Impact of *Moringa oleifera* leaf extract in reducing the effect of lead acetate toxicity in mice

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**Abstract**

This study aimed to assess the impact of *Moringa oleifera* (M. oleifera) leaf extract against the poisoning of lead acetate; therefore, sixty mice were allocated into 4 groups with 15 in each, as G1) blank control, G2) supplied with 300 mg/kg body weight (BWT) of *M. oleifera* extract, G3) supplied with 60 mg/kg BWT of lead acetate [Pb(C2H3O2)2], and G4) supplied with extract of *M. oleifera* + lead acetate. The liver enzymes were elevated post-treatment with Pb(C2H3O2)2, which then lowered to almost the normal level when *M. oleifera* was supplied to mice previously treated with Pb(C2H3O2)2. The values in (G3) decreased when compared with G1 (92.33 ± 12.99, 21.67 ± 2.91 and 98.00 ± 13.20 U/L, respectively. Also, the cholesterol and low-density lipoprotein levels were elevated post-supplementation with *M. oleifera* and Pb(C2H3O2)2. Pb(C2H3O2)2 improves the lipid profile, whereas *M. oleifera* pretreatment reduced cholesterol (CHOL), high density low cholesterol (HDL-c), and low-density low cholesterol (LDL-c) levels in animals fed Pb(C2H3O2)2. Pb(C2H3O2)2 elevates the total protein but lowers the total bilirubin and triglycerides post *M. oleifera* treatment and Pb(C2H3O2)2 when contrasted with G1. The protective effect of *M. oleifera* was caused by the fact that it lowered triglycerides (TG) and total bilirubin (TBIL) and raised total protein (TP). After administration of Pb(C2H3O2)2, the histological examination revealed alterations in the hepatocytes and kidneys of G3. Also, the liver and kidney cells in mice supplied with *M. oleifera* after Pb(C2H3O2)2 poisoning recovered. In conclusion, Pb is toxic, and the usage of *M. oleifera* partially enhances the negative impacts induced by Pb(C2H3O2)2.

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1. Introduction

Engineering, traffic, agriculture, and waste pollute the environment, resulting in toxic substances smogging the air, soil, food, and water, such as heavy metals (HMs), which endanger human health (Nagajyoti et al., 2010). HMs are considered the most poisonous ecological contaminants (Masindi and Muedi, 2018; El Zlitne, 2022).

Even at low levels, HMs have neurotoxic and oncogenic impacts on humans (Castro-González and Méndez-Armenta, 2008). Lead (Pb), mercury, cadmium, arsenic, and chromium are the most common heavy metals that can poison people, plants, animals, and fish. In addition, these HMs have various toxic impacts on different tissues (Balali-Mood et al., 2021). In 2016, Pb was deemed the cause of 540,000 deaths globally (Mu et al., 2019), and Pb contact is expected to be responsible for 0.6% of the world’s problem of diseases, especially in developing countries (WHO, 2011).

Pb is employed in many industrial processes, including the manufacture of ammunition, batteries, metal outcomes (solder and pipes), X-ray shielding devices, gasoline, paints, lead-based paint, toys, and cosmetics (Martin and Griswold, 2009; Nag and Cummins, 2022). Pb may be absorbed from the integument; it is mostly uptaken from the respiratory and alimentary tracts, leading to neurological, immunological, respiratory, renal, cardiovascular, skeletal, hematological, embryonic, and reproductive disorders because of disrupting the equilibrium of the oxidant-antioxidant agents and causing inflammation in different tissues (Guo et al., 2018; Zwolak et al., 2019; Usman et al., 2022).

The global blood level for Pb intoxication is 10 μg/dl (Kianoush et al., 2013). Wang et al. (2013) reported a marked elevation in the
concentrations of AST, ALT, uric acid, creatinine, and serum urea in lead-exposed rats. Elmenoufy (2012) found that Pb treatment increased the creatinine, uric acid, bilirubin, and urea levels in exposed rats; moreover, Pb-exposed rats exhibited increased levels of total cholesterol, LDL, HDL, and TG, and also elevated ALP, GPT, and GOT enzymes. Pb(C₂H₃O₂)₂ altered hematological and biochemical profiles and revealed renal and hepatic damage via a significant increase in reactive oxygen species (ROS) formation, resulting in oxidative stress (OS), elevated lipid peroxidation, and a decrease in glutathione (GSH) levels in tissues (Ibrahim et al., 2011; Liu et al., 2012).

