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The effect of alcoholic and aqueous extract of *Capparis spinosa* leaves on histological and physiological structure in the kidneys of male rats injected with lead acetate intraperitoneally

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Abstract---The current study aimed to investigate the curative and preventive effect of alcoholic and aqueous extract of *Capparis spinosa* leaves on the histological structure of the kidneys and some biochemical parameters of male rats injected intraperitoneally with lead acetate. Biometrics included urea, creatinine, uric acid and total protein levels and total antioxidants (T-AOX), glutathione (GSH) and malondial aldehyde (MDA) assay. The study included 40 male laboratory male albino rats of the Sprague dawley breed, with weights ranging between 170-200 grams, and they were randomly divided into eight groups. The second group injected intraperitoneally with lead acetate, the third group was injected with the alcoholic extract of capers leaves, the fourth group was injected with aqueous extract of capers leaves, the fifth group was injected with britonia with lead acetate for 30 days and then it was injected with the alcoholic extract of capers leaves for 30 days, the sixth group was injected with britonia with acetate Lead for 30 days and then dosed with aqueous extract of capers leaves, the seventh group dosed with alcoholic extract of capers leaves and after 3 hours injected Britonia with lead acetate, the eighth group dosed with aqueous extract of capers leaves and after 3 hours injected Britonia with lead acetate. The results showed that the peritoneal injection of lead acetate to male rats caused a significant

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increase at the probability level (P≤0.05) in the concentration of urea, creatinine, uric acid, total protein and malondialdehyde (MDA), while there was a significant decrease (P). ≤0.05 in the level of total antioxidants (T-AOX) and glutathione (GSH) in the blood serum compared with the control group.The results of groups that were injected peritonia with lead acetate for 30 days and then dosed with alcoholic extract of capers leaves for another 30 days as well as the groups that were dosed First with alcoholic extract and aqueous extract of capers leaves and after 3 hours Britonia injected with lead acetate showed a significant decrease at the probability level ((P≤0.05) in the level of urea, creatinine, uric acid, total protein and malondialdehyde (MDA) compared to With the group that injected intraperitoneally with lead acetate, while the results showed a significant increase in the total antioxidants (T-AOX) and glutathione (GSH) compared with the group that injected intraperitoneally with acetate. Lead. The results of the study for groups that were dosed with alcoholic extract of capers leaves only showed no significant changes at the probability level ((P≤0.05) in the level of urea, creatinine, malondialdehyde (MDA), total antioxidants (T-AOX) and glutathione (GSH). Except for uric acid and total protein, which had a significant decrease compared to the control group, while the groups that were dosed with aqueous extract of caper leaves did not show any significant changes at the probability level ((P≤0.05) in any of the studied variables compared with the control group. The current study also showed significant histological changes in the kidney tissue in the group that injected Britonia with lead acetate, while the groups treated with alcoholic and aqueous extract of capers leaves showed an improvement in the histological picture of the kidney tissues.

Keywords---lead acetate, kidney, urea, creatinine, glutathione, capers.

Introduction

Lead (Pb) is considered one of the heavy and toxic metals in the environment. It is one of the non-essential elements for the body because it does not affect the vital functions of the body. It is characterized by its high stability, abundance, low price and many uses as it is used in various activities and industrial applications due to its physical and chemical properties (Sohrabi). et al., 2021). There is lead either in organic form, which is lead acetate and tetraethyl lead, which is added to vehicle fuels as an anti-explosion material, or it is found inorganic and humans are exposed to it mainly through polluted water, and there are many other potential sources, which include cosmetics, folk medicines Paints, gasoline, the coal combustion process, and in industries such as batteries, pipes, ceramic tableware, toys and pencils and is an essential component in the manufacture of food cans (Budnik and Casteleyn, 2019). The danger of lead lies in the difficulty of detecting poisoning with it, because even seemingly healthy people may have a high level of lead in the blood and do not show any symptoms or signs of poisoning until after dangerous amounts of lead have accumulated in the body. All forms of lead are toxic to humans and most In adults, the effect of lead is so

great that more than 900,000 premature deaths annually are attributable to lead exposure (Kocarnik et al., 2022). Lead enters the body through ingestion or absorption through the skin and respiratory tract and accumulates in the blood, bones and soft tissues such as the liver, kidneys and spleen (Aktepe et al., 2022). Because of the cumulative property of lead, exposure to low concentrations of it may lead to serious disease states such as neurological deficits, cardiovascular diseases, strokes, endocrine diseases, immune diseases, respiratory system, and urinary system (Al-Megrin et al. 2019).

