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Original Research Article

Ameliorative effects of *Spirulina* on acute lead acetate toxicity complications in male rats

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Abstract

Objective: Lead toxicity, a global health concern, damages many organs. *Spirulina* is a blue-green algae which has vitamins, minerals, and antioxidant properties, may alleviate injury resulting from lead toxicity. This investigation aimed to determine the protective benefits of *Spirulina* on acute lead toxicity.

Materials and Methods: Thirty-two Wistar rats were divided into four groups of 8: Control, lead toxicity group which received lead acetate (50 mg/kg/day, i.p), EDTA group which received lead acetate + EDTA (Ethylenediaminetetraacetic acid, 50 mg/kg/day, i.p) and *Spirulina* group received lead acetate + *Spirulina* (1000 mg/kg/day, oral gavage). After one week, blood samples were taken for serum liver enzymes, testosterone, BUN (Blood Urea Nitrogen), and creatinine determination. Additionally, the livers, kidneys, and testes were dissected, weighed, and saved for evaluation of oxidant-antioxidant factors and histopathological studies. Antioxidant status was assessed by measuring the levels of malondialdehyde (MDA) and the activities of superoxide dismutase (SOD) and catalase in liver, kidney and testis homogenates.

Results: Our results showed that lead toxicity caused a reduction in the organ index, which was improved by EDTA and *Spirulina* treatment. Lead toxicity significantly increased serum glutamic oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), alkaline phosphatase (AlkP), and creatinine, which were significantly reduced by *Spirulina* treatment. Histological studies indicated that treatment by EDTA and *Spirulina* improved histological changes in liver, kidney and testis organs. In addition, treatment with *spirulina* reduced MDA and increased SOD and catalase in liver and testis tissues.

Conclusion: *Spirulina* improved complications of lead toxicity by improving redox balance. These promising results suggest its potential as a protective agent, though further studies are warranted to elucidate the precise mechanisms and clinical applicability.

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Introduction

Heavy metals are components of the Earth's crust that accumulate due to their stability and resistance to degradation. In addition, human industrial interventions and manipulation of marine and terrestrial habitats have caused a rapid increase in these metals. In the past three centuries, due to human interventions, environmental pollution with lead has increased by nearly 1000 times. Plants absorb these metals along with essential substances, including cadmium, mercury, chromium, and lead. The consumption of these plants by animals and humans causes the accumulation of heavy metals in the body and impairs health (Aslam et al. 2020). Lead enters the body through ingestion, inhalation, or contact with the skin and eyes, mainly originating from lead paint, gasoline, counterfeit opium, and the workplace (Balali-Mood et al. 2025). As a cumulative toxin, lead affects cardiovascular, renal, neurological, skeletal, blood, immune, respiratory, digestive, reproductive, and endocrine systems (Mitra et al. 2017). Lead is excreted through the kidneys, so the kidney is exposed to lead more than other tissues, and because most of the lead is excreted through the proximal tubule, this part is more susceptible to damage (Lian et al. 2023; Vargas Robles et al. 2002). One of the complications of lead toxicity is kidney damage, which is manifested by changes in kidney tissue, renal index, as well as changes in serum BUN (Blood Urea Nitrogen) and creatinine concentrations, which indicate impaired kidney function (Liu et al. 2017). Also, lead toxicity impairs liver function and decreases antioxidant enzymes such as superoxide dismutase (SOD) and catalase in liver and kidney tissues (Asiwe et al. 2022). In a study of lead administration, the kidney, spleen, and especially the liver, showed increased liver enzymes and reduced serum albumin. The consumption of broccoli extract due to its antioxidant and anti-inflammatory properties, adjusted to these complications (Shahbazi et al. 2024). In another study, rats were exposed to lead, and in these animals, lead in the blood, liver, and kidney increased, resulting in DNA strand breakage, apoptosis of hepatocytes, and increased caspase-3 activity. It also increases liver enzymes in the serum and increases serum creatinine, in addition to decreasing sperm count, sperm motility, and increasing sperm abnormality, but treatment with vitamin C has reduced these complications due to its antioxidant properties (Shalan 2025a). Lead exposure has been shown to induce oxidative stress and degenerative alterations in the testicular tissue, which consequently leads to a marked atrophy of the testicular structures, as well as a pronounced loss of the spermatogenic series, thereby adversely affecting the overall reproductive health and functionality of the male reproductive system (Abbaszadeh et al. 2021; Elhemiely et al. 2023).

Lead poisoning is generally treated with chelators like EDTA (Ethylenediaminetetraacetic acid). However, the use of these synthetic agents imposes great limitations due to their non-specific binding of essential metals, nephrotoxicity, and limited effectiveness in removing intracellular heavy metals which may lead to rebound poisoning (Flora and Pachauri 2010). For these reasons, it would be important to find alternative treatments with fewer side effects. Today, the use of medicinal plants has become popular due to fewer side effects and lower costs. *Spirulina*, a planktonic algae, is a strong candidate due to its basic compounds, protein, carbohydrates, lipids, vitamins, minerals, and bioactive molecules such as phenols, flavonoids, alkaloids, and terpenoids that contain anti-inflammatory, antioxidant, anti-diabetic, and anti-apoptotic properties (Althobaiti 2023). *Spirulina* could reduce lead effects through its antioxidant mechanisms while potentially avoiding the side effects associated with traditional chelators, (Aladaileh et al. 2020). Furthermore, due to these properties, *Spirulina* has a favorable effect on the rat reproductive system, including improvement in testicular tissue, an increase in androgen receptors, and thus increases spermatogenesis, as well as testosterone levels (Ibrahim et al. 2021b). This study aimed to investigate the effect of *Spirulina* supplementation on lead-induced hepatic, renal, and testicular damage in an animal model of acute lead toxicity.

