Journal of Pharmacology &Drug Development

eISSN: 2958-6801

OPEN ACCESS

Hepatoprotective Role of Zinc Gluconate against Hepatotoxicity Induced by Mitoxantrone In Rats

Taif M. Maryoosh [*1] Kasim S. Hmood [2] Raghad A. Khaleel [3] Dhilal dhiaa Nasser [4] Noor Fadhil [1]

[1] *Department of Pharmacology and Toxicology, College of Pharmacy, University of Kut, Wasit, Iraq.*

[2] *Department of Pharmaceutical Chemistry, College of Pharmacy, University of Kut, Wasit, Iraq.*

[3] *University of Al-Iraqia College of Medicine Department of Pharmacology, Baghdad, Iraq*

[4] *Department of Aesthetic and Laser Techniques, College of Health and Medical Techniques, University of Kut,Wasit.*

***Corresponding author**

Received 1 Dec , Accepted 6 Feb , Published 1 Jun

ABSTRACT

Objective: Mitoxantrone is a chemotherapeutic very effective against a variety of human malignancies. Administration of Mitoxantrone is associated with hepatotoxicity. It's impossible to find an effective therapeutic option against chemotherapy-induced liver injury. Zinc is considered a mineral that is required for cell division as well as the creation of DNA and proteins; moreover, such mineral has a protective effect in liver illness. This study aimed to determine the role of zinc gluconate as a hepatoprotective agent in Mitoxantroneinduced hepatotoxicity in rats.

Methods: For this investigation, there were twenty-four male and female rats used. Rats were divided up Into three groups, each consisting of eight animals. Distilled water is in **Group I** (negative control). **Group II:** Mitoxantrone was delivered intraperitoneally with a dosage of 2.50 mg/ kg in order to achieve a cumulative complete dosage of 7.50 mg /kg by day 20. **Group III:** Zinc gluconate was orally provided at a dosage of 20 mg/ kg/day, and Mitoxantrone was injected intraperitoneally at a rate of 2.50 mg/kg. The goal was to attain a cumulative total dosage of 7.50mg/ kg by day 20.After 48 hours following the completion of the treatment period, diethyl ether was used to euthanize each animal (i.e., on day 22).

Following cervical dislocation, blood was drawn via intracardiac puncture, and serum was used to determine the activity of the alanine aminotransferase (ALT) and aspartate aminotransferase (AST) enzymes. Each animal's liver was removed in order to perform a terminal deoxynucleotidyl-transferase-mediated-deoxyuridine-triphosphate, necked labeling (TUNEL) test to detect DNA fragmentation.

Results: Zinc gluconate significantly ($P<0.05$) decreased blood ALT and AST, and group III showed a higher percentage of normal hepatocyte cells and a lower percentage of apoptotic cells than group II.

Conclusions: Zinc gluconate may have a protective effect against the hepatotoxicity induced by Mitoxantrone in rats.

Keywords: Alanine aminotransferase ,Aspartate aminotransferase Hepatotoxicity, Hepatoprotective agent, Mitoxantrone, Zinc gluconate, necked labelin.

Journal of Pharmacology &Drug Development eISSN: 2958-6801

How to cite: Maryoosh TM, Hmood KS, Khaleel RA, Nasser DD, Fadhil N. A Review: Hepatoprotective Role of Zinc Gluconate against Hepatotoxicity Induced by Mitoxantrone In Rats. J Pharm Drug Dev.2026: Vol 4 (1);124-131.

INTRODUCTION

Mitoxantrone is an immunosuppressive and antitumor medication that has been used to treat cancers like acute lymphoblastic leukemia, breast, prostate, and lymphoma[1], as well as secondary progressive multiple sclerosis[2]. By stabilizing the complex that is produced between DNA and topoisomerase II, Mitoxantrone is thought to act as an intercalating agent that breaks DNA[3]. Depending on the patient's clinical condition and the progression of the disease, different administration schedules for Mitoxantrone are used[4]. Generally, usual dosages range between 12 and 14 mg/m2, with a cumulative total dose of 140 mg/m2 [1]. The late and irreversible cardiotoxicity associated with Mitoxantrone therapy is one of the most serious side effects[5-7].

