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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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

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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HISTOLOGICAL EFFECTS OF CO ENZYME Q10 ON DOXORUBICIN-INDUCED DEFICITS OF CARDIOPULMONARY AXIS IN WHITE ALBINO RATS

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Abstract.

Doxorubicin is the common chemotherapeutic agent that has been harnessed for the treatment of various types of malignancy including the treatment of soft tissue and osteosarcoma and cancers of the vital organs like breast, ovary, bladder, and thyroid. It is also used to treat leukaemia and lymphoma, however, this is an obstacle because of their prominent side effects including cardiotoxicity and lung fibrosis, we do aim to determine the role of CoQ10 as an antioxidant on the impeding the deleterious impacts of doxorubicin on tissue degenerative effects. To do so, 27 rats were subdivided into 3 groups of 9 each; CoQ10 exposed group, Doxorubicin exposed group, and CoQ10 plus Doxorubicin group. At the end of the study, the animals were sacrificed and lungs with hearts were harvested, and slides were prepared for examination under a microscope. The results indicated that doxorubicin induced abnormal cellular structure resulting in damaging cellular structures of the lung and heart while CoQ10 impeded these damaging effects and nearly restoring normal tissue structure. As a result, CoQ10 will maintain normal tissue of the lung and heart.

Key words. Doxorubicin, CoQ10, histopathology, lung, cardiotoxicity.

Introduction.

Doxorubicin is a commonly used anticancer drug used for the treatment of haematological and solid tumours [1,2]. The efficacy of doxorubicin is drawbacked by its side effects on the vital organs, including liver, kidney, heart, respiratory, testis, and haematological toxicity [3,4]. The mechanism by which doxorubicin-induced toxicity is lured by cellular apoptosis, DNA/RNA damage, oxidative stress and inflammatory reactions [2,5]. Therefore, medications or products with antioxidant activity will potentially provide cytoprotective effects against doxorubicin [6-8]. Many natural remedies have been suggested as a candidate product that could be used to mitigate the cytotoxicity of anticancer, including Lycopene [9], Curcumin [10], chalcone [11], Catechin [12], Coumaric acid [13], Rutin [14], Caffeic acid phenylmethyl ester [15], and Melatonin [16].

Cardiac side effects of doxorubicin are reported to be common, especially congestive heart failure and the risk of toxicity is higher when doxorubicin is co-administered with another anticancer agent [17]. The mode of toxicity principally related to redox imbalances resulted from reactive oxygen species generation [18-20]. The cardiac tissue is highly vulnerable to free radical toxicity generated by doxorubicin [21,22]. These oxygen species particularly damage DNA, protein, lipid, and other important biomolecules [22,23]. The highly sensitive part of cardiac cell structures are mainly mitochondria, nucleus, myofibrils, and sarcoplasmic reticulum [24-27], these cardiotoxicities might be permanent resulting in necrosis and cellular apoptosis [28]. Moreover, doxorubicin has been also reported to induce lung toxicity [29]. Doxorubicin is characterized by the accumulation in lung tissues thereby increasing the susceptibility of lung tissue to damage compared to other tissues [30]. The mechanism seems similar to cardiotoxicity involving lipoid peroxidation and oxidative stress mechanism [31,32], These pulmonary deficits are more apparent when doxorubicin is used in combination with other anticancer therapy [33,34].

CoQ10 is an intrinsic cofactor that is present in all cellular mitochondria and involved in oxidative stress during metabolic activity to tackle the reactive oxygen species maintaining intracellular equilibrium [35]. The present study aimed to investigate the protective role of CoQ10 in protecting the tissue of the lung and heart from doxorubicin-induced oxidative stress using rats as a model via histological study of heart and lung tissue.

Materials and Methods.

Materials: The CoQ10 (manufactured by 21st Century®, USA) was prepared by overnight mixing CoQ10 with normal saline (0.9% NaCl) mixed with Tween-80 1% (v/v). The doxorubicin (manufactured by Saba-Turky) was ready to use.

