improve blood flow and reduce blood viscosity, make it a promising therapy for cardiovascular diseases. Further research is needed to fully understand the potential benefits of CoQ10 in the treatment of heart disease, but the evidence so far is encouraging.


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