Cardiotoxic medications like Mitoxantrone are known to have the potential to result in acute liver failure, due to primary congestive heart failure with insufficient cardiac output, resulting, diminished hepatic blood flow[8]. When compared to other anti-cancer medications like doxorubicin, Mitoxantrone is more hepatotoxic[9]. A temporary increase in the serum bilirubin level and liver enzymes are two signs of Mitoxantrone-induced hepatotoxicity in humans that occur in some of the treated patients[10]. Undoubtedly, the cytotoxicity of Mitoxantrone was prevented by inhibiting CYP-450 metabolism in rat hepatocytes and HepG2 cells[11]. At least one metabolite of Mitoxantrone, naphthoquinoxaline (8,11-dihydroxy-4-[2-hydroxyethyl]), is toxicologically and pharmacologically related. -6-[2-hydroxyethylamino]1,2,3,4,7,12-hexahydronaphtoo-[2,3]-quinoxaline-7-12-dione), which is linked to Mitoxantrone toxicity and has been demonstrated to have antitumor effects.[10]. The naphthoquinoxaline metabolite of Mitoxantrone was shown in studies to be transported to more perfused tissues and accumulated in organs like the heart and liver of the rats[5]. However, it can be difficult to pinpoint whether liver failure is caused directly by or as a result of cardiomyopathy because early clinical indications of cardiac decompensation may go unnoticed[8]. Toxic metabolite of Mitoxantrone may cause direct liver poisoning as a consequence of prolonged exposure to Mitoxantrone. Zinc (Zn), which is considered a crucial element for the division of cells and the synthesis of proteins and DNA, and enzymes that decompose carbohydrates, proteins, and fats in the body, depends on it[12]. This research aimed to investigate the possible hepatoprotective impact of zinc gluconate on liver damage resulting from Mitoxantrone treatment in rats.

MATERIALS AND METHODS

To get 1 mg/ml of Mitoxantrone, the 20 mg/10 ml vial of Mitoxantrone was diluted with 10 ml of D.W., and then 2.5 mg/kg was injected intraperitoneal (IP). Each 50mg of zinc gluconate capsule was dissolved with 10ml of D.W. to make 5mg/ml, which was then given by oral gavage at a dose of 20mg/kg .

Animals

In this experiment, we utilized Twenty-four (24) healthy male and female Wistar albino rats, which were three months old and weighed between 130 and 200 g each; Rats were kept under typical temperature, humidity, and light/dark cycle conditions. Throughout the trial period, rats were given commercial pellets and unlimited access to tap water. For three weeks, there was no contact to allow them to acclimate.

Experimental protocol

Three groups of eight healthy rats, each with four males and four females, were randomly assigned as in the following manner :

Rats in **Group I** were injected with 0.5ml of distilled water(D.W) every day for 20days; this group was used as a negative control. Rats in **Group II** were given 2.50 mg/kg of Mitoxantrone by intraperitoneal (IP) injection on days 0, 12, and 20 to approach a cumulative total dosage of 7.50mg/ kg by day20. This group was used as a positive control[13]. Rats in **Group III** started taking zinc gluconate by mouth at a dosage of 20 mg /kg /day for 20days. They also got Mitoxantrone administered intraperitoneally (IP) at a dosage of 2.5 mg/kg on days 0, 12, and 20 to achieve a cumulative total dosage of 7.5mg/ kg on day 20 [14]. Diethyl ether was used to euthanize each animal 48 hours following the treatment period (on day 22). Following dislocation of the cervical region, two and a half (3) ml of blood was collected using an intracardiac puncture, transferred to a gel tube, and left 30 minute in order to clot. To get serum, the blood was then centrifuged at 3000 rpm for 15 minutes. The serum was collected with a rubber micropipette, split into tiny portions in labeled-Eppendorf tubes, and adjusted at -50°C. The blood was used to measure the activity of the enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) using the ELISA method, and a section of the liver was examined immunohistochemically using the TUNEL test, which is mediated by terminal deoxynucleotidyl transferase.

