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Research Article

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Chenopodium botrys extract: The preventive effects on the hepatotoxicity induced by Adriamycin

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Abstract

Adriamycin, as a drug, is known to induce hepatotoxicity at high doses. This study investigated the preventive effect of Chenopodium botrys extract on Adriamycin-induced liver damage in rats.

Twenty-four rats were randomly divided into control, Adriamycin, and prevention groups, including the extract of *Chenopodium botrys* combined with Adriamycin and silymarin combined with Adriamycin. The experimental period was 30 days. Ultimately, blood was drawn, and liver tissue was removed for evaluation of oxidation markers and biochemical analysis.

Administration of *Chenopodium botrys* significantly decreased the biochemical parameters related to liver function, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), compared to the Adriamycin group. Oxidative parameters, including total thiol content, superoxide dismutase (SOD), and catalase, were improved in the preventive groups compared to Adriamycin in liver tissues.

The data confirm that Adriamycin induces hepatic oxidative stress and liver damage. At the same time, co-treatment with the *Chenopodium botrys* effectively attenuates these adverse effects by restoring redox balance and preserving liver integrity. These findings highlight the therapeutic potential of natural antioxidants in preventing Adriamycin-induced hepatotoxicity.

Keywords: *Chenopodium botrys*; Hepatotoxicity; Adriamycin;Oxidative stress.

1. Introduction

Adriamycin, also known as Doxorubicin, is a compound from the anthracycline family used as a chemotherapeutic agent due to its effectiveness against various types of cancer. These include carcinomas, sarcomas, and hematological malignancies, such as breast, prostate, uterine, ovarian, esophageal, stomach, and liver cancers, as well as acute lymphoblastic leukemia in both pediatric and adult patients. However, serious side effects such as nausea, vomiting, extravasation, severe cardiotoxicity, and hepatotoxicity have been documented [1, 2]. Although Adriamycin is

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the most effective drug for cancer tissue, it unfortunately causes adverse effects in non-cancerous tissues, including the liver, kidneys, heart, brain, immune system, and testis [3]. Numerous studies have suggested that the toxic effects of Adriamycin are related to the generation of oxidative stress in the liver. Therefore, certain antioxidants (such as selenium, Vitamin E, and NAC) can reduce Adriamycin-induced liver damage [4]. It is also well-documented that Adriamycin significantly increases lipid oxidation and mitochondrial ROS content, while decreasing liver antioxidant enzyme activity and mitochondrial function [5].

Chenopodium botrys, a member of the Chenopodiaceae family, exhibits significant antioxidant activity attributed to its rich phytochemical profile, including condensed tannins, saponins, flavonoids, and phenolic compounds. The antioxidant effects of *Chenopodium botrys* extracts are mediated through several mechanisms: scavenging reactive oxygen and nitrogen species such as superoxide anion (O2·-), nitric oxide (·NO), and hydroxyl radicals (HO·), thereby protecting cellular components like lipids, proteins, and DNA from oxidative damage; demonstrating strong reducing power via electron donation, which disrupts free radical chain reactions and mitigates oxidative stress; and chelating transition metal ions (e.g., Fe^{2+}), thus inhibiting metal-catalyzed radical generation through Fenton and Haber-Weiss reactions and reducing the production of highly reactive hydroxyl radicals. [6]

Based on previous research, Adriamycin-induced hepatotoxicity has been strongly associated with free radical generation and oxidative stress. The use of *Chenopodium botrys* can be effective in mitigating hepatotoxicity.

Therefore, this study aimed to investigate, evaluate, and confirm the potential hepatoprotective effects of *Chenopodium botrys* in rats after a multi-dose administration of doxorubicin.

2. Materials and Methods

2.1. Animals

Twenty-four male Wistar rats (220–300 g) were maintained in a controlled laboratory environment with free access to standard chow and water. Environmental conditions were maintained at a temperature of 23 ± 2°C, a relative humidity of 50–60%, and a 12-hour light/dark cycle. All animal procedures were approved by the Ethics Committee at Mashhad University of Medical Sciences (IR.MUMS.AEC.1402.138).