The histology and biochemistry of blood, kidney, liver and encephalonic tissues were altered by Pb(C₂H₃O₂)₂ (Ozsoy et al., 2011). Recently, the world has been paying more attention to using natural products to improve the health of livestock (Alagawany et al., 2021; Abd El-Hack et al., 2022a, b; Arif et al., 2022). Chemical preparations can be dangerous (Alagawany et al., 2021; Abd El-Hack et al., 2022a, b; Arif et al., 2022) As a result, there is a high demand for the creation of antioxidant agents. Moringa species (sp.) are found in many tropical and sub tropical parts of the world. Thirteen species of Moringa have been found (Lakshmidevamma et al., 2021).

Medicinal plants have many applications due to their efficiency, lower side effects, and content of phytochemical compounds that efficiently treat many diseases. Treatment of these diseases using efficient medicinal plants prevents or decreases infections. The global demand for natural goods has soared. Folk medicine, particularly herbal medications, is used to treat around 85% of the population in underdeveloped nations. These requests are mostly motivated by the negative consequences of synthetic medications. As a result, the relevance of therapeutic herbs has grown dramatically. Identifying active herbal constituents can lead to new possible therapeutic uses and the manufacturing of natural pharmaceuticals, despite the long history of plant medicine use in traditional treatment systems. Great efforts should be made in the quality control of raw and manufactured pharmaceuticals to verify their use in the current healthcare system. Biological and clinical investigations are required to maximize the profitability of these plants. Furthermore, a practical plan for preserving medicinal plant resources should be devised. Medicinal herbs are used not only for adjuvant illness therapy but also for disease prevention and health maintenance.

M. oleifera Lam. is an abundant multipurpose plant of great importance. Almost every part of the tree is useful and has many industrial uses. This plant is considered a high-value crop due to its nutritive, curative, and preventative properties, which are linked to its high content of potent bioactive compounds (Lakshmidevamma et al., 2021; Brazales-Cevallos et al., 2022). M. oleifera has various therapeutic properties such as anti-cancer, anti-inflammatory, ulcer-healing, and antioxidant activities. The antioxidant and ROS-clearing properties of M. oleifera are attributed to its phenolic content (Paliwal et al., 2011; Chigurupati et al., 2022; Kandeepan et al., 2022).

Studies revealed the different dose-dependent impacts of extracts of M. oleifera on rats’ renal tissues (Kasolo et al., 2012). Also, Nagarshree et al. (2011) estimated the impact of M. oleifera on acute arsenic poisoning in rats, and they found that the extract reduced the negative impact of arsenic. In addition, in rabbits, M. oleifera extracts reduced renal and hepatic histopathological changes caused by Pb(C₂H₃O₂)₂ (Mohamed et al., 2020). Therefore, this work was designed to determine the protective impact of M. oleifera leaf extract on blood chemistry. The tissue histopathology of mice subjected experimentally to lead acetate toxicity action revealed alterations in the hepatocytes and kidneys of G3. Also, the liver and kidney cells in mice supplied with M. oleifera after Pb(C₂H₃O₂)₂ poisoning recovered.

2. Materials and methods

2.1. M. oleifera leaves extraction

The leaves were carefully rinsed and dried at (20–25 °C), then powdered and preserved in a dry container according to Al-Attar and Abu Zeid (2013) with a few adjustments. After six hours, fifty grams of the powder were added to a flask containing 1.5 of hot water, and after six hours, the mix was gently boiled for 45 min. Post-treatment, the mix was cooled and then softly exposed to an electric mixer for 10 min. After that, the solution was filtrated with 250 mm filter paper, and then the filtrate was heat-treated at 40 °C to be evaporated and obtain dried active principles. The end product of the M. oleifera extracts was 16.4 % refrigerated for further work.