Statistical Analysis

Statistics were measured using the Statistical Package for Social Sciences (SPSS) version 24. The results were determined as mean ± standard error of means (SEM). A one-way analysis of variance (ANOVA) was employed to compare groups. When the P value was less than 0.05, we regarded the differences to be statistically significant.

RESULTS AND DISCUSSION

Effects of zinc gluconate on serum liver biomarkers

Table 1 showed that rats given a cumulative total dosage of 7.50mg/ kg of Mitoxantrone **(Group II)** (positive control) had a significant increase ($P< 0.05$) in the level of **ALT** and **AST** enzymes in their blood, compared to the level of those enzymes in the blood of rats in the negative control group **(Group I).**

Moreover, Serum levels of ALT and AST dropped significantly ($P<0.05$) when zinc gluconate (20 mg/kg/day) was given to rats with a cumulative total dosage of 7.50mg/ kg of Mitoxantrone (**Group III**) compared to positive control group rats IP administered with a cumulative doses of Mitoxantrone of 7.50 mg/ kg (**Group II**).

Immunohistochemistry(TUNEL test) on Rat Liver Tissue

Apoptosis (green-colored cells) was not seen in the liver tissue of the Group I (negative control rats given D.W), which revealed normal hepatocyte cells.

Figures 1-A Immunohistochemistry changes in the hepatocyte cells of rats that were intraperitoneally treated with 7.50 mg/ kg of Mitoxantrone on the day 20 (**Group II**) were detected, that distinguished by the existence of brown colored cells (apoptotic cells) and a lower proportion of normal green hepatocyte cells. As well, liver sections of rats of orally delivering 20 mg/kg zinc gluconate with Mitoxantrone IP injected at a dosage of 2.50 mg/kg. (**Group III**) illustrated fewer apoptotic cells (cells with a brownish color) and a greater proportion of normal hepatocyte cells (cells with a green color). Figure 1-C.

Table 1. Effects of different treatments on serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels in rats.

Group	Serum AST levels (IU/L)	Serum ALT levels (IU/L)
Group I	**175.8 ± 5.2**	**44.25±3.71**
Group II	**293.87±11.83***	**65.37±2.68***
Group III	**209 ± 7.4 #**	**48±31#**

The mean ± standard error of means (SEM) was used to represent the data.
GroupI: Negative control[Distilled water (DW)]
Group II: Mitoxantrone 7.50mg/kg)
Group III: Zinc Gluconate (20 mg/kg/day) with Mitoxantrone (7.50mg / kg).
*: Significant difference ($P<0.05$) in comparison to the negative control group
(Group I)
# $P<0.05$: Significant difference in comparison to **Group II**