The animals were randomly assigned to four experimental groups, each consisting of six rats. The experimental groups were as follows:

1- Healthy control group: received daily administration of normal saline.

2-Adriamycin group: received a single intravenous injection of Adriamycin (5 mg/kg) [7] on the second day.

3- *Chenopodium botrys* preventive group: received daily oral administration of *Chenopodium botrys* extract (12 mg/kg) [8] plus Adriamycin

4-Silymarin preventive group: received daily oral administration of silymarin (200 mg/kg) [9] plus Adriamycin

The effective dose of *Chenopodium botrys* extract (12 mg/kg) was selected based on a preliminary pilot study in previous research. The extract was administered orally via gavage for a total duration of 30 days. Adriamycin was administered as a single intravenous injection (5 mg/kg) into the tail vein on the second day of the study. Treatment with the extract began one day prior to Adriamycin administration and continued for 28 days thereafter.

2.2. Extraction

The hydroalcoholic extract of *Chenopodium botrys* was obtained through the maceration technique. Briefly, 100 grams of dried plant material were immersed in 70% ethanol and kept at a constant temperature of 25°C for 72 hours with occasional stirring to enhance extraction efficiency. The mixture was then filtered to remove plant debris, and the filtrate was concentrated under reduced pressure using a rotary evaporator. The resulting semi-solid extract was placed in an incubator at 45°C to ensure complete evaporation of the remaining solvent, yielding a dry, purified extract suitable for experimental use [10].

2.3. Experiment

The rats were weighed on both the first and final days of the experimental period. Blood samples were collected at the end of the study for biochemical assessments. Liver tissue samples were also obtained for the

evaluation of oxidative stress markers and biochemical analyses. On day 0, all rats were weighed. At the end of the experiment, animals from all groups were weighed again, anesthetized with 100 mg/kg ketamine and 10 mg/kg xylazine [8], and cardiac blood samples were collected. Subsequently, liver specimens were excised, and the animals were humanely euthanized. Liver samples were stored at –80°C for future analyses of oxidative stress markers, including thiol groups, superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (MDA), as well as nitrite concentration.

Serum samples were analyzed for hepatic enzyme activities, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) using commercially available assay kits (Purchased from Pars Azmoon Co.).

2.4. Statistical Analysis

Data analysis was performed using one-way analysis of variance (ANOVA) followed by the appropriate post hoc test when normality assumptions were met. Results are presented as mean ± standard error of the mean (SEM) for each group, and a p-value of less than 0.05 was considered statistically significant.

3. Results and Discussion

As illustrated in **Figure 1,** hepatic MDA levels were significantly elevated in the Adriamycin-treated group compared to the control group ($P < 0.001$). Co-administration of the extract with Adriamycin significantly reduced levels of hepatic MDA compared to the Adriamycin group ($P < 0.001$). Co-administration of silymarin with Adriamycin demonstrated a notable reduction of hepatic MDA levels compared to the Adriamycin-alone group ($P<0.01$).

Hepatic nitric levels were significantly elevated in the Adriamycin-treated group compared to the control group ($P<0.001$). Co-administration of extract and silymarin with Adriamycin significantly reduced levels of hepatic nitric compared to the Adriamycin group ($P<0.001$).

According to **Figure 2**, hepatic total thiol levels were significantly decreased in the Adriamycin-treated group compared to the control group ($P < 0.001$). Co-administration of extract and silymarin with Adriamycin significantly increased levels of hepatic total thiol compared to the Adriamycin group ($P<0.001$). Hepatic SOD activity was markedly decreased in the Adriamycin-treated group compared to the control group ($P<0.001$). However, co-administration of the extract and silymarin significantly restored SOD activity compared to the Adriamycin group ($P < 0.001$). Hepatic catalase (CAT) activity was significantly suppressed in the Adriamycin-treated group compared to the control group ($P<0.001$). Co-treatment with extract and silymarin significantly ameliorated this reduction, resulting in a marked elevation in CAT activity compared to the Adriamycin group ($P < 0.001$).