Materials and Methods

Drugs and chemicals

Spirulina was purchased from Rehyhan Naghshe Jahan (IRAN). Lead acetate and EDTA were purchased from Merck Company, Germany. Materials for the measurement of oxidative stress factors were purchased from Sigma. Co, USA. Serum parameters were measured using commercially available kits.

Study design and animals

Experiments were carried out on male Wistar rats weighing 200-250 g. The animals were obtained from the Medical Faculty animal house of Mashhad University of Medical Sciences to conduct this experimental study. Rats were housed in a room at a constant temperature of 22±2°C with 12-hr light/dark cycles and fed standard pellet chow and water *ad libitum*. The ethical committee of the university approved the study.

In this study, 32 Wistar rats were divided into four groups, each consisting of 8 animals: Control group received 1 ml normal saline, i.p, daily; lead toxicity group received lead acetate (50 mg/kg/day, i.p.)(Yaman et al. 2025); EDTA group received lead acetate + EDTA (50 mg/kg/day, i.p.) and *Spirulina* group received lead acetate + *Spirulina* (1000 mg/kg/day, oral gavage)(Bin-Jumah et al. 2021). Both treatments (EDTA and Spirulina) were administered concurrently with lead acetate throughout the 7-day experimental period to assess their protective efficacy. During one-week treatment, body weight gain/loss was calculated as the difference in initial body weight on day 1 of administration and final body weight at the time of sacrifice (Figure 1) and also the weight of liver, kidney, and testis were calculated. Then, the percentage of each organ's weight relative to body weight was determined as the organ index.

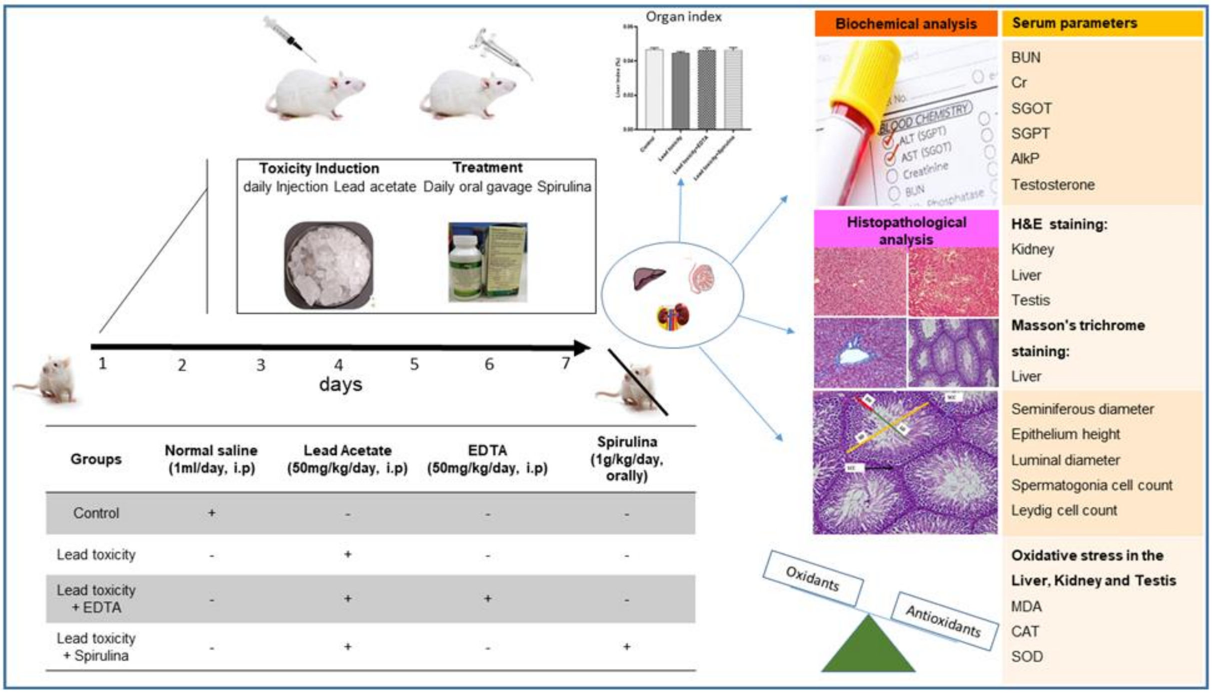

Figure 1. Experimental design

Serum biochemical assay

At the end of the experiment, blood samples were taken via retro-orbital vein under light anesthesia by injection of ketamine (70 mg/kg, ip) and xylazine (7 mg/kg, ip) for measurement of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), alkaline phosphatase (AlkP), testosterone, BUN, and creatinine using available diagnostic kits (Snibe Co., Ltd, PRC). Then, the animals were euthanized by CO_2, and the livers, kidneys, and testes were dissected out, weighed, and the organ weight to body weight ratio was calculated. Then, part of the tissues were put in formalin solution 10% for histological evaluations, and another parts were put in -70°C for oxidant/antioxidant marker measurements.