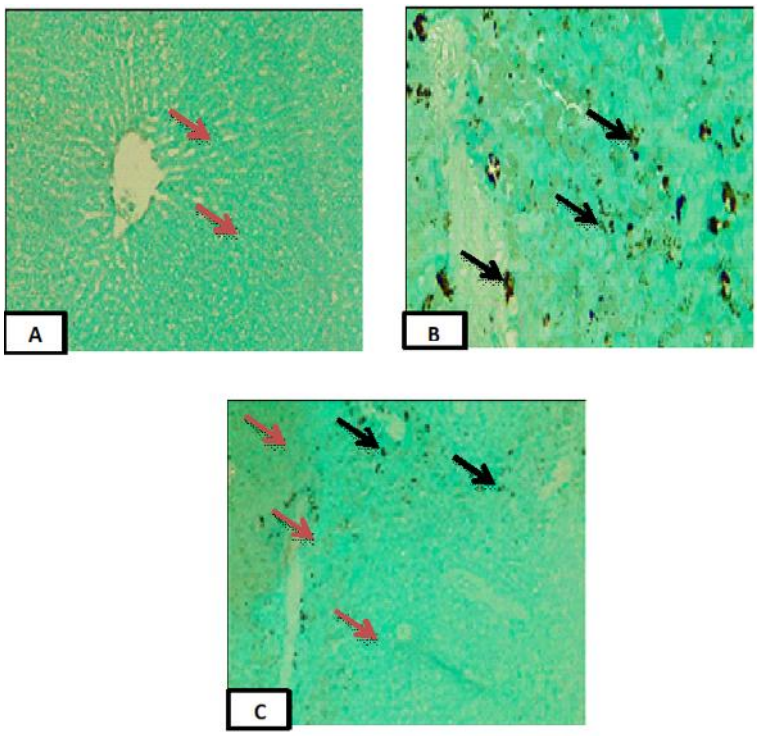

Figure 1. Immunohistochemical section of liver taken from each of the four distinct groups of test rats; (TUNEL assay; ×40).
(A) Group I (negative control (D.W)
(B) Group II Mitoxantrone dose of 7.50 mg/ kg
(C) Group III zinc (20mg/kg/day) with an IP (Mitoxantrone 7.50 mg/ kg).
Green colour was present in normal hepatocyte cells, which were denoted by the red arrow; brown colour was present in apoptotic cells, which were denoted by the black arrow.

Discussion

Hepatotoxicity is a potentially life-threatening clinical complication that may be caused by chemotherapy; there is no safe and effective treatment against these complications[15].
Therefore, finding novel therapy modalities may be useful clinically. Mitoxantrone is amongst the hepatotoxic anticancer agents. Mitoxantrone is one of the anticancer drugs that may damage the liver. There have been reports of many cases of liver damage caused by mitoxantrone treatment [16.17,18]. The objective of the present study was to investigate the role of Zinc Gluconate against mitoxantrone-induced hepatic toxicity .
Mitoxantrone structurally resembles doxorubicin. Doxorubicin is a recognized oxidative stress aggravating agent and a mitochondrial toxin, which induces lung injury , cardiotoxicity and hepatotoxicity[19].

It has been widely recognized that the oxidative stress is a major cause of toxicity caused by chemotherapy. Oxidative stress is one of the main causes of liver damage caused by drugs. Drugs and chemicals that cause oxidative stress have the potential to influence a wide variety of cellular targets, ultimately causing organ damage[20].

Additionally, it seems that the oxidative stress is a key player in the pathophysiology of Mitoxantrone-induced cytotoxicity[21]. When Mitoxantrone is converted to reactive metabolites, these may interact with many intracellular components and cause oxidative stress[22]. As long as the liver is exposed to Mitoxantrone and its active metabolite, naphthoquinoxaline, it may cause damage to the liver. Therefore, antioxidants may provide defense against this problem[23]. The current study's findings indicated that mitoxantrone produced hepatotoxicity, as evidenced by a significant ($P<0.05$) increase in ALT and AST serum activity compared to the negative control group. The results were consistent with previous rodent researches by Niknahad et al., 2017 reported hepatotoxic signs by increased in serum level of in ALT and AST in rat liver with mitoxantrone treatment, confirming the mitoxantrone-induced hepatotoxicity in rat [24] .The recognized hepatotoxic impact of mitoxantrone, which causes

cellular injury and the release of these enzymes into the extracellular environment, may be the cause of the increase in the serum activity of the targeted enzymes.