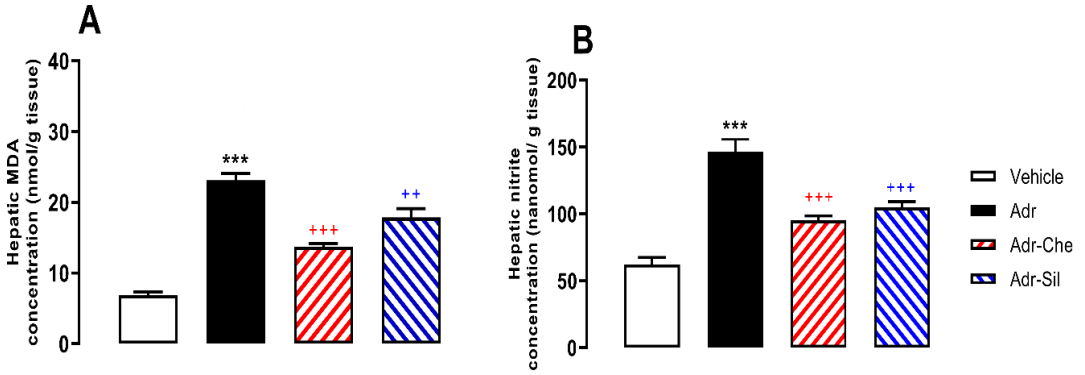

Figure 1: The MDA (A) and nitrite (B) levels in liver tissue in different groups. ***P<0.001 compared to the control, ++P<0.01, +++P<0.001 compared to the Adriamycin group.

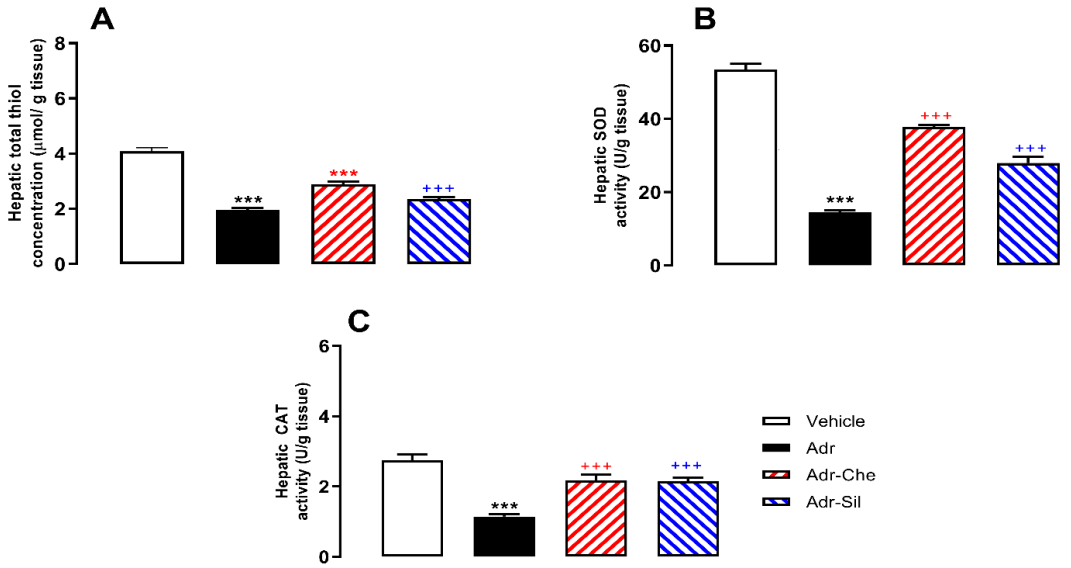

Figure 2. The total thiol (A), SOD (B), and CAT (C) levels in liver tissue in different groups. ***P<0.001 compared to the control, +++P<0.001 compared to the Adriamycin group.