Histopathological evaluation

A part of the livers, testes, and kidneys were fixed in 10% buffered formalin solution for 48 hr, washed, dehydrated, and embedded in paraffin. Sections of 5µm thickness were stained with Hematoxylin and Eosin (H&E) and Masson's trichrome staining for evaluation of liver fibrosis. For Leydig cell count, the number of Leydig cells in 50 random intertubular areas (area enclosed by three seminiferous tubules) was counted using a 40× objective, and from each animal, 50 seminiferous tubules were chosen for assessment of the number of spermatogonia cells. During histological analysis of the testis, the diameter of a seminiferous tubule was defined as the shortest distance when the length of the outer edge of the tubule, measured by two vertical measuring scales, is equal. The seminiferous epithelial height was defined as the shortest distance between the germ cell that is closest to the center of the lumen and the basement membrane (Rigi et al. 2025). All the measurements were obtained using Image J software.

Oxidant/antioxidant assay

For evaluation of oxidative markers, the liver, kidney and testis tissues were homogenized. Then, the homogenates were centrifuged for 5 min at 5000 x g using a cooling centrifuge. Next, the supernatants were removed immediately and assayed for malondialdehyde (MDA), SOD, and catalase. For measurement of SOD activity, the definition of one unit of SOD activity is the enzyme amount that can inhibit the auto-oxidation of pyrogallol by 50%. The results are interpreted with respect to the total protein content, measured as SOD units per milligram of protein (Nazari et al. 2023; Rahmani et al. 2020). Catalase activity was evaluated by adding 0.1 ml of each tissue homogenate to 4.9 ml of distilled water. Then, 1 ml of the mixture was added to H_2O_2 and phosphate buffer mixture at 100°C. The rate of breakdown of H_2O_2 was proportional to the reduction in absorbance at 600 nm. The difference in the absorbance per unit was expressed as catalase units/mg protein and recorded as the activity (Eskandari et al. 2022; Nazari et al. 2022). Lipid peroxidation was assessed by measuring the MDA-thiobarbituric acid reactive adduct formed a pink coloration in the reaction. The quantification was done spectrophotometrically at 535 nm and was considered the index of lipid peroxidation (Asgharzadeh et al. 2021; Eskandari et al. 2022).

Statistical analysis

SPSS 22 software was used for data analysis. Results are expressed as mean ± SEM. The One-Way analysis of Variance (ANOVA) followed by post-hoc tukey's test was utilized. A p value less than 0.05 was considered statistically significant.

Results

Effect of *Spirulina* on body weight and organ index

Our results showed that the animals with acute lead toxicity had significant weight loss during the experiment, which improved in the treated groups by EDTA or *Spirulina*. Acute lead toxicity resulted in a reduction in liver, kidney, and testis index, which was statistically significant in the kidney index compared to control group. Administration of EDTA or *Spirulina* improved the organ index (Table 1).

Table 1. Effect of acute lead toxicity and treatment with EDTA and Spirulina on weight loss and organ index.

Groups **Index**	**Control**	**Lead toxicity**	**Lead toxicity** **+ EDTA**	**Lead toxicity** **+ Spirulina**
Weight loss (%)	0.79±0.52	-13.02±1.49***	-11.08±1.13***	-10.88±0.96***
Liver index	0.05±0.001	0.04±0.0007	0.05±0.001	0.05±0.002
Kidney index	0.01±0.0001	0.005±0.0002*	0.006±0.0002	0.006±0.0002
Testis index	0.01±0.0002	0.01±0.0002	0.01±0.0002	0.01±0.0002

The values represent mean ± SEM. *p<0.05 and ***p<0.001 compared to the control group.

Effect of *Spirulina* on liver function tests

Acute lead toxicity resulted in a significant increase in liver function tests, including SGPT, SGOT, and AlkP compared to control group. Administration of *spirulina* or EDTA significantly decreased SGPT and AlkP compared to the lead toxicity group, while there was no significant difference in serum liver enzymes between EDTA and *Spirulina* groups (Figure 2A-C).

Effect of *Spirulina* on liver histopathology

The findings of histopathological evaluation showed significant alterations in liver tissue in lead toxicity group. As shown in Figure 2D, which was stained by H&E, lead toxicity induced leukocyte infiltration in hepatic parenchyma, hepatic congestion, hemorrhage, sinus dilatation, and hepatocyte necrosis, and treatment with *spirulina* or EDTA improved histological changes and reversed lead-induced liver injury. Interestingly, treatment with *Spirulina* revealed more improvement in histological changes. Histopathological evaluation of Masson trichrome staining in liver tissue indicated more perivascular fibrosis in toxicity group, which was reduced by treatments with EDTA and *Spirulina* (Figure 2E).

Effect of *Spirulina* on serum BUN and Cr and renal histology

Administration of lead acetate resulted in significantly increased serum Cr level compared to control group. Interestingly, treatment with *Spirulina* decreased serum Cr more than EDTA compared to lead toxicity group. There was no significant difference in serum BUN between groups (Figure 3A and B).

Histological evaluation of renal tissue showed that lead toxicity caused degeneration and atrophy in renal corpuscles, degeneration and desquamation of epithelial cells in renal tubules, and congestion in renal parenchyma, which were improved by treatments with *Spirolina* or EDTA compare to control group (Figure 3C).