Apoptosis may contribute to the effectiveness of anthraquinone-based anticancer agents on neoplastic cells [25]. The immunohistochemistry changes observed in the current investigation were used to determine the apoptosis and DNA fragmentation by employing terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining technique of hepatocyte cells in Mitoxantrone-treated rats; It is distinguished by an increase in the number of apoptotic (brown-colored) cells,these results were similar with a study by See-Hyoung Park . It was reported that Mitoxantrone induced apoptosis in osteosarcoma cells through the use of the TUNEL assay [26].Additionally, other study showed that the mitroxantrone administration caused apoptosis in the hepatocellular carcinoma cells lines[27]. In contrast , co-exposure to zinc repaired the architecture of the liver and modified the activity of enzymes and the concentrations of metabolic products. Zinc has been shown to protect the liver from damage by other environmental pollutants, such as lead[28] and thallium[29].In the current study, Zinc gluconate administered at a dosage of 20mg/kg /day with Mitoxantrone (7.50 mg/kg) significantly (P<0.05) lowered serum levels of ALT, AST in comparison to the positive control group. Additionally, there were improvement in liver sections of rats delivered zinc gluconate orally at a dose of 20mg/kg/day with Mitoxantrone (**Group III**) that by a decrease in apoptotic cells (brown color) and a rise in the percentage of normal hepatocyte cells (green color); Figure 1-c] in comparison to those seen in **Group II** (Mitoxantrone -treated).

Similar to this research, a study of Hiroki Yoshioka and Satomi Onosaka[30] found that mice are protected from CCl4-induced acute hepatotoxicity through prophylaxis with zinc, which is believed to be achieved by increasing the expression of free radical-scavenging MT. Zinc treatment resulted in normalization of the structure of hepatocytes in acetaminophen-induced hepatotoxicity in mice[31]. Furthermore, Fadi Choucaire et al. (2018) found that zinc significantly reduced DNA fragmentation of the sperm(32). additionally, Susmita Barman and Krishnapura Srinivasan (2017) indicated that the supplementation of the Zn exerted a protective action against apoptosis, mainly by reestablishing the balance between Bax and Bcl-2 proteins; the reduction of raised Bax levels and the upregulation of Bcl-2 expression implied the anti-apoptotic properties of Zn [33].These findings agree with this study that zinc management reduced the hepatocyte damage. Many mechanisms might be responsible for the zinc hepatoprotective effect, by its antioxidative, antiapoptotic and anti-inflammatory action, ability to stimulate regenerative processes in the liver tissue, its ability to normalize hepatocytes' biomembranes, capacity to decrease collagen accumulation in the liver, and its role in maintaining homeostasis through governing protein metabolism, which in turn controls the levels of transaminases [34].

CONCLUSION

Findings from the present study indicate that zinc gluconate confers significant hepatoprotective effects against Mitoxantrone-induced hepatotoxicity in rats

ACKNOWLEDGMENT

The authors gratefully thank the College of Pharmacy, University of Kut , for supporting the present work.

CONFLICTS OF INTEREST

The authors did not disclose any conflicts of interest.

FUNDING

There was no external funding for this study.

ETHICS STATEMENTS

The study was approved by the Institutional Review Board (IRB) of the College of Pharmacy/ Kut University Wasit, Iraq. (acceptance number13 on 10/12/2023)

REFERENCES

1. Seiter K. Toxicity of the topoisomerase II inhibitors. Expert opinion on drug safety. 2005;4(2):219-34. https://doi.org/10.1517/14740338.4.2.219.
2. Neuhaus O, Kieseier BC, Hartung H-P. Therapeutic role of mitoxantrone in multiple sclerosis. Pharmacology & therapeutics. 2006;109(1-2):198-209.https://doi.org/10.1016/j.pharmthera.2005.07.002.
3. Kathiravan MK, Khilare MM, Nikoomanesh K, Chothe AS, Jain KS. Topoisomerase as target for antibacterial and anticancer drug discovery. Journal of enzyme inhibition and medicinal chemistry. 2013;28(3):419-35 .https://doi.org/10.3109/14756366.2012.658785.
4. Maryoosh TM, N. Al-Shawi N, S. Salih E. Effects of Two Different Doses of Zinc Sulfate on Serum Troponin I 3 Enzyme Level and Cardiac Malondialdehyde Contents in Mitoxantrone-Induced