Purchasing and acclimatization of animals study:

The animal house in the College of Veterinary Medicine has kindly provided 27 rats (Male rats, aged 8-10 weeks, weighing 225-275 g) to complete this study. The study was ethically approved by the Scientific and ethical committee in the university (Approval Letter UM.VET.2021.33). The animals were treated according to standard conditions of temperature, light-dark cycle, and free access to water and food [36,37].

Animals groupings:

The rats were divided into 3 groups (9 each) (Figure 1):

Group 1: treated by oral CoQ10 (10mg/day for 17 days) with day 13 given IP dose normal saline.

Group 2: treated by oral normal saline for 17 days with day 13 given IP dose Dox (15mg/kg).

Group 3: treated by oral CoQ10 (10mg/day for 17 days) with day 13 given IP dose Dox (15mg/kg).

Preparation of histological tissues:

To prepare microscopic slides of lung and heart: At the end of the study the rats were euthanased and killed by cervical spine dislocation, and the lung and heart were harvested for slide preparation. The organs were washed with normal saline twice and then kept in 10% formalin overnight. The next day, the fixed organ was washed to remove the formalin solution [38,39].

The tissue is then dehydrated by a series of alcohol-increasing concentrations. The tissue was placed in cassettes for preparation of tissue block. The cassettes were then paraffin-embedded, and tissue blocks then underwent cutting by microtome to the desired slides which were then stacked into slides. Before staining slides with hematoxylin and eosin, the paraffin was

removed by xylene. The prepared slides were then examined under a light microscope for assessment.

Results.

The diagnosis of the heart slides under the light microscope has revealed that the group of rats exposed to CoQ10 has shown intact tissue structure of normal myocardial muscles and muscle fibres (Figure 2). The heart slides of rats exposed to doxorubicin have shown damaging of the normal tissue architecture resulting in hyaline degeneration, and necrosis of myocardial muscles with characteristic oedema at intracellular area (Figure 3). The heart slides of rats exposed to a combination of doxorubicin and CoQ10 revealed that the heart architectural structures were nearly intact represented by intact myocardial muscles with congestion of blood vessels and mild edema (Figure 4).

The diagnosis of the lung slides under the light microscope has revealed that the group of rats exposed to CoQ10 has shown intact tissue structure of lung represented by bronchioles, alveoli, and blood vessels (Figure 5). The lung slides of rats exposed to doxorubicin have shown degradation of the normal lung architecture resulting in infiltration of inflammatory cells surrounding bronchioles and alveoli, emphysema, atelectasis, tissue necrosis, and loss of epithelium of bronchiole (Figure 6). The lung slides of rats exposed to a combination of doxorubicin and CoQ10 revealed that the lung architectural structures were nearly intact represented by intact bronchioles and alveoli with mild atelectasis (Figure 7).