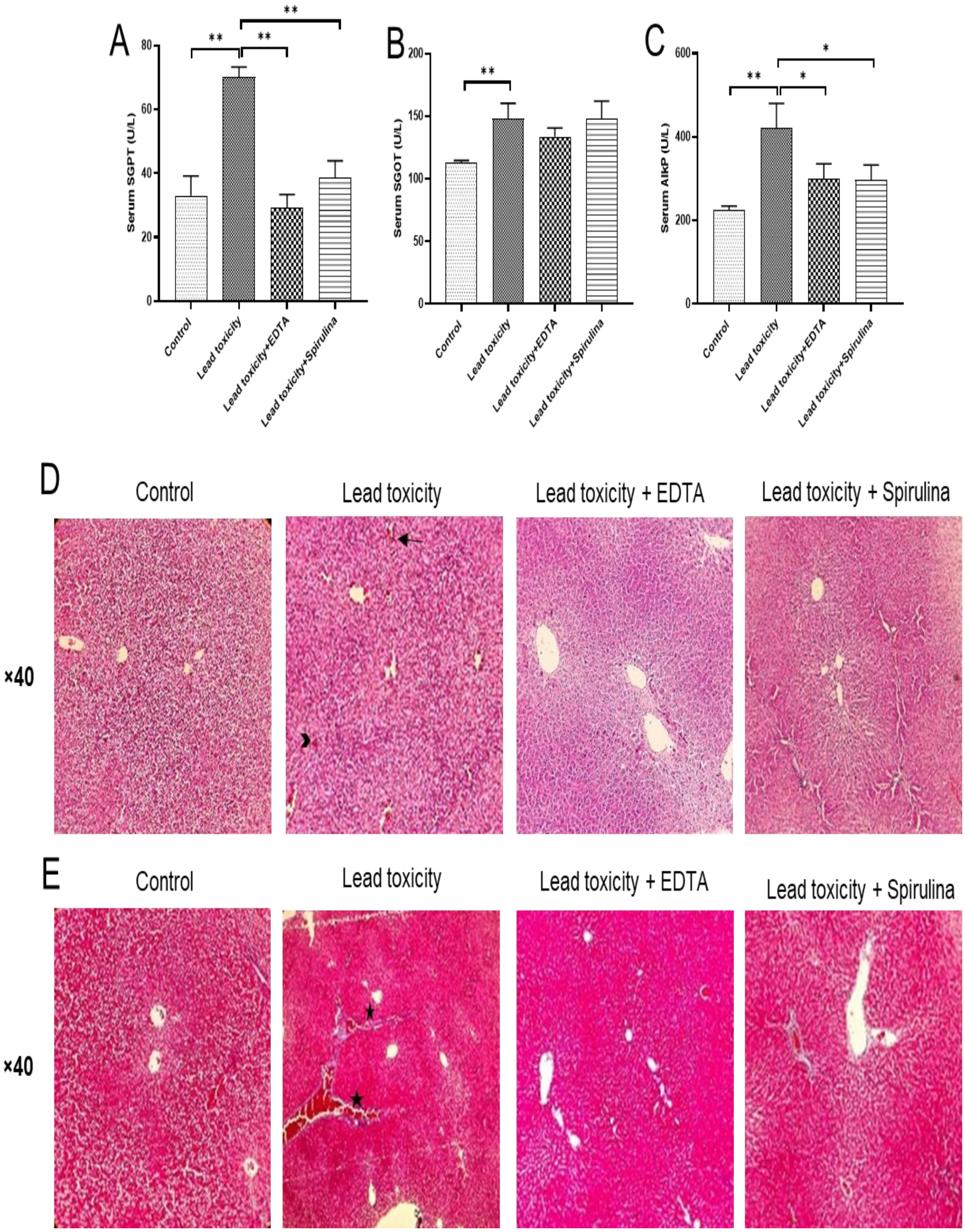

Figure 2. A. serum SGPT, B. serum SGOT, C. serum AlkP, D. Light micrographs of liver section stained with H&E, and E. Masson's trichrome staining exhibiting effects of administration of EDTA and Spirulina on liver against lead toxicity. Hemorrhage (thick arrow), congestion (thin arrow), necrosis (stars). The values represent mean ± SEM. **$p<0.01$ and *$p<0.05$.