Cardiotoxicity in Rats. Iraqi Journal of Pharmaceutical Sciences.. 25 2025 Feb.;29(1):115-22 https://doi.org/10.31351/vol29iss1pp115-122

5. Rossato LG, Costa VM, de Pinho PG, Arbo MD, de Freitas V, Vilain L, et al. The metabolic profile of mitoxantrone and its relation with mitoxantrone-induced cardiotoxicity. Archives of toxicology. 2013;87(10):1809-20. https://doi.org/10.1007/s00204-013-1040-6.
6. Taif M. Maryoosh, Nada N. Al-Shawi, Eman S. Saleh, Suhair H. Alkutbi. Journal of Global Pharma Technology 2019 ;11 (9) :340-347.
7. Rossato LG, Costa VM, Vilas-Boas V, de Lourdes Bastos M, Rolo A, Palmeira C, et al. Therapeutic concentrations of mitoxantrone elicit energetic imbalance in H9c 2cells as an earlier event. Cardiovascular toxicology. 2013;13(4):413-25. https://doi.org/10.1007/s12012-013-9224-0
8. Saner F, Heuer M, Meyer M, Canbay A, Sotiropoulos G, Radtke A, et al. When the heart kills the liver: acute liver failure in congestive heart failure. European journal of medical research. 2009;14(12):541-6. https://doi.org/10.1186/2047-783x-14-12-541
9. King PD, Perry MC. Hepatotoxicity of chemotherapy. The oncologist. 2001;6(2):162-76. https://doi.org/10.1634/theoncologist.6-2-162
10. Gunes AK, Serin I, Demir I, Sarifakioglullari S, Durusoy SS, Akkurt DM, et al. Comparison of mitoxantrone–melphalan and BEAM conditioning regimens in patients with lymphoma. Hematology/Oncology and Stem Cell Therapy. 2021. https://doi.org/10.1016/j.hemonc.2021.03.005
11. Juntti-Patinen L, Kuitunen T, Pere P, Neuvonen PJ. Drug-related visits to a district hospital emergency room. Basic & clinical pharmacology & toxicology. 2006;98.7-212:(2) https://doi.org/10.1111/j.1742-7843.2006.pto_264.x
12. Deshpande JD, Joshi MM, Giri PA. Zinc: The trace element of major importance in human nutrition and health. Int J Med Sci Public Health. 2013;2(1):1-6. DOI:10.5455/ijmsph.2013.2.1-6
13. Rossato LG, Costa VM, Dallegrave E, Arbo M, Silva R, Ferreira R, et al Mitochondrial cumulative damage induced by mitoxantrone: late onset cardiac energetic impairment. Cardiovasc Toxicol . 2014; 14(1): 30-40. https://doi.org/10.1007/s12012-013-9230-2
14. Al-bayti, Ayoub & Ahmed, Fidan & Abdullah, Sami & Ghareeb, Ozdan. (2022). The protective effect of zinc and its relationship with some hematological, biochemical, and histological parameters in adult male rats. Archivos Venezolanos de Farmacologia y Terapeutica. 41. 400-405.
15. Thatishetty AV, Agresti N, O'Brien CB. Chemotherapy-induced hepatotoxicity. Clinics in liver disease. 2013;17(4):671-86. .https://doi.org/10.1016/j.cld.2013.07.010
16. King PD, Perry MC. Hepatotoxicity of Chemotherapy. The Oncologist. 2001;6;162-76.
17. Llesuy SF, Arnaiz SL. Hepatotoxicity of mitoxantrone and doxorubicin. Toxicology. 1990;63;187-98.
18. Kingwell E, Koch M, Leung B, Isserow S, Geddes J, Rieckmann P, Tremlett H. Cardiotoxicity and other adverse events associated with mitoxantrone treatment for MS. Neurology. 2010;74;1822-6
19. Volkova M, Russell R. Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. Current cardiology reviews. 2011;7(4):214-20https://doi.org/10.2174/157340311799960645
20. Suk KT, Kim DJ. Drug-induced liver injury: present and future. Clinical and molecular hepatology. 2012;18(3):249https://doi.org/10.3350/cmh.2012.18.3.249.
21. Duthie SJ, Grant MH. The role of reductive and oxidative metabolism in the toxicity of mitoxantrone, adriamycin and menadione in human liver derived Hep G2 hepatoma cells. Brit J Cancer. 1989;60;566-71.
22. Stephens C, Andrade RJ, Lucena MI. Mechanisms of drug-induced liver injury. Current opinion in allergy and clinical immunology. 2014;14(4):286-92https://doi.org/10.1097/ACI.0000000000000070
23. Liebler DC. Protein damage by reactive electrophiles: targets and consequences. Chemical research in toxicology. 2008;21(1):117-28. https://doi.org/10.1021/tx700235t
24. Niknahad H, Hosseini H, Gozashtegan F, Ebrahimi F, Azarpira N, Abdoli N, et al. The hepatoprotective role of thiol reductants against mitoxantrone-induced liver injury. Trends in Pharmaceutical Sciences. 2017;3(2):113-22. DOI:10.1111/tips.v3i2.123
25. Pistritto G, Trisciuoglio D, Ceci C, Garufi A, D'Orazi G. Apoptosis as anticancer mechanism: function and dysfunction of its modulators and targeted therapeutic strategies. Aging (Albany NY). 2016 Apr;8(4):603-19. doi: 10.18632/aging.100934. PMID: 27019364; PMCID: PMC4925817.
26. Park SH, Lee J, Kang MA, Jang KY, Kim JR. Mitoxantrone induces apoptosis in osteosarcoma cells through regulation of the Akt/FOXO pathway. Oncol Lett. 2018; 15(6): 9687–9696.
27. Xie B, He X, Guo G, Zhang X, Li J, Liu J, Lin Y. High-throughput screening identified mitoxantrone to induce death of hepatocellular carcinoma cells with autophagy involvement. Biochem Biophys Res Commun. 2020 Jan 1;521(1):232-237. doi: 10.1016/j.bbrc.2019.10.114. Epub 2019 Oct 22. PMID: 3165334
28. Bandhu H, Dani V, Garg M, Dhawan D. Hepatoprotective role of zinc in lead-treated, protein-deficient rats. Drug and chemical toxicology. 2006;29(1):11-24 .https://doi.org/10.1080/01480540500408507.