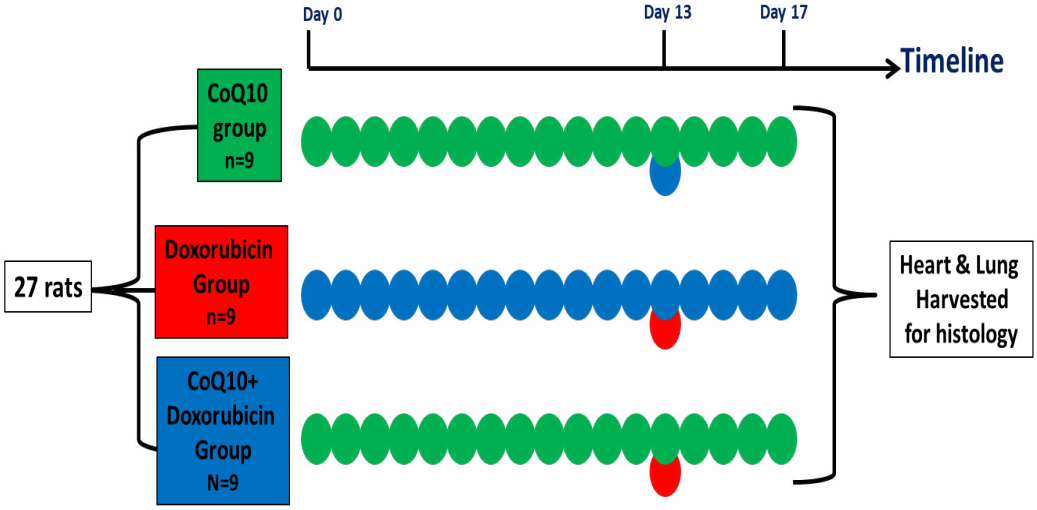

Figure 1. *A schematic diagram describing the workflow of the study design involving 27 rats (9 in each group). Group 1 represented the CoQ10 group. Group 2 represented the Dox group. Group 3 represented the CoQ10+Dox group. Each circle represent a day in the study period. Green Circle= CoQ10, Blue circle= Normal Saline, Red Circle=Dox.*

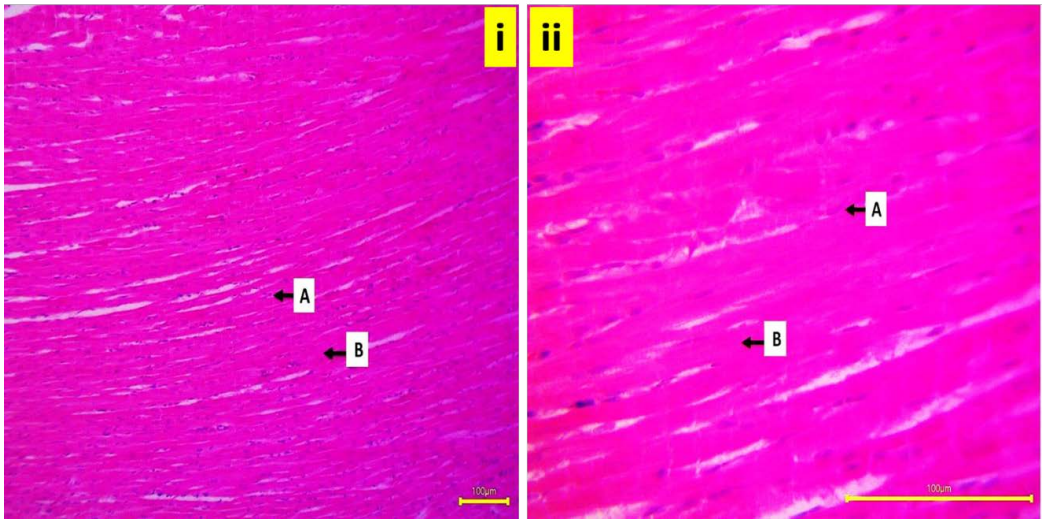

Figure 2. *A representative image for rat heart sections treated by CoQ10 showing normal structural architecture represented by myocardial muscle cells (A) and fibres (B). H&E stain, Scale bar = 100µm (i), 400µm (ii).*