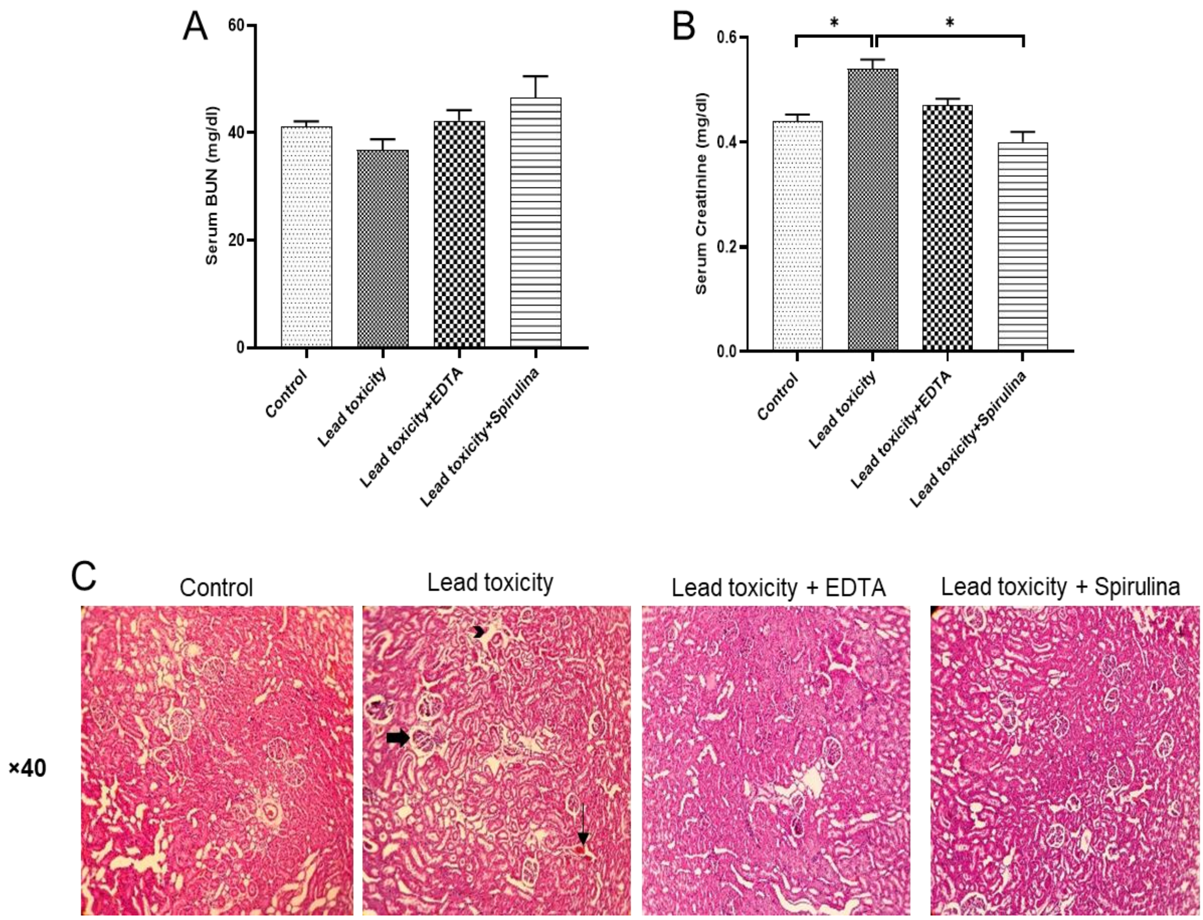

Figure 3. A. Serum BUN, B. serum creatinine, C. Light micrographs of kidney section stained with H&E (×40 magnification) exhibiting effects of administration of EDTA and Spirulina against lead toxicity. Degeneration and atrophy in renal corpuscle (thick arrow), degeneration and desquamation of epithelial in renal tubule (arrow head), congestion (thin arrow). The values represent mean ± SEM. *p<0.05 and *p<0.05

Serum testosterone level

Administration of lead acetate for seven days caused a significant decrease in serum testosterone level in groups of lead toxicity and lead toxicity + EDTA compared to control. Treatment with *Spirulina* partially increased serum testosterone level, which was higher than EDTA group (Figure 4A).

Effect of *Spirulina* on testis histopathology

In control group, normal testicular histopathology, seminiferous tubules, seminiferous epithelial cells, and interstitial connective tissue were observed, whereas significant deterioration was observed in lead toxicity group. Observations included degeneration of the seminiferous epithelium, irregularly shaped seminiferous tubules, and interstitial connective tissue edema. The animals treated with EDTA and *Spirulina* showed significant improvement in the architecture of the seminiferous tubules, with reduced degeneration (Figure 4G). In detail, Leydig cell count in the interstitial space and spermatogonial cell count were significantly decreased in lead toxicity group compared to control group, while no significant difference was observed between the groups of lead toxicity + *Spirulina* and lead toxicity + EDTA compared to control group. (Figure 4B and C). Epithelium height was significantly lower in lead toxicity group, which was improved by EDTA and *Spirulina* treatment. In addition, seminiferous tubule diameter and luminal diameter of the seminiferous tubule in lead toxicity group were significantly higher than control group, which were markedly reduced in the treatment groups, especially in *Spirulina* group (Figure 4D-F).

