doi:10.22100/ijhs.v12i1.1290
Original Article

SJMS 2026;12(1):23-26
sjms.shmu.ac.ir

SJMS
Shahroud Journal of Medical Sciences

The Beneficial Effects of Exercise and Date Palm Pollen Supplement on Liver Histopathology in the Cadmium Chloride Toxicity Model

Amir Delshad[1], Maryam Azimzadeh[2], Fereshteh Salimi[1], Mohsen Eslami Farsani[3,4], Shima Ababzadeh[3,5], Reihaneh Seyedebrahimi[3,4*]

[1] Department of Sport Science, Faculty of Literature and Humanities, Qom University, Qom, Iran.
[2] Department of Medical Laboratory Sciences, Khomein University of Medical Sciences, Khomein, Iran.
[3] Cellular and Molecular Research Center, Qom University of Medical Sciences, Qom, Iran.
[4] Anatomy Department, Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran.
[5] Department of Tissue Engineering and Applied Cell Sciences Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran.

Received: 30 June 2025
Accepted: 7 October 2025

Abstract

Background: *Cadmium (Cd) is a highly toxic heavy metal that poses a significant health risk in vital organs such the liver. This study investigates the protective effects of aerobic exercise and hydroalcoholic extract of Date Palm Pollen (DPP) in rat Cd toxicity model.*

Methods: *Thirty-six male Wistar rats (230-250 g) divided to six experimental groups (n=6): control, exercise, Cd, Cd-exercise, Cd-exercise-200 DPP, and Cd-Exercise-400 DPP. Each group received a daily dose of 3mg/kg of Cd chloride via gavage. Then, DPP extract was administered intraperitoneally at doses of 200 and 400 mg/kg/day. The aerobic exercise protocol was involved the rats running on a treadmill at a speed of 27 meters/min, with an additional minute added to the training duration each day. The enzyme levels (AST, ALT, GGT) were measured and the histopathological analysis of liver tissue were performed after 5 weeks.*

Results: *Results demonstrated that treatment groups have the significant decrease of GGT and ALT serum levels compared with Cd group (GGT; P-value<0.001, ALT; P-value<0.05). However, there were no significant difference in AST serum level between different groups. Besides, the histopathological findings revealed the number of necrotic areas, sinusoids congestion, and inflammation in Cd group while these alternations were decreased in treatment groups compared with injured group.*

Conclusions: *The findings demonstrating that the combination of aerobic exercise and DPP extract effectively reduce inflammation and cellular damage in liver tissue. So, DPP extract with 200 mg/kg concentration along with regular exercise has hepatoprotective potential effect.*

Keywords: Cadmium chloride, Exercise, Date palm pollen, Liver.
***Corresponding to:** R Seyedebrahimi, **Email:** Reihaneh.s.ebrahimi@gmail.com

Please cite this paper as: Delshad A, Azimzadeh M, Salimi F, Eslami Farsani M, Ababzadeh S, Seyedebrahimi R. The Beneficial Effects of Exercise and Date Palm Pollen Supplement on Liver Histopathology in the Cadmium Chloride Toxicity Model. Shahroud Journal of Medical Sciences 2026;12(1):23-26.

Introduction

Scientists classify cadmium (Cd) as the most toxic metal in soil which its absorption with plants leading to a global threat to public health [1]. Cd is a toxic element with the detrimental effects on human tissues particularly liver and kidney through the multiple biological mechanisms. Recent studies have shown that Cd, by inducing peroxidation of unsaturated fatty acids, disrupts the biological activity of cells and consequently impairs protein synthesis as well as the metabolism of lipids, carbohydrates, and amino acids [2]. It also prevents their methylation and thereby increases the rate of DNA mutation. Additionally, it appears to play a role in the reduction of cellular antioxidants. The induced oxidative stress is likely one of the mechanisms responsible for several diseases [3]. Also, it has the potential to lead to clinical features in blood (e.g., anemia and elevated levels of eosinophils), bone (weakened bones and fractures), diabetes, activation of cancer-causing genes, and respiratory issues [4, 5]. However, the precise mechanism is not well understood.