As illustrated in **Figure 3**, serum AST levels were significantly elevated in the Adriamycin-treated group compared to the control group (P < 0.001). Co-administration of the extract and silymarin with Adriamycin significantly reduced serum AST levels compared to the Adriamycin group (P < 0.001). In parallel, serum ALT levels also showed a significant increase following Adriamycin administration compared to the control (P < 0.001). Co-treatment with extract and silymarin significantly mitigated the elevation in ALT levels compared to the Adriamycin group (P < 0.001). Serum ALP levels were significantly elevated in the Adriamycin-treated group compared to the control group (P<0.001). Co-treatment with extract and silymarin markedly reduced ALP levels relative to the Adriamycin group (P<0.001).

Additionally, a comparison between the extract and silymarin was performed for all data, but no significant change was observed.

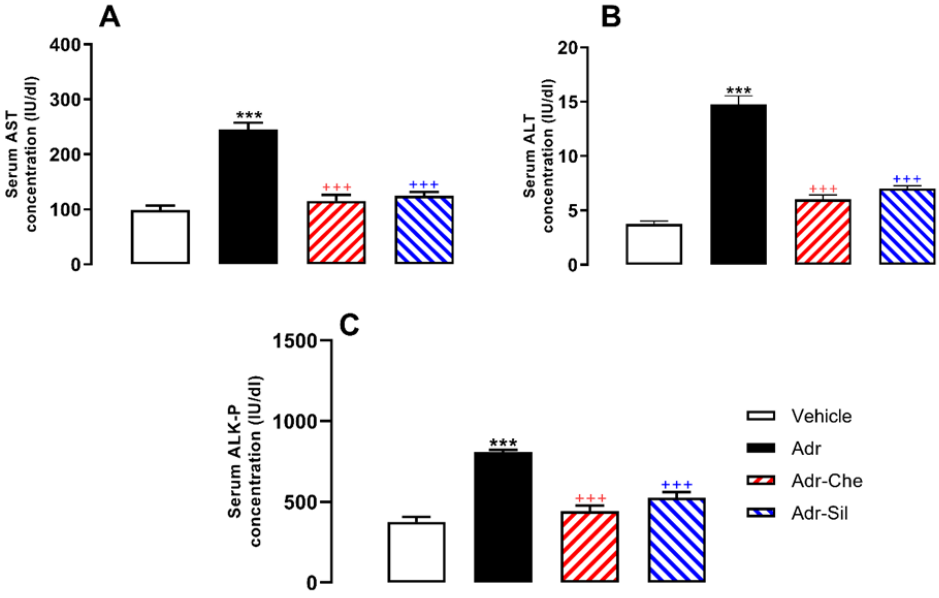

Figure 3. The AST (A), ALT (B), and ALP levels in serum in different groups. ***P<0.001 compared to the control, +++P<0.001 compared to the Adriamycin group.

3.1. Discussion

The present study demonstrates that Adriamycin administration induces significant hepatic oxidative stress and liver injury, as evidenced by elevated levels of malondialdehyde (MDA) and nitric oxide, decreased total thiol content, and suppressed activities of antioxidant enzymes (SOD and catalase). These biochemical alterations were accompanied by marked increases in serum liver enzymes (AST, ALT, ALP), indicating hepatocellular damage.

The significant elevation of hepatic MDA and nitric oxide levels in the Adriamycin-treated group confirms enhanced lipid peroxidation and nitrosative stress, consistent with Adriamycin's known mechanism of generating reactive oxygen species (ROS) and reactive nitrogen species that damage cellular membranes and macromolecules[7, 11-15]. The concomitant decrease in total thiol levels and antioxidant enzymes (SOD and catalase) further reflects a compromised hepatic antioxidant defense system due to Adriamycin-induced oxidative stress [11, 16]. These findings align with previous reports, where Adriamycin impairs liver function by inducing oxidative damage and depleting endogenous antioxidants, leading to hepatocyte injury and dysfunction [17, 18].