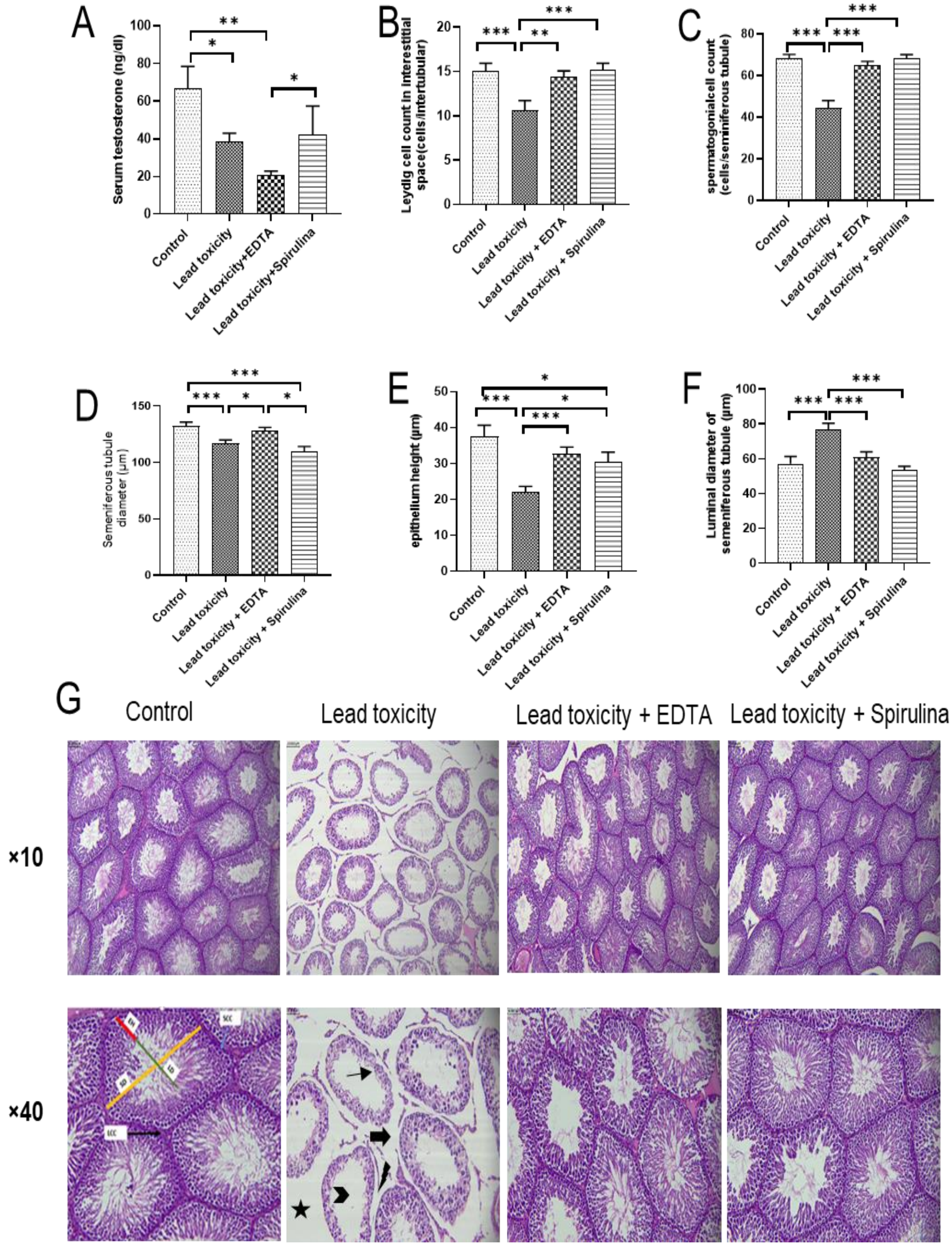

Figure 4. A. serum testosterone, B. Leydig cell count interstitial space, C. Spermatogonia cell count, D. Seminiferous tubule diameter, E. epithelium height, F. Luminal diameter of seminiferous tubule, G. Light micrographs of testis section stained with H&E exhibiting effects of administration of EDTA and Spirulina against lead toxicity. Degeneration of the seminiferous epithelium (thin arrow), irregular shapes of the seminiferous tubules (lightning Bolt), edema in the interstitial connective tissue (star). Decline Spermatozoa in the lumen (arrowhead). Decline number of Leydig cells in the interstitial tissue (thick arrow). The values represent mean ± SEM. *p<0.05, **p<0.01, and ***p<0.001. Epithelial height (EH), diameter of the seminiferous tubules (SD), diameter of the tubular lumen (LD), spermatogonia cell count (SCC), and leydig cell count (LCC).

Figure 5 indicates the tissue level of MDA, as an oxidant marker, and SOD and catalase, as antioxidant factors, in the kidney (Figure 5A-C), liver (Figure 5D-F), and testis (Figure 5G-L).

In the kidney, we found that markers of antioxidant status, including SOD and catalase were significantly lower and MDA was significantly higher in lead toxicity group. All of these factors were partially improved by treatment with EDTA or *Spirulina*, although not statistically significant.

In the liver, tissue level of MDA in toxicity group was significantly higher and SOD and catalase were lower than control group. Administration of EDTA or *Spirulina* partially improved MDA and SOD in liver tissue. However, importantly, treatment with *Spirulina* significantly increased liver catalase, which reached to control level.

In testicular tissue, lead toxicity showed the same changes of MDA, SOD and catalase as liver and kidney and treatment with *Spirulina* significantly reduced MDA level and partially increased SOD and catalase level.