Cd is excreted from the body which the liver and kidney have the ability to synthesize metallothioneins (MT) which are inducible proteins that bind tightly to Cd ions and protect the cells [6]. However, excretion rate of Cd is low and it can remain for approximately 20-30 years in body that it has enough opportunity for damage to target organs such as kidney and liver [7].

So, finding a way to reduce the toxic effects of Cd is important. It is believed that regular physical activity is a protective approach against metabolic disorders and could be considered as a best way to maintain healthy liver conditions. Moreover, physical activity has by enhancing beta-oxidation and reducing lipogenesis is considered one of the main regulators of liver metabolism [8].

Moreover, the nutritional status affects on the Cd accumulation and toxicity. In this respect, it has been reported that several mineral elements such as calcium, zinc, selenium and iron play an significant role in protecting against Cd toxicity [9]. Date palm pollen (DPP) is a natural product derived from male palm flowers which is rich source of flavonoids, amino acids, nucleic acids, minerals and vitamins, as well as saturated and unsaturated fatty acids with the antioxidant properties [10]. Accordingly, the DPP physiological role in the anti-inflammatory and anti-proliferative, anti-diabetic, and antioxidant activities has been documented [11].

Given the antioxidant properties of DPP as well as the beneficial effects of physical activity, the current research aimed to investigate a period of aerobic exercise and the consumption of the hydroalcoholic DPP extract on the liver function enzymes and histological indices in in the rat with Cd exposure.

Materials and Methods

The DDP plant were purchased from center of medicinal plants in Qom and confirmed by Herbarium of Qom Agriculture Education and Research Center. DPP was extracted according by soxhlet method. Briefly, the dried plant was placed in a white cloth and it put on soxhlet with 70% ethanol. Then, 250 ml of distilled water was added into the soxhlet balloon. The solvent was heated up to boiling in a water bath. Then, the solvent was gradually evaporated by heat and the extract was collected in the central compartment [12].

This study was approved by the Ethics Committee of the Qom University of Medical Sciences (IR.MUQ.AEC.1400.005). 36 healthy male Wistar rats, 12 weeks old and weighing between 230-250 g, were placed in a standard condition which included access to clean water and food, maintenance of a normal biological rhythm (dark/light period of 12 h), and a temperature range of 22-25°C.

The animals were divided into 6 experimental groups (n=6) as follows: the control group without treatment, exercise group, injury group, injury and exercise group, groups treated with DPP herbal extract and exercise.

Injury group received daily 3 mg/kg/days of Cd (diluted in distilled water) via gavage to induce toxicity for 5 weeks. The exercise groups which were subjected to daily forced aerobic exercise. The treated that subjected exercise and herbal extract of DPP (200 or 400 mg/kg) was administrated as intraperitoneal (IP) and after induction of liver toxicity by Cd.

Rats in the exercise groups were familiarized with daily running sessions on a level motor-driven treadmill (Pishroo Andisheah Senate, A1400Y10, Iran) at 10-12 m/min for seven days. The procedures were performed for 5 weeks (5 d/week). During this period, the exercise sessions began with a duration of 16 min which increased slowly until the rats were able to run for 30 min at 27 m/min daily in the 5th week [13].

The rats were anesthetized with ketamine (100mg/kg) and xylazine (10mg/kg). Then, the cardiac perfusion of rats was performed after 14 days of treatment. Blood samples were separated in a centrifuge at 4000 rpm for 5 min and finally, level of Aspartate aminotransferase (AST), Alkaline phosphatase (ALP) and Gamma-glutamyl Transferase (GGT) enzymes were measured by ELISA kits [14].