Medicinal plants have gained in modern times a special importance in conjunction with the great acceleration in the discovery of the effective chemical components of these plants and their role in the treatment of many diseases (Anand et al., 2019). Which makes it a very important source of therapeutic materials, medicinal plants and their extracts have been widely used in the prevention of animal diseases (Kuralkar and Kuralkar, 2021). It was reported (Tiwari et al., 2021) that natural biomolecules such as phenolic compounds, carotenoids and polysaccharides, were effective in inhibiting reactive oxygen species caused by organ diseases. Furthermore, there is a growing preference for natural antioxidants rather than synthetic molecules due to the safety of natural sources (Lourenço et al., 2019). The plant *Capparis spinosa* is one of the aromatic perennials that is widely used in the medical field (Rad et al., 2021). It has been used since ancient times in the treatment of many diseases that affect humans, such as cold, fever, stomach pain, laxative and anti-inflammatory. 2018).

Aim of the study

- Estimation of nephrotoxicity indicators in the serum of male rats, including measuring the level of urea, creatinine, uric acid and total protein.
- Estimation of oxidative stress indicators by measuring the level of Malondialdehyde and estimating the level of total antioxidants. Total anti-oxidant and glutathione estimation.
- Study of histological variables in the kidneys.

Materials and working methods

Preparation of the alcoholic extract of capers leaves

The alcoholic extract of capers leaves was prepared using the extraction device (Soxhlet), where 50 g of capers leaves powder was placed in a thimble tube made of strong filter paper and placed in the tube of the device, then alcohol was added to it Gradually released ethyl ethanol, then the device was run at a temperature of (65 °C) for four hours, and after the extraction process was completed, the extract was taken and placed in ceramic jars and placed in the electric oven at a temperature of (60 °C) and left to dry, then the remaining extract was collected And put it in dark containers and kept until use (Daher and Muraih, 2021; Redfern et al., 2014)

Preparation of the aqueous extract of capers

The aqueous extract of capers was prepared on a daily basis by placing (15) gm of dry powder of capers leaves in a glass beaker of (250) ml capacity, 150 ml of distilled water was added to it and left The hot plate with magnetic stirre was heated for an hour with continuous stirring at a temperature of 50°C, after that it was left to cool and then filtered with three layers of gauze to separate the large plankton, after which an extract was obtained ready to dose the animals (Samari et al. , 2019).

Preparation of lead acetate

Lead acetate powder was dissolved in physiological solution, and the animals were injected intraperitoneally at a concentration of 20 mg / kg of body weight and at a dose (0.2 ml) twice a week for 60 days (El-Khadragy et al., 2020; Ito et al., 1985).

Animals used in the study

(40) males Albino rates of white rats of the type (Sprague Dawley) Rattus norvagegicus were used in this study, whose ages ranged between (14-12) weeks, and their weights ranged between (200-170) grams. In cages prepared for this purpose at a temperature of (25 ± 3◦C) with a light period of 12 hours and a period of darkness of 12 hours, the standard diet and adequate water were given. The animals were randomly divided into 8 groups, each group included 5 animals. The first group (negative control) was given orally 5 ml per kg of saline solution (Normal Saline 0.9%). The second group, the positive control, was injected peritoneally with a dose of (0.2 ml) lead acetate at a concentration of 20 mg/kg. The third group was dosed with (3 ml) of alcoholic extract of capers leaves at a concentration of 300 mg/kg. The fourth group was dosed with (3 ml) of aqueous extract of capers leaves at a concentration of 300 mg / kg. The fifth group injected Britonia with 20 mg/kg of lead acetate at a dose (0.2 ml) for a period of 30 days, and then dosed with an amount (3 ml) at a concentration of 300 mg/kg of alcoholic extract of capers leaves for 30 days.

The sixth group injected Britonia with 20 mg/kg of lead acetate at a dose (0.2 ml) for 30 days, and then dosed with (3 ml) at a concentration of 300 mg/kg of aqueous extract of capers leaves for 30 days. The seventh group dosed (3 ml) of alcoholic extract of capers leaves at a concentration of 300 mg / kg 3 hours before injecting lead acetate with peritonia at a dose (0.2 ml) of lead acetate at a concentration of 20 mg / kg. The eighth group dosed (3 ml) of aqueous extract of capers leaves at a concentration of 300 mg / kg 3 hours before injecting lead acetate with peritonia at a dose (0.2 ml) of lead acetate at a concentration of 20 mg / kg. Lead acetate was injected twice a week, while the extracts were dosed from day to day for 60 days at a rate of three doses per week. After the end of the experiment for (60) days, the animals starved for 24 hours. After anesthesia, the animals were sacrificed and blood was collected using the heart puncture method. The blood serum was obtained using a centrifuge at 3000 rpm for (15 minutes) and the serum was saved. At -20°C, the kidneys were removed, washed with

physiological solution, and placed in 10% formalin solution until tissue excision was performed.