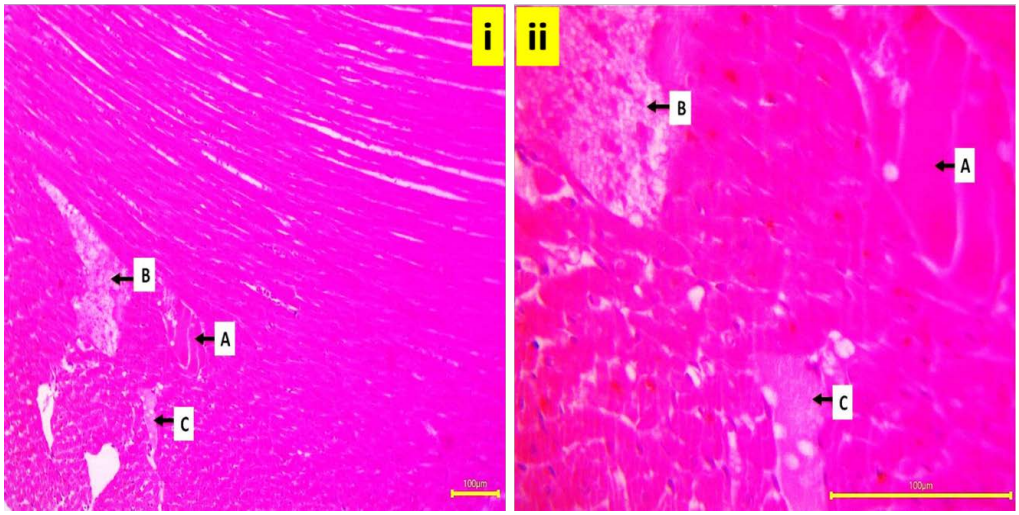

Figure 3. *A representative image for rat heart sections treated by doxorubicin showing abnormal structural architecture represented by hyaline degeneration (A) and necrosis (B) of myocardial cells and the presence of oedema (C). H&E stain, Scale bar = 100µm (i), 400µm (ii).*

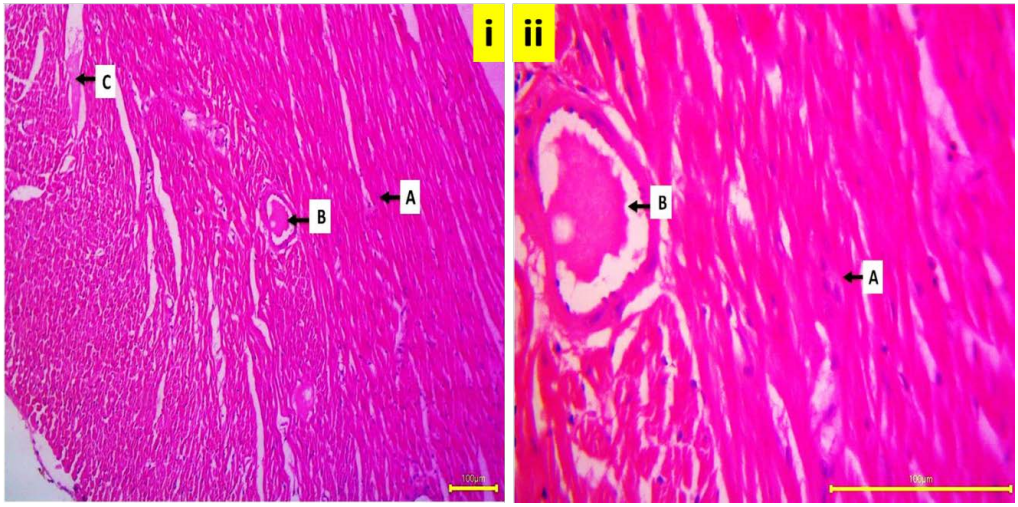

Figure 4. *A representative image for rat heart sections treated by doxorubicin+CoQ10 showing nearly normal structural architecture represented by intact myocardial muscles (A) with congestion of blood vessels (B) and mild oedema (C). H&E stain, Scale bar = 100µm (i), 400µm (ii).*