The liver tissue of rats was collected after anesthesia and cardiac perfusion. First, the samples fixed in 10% formalin. After dehydration and cleaning, the paraffin-embedded tissue blocks were obtained. The tissue sections was done at a 5 µm thickness with the rotary microtome. The tissue sections were stained with hematoxylin and eosin (H&E). Finally, the transverse sections of the liver tissue were observed under a light [14].

Data are expressed as mean±standard deviation. The statistical analysis was performed using one-way analysis of variance (ANOVA). P-value<0.05 was considered as statistically significant.

Results

The findings indicated that all treatment groups had a significant decrease of GGT and ALT serum levels in comparison to Cd group (GGT; P-value≤0.001, ALT; P-value≤0.05). However, there was no significant difference in AST serum level between different group (P-value≥0.05) (Figure 1).

As shown in Figure 2, the hepatocyte cells have distinct nuclei and normal cell boundaries without fat vacuoles, also, sinusoidal spaces were visible in control and exercise groups. There were the necrotic areas along with dilation and congestion in the sinusoids in Cd group (Figure 2).

Moreover, the necrotic hepatocytes with pyknosis nuclei were detected in Cd group. However,

rats treated with DPP and exercise had a small number of cellular destructions with necrotic foci compared with Cd group. Very few numbers of hepatocyte with condensation nuclei (pyknosis) was found in treated group, and also, the administration of DPP at a dose of 200 and 400 was prompted the organized arrangement of hepatocyte and average diameter of sinusoids. However, the inflammatory infiltration was obvious with increasing the dose of DPP (400 mg/kg) (Figure 2).

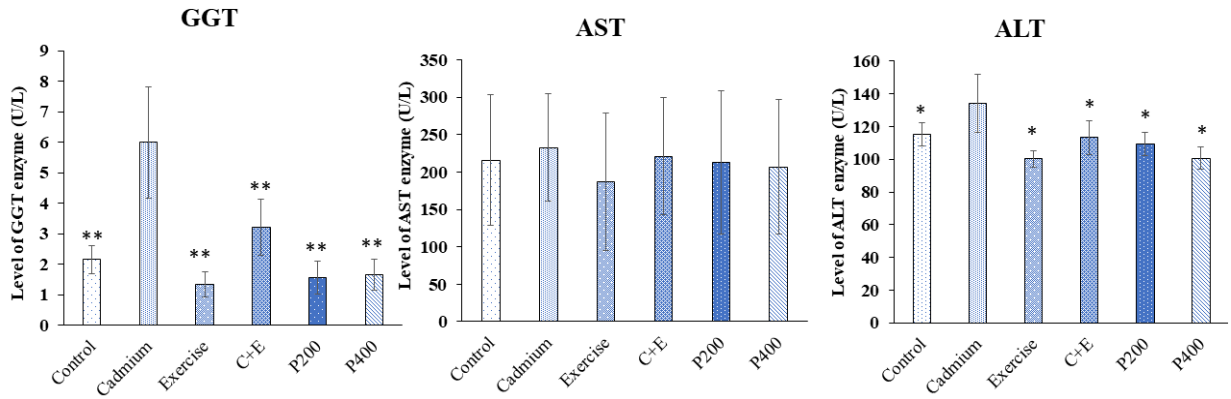

Figure 1. A) The comparison of GGT serum level in experimental groups. (B) The comparison of AST serum level in different groups. (C) The comparison of ALT serum level in different groups. Control (without any treatment), Cadmium (received daily 3 mg/kg/days of Cd only), exercise (received daily forced aerobic exercise), C+E (received Cd and exercise), C+P200 (received Cd and 200 mg/kg DPP extract along with exercise), C+P400 (received Cd and 400 mg/kg DPP extract along with exercise), (* P-value<0.05 and ** P-value<0.05 indicate a significant difference between Cd group with other groups).