2.2. Laboratory animals

The mice were reared in cages and kept below normal lab circumstances such as humidity (65 %), temperature (20 ± 1 °C) and half in a half-light/dark cycle. Animals were fed ad libitum on a balanced ration with ad libitum clean water. Mice were adapted to the house for ten days prior to the beginning of the trial. The trial design and the animal handling procedures followed the ethical rules of the Animal Care and Use Committee of King Abdulaziz University. As seen in Fig. 1, a total of 60 mice were allotted into 4 main groups (15 mice each) where.

1. Control group (G1): mice supplied daily with distilled water via gastric intubations for 6 weeks,
2. M. oleifera leave extract supplied group (G2): animals were treated via oral route with 300 mg/kg BWT of M. oleifera leaves extract dose via the gastric intubation day post day for 6 weeks,
3. Lead acetate-supplied group (G3): mice treated orally with 1/10 LD50 of Pb(C₂H₃O₂)₂ (60 mg/kg BWT) via the stomach tube, day post day for 45 days.
4. M. oleifera Leave extract supplied group + lead (G4): mice orally administered 300 mg/kg BWT of M. oleifera leaves extract then given 60 mg/kg BWT Pb(C₂H₃O₂)₂ days after day for 45 days.

The BWT of mice was measured at the start of the trial and the end by a digital balance, and the health status was observed daily. Blood was collected for biochemical assessment at the end of the trial (6 weeks). Animals in all groups were ethically slaughtered and examined, and sections of hepatic and renal tissues were taken for further histopathological examination.

2.2.1. Serum analysis

Mice abstained for 12 h with a constant water supply before being ethically sedated with diethyl ether. Blood was obtained from the orbital venous plexus in plain tubes and centrifuged at 2500 rpm for 15 min. The sera were separated and kept at 4 °C before direct evaluation of AST, ALT, ALP, Total bilirubin (TBIL), Lactate dehydrogenase (LDH), Total protein (TP), Glucose (GLU), Triglycerides (TG), Cholesterol (CHOL), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), and Urea (BUN) (Abou-Kassem et al., 2021; Reda et al., 2021). Analysis was adopted via an automated clinical chemistry analyzer (RX Daytona™; Randox Laboratories, Crumlin, County Antrim, UK).

2.2.2. Histological examination

Mice were ethically dissected, and the livers and parts of the kidneys were kept in 10 % formal saline (Culling and Dunn, 1974; El-Saadony et al., 2021a). All liver and kidney specimens were
processed and stained with H&E stain, then microscopically examined (Olympus BX61-USA) and snapped by a camera (Olympus DP72-USA) in the microscope unit at King Fahd Medical Research Center.

2.3. Heavy metals:

Samples of lead acetate and the rest of the chemicals were obtained from chemical companies in Jeddah.

2.3.1. Determination of LD50

The lethal and sub-lethal doses lethal dose (LD50) for Pb(C2H3O2)2 were determined in mice, and it was 600 mg/kg BWT.

2.4. Statistical analysis

The Statistical Package for Social Sciences (SPSS for Windows, version 12.0) was used to analyze the results. Values were articulated as means ± Standard Error, and values were tested by one-way analysis of variance (ANOVA). Afterward, the smallest significant difference (LSD) test was carried out to decide differences among the means of different groups, and p-values lower than 0.05 were significant.

3. Results

3.1. Biochemical findings:

3.1.1. The activity of ALT, AST, and ALP

As shown in Table 1, group 2 AST enzyme activities were significantly higher (p < 0.05) when compared to G1 (187.40 ± 33.30 U/L) and increased for ALT and ALP when compared to G1 (36.25 ± 1.84 and 75.20 ± 12.02 U/L, respectively). The values in (G3) decreased when compared with G1 (92.33 ± 12.99, 21.67 ± 2.91 and 98.00 ± 13.20 U/L, respectively). When using *M. oleifera* leaves extract + Pb(C2H3O2)2 (G4), the mean values for the enzyme’s activities were significantly lowered (p < 0.05) for AST and ALT when contrasted with G2 (97.00 ± 11.69 and 18.25 ± 3.17 U/L), but for ALP it was decreased (65.50 ± 15.06 U/L).