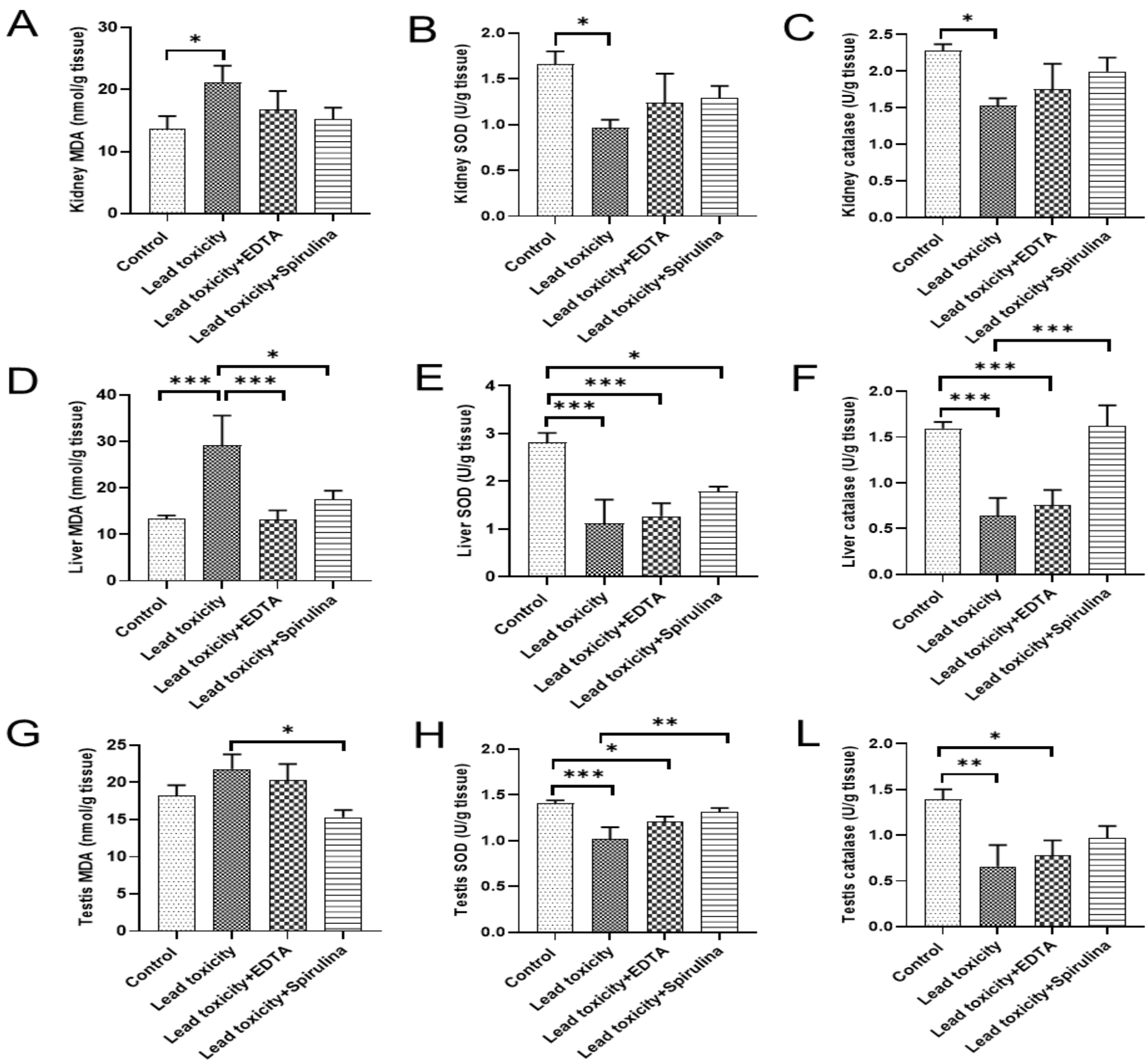

Figure 5. Properties of EDTA and Spirulina on the lead-induced alterations in the activities of SOD and catalase and the level of MDA in the liver, testis and kidney of rats. The values represent mean ± SEM. *$p<0.05$, **$p<0.01$, and ***$p<0.001$.

Discussion

This investigation was conducted to determine the protective benefits of *Spirulina* in countering lead-related damage to the liver, kidney, and testis. We found that lead-exposed rats exhibited notable organ damage in the kidney, liver, and testis and impaired oxidant-antioxidant balance and treatment with *Spirulina* improved organ function, histological changes and oxidant-antioxidant balances in these tissues, which shows the reduced complications of acute lead toxicity.

Our results showed that acute lead toxicity triggered a significant decrease in body weight. Body weight loss is an essential indicator of the disruption in general health, and organ weight reduction is vital in determining organ toxicity. We found that liver and kidney index in lead toxicity group was significantly diminished in comparison to control. These results are consistent with previous studies. In a study, lead exposure significantly reduced body weight (Shalan 2025b). In a separate investigation, the administration of lead acetate (100 mg/kg intraperitoneally) resulted in a notable reduction in body weight among the rodent subjects (Ansari et al. 2013). In another study, administration of lead acetate (100 mg/kg i.p.) for seven days caused weight loss in rats (Allam et al. 2025). Loss of body weight might be a direct effect of lead on the gastrointestinal tract, resulting in malabsorption of food intake as lead influences food satiety signals. Administration of *Spirulina* significantly prevented the weight loss, which might have been a result of providing the body with essential substances present in *Spirulina*, such as proteins, vitamins, and amino acids, and these substances might be beneficial in restoring the body weight (Khalil et al. 2018).

We also found that lead acetate toxicity caused structural histological changes in liver, congestion and liver fibrosis and increased serum liver function tests including SGPT, SGOT and AlkP. These findings align with several prior investigations that demonstrated that administration of lead acetate at a concentration of 0.6 g/L via drinking water for a duration of 10 days resulted in a significant elevation of SGPT, SGOT and AlkP levels in serum. Hepatocyte damage and hepatocyte necrosis cause leakage of intracellular enzymes into the bloodstream, resulting in an increase in SGPT, SGOT and AlkP level (Asgharian et al. 2023). In our study, supplementation with *Spirulina* decreased SGPT, SGOT and AlkP levels in serum and this advantage of *Spirulina* was similar to EDTA treatment.

A large volume of blood is filtered by the kidneys, which results in toxins coming into direct contact with the kidneys and causing kidney damage. In our study, lead toxicity significantly increased Cr levels in serum. In previous studies, the animals that received lead acetate, showed increased serum concentrations of Cr, sodium, and urea (Akbaribazm et al. 2024b; Dwi et al. 2024). Lead has the potential to adversely affect renal function through various mechanisms. It causes tubular degeneration and disruption of the urinary-plasma ion balance by inhibiting endogenous antioxidant enzymes and damaging the microvilli of the proximal convoluted tubule. It also causes damage by activating intracellular apoptotic vesicles. It also causes changes in the activity of transporters by binding to membrane phospholipids and increasing lipid peroxidation (Akbaribazm et al. 2024a). In this study, treatment with *Spirulina* significantly decreased Cr level and improved histological changes in renal tissue. It is possible that the flavonoids and potassium in *Spirulina* can cause diuresis, and the phycocyanin in it improves renal tubular dysfunction (Bin-Jumah et al. 2021).