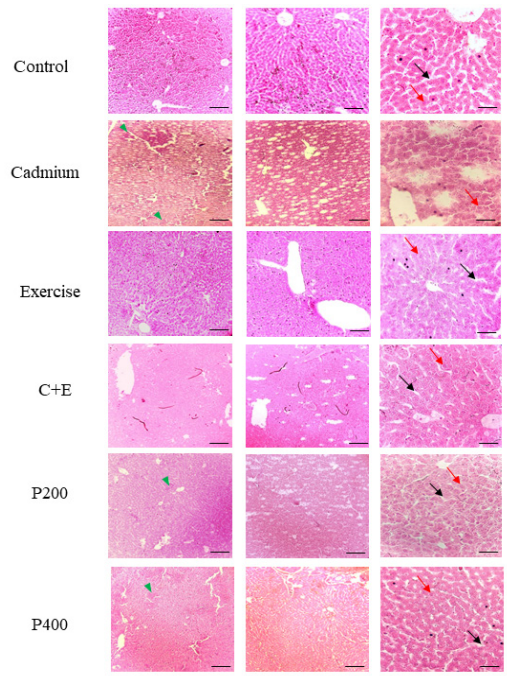

Figure 2. Histopathology of hepatic changes with H & E staining under light microscopy at 5 weeks after treatment in different groups. Control, Cadmium, Exercise, C+E (cadmium and exercise), P200 (injury with cadmium and treatment with 200 mg/kg of DPP and exercise), P400 (injury with cadmium and treatment with 400 mg/kg of DPP and exercise). The black arrows point to sinusoids, the hepatocytes are shown by red arrow and green arrows point to necrotic areas in different group.

Discussion

Prolonged exposure to Cd can result in organ toxicity such as liver. Evidence was noted the marked association between liver enzyme levels and urinary Cd concentrations suggesting that chronic exposure to Cd may lead to human hepatotoxicity [15]. The multiple cellular response are involved in The hepatotoxicity caused by Cd included the apoptosis, inflammation, oxidative stress, and adipogenesis [16].

The histopathology findings of current investigation revealed that the necrotic hepatocytes and congested central veins were detected in Cd group while administration of DPP and the physical activity decreased necrotic status in liver tissue. In fact, the physical activity play a significant role on the immune system and may serve as an effective strategy for treating and managing chronic conditions [17]. Consistently, Delshad et al documented that engaging in moderate-intensity regular exercise, combined with DPP, increased the levels of microRNAs linked to kidney toxicity in mice treated with Cd [13]. Moreover, Mohamed et al indicated that DPP elevated the levels of anti-oxidant enzymes (e.g., glutathione and superoxide dismutase) in gonadal tissue of diabetic model [18]. The DPP potential to decrease the inflammatory markers such as IFN-γ, iNOS, TNF-α, and IL-6 in rats suffering from prostate and intestinal inflammation, suggesting that palm pollen possesses both anti-inflammatory and anti-apoptotic effects [19, 20]. Accordingly, co treatment of exercise and DPP could have the positive impact in reducing inflammation and cellular damage.

The ELIZA findings of current investigation demonstrated that the treatment groups had the significant decrease of GGT and ALT serum levels in comparison to Cd group. Supporting this, Kratz et al. observed significant increases in ALP and AST levels in marathon runners 24h after the race, underscoring the impact of exercise type on enzyme responses [21]. Barquilha et al. reported a significant increase in plasma keratin kinase activity [22]. However, the specific type and duration of physical activity could have on enzyme levels. For example, the study conducted by Fatouros et al. revealed that anaerobic exercise sessions did not significantly affect liver enzyme levels [23]. On the other aspect, Palm pollen provides protective benefits through its beneficial compounds (e.g., flavonoids phenolics, carotenoids, and fatty acids). Al-Asmari et al investigated the DPP effect on Paracetamol-Induced Hepatorenal Toxicity in Rats. The results revealed the pretreatment with DPP at doses of 50 and 100 mg/kg body

weight significantly prevented alterations in serum biomarkers of liver damage—including AST, ALT, GGT, and ALP induced by paracetamol [24].