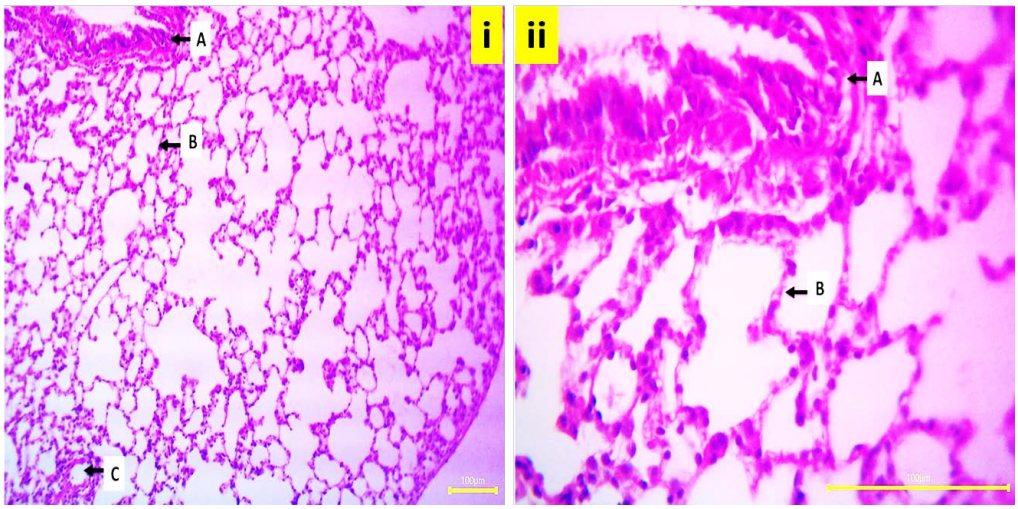

Figure 5. *A representative image for rat heart sections treated by CoQ10 showing normal structural architecture represented by bronchioles (A), alveoli (B) and blood vessels (C). H&E stain, Scale bar = 100µm (i), 400µm (ii).*

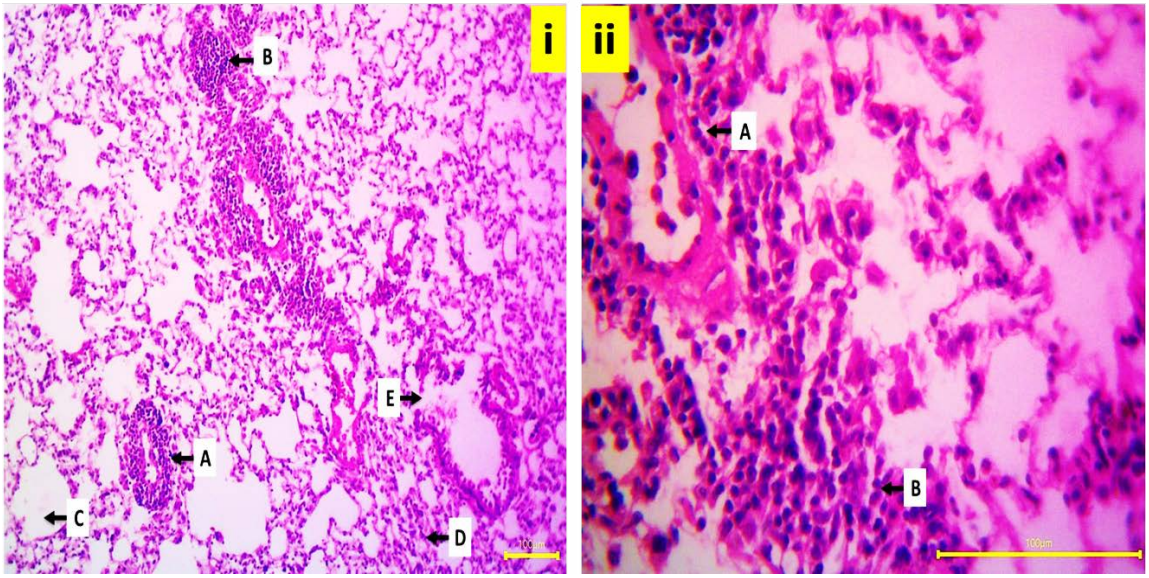

Figure 6. *A representative image for rat heart sections treated by doxorubicin showing abnormal structural architecture represented infiltration of inflammatory cells surrounding bronchioles (A) and alveoli (B), emphysema (C), atelectasis (D) and necrosis and loss of epithelium of bronchiole (E). H&E stain, Scale bar = 100μm (i), 400μm (ii).*