3.1.2. Levels of HDL-C, CHOL and LDL-C

Table 2 illustrates the data when contrasting the mean values in *M. oleifera* leaves extract treated group (G2) with (G1) CHOL, and LDL-C were increased to 3.49 ± 0.29 and 0.29 ± 0.03 g/dl, respectively, while for HDL-C it was decreased (65.50 ± 15.06 U/L).

![Fig. 1. Experimental design and groups classification.](image-url)
The values in (G3) were elevated for CHOL and HDL-C (3.98 ± 0.17 and 3.30 ± 0.003 g/dl, respectively) when compared with G1, but for LDL-C (0.64 ± 0.17 g/dl), it was significantly elevated (p < 0.05) when contrasted with G1.

When using *M. oleifera* + Pb(C2H3O2)2 in group (G4), the mean values decreased when compared with group 3 (3.33 ± 0.20, 3.15 ± 0.09 and 0.41 ± 0.04 g/dl, respectively).

### 3.1.3. The results of LDH, GLU and BUN

Table 3 shows the results of the lactate dehydrogenase enzyme activity (LDH), (GLU), and (BUN) in various groups examined. In (G1), the mean values ± SE for LDH, GLU, and BUN were 576.50 ± 13.25 U/L, 3.88 ± 0.80 and 8.44 ± 0.41 g/dl, respectively. When contrasting the mean values in the *M. oleifera* leaf extract treated group (G2) with (G1), the enzyme LDH was increased (599.20 ± 0.80 U/L) while GLU and BUN were decreased (2.86 ± 0.20 and 8.26 ± 1.02 g/dl, respectively).

The mean values in (G3), when compared with (G1), were not changed for LDH enzyme (577.00 ± 20.08 U/L) and increased for BUN (12.30 ± 3.01 g/dl) and GLU (3.28 ± 1.02 g/dl). When using *M. oleifera* leaves extract + Pb(C2H3O2)2 (G4), the mean value of LDH was significantly decreased (478.25 ± 73.49 U/L) when compared with groups I and II, GLU was decreased (3.05 ± 0.39 mg/dl) when compared with G1 and BUN was significantly decreased (7.03 ± 1.16 g/dl) when compared with group IV.

### Table 3

Mean values ± SE of lactate dehydrogenase (LDH) enzyme activity, glucose (GLU) and blood urea nitrogen (BUN) in different groups.

| Parameters              | Groups                          | LDH (U/L)   | GLU (g/dl) | BUN (g/dl)  |
|-------------------------|---------------------------------|-------------|------------|-------------|
| Control                 | 576.50 ± 13.25                  | 3.88 ± 0.80 | 8.44 ± 0.41|
| *M. oleifera*           | 599.20 ± 0.80                  | 2.86 ± 0.20 | 8.26 ± 1.02|
| Lead acetate            | 577.00 ± 20.08                  | 3.28 ± 1.029| 12.30 ± 3.01|
| *M. oleifera* + Lead acetate | 478.25 ± 73.49               | 3.05 ± 0.39 | 7.03 ± 1.16 |

Values are given as means ± SE for 6 mice in each group.

b: Significantly decreased when compared with *M. oleifera* group (G2).

c: Significantly decreased when compared with control group (G1).

d: Significantly decreased when compared with lead acetate group (G3).

### Table 4

Mean values ± SE of total protein (TP), total bilirubin (TBIL) and triglycerides (TG) in different groups.

| Parameters          | Groups                          | TP (g/dl) | TBIL (g/dl) | TG (g/dl) |
|---------------------|---------------------------------|-----------|-------------|-----------|
| Control             | 53.33 ± 1.52                    | 5.00 ± 0.26| 0.92 ± 0.12 |
| *M. oleifera*      | 59.00 ± 2.12a                   | 4.80 ± 0.58| 0.73 ± 0.08 |
| Lead acetate        | 57.50 ± 2.53                    | 4.75 ± 0.48| 0.72 ± 0.22 |
| *M. oleifera* + Lead acetate | 52.00 ± 2.86                  | 3.75 ± 0.25| 0.83 ± 0.04 |

Values are given as means ± SE for 6 mice in each group.

a: Significantly increased when compared with control group (G1).