29. Al-Jawad FH, Sharquie KE, Raghif AA, Nashtar SB. Hepatoprotective effects of zinc sulphate and silymarin against thallium-induced poisoning in rats. AL-yarmouk Journall. 2015(1): 42-57.https://www.iasj.net/iasj/download/04667c65079ff11d
30. Yoshioka H, Onosaka S. Zinc sulfate pretreatment prevents carbon tetrachloride-induced lethal toxicity through metallothionein-mediated suppression of lipid peroxidation in mice. Fundamental Toxicological Sciences. 2016;3(4):151-6. https://doi.org/10.2131/fts.3.151
31. Chengelis C, Dodd DC, Means JR, Kotsonis FN. Protection by zinc against acetaminophen induced hepatotoxicity in mice. Toxicological Sciences. 1986;6(2):278-84. https://doi.org/10.1016/0272-0590(86)90241-1
32. Choucair F , Saliba E, Jaoude IA, Hazzouri M. Antioxidants modulation of sperm genome and epigenome damage: Fact or fad? Converging evidence from animal and human studies. Middle East Fertility Society Journal 2018; 23(2): 85-90
33. Barman S and Srinivasan K. Attenuation of oxidative stress and cardioprotective effects of zinc supplementation in experimental diabetic rats.British Journal of Nutrition 2017; 117: 335–350.
34. Rogalska J, Pilat-Marcinkiewicz B, Brzóska MM. Protective effect of zinc against cadmium hepatotoxicity depends on this bioelement intake and level of cadmium exposure: a study in a rat model. Chem Biol Interact. 2011 Sep 30;193(3):191-203. doi: 10.1016/j.cbi.2011.05.008. Epub 2011 May 24. PMID: 21627960.