In testicular tissue, this study showed that acute lead toxicity significantly lowered serum testosterone, that consistent with previous studies. In a study, administration of lead acetate significantly decreased serum testosterone, FSH (follicle-stimulating hormone) and LH (luteinizing hormone) (Saronee and Olumeni 2025). Studies suggested that the decrease in testosterone levels after exposure to lead may result from the indirect effects of lead on the hypothalamic-pituitary–testicular axis, and the structural and functional integrity of reproductive organs (Allam et al. 2025; Hassan et al. 2019). Toxicity by lead can cause testosterone reduction by inhibiting Leydig cell activity through the extrinsic apoptosis pathway and reducing the response of Leydig cells to LH by causing oxidative stress in Leydig cells. In this study, treatment with *Spirulina* reduced the damage caused by lead to testicular tissue and improved testosterone levels in the blood. Other studies have also shown the beneficial effects of *Spirulina* on testicular tissue and sex hormones (Abd El-Hakim et al. 2018; Ibrahim et al. 2021a). These beneficial effects of *Spirulina* are probably attributed to antioxidant active ingredients of *Spirulina*, such as phenols, which scavenge ROS (reactive oxygen species) and improve antioxidant status, and C-phycocyanin, that revealed antioxidant and antiapoptotic properties.

For this purpose, we measured oxidant and antioxidant factors in the liver, kidney, and testis, and we found that lead toxicity reduced antioxidant enzymes (SOD and catalase) and increased MDA in the kidney, liver and testis and treatment by *Spirulina* significantly improved oxidative balance. In previous studies, exposure to lead decreased catalase and SOD activity and increased MDA levels (Soleimanzadeh et al. 2020; Soleimanzadeh et al. 2018). A recent study indicated that administration of lead acetate (100 mg/kg body weight for seven days) increased content of MDA and decreased SOD and catalase levels in testis (Allam et al. 2025). Testicular tissue has a high content of unsaturated lipids in its cell membranes, which are sensitive to oxidative stress. Lead can cross the blood-testicular barrier and cause oxidative stress, lipid peroxidation, and damage to DNA(Soleimanzadeh et al. 2020). In a study, the rats that received oral 30 mg/kg/day lead acetate showed higher urea and Cr levels decreased catalase, GSH, GPx and SOD levels (Kucukler et al. 2021). In another study, lead toxicity disrupted the oxidant/antioxidant balance in the kidney tissue, as shown by the decline in antioxidant proteins (glutathione, glutathione reductase, glutathione peroxidase, catalase, and superoxide dismutase) and elevation of oxidants (lipid peroxidation and nitric oxide)(Abdel-Daim et al. 2020). It is suggested that lead, by penetrating tissues and interacting with enzymes and proteins, disrupts the antioxidant system, which leads to an increase in ROS, resulting in oxidative stress and triggering inflammatory processes(Asgharian et al. 2023). Lead also induces expression of *iNOS* (inducible nitric oxide synthase) gene. The enzyme iNOS facilitates the production of nitric oxide, which reacts with superoxide anions to create peroxynitrite anions ($ONOO^-$), which are potent reactive oxygen species capable of inducing lipid peroxidation in cell membranes. Furthermore, lead modifies the function of antioxidant enzymes by either directly inhibiting the active SH groups present in these enzymes or by attaching to metal cofactors such as copper, zinc, and manganese (Soleimanzadeh et al. 2020).

In the current study, treatment with *spirulina* in rats with lead intoxication led to an increase in SOD and Catalase decrease MDA in hepatic, renal and testis homogenate. The beneficial effect of *Spirulina* on the oxidant-antioxidant defense system could be attributed to alleviating lipid peroxidation that stabilizes the cell membrane, increasing the antioxidant enzyme activities, aborting the proinflammatory response, and the radical scavenging activity. In addition, high quantities of phycocyanin and phenolic compounds and the antioxidant capacity of *Spirulina* may be the cause (Bin-Jumah et al. 2021). It is indicated that acrylamideintoxicated rats treated with *Spirulina* showed a marked reduction in MDA and NO and an increase in Glutathione, Glutathione peroxidase, SOD, and catalase levels in hepatic, renal, and brain homogenates. The abundant content of antioxidant active ingredients, such as C-phycocyanin, vitamins, ß-carotene, and minerals in *Spirulina* can be the cause (Bin-Jumah et al. 2021). The limitation of this study is that we evaluated the toxic effect of lead toxicity and effect of *Spirulina* on three major organs, however, we didn't evaluate the effect of acute lead toxicity on other major organs such as heart or brain.

In conclusion, treatment with *Spirulina* reduced complications of acute lead toxicity on liver, kidney and testicular tissues, improved liver and kidney function tests and histological changes by improving oxidative and antioxidative balance, which was similar to standard drug, EDTA and can be considered in lead toxicity in patients with acute lead toxicity.

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Conflicts of interest

The authors have declared that there is no conflict of interest.

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Ethical Considerations

Ethical approval for this study was obtained from the Ethics Committee of Mashhad University of Medical Sciences.

Code of Ethics

IR.MUMS.AEC.1404.018 SE.N

Authors' Contributions

Conceptualization, M.K., M.S.; Methodology, M.K., M.S, MT.K, K.K and SE.N.; formal analysis, M.S, MT.K, K.K.; investigation, M.S, MT.K, K.K and SE.N; writing—original draft preparation, M.S, MT.K; writing—review and editing, M.K. ,M.S, MT.K, K.K and M.B; supervision, M.K. All authors have read and agreed to the published version of the manuscript.

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