Importantly, co-administration of the tested extract and silymarin significantly ameliorated these oxidative stress markers and restored the activities of antioxidant enzymes. The reduction in hepatic MDA and nitric oxide levels, along with the restoration of total thiol content and SOD and catalase activities, suggests that both agents exert potent hepatoprotective effects by scavenging free radicals and enhancing the antioxidant defense system[11, 16]. This protective effect is further supported by the significant decrease in serum AST, ALT, and ALP levels following extract and silymarin treatment, indicating a mitigation of hepatocellular membrane damage and improved liver function [11, 17].

Silymarin's hepatoprotective properties are well-documented, primarily attributed to its antioxidant, anti-inflammatory[19], and membrane-stabilizing effects, which counteract Adriamycin-induced oxidative injury. The extract's comparable efficacy suggests that it may contain bioactive compounds with similar antioxidative and cytoprotective mechanisms, warranting further phytochemical and mechanistic investigations [11, 16].

Chenopodium botrys has demonstrated significant hepatoprotective effects in experimental models of liver toxicity. Studies show that both methanolic and aqueous extracts of *Chenopodium botrys* can effectively ameliorate liver damage induced by toxic agents, such as lead acetate, by restoring biochemical parameters to near-normal levels, indicating their ability to counteract oxidative stress and cellular injury in hepatic tissue [20]. The hepatoprotective potential is largely attributed to its rich content of bioactive compounds [8, 10], including flavonoids, alkaloids, terpenoids, and phenolic components, which exhibit strong antioxidant properties capable of scavenging free radicals and enhancing endogenous antioxidant defenses [21, 22]. Additionally, *Chenopodium botrys* essential oil contains ascaridole, a compound with known anti-inflammatory and cytoprotective effects, which may contribute to its protective action against hepatotoxicity [22].

Finally, a comparison between the extract and silymarin-received groups showed that there is no significant change in all data. This issue indicated that the extract could improve toxicity induced by Adriamycin in parallel with the known drug, silymarin. The extract's effects on toxicity improvement are comparable to those of silymarin, based on our experimental data. Therefore, it can be replaced by silymarin in future research. Of course, clinical studies are also needed to approve it.

4. Conclusion

In summary, the data confirm that Adriamycin induces hepatic oxidative stress and liver damage. At the same time, co-treatment with *Chenopodium botrys* effectively attenuates these adverse effects by restoring redox balance and preserving liver integrity. These findings highlight the therapeutic potential of natural antioxidants in preventing Adriamycin-induced hepatotoxicity, which remains a significant limitation in clinical oncology. Future studies should explore the molecular pathways involved and evaluate the clinical applicability of these protective agents.

Ethics approval

All the procedures were conducted under the Animal Experimentation Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.AEC.1402.138).

Conflict of interest

The authors declare that there is no conflict of interest.

Data availability

Data are available at editor request.

Authors Contributions

RM: Study design, animal work, data collection and analysis and manuscript drafting and final approve.
FS and FA: Animal work and manuscript drafting and final approve.
MSA: plant collection and extraction, final approve.

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Using artificial intelligence chatbots

There was no use of artificial intelligence in the making of this article.