Biochemical tests

The tests included estimating the levels of urea, creatinine, uric acid and total protein, as a ready-made analysis kit from the Spanish company LINEAR was used. As for malondialdehyde, total antioxidants and glutathione, they were measured using a ready-made analysis kit from the American company Elabscience.

Histological sections

Histological sections of the kidneys were made according to sequential steps based on (Bancroft and Stevens, 1999). Washing, Dehydration, Clearing, Embedding and Infiltration and Sectioning Trimming and were performed on it, cutting with a thickness of (5-6) microliters, and finally hematoxylin and eosin dye was used. German made.

Statistical analysis

The significant differences between the means were tested using the least significant difference test (L.S.D). At the probability level of 0.05, Analysis of variance was analyzed using the ANOVA Table using the SPSS statistical program.

Results

Analysis of urea, creatinine, uric acid, and total protein

Figure 2, 3, 4, 5 showed that peritoneal injection with lead acetate caused an increase in the concentration of urea, creatinine and uric acid compared to the control group, and it decreased in the group treated with plant extracts compared to the second group that was injected peritoneally with lead acetate.

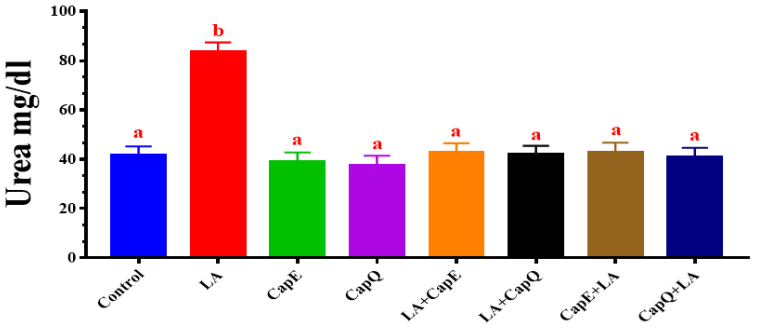


Figure 1. Effect of aqueous and alcoholic extracts of capers leaves on urea concentration in serum of male rat

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P.(≥

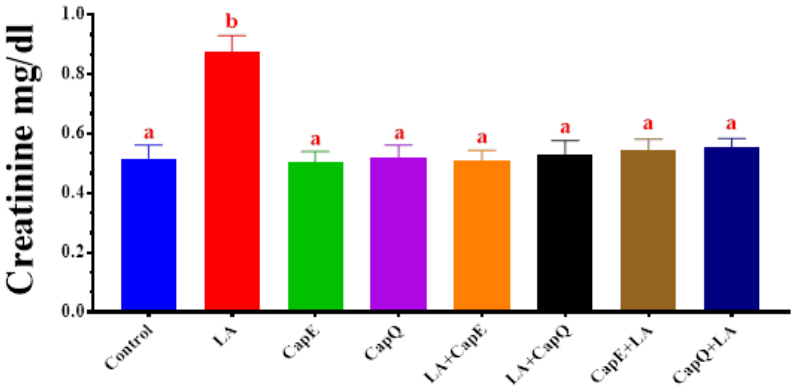


Figure 2. Effect of alcoholic and aqueous extract of capers leaves on creatinine concentration in the blood serum of male rats

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P.(≥

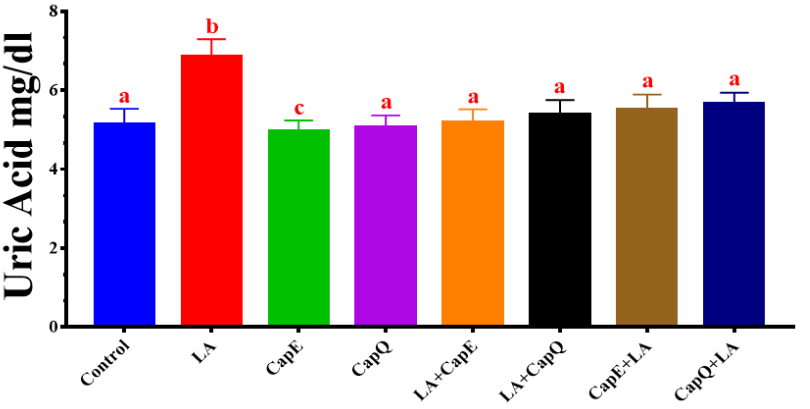


Figure 3. Effect of alcoholic and aqueous extract of capers leaves on the concentration of uric acid in the blood serum of male rats

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P ≤).