### 3.1.4. The results of LDH, GLU and BUN

Table 3 shows the results of the lactate dehydrogenase enzyme activity (LDH), (GLU), and (BUN) in various groups examined. In (G1), the mean values ± SE for LDH, GLU, and BUN were 576.50 ± 13.25 U/L, 3.88 ± 0.80 and 8.44 ± 0.41 g/dl, respectively. When contrasting the mean values in the *M. oleifera* leaf extract treated group (G2) with (G1), the enzyme LDH was increased (599.20 ± 0.80 U/L) while GLU and BUN were decreased (2.86 ± 0.20 and 8.26 ± 1.02 g/dl, respectively).

The mean values in (G3), when compared with (G1), were not changed for LDH enzyme (577.00 ± 20.08 U/L) and increased for BUN (12.30 ± 3.01 g/dl) and GLU (3.28 ± 1.02 g/dl). When using *M. oleifera* leaves extract + Pb(C2H3O2)2 (G4), the mean value of LDH was significantly decreased (478.25 ± 73.49 U/L) when compared with groups I and II, GLU was decreased (3.05 ± 0.39 mg/dl) when compared with G1 and BUN was significantly decreased (7.03 ± 1.16 g/dl) when compared with group IV.

### Table 4

Mean values ± SE of total protein (TP), total bilirubin (TBIL) and triglycerides (TG) in different groups.

| Parameters          | Groups                          | TP (g/dl) | TBIL (g/dl) | TG (g/dl) |
|---------------------|---------------------------------|-----------|-------------|-----------|
| Control             | 53.33 ± 1.52                    | 5.00 ± 0.26| 0.92 ± 0.12 |
| *M. oleifera*      | 59.00 ± 2.12a                   | 4.80 ± 0.58| 0.73 ± 0.08 |
| Lead acetate        | 57.50 ± 2.53                    | 4.75 ± 0.48| 0.72 ± 0.22 |
| *M. oleifera* + Lead acetate | 52.00 ± 2.86                  | 3.75 ± 0.25| 0.83 ± 0.04 |

Values are given as means ± SE for 6 mice in each group.

a: Significantly increased when compared with control group (G1).

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**Fig. 2.** Histological section of A: liver in control group (G1) showing the hepatic lobules with its central vein (CV), notice the arrangement of hepatocytes as cords (H) separated by liver sinusoids (S), also appears Kupffer cells (K) also, a branch of the portal vein (PV) in the portal area (H & E stain X = 200); B: liver in control group (G1) showing branch of the portal vein (PV) and branch of the bile duct (BD) in the portal area, also hepatocytes (H) appeared normal with rounded nuclei (N) hepatocytes arranged in cords which are separated by liver sinusoids (S) also seen are Kupffer cells (K) (H & E stain X = 200); C: liver in *M. oleifera* group (G2) showing normal arrangement of hepatocytes in cords (H) with rounded nuclei found in the middle of the cytoplasm (N) in addition, blood sinusoids appeared between hepatic cords (S), branch of the portal vein (PV), branch of the bile duct (BD) and Kupffer cells (K) are seen, and notice cytoplasmic vacuolation (V) (H & E stain X = 400); and D: liver in *M. oleifera* group (G2) showing normal arrangement of hepatocytes in cords (H) with rounded nuclei found in the middle of the cytoplasm (N) also, blood sinusoids appeared between hepatic cords (S), branch of the portal vein (PV), branch of the bile duct (BD) and Kupffer cells (K) are seen, and notice cytoplasmic vacuolation (V) (H & E stain X = 400).
3.1.4. Levels of TP, TBIL and TG

Table 4 shows the results of TP, TBIL, and TG in all groups. In G1, the mean values ± SE for TP, TBIL, and TG were 53.33 ± 1.52, 5.00 ± 0.26 and 0.92 ± 0.12 g/dl, respectively.

When contrasting the mean values in the *M. oleifera* leaf extract treated group (G2) with (G1), the TP was significantly increased (59.00 ± 2.12 mg/dl) while TBIL and TG were decreased (4.80 ± 0.58 and 0.73 ± 0.08 g/dl, respectively).

When comparing the mean values in (G3) with (G1), TP was increased (57.50 ± 2.53 g/dl), but TBIL and TG were decreased (4.75 ± 0.48 and 0.72 ± 0.22 g/dl, respectively).