This study demonstrated that Cd exposure causes significant liver damage, elevated liver enzyme levels and histopathological alterations of liver tissue. However, combination of exercise and extract especially consumption of 200 mg/kg DPP significantly alleviated adverse effects related to Cd and appears to effectively reduce inflammation and cellular damage of liver tissue. The protective role of DPP is likely due to its rich antioxidant and anti-inflammatory compounds, while physical activity contributes to enhancing liver metabolism and immune regulation. Together, these interventions may offer an effective strategy for reducing Cd-induced hepatotoxicity and improving liver health.

Ethical Considerations

This study was approved by the Ethics Committee of the Qom University of Medical Sciences (Code: IR.MUQ.AEC.1400.005).

Acknowledgment

The authors are grateful to Qom University of Medical Sciences and Qom University for their support.

Conflict of Interest

The authors declare that there is no conflict of interests.

Funding

This research is supported by Qom University of Medical Sciences and Qom University.

References

1. El Rasafi T, Oukarroum A, Haddioui A, et al. Cadmium stress in plants: A critical review of the effects, mechanisms, and tolerance strategies. Critical Reviews in Environmental Science and Technology. 2022;52(5):675-726. doi: 10.1080/10643389.2020.1835435

2. Rahmani Talatappeh N, Ranji N, Beigi Harchegani A. The effect of N-acetyl cysteine on oxidative stress and apoptosis in the liver tissue of rats exposed to cadmium. Archives of Environmental & Occupational Health. 2021;76(8):518-525. doi: 10.1080/19338244.2021.1887796

3. Cichoż-Lach H, Michalak A. Oxidative stress as a crucial factor in liver diseases. World journal of gastroenterology: WJG. 2014;20(25):8082. doi: 10.3748/wjg.v20.i25.8082

4. Waisberg M, Joseph P, Hale B, Beyersmann D. Molecular and cellular mechanisms of cadmium carcinogenesis. Toxicology. 2003;192(2-3):95-117. doi: 10.1016/S0300-483X(03)00305-6

5. Yazdankhah A, Moradi S, Amirmahmoodi S, Abbasian M, Shoja SE. Enhanced sorption of cadmium ion on highly ordered nanoporous carbon by using different surfactant modification. Microporous and mesoporous materials. 2010;133(1-3):45-53. doi: 10.1016/j.micromeso.2010.04.012

6. Sakulsak N. Metallothionein: an overview on its metal homeostatic regulation in mammals. Int J Morphol. 2012;30(3):1007-1012. doi: 10.4067/S0717-95022012000300039

7. Branca JJV, Morucci G, Pacini A. Cadmium-induced neurotoxicity: still much ado. Neural regeneration research. 2018;13(11):1879-1882. doi: 10.4103/1673-5374.239434

8. Melo L, Bilici M, Hagar A, Klaunig JE. The effect of endurance training on non-alcoholic fatty liver disease in mice. Physiological Reports. 2021;9(15):e14926. doi: 10.14814/phy2.14926

9. Chen Z, Shi K, Kuang W, Huang L. Exploration of the optimal strategy for dietary calcium intervention against the toxicity of liver and kidney induced by cadmium in mice: An in vivo diet intervention study. PloS one. 2021;16(5):e0250885. doi: 10.1371/journal.pone.0250885

10. Elblehi SS, El-Sayed YS, Soliman MM, Shukry M. Date palm pollen extract avert doxorubicin-induced cardiomyopathy fibrosis and associated oxidative/nitrosative stress, inflammatory cascade, and apoptosis-targeting Bax/Bcl-2 and Caspase-3 signaling pathways. Animals. 2021;11(3):886. doi: 10.3390/ani11030886

11. Saleh M, Kokoszyński D, Mousa MA-A, Abuoghaba AA-K. Effect of date palm pollen supplementation on the egg production, ovarian follicles development, hematological variables and hormonal profile of laying hens. Animals. 2021;11(1):69. doi: 10.3390/ani11010069

12. Karimi Arab M, Heidarieh N, Jamalloo F. Effect of hydroalchoholic extract sumac (rhus coriaria L.) on expression of passive avoidance learning in gonadectomized male rats. SSU_Journals. 2017;25(5):404-413.