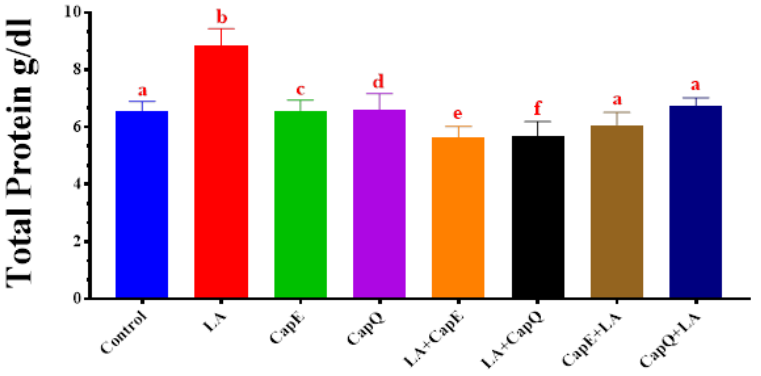


Figure 4. Effect of alcoholic and aqueous extract of caper leaves on total protein concentration in serum of male rat.

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P ≤).

Total anti oxidant and glutathione analysis

Figure 6, 7 showed that the group that injected Britonia with lead acetate had a significant increase in the level of total antioxidants and glutathione compared to the normal control group, and the levels of total antioxidants and glutathione decreased in the groups treated with alcoholic extract and aqueous extract of caper leaves compared to the pathogenic group by injecting them Britonia lead acetate.

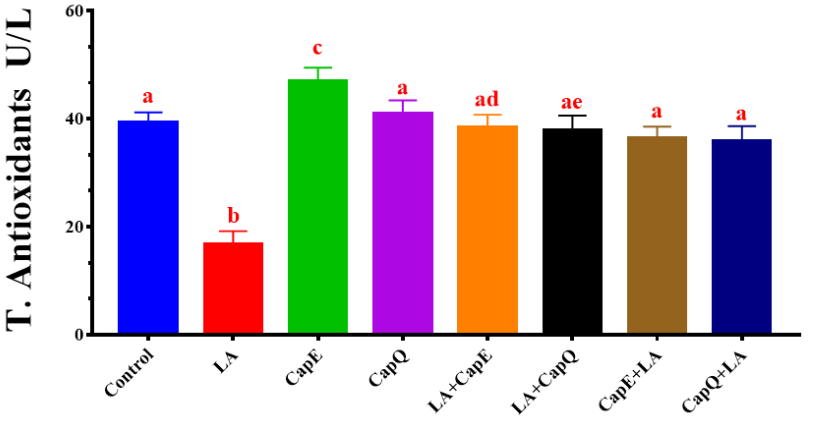


Figure 5. Effect of alcoholic and aqueous extract of capers leaves on the level of total antioxidants (T-AOX) in the blood serum of male rats

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P ≤).

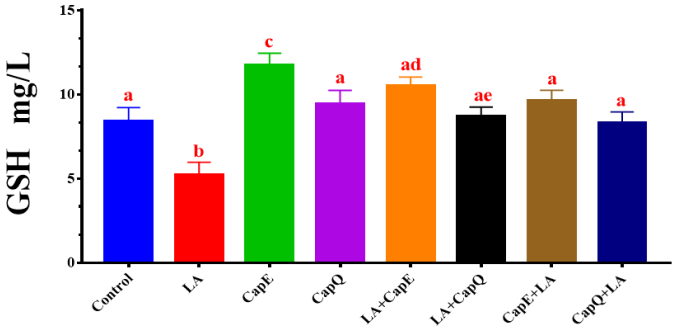


Figure 6. Effect of alcoholic and aqueous extract of capers leaves on the activity of glutathione (GSH) in the serum of male rats

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P ≤).

MDA Malone Dialdehyde Analysis

Figure 8 showed a significant increase in lipid peroxidation (MDA) in the group injected with lead acetate intraperitoneally compared with the control group, while it decreased in the groups treated with alcoholic extract and aqueous extract of caper leaves compared with the nurse group injected with lead acetate intraperitoneally.

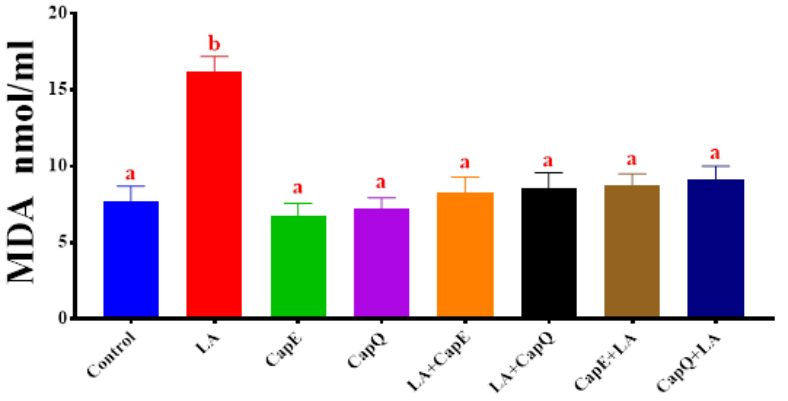


Figure 