When using *M. oleifera* leaf extract + Pb(C₂H₃O₂)₂ (G4), the mean values were decreased when compared with GIII for TP and TBIL (52.00 ± 2.86 and 3.75 ± 0.25 g/dl, respectively), but for TG it was increased (0.83 ± 0.04 g/dl).

3.2. Histological results

3.2.1. Liver

3.2.1.1. Light microscopy observations in (G1). The liver tissues of G1 appear to be in normal shape. Fig. 2 shows the hepatic lobules, polygonal-appearing epithelial cells called hepatocytes, radiating from a central vein (CV). Hepatocytes make up each interconnected plate-like brick in a wall, and the plates are over the CV. The CV of every part is indicated by its location in the middle of each lobule, where portal areas are found at its periphery. Hepatocytes showed healthy and intact architecture with no necrosis of the liver cells. Blood sinusoids (liver sinusoids) lined with endothelial cells appeared as flattened cells with flattened nuclei. Specified cells, known as Kupffer cells (K) or satellite macrophages, are easily identifiable with H & E stain and found between sinusoidal endothelial cells (Fig. 2).

3.2.1.2. Light microscopy observations in (G2). The liver section of (G2) appears to have a normal structure as (G1), where the hepatocytes appeared normal with rounded centrally located nuclei arranged in cords and blood sinusoids among the hepatic cords. Kupffer cells are clear with darkly stained nuclei (Fig. 2).

3.2.1.3. Light microscopy observations in (G3). Histological liver testing in (G3) showed clear alterations in the hepatocytes represented by cytoplasmic vacuolation, granulation in some cells and pyknosis of the nuclei. In addition, some hepatocytes appeared to be undergoing necrosis and loss of their nuclei; in some sections,
inflammatory cells appeared between hepatocytes, and there was congestion in blood vessels (Fig. 3).

3.2.1.4. Light microscopy observations in (G4). Examination of the liver in Pb(C₂H₃O₂)₂ + *M. oleifera* group (G4) revealed that the hepatic tissue appeared normal, resembling G1, where the hepatic cords were seen normal in arrangement and radiating around the central vein. The hepatic cells appeared normal with rounded nuclei and centrally located in the cytoplasm; some hepatic cells had vacuolated cytoplasm and faintly stained nuclei, and blood sinusoids and Kupffer cells appeared normal (Fig. 3).

3.2.2. Kidney

3.2.2.1. Light microscopy observations in (G1). The histological examinations of the kidney in (G1) revealed that the renal tissue could appear as a cortex and medulla. Each kidney contains millions of nephrons. A major part of each nephron is the corpuscles; a cortex dilated portion, proximal convoluted tubule and distal convoluted (Fig. 4) loop of Henle, which is thin and thick limbs, followed by the medulla back to the cortex. Collecting tubules (Fig. 4) from nephrons unite within collecting ducts to hold urine to the ureter. The renal capsule comprises a tuft of capillaries, the glomerulus, enclosed by a double-walled epithelial capsule, the Bowman's capsule, and the internal layer (the visceral layer) of the capsule envelops the capillaries of the glomerulus. The outer layer forms the limit of the renal capsules. Between the bilayers of Bowman’s capsule is the urinary space. The parietal layer of Bowman’s capsule, composed of simple squamous epithelium, rests on a basement membrane.

3.2.2.2. Light microscopy observations in (G2). Light microscopy observations of the kidney in the *M. oleifera* leaves extract treated group (G2) shows the normal kidney structure in both the cortex and medulla, where no changes in the glomerulus or the medullary rays (Fig. 4). While the structure of collecting tubules, thin and thick limb of Henle’s loop also revealed normal structure (Fig. 4).

3.2.2.3. Light microscopy observations in (G3). In (G3), the histological examination of kidneys of this group (Fig. 5) revealed significant alterations in proximal and distal convoluted tubules and collecting tubules (CT), thick Henle’s loop (K) which characterized by vacuolation and necrosis of cells (Ne) with pyknotic nuclei also, the blood vessel (BV) among the tubules and the Henle loops were filled with blood with necrotic cells.