References

1. Aljobaily, N., et al., Creatine Alleviates Doxorubicin-Induced Liver Damage by Inhibiting Liver Fibrosis, Inflammation, Oxidative Stress, and Cellular Senescence. Nutrients, 2020. 13(1).
2. Navarro-Hortal, M.D., et al., Role of flavonoids against adriamycin toxicity. Food Chem Toxicol, 2020. 146: p. 111820.
3. Taskin, E., et al., The Cooperative Effect of Local Angiotensin-II in Liver with Adriamycin Hepatotoxicity on Mitochondria. Med Sci Monit, 2016. 22: p. 1013-21.
4. Wang, B., et al., NAD(+) administration decreases doxorubicin-induced liver damage of mice by enhancing antioxidation capacity and decreasing DNA damage. Chem Biol Interact, 2014. 212: p. 65-71.
5. Diamanti, J., et al., Doxorubicin-induced oxidative stress in rats is efficiently counteracted by dietary anthocyanin differently enriched strawberry (Fragaria × ananassa Duch.). J Agric Food Chem, 2014. 62(18): p. 3935-43.
6. Ozer, M.S., C. Sarikurkcu, and B. Tepe, Phenolic composition, antioxidant and enzyme inhibitory activities of ethanol and water extracts of Chenopodium botrys. RSC Advances, 2016. 6(69): p. 64986-64992.
7. Mohebbati, R., et al., Effects of standardized Zataria multiflora extract and its major ingredient, Carvacrol, on Adriamycin-induced hepatotoxicity in rat. Biomedical journal, 2018. 41(6): p. 340-347.
8. Momeni-Moghaddam, M.A., et al., Chenopodium botrys Extract Affects Acute Kidney Injury Caused by Rhabdomyolysis in Rats Through TNF/NF-κB Signaling Pathway. Food Science & Nutrition, 2025. 13(1): p. e4667.
9. Tsai, J.H., et al., Effects of silymarin on the resolution of liver fibrosis induced by carbon tetrachloride in rats. Journal of viral hepatitis, 2008. 15(7): p. 508-514.
10. Mohebbati, R., et al., Investigating the analgesic effects of the Chenopodium Botrys L. hydroalcoholic extract using behavioral tests on mice. Iranian Journal of Pharmaceutical Sciences, 2023. 19(3): p. 208-216.
11. Khairani, D. and S. Ilyas, Flavonoids for hepatoprotection: Potential natural approaches to mitigate doxorubicin-induced liver toxicity: A mini review. Journal of Medicinal and Pharmaceutical Chemistry Research, 2025. 7: p. 1464-1485.
12. Prasanna, P.L., K. Renu, and A.V. Gopalakrishnan, New molecular and biochemical insights of doxorubicin-induced hepatotoxicity. Life sciences, 2020. 250: p. 117599.
13. Mohebbati, R., et al., Hepatoprotective effects of combination hydroalcoholic extracts of Nigella sativa and Curcuma longa on adriamycin-induced oxidative stress in rat. Journal of reports in pharmaceutical sciences, 2017. 6(2): p. 105-114.
14. Khajavi Rad, A., et al., A standardized extract of Ziziphus jujuba Mill protects against adriamycin-induced liver, heart, and brain toxicity: An oxidative stress and biochemical approach. Journal of Food Biochemistry, 2021. 45(4): p. e13698.
15. Khazdair, M.R., et al., The protective effects of Curcuma longa extract on oxidative stress markers in the liver induced by Adriamycin in rat. Physiology and Pharmacology, 2016. 20(1): p. 31-37.
16. Roomi, M.W., et al., Prevention of Adriamycin-induced hepatic and renal toxicity in male BALB/c mice by a nutrient mixture. Exp Ther Med 7: 1040–1044. 2014.
17. Mosaad, R.M., A. Samir, and H.M. Ibrahim, Median lethal dose (LD50) and cytotoxicity of Adriamycin in female albino mice. Journal of Applied Pharmaceutical Science, 2017. 7(3): p. 077-080.
18. Taskin, E. and N. Dursun, Recovery of adriamycın induced mitochondrıal dysfunctıon in liver by selenium. Cytotechnology, 2014.
19. Mohebbati, R., et al., The comparison of the effects of nano-silymarin and silymarin on high-fat diet-induced fatty liver of adult male rats. Avicenna Journal of Phytomedicine, 2024. 14(3): p. 365.
20. Gupta, N., R. Sagar, and M.L. Kori, Hepatoprotective Potential of Methanolic and Aqueous Extract of Chenopodium botrys against Lead-induced Toxicity. International Journal of Pharmaceutical Investigation, 2021. 11(2).
21. Sezer, E.N.Ş. and T. Uysal, Phenolic screening and biological activities of Chenopodium botrys L. extracts. Anatolian Journal of Botany, 2021. 5(2): p. 78-83.
22. Morteza-Semnani, K., A Review on Chenopodium botrys L.: traditional uses, chemical composition and bio*logical activities.* Pharmaceutical and Biomedical Research, 2015. **1**(2): p. 1-9.