التأثير الواقي للكبد للزنك ضد السمية الكبدية المستحثة الناجم عن المايتوزانترون في الجرذان

طيف مريوش [1]، قاسم حمود [2]، رغد خليل [3]، ظلال ضياء ناصر[4]، نور فاضل [1]

[1] قسم الأدوية والسموم، كلية الصيدلة، جامعة الكوت، واسط، العراق.

[2] قسم الكيمياء الصيدلانية، كلية الصيدلة، جامعة الكوت، واسط، العراق.

[3] قسم الأدوية، كلية الطب، الجامعة العراقية، بغداد، العراق.

[4] قسم تقنيات التجميل والليزر، كلية التقنيات الصحية والطبية، جامعة الكوت، واسط .

الخلاصة

المايتوزانترون هو علاج كيمائي فعال للغاية ضد مجموعة متنوعة من الأورام الخبيثة البشرية. يرتبط المايتوزانترون بتسمم الكبد. من الصعوبة العثور على خيار علاجي فعال ضد إصابة الكبد التي يسببها العلاج الكيميائي. يعتبر الزنك معدنًا ضروريًا لتقسيم الخلايا وكذلك لإنشاء الحمض النووي والبروتينات ؛ علاوة على ذلك ، فإن هذا المعدن له تأثير وقائي في أمراض الكبد. تهدف هذه الدراسة إلى تحديد دور غلوكونات الزنك كعامل وقائي للكبد في الجرذان ضد تسمم الكبد المستحث الناجم عن المايتوزانترون .

الطريقة: في هذه الدراسة ، تم استخدام أربعة وعشرين جرذا من الذكور والإناث. تم تقسيم الجرذان إلى ثلاث مجموعات ، كل مجموعة تتكون من ثمانية حيوانات. في **المجموعة الأولى** الماء المقطر (مجموعة السيطرة). **المجموعة الثانية**: حقنة داخل الصفاق بالمايتوزانترون تم إعطاؤها بجرعة 2.5 ملغم / كغم من أجل للوصول إلى جرعة إجمالية تراكمية تبلغ 7.5 ملغم / كغم في اليوم 20. **المجموعة الثالثة**: 20 ملغم / كغم / يوم غلوكونات الزنك فمويا مع المايتوزانترون بطريقة الحقن داخل الصفاق بجرعة 2.5 ملغم / كغم للوصول للجرعة التراكمية قدرها 7.5 ملغم / كغم في اليوم 20. بعد 48 ساعة بعد نهاية فترة العلاج (أي في اليوم 22)بعد خلع العنق ، تم سحب الدم عن طريق ثقب داخل القلب ، وتم اعداد مصل لتحديد نشاط إنزيمات alanine aminotransferase (ALT) وaspartate aminotransferase (AST).

بالإضافة الى قطع كبد الحيوان لإجراء اختبار(TUNEL) الديوكسيوريدين ثلاثي الفوسفات والنيكند ووضع العلامات , وسيلة للكشف عن تجزئة الحمض النووي. اظهرت الدراسة ان غلوكونات الزنك ادى الى انخفاض معنوي($P < 0.05$) في مستوى نشاط مصل ALT و AST وكذلك انخفاض في نسبة الخلايا المبرمجة وزيادة في نسبة خلايا الكبد الطبيعية في المجموعة الثالثة مقارنة بالمجموعة الثانية. و بذلك يمكن الاستنتاج إن غلوكونات الزنك لها تأثير وقائي ضد السمية الكبدية التي يسببها المايتوزانترون في الجرذان .

الكلمات المفتاحية: ،سمية الكبد،عامل حماية الكبد، المايتوزانترون ،غلوكونات الزنك