3.2.2.4. Light microscopy observations in (G4). Mice in (G4) revealed normal structures of glomeruli, which appeared in the Bowman’s capsules. The urinary space appeared clear, with the parietal layer of the Bowman’s capsule appeared covered by squamous cells, and proximal and distal convoluted tubules also appeared normal in the cortex. However, in some sections, the distal convoluted tubules showed little changes, like cells with vacuolated cytoplasm and pyknotic nuclei. In the medulla, collecting tubules, thin and thick limbs of Henle’s loop also showed normal structures (Fig. 5).

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**Fig. 4.** Histological section of A: kidney of mice of the control group (G1) showing the cortex with renal corpuscles (glomerulus) (G), inside the Bowman’s capsule (BC) and the urinary space (US), proximal (PT), and distal (DT) convoluted tubules, which appeared normal with normal nuclei (N) (H & E stain X = 600); B: kidney of mice of the control group (G1) showing the medulla with normal collecting tubules (CT), thin limb of Henle’s loop (T), thick limb of Henle’s loop (K) with normal healthy nuclei (N) (H & E stain X = 400); C: kidney of mice treated with *M. oleifera* leaves extract (group G2) showing normal structures in cortex (C), medulla (M), glomerulus (G) and medullary rays (MR) (H & E stain X = 200); and E: kidney of mice treated with *M. oleifera* leaves extract (group G2) showing normal collecting tubules (CT), thin (T) and thick (K) limbs of Henle’s loop (T) (H & E stain X = 200).
4. Discussion

Medicinal plants and natural secondary metabolites have recently grown in prominence in modern medical practice (Abd El-Hack et al., 2022c,d; El-Shall et al., 2022; El-Saadony et al., 2021b). Because herbal products are widely available, acceptable, inexpensive, and safe, there is trust in their use (Saad et al., 2021a,b,c; El-Saadony et al., 2020; El-Saadony et al., 2022a). As a result, the quality, efficacy, and safety of plant medicines have become major problems in both developed and developing countries. Moringa rich in antioxidants and other nutrients such as vitamins, minerals and amino acids, carotenoids, polyphenols, phenolic acids, flavonoids, alkaloids, glucosinolates, isothiocyanates, tannins and saponins (Swelum et al., 2021a,b; El-Saadony et al., 2022b). Therefore, the use natural components such as peptides (Abd El-Hack et al., 2021; Yaqoob et al., 2021), nano fertilizers (El-Saadony et al., 2021c,d; Elnahal et al., 2022), biofertilizers (Desoky et al, 2020b) in increasing Moringa trees growth and quality are crucial to worldwide trend in using the pure medicine. Heavy metals toxicity is a serious global human health hazard (Usman et al., 2022; Desoky et al, 2020a). Therefore, the use natural components such as peptides (Abd El-Hack et al., 2021; Yaqoob et al., 2021), nano fertilizers (El-Saadony et al., 2021c,d; Elnahal et al., 2022), biofertilizers (Desoky et al, 2020b) in increasing Moringa trees growth and quality are crucial to worldwide trend in using the pure medicine.

Impact of Pb toxicity on the serum AST, ALT, and ALP levels and reported that increased AST, ALT, and ALP levels result from Pb liver toxicity. Pb(C$_2$H$_3$O$_2$)$_2$-mediated hepatorenal toxicity and damage in male mice with significantly increased enzymatic activities of ALP, ALT, and AST (Götz et al., 1994; Farrag et al., 2007; Elmenoufy, 2012; Wang et al., 2013).

In this work, ALP, ALT, and AST activities were elevated post-treatment with lead and then lowered nearly to the normal level when supplied with M. oleifera to animals in (G4). These findings may be because of the protecting impact of M. oleifera. Kothandaraman and Dawood Sharief (2013) observed that administration of stannous chloride significantly increased AST, ALT, ALP, and ACP in blood serum compared with control. They added that the enzyme parameters significantly decreased in animals treated with M. oleifera, nearing the control values. Therefore, they reported that supplementing with M. oleifera could minimize the toxic effects of stannous chloride. Also, Sharifudin et al. (2013) evaluated the impact of M. oleifera hydroethanol extract versus hepatic damage by hepatotoxicity and acetaminophen, revealing an elevated level of (ALT & AST) in animals. They found that M. oleifera crude extracts decreased these enzymes activities, thus lowering the seriousness of the liver injury. They suggested that M. oleifera leaf extract plays a critical role in treating the cause of acute hepatic damage in rats.