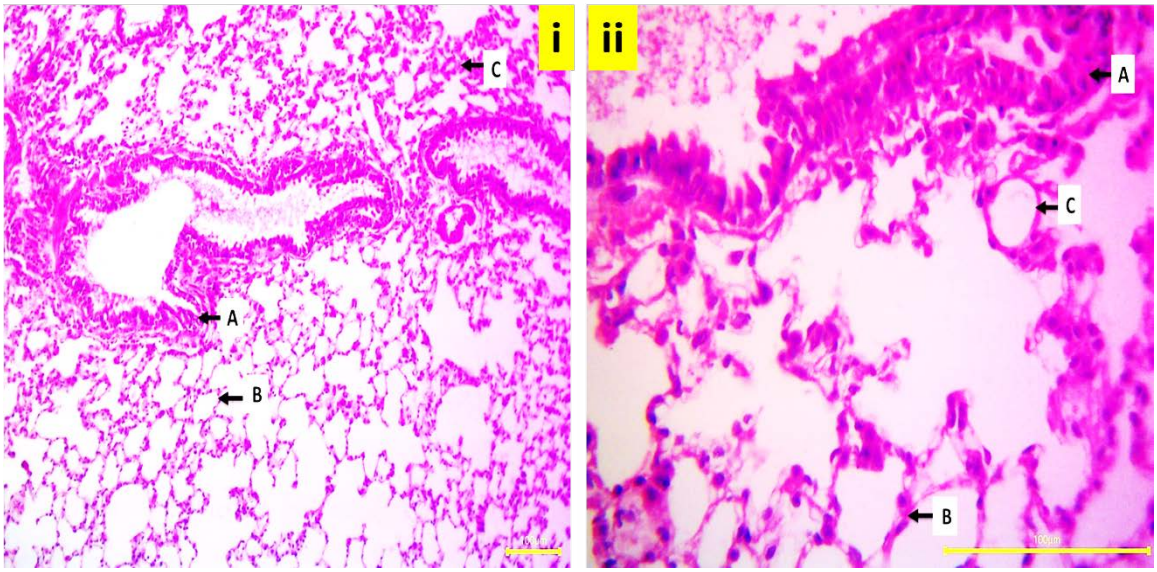

Figure 7. *A representative image for rat heart sections treated by doxorubicin+CoQ10 showing nearly normal structural architecture represented by intact bronchioles (A) and alveoli (B) with mild atelectasis (C). H&E stain, Scale bar = 100μm (i), 400μm (ii).*

Discussion.

In the present study, doxorubicin has ruined the tissue architecture of the heart represented by hyaline degeneration and myocardial necrosis with the presence of edema. Similar results were obtained in a study conducted earlier by Ichikawa et al. (2014) [3], Zhan et al. (2016) [4], and El-Sayed et al. (2016) [6], who have found that doxorubicin-induced cardiotoxicity in experimental animal models [3,4,6]. The mechanism of cardiotoxicity has been related to the induction of inflammatory reaction together with oxidative reaction and cellular apoptosis [6-10]. Moreover, antioxidant molecules have balanced these reactive oxygen species biomolecules minimizing their deleterious impact and restoring the quasi equilibrium to the milieu thereby protecting against these detrimental deficits induced by doxorubicin [1,2,6,10,15].

Regarding lung tissue, doxorubicin has been reported to have fibrotic activity against lung tissue resulting in tissue damage and apoptosis [40,41].

Recently, CoQ10 has found a clinical application due to its antioxidant and cytoprotective effects in experimental and clinical studies. Doxorubicin-induced damage has been tackled by CoQ10 through reducing cellular apoptosis, reducing oxidative reactions, and proinflammatory mediators [42,43] maintaining cellular and tissue shape and architecture [44].

Conclusion.

Doxorubicin as an anticancer drug induces cellular toxicity of normal tissue of the heart and lung resulting in tissue damage due to the capacity of the lung and heart to accumulate

doxorubicin. The deleterious impact has been attributed to redox imbalances of exposed tissue leading to organ damage. CoQ10 as an antioxidant reduces oxidative stress and improves the structural architecture of the lung and heart maintaining cellular architecture.

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