13. Delshad A, Salimi F, Valipour S. The effect of physical activity along with the consumption of hydroalcoholic extract of date pollen on the expression of some microRNAs in cadmium-induced toxicity in rat kidney tissue. Med J Tabriz Uni Med Sciences. 2024;46(2):88. doi: 10.34172/mj.2024.023

14. Seyedebrahimi R, Azimzadeh M, Ababzadeh S, Heidarieh N, Bahrami M, Farsani ME. Histopathological and Enzymological Evaluation of Opium Tincture and Protective Effects of Chicory Extract on Liver Structure in Adult Male Rats. Pharmaceutical Chemistry Journal. 2023;57(3):395-400. doi: 10.1007/s11094-023-02896-z

15. Hong D, Min J-Y, Min K-B. Association between cadmium exposure and liver function in adults in the United States: a cross-sectional study. Journal of Preventive Medicine and Public Health. 2021;54(6):471. doi: 10.3961/jpmph.21.435

16. Souza-Arroyo V, Fabián JJ, Bucio-Ortiz L, Miranda-Labra RU, Gomez-Quiroz LE, Gutiérrez-Ruiz MC. The mechanism of the cadmium-induced toxicity and cellular response in the liver. Toxicology. 2022;480:153339. doi: 10.1016/j.tox.2022.153339

17. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. Journal of sport and health science. 2019;8(3):201-217. doi: 10.1016/j.jshs.2018.09.009

18. Mohamed NA, Ahmed OM, Hozayen WG, Ahmed MA. Ameliorative effects of bee pollen and date palm pollen on the glycemic state and male sexual dysfunctions in streptozotocin-Induced diabetic wistar rats. Biomedicine & Pharmacotherapy. 2018;97:9-18. doi: 10.1016/j.biopha.2017.10.117

19. Saryono S, Taufik A, Proverawati A, Efendi F. Dietary supplementation of Phoenix dactylifera L. seeds decreases pro-inflammatory mediators in CCl4-induced rats. Journal of Herbmed Pharmacology. 2019;8(3):212-217. doi: 10.15171/jhp.2019.31

20. Mohamadi Yarijani Z, Madani SH, Changizi-Ashtiyani S, Najafi H. Protective effects of date palm pollen extract on gentamicin-induced hepatotoxicity. Physiology and Pharmacology. 2021;25(3):251-260. doi: 10.52547/ppj.25.3.251

21. Kratz A, Lewandrowski KB, Siegel AJ, et al. Effect of marathon running on hematologic and biochemical laboratory parameters, including cardiac markers. American journal of clinical pathology. 2002;118(6):856-863. doi: 10.1309/14TY-2TDJ-1X0Y-1V6V

22. Barquilha G, Uchida M. Characterization of the effects of one maximal repetition test on muscle injury and inflammation markers. 2011.

23. Fatouros I, Chatzinikolaou A, Paltoglou G, et al. Acute resistance exercise results in catecholaminergic rather than hypothalamic-pituitary-adrenal axis stimulation during exercise in young men. Stress. 2010;13(6):461-468. doi: 10.3109/10253891003743432

24. Al-Asmari AK, Al-Said MS, Abbasmanthiri R, Al-Buraidi A, Ibrahim KE, Rafatullah S. Impact of date palm pollen (Phoenix dactylifera) treatment on paracetamol-induced hepatorenal toxicity in rats. Clinical Phytoscience. 2020;6:1-12. doi: 10.1186/s40816-020-0151-x