Similarly, Sharma et al. (2012) assessed the efficacy of M. oleifera as a liver protectant and antioxidant in comparison to...
In this work, the histological investigation of renal tissue of animals orally taken with Pb revealed severe alterations in renal tissues. These data concur with those of Farrag et al. (2007). They noticed that in rats supplied on the basal diet and eaten Pb, the renal corpuscle revealed congestion and hypercellularity, degeneration of the tubules, inflammatory infiltration, congested renal corpuscle and hemorrhagic parts in the interstitial region.

Also, the influence of lead exposure on the kidney of Wistar rats was evaluated by Missoun et al. (2010). They noticed an elevation of blood calcium, phosphaturia and calcium in rats supplied with lead contrasted with control ones, and the elevation of these showed a renal shortage that was inveterate by a lowering of creatinine and urea in urine samples and the existence of calcium oxalate dihydrate crystals in urine samples of exposed rats. All Pb-supplied animals in this trial revealed intranuclear inclusion bodies in the renal proximal tubular. The estimation of the level of Pb in the blood revealed that this agent elevated between supplied animals, also, they found that Pb supplied orally induces kidney defects in the rats.

Additionally, Fakurazi et al. (2008) recorded the hepatoprotective impact of M. oleifera via the restoration of the hepatic enzymes in rats induced with acetaminophen. They also noticed that the pretreatment with this plant significantly saved rat hepatic histology. They recommended that the plant extract had action in maintaining basic cell integrity of the hepatocellular membrane, thus inhibiting enzyme leakage into the blood circulation. However, they also proposed that the caring impacts of M. oleifera leave versus chemical-caused liver toxicity were because of its ability to stimulate the phase II detoxification pathway through promoting GSH conjugation with toxic metabolites generated from CYP450 pathway (Fakurazi et al., 2008).

Azab (2014) investigated the liver protective effect of sesame oil versus Pb caused liver damage in albino mice from the histological and biochemical characteristics; they noticed that lead-supplied animals showed huge structural injury in the hepatocytes, and there were necrotic and degenerative alterations along with the presence of the inflammatory cell.

Sirimongkolvorakul et al. (2012) assessed the impact of M. oleifera on lowering the lead toxicity in Puntius Altus via histopathological examination in fishes, which were classified into three groups for supply with various M. oleifera levels; 0, 20, and 60 mg g-1 fish food, past month, they exposed fish to 93.8 mg/L Pb(C2H3O2)2 exposure revealed glomerular and tubulointerstitial alterations accompanied by glycosuria, proteinuria, kidney failure, and hypertension (Kim et al., 1996; Loghman-Adham, 1997). These findings support the current research results of lead intoxication of the kidney.

In addition, Ghorbe et al. (2001) found that orally supplied with Pb revealed a considerable elevation in the blood urea and serum creatinine. In parallel, Pb intoxication reveals interstitial fibrosis and hyperplasia and gradual atrophy of tubules and glomeruli (Goyer, 1989; Nolan and Shaikh, 1992). Pb(C2H3O2)2 exposure revealed glomerular and tubulointerstitial alterations accompanied by glycosuria, proteinuria, kidney failure, and hypertension. Also, the influence of lead exposure on the kidney of Wistar rats was highlighted by Farrag et al. (2007), who stated that lead intoxication revealed a marked elevation in the blood urea and serum creatinine. In parallel, Pb intoxication reveals interstitial fibrosis and hyperplasia and gradual atrophy of tubules and glomeruli (Goyer, 1989; Nolan and Shaikh, 1992). Pb(C2H3O2)2 exposure revealed glomerular and tubulointerstitial alterations accompanied by glycosuria, proteinuria, kidney failure, and hypertension. However, M. oleifera feeding fishes, particularly those with higher levels, noticed smaller scores in the histological changes when contrasted with the control fishes. Thus, these data indicate that pre-supplying M. oleifera would lower Pb(C2H3O2)2 damage in fish subjected to an ecosystem polluted with waterborne Pb(C2H3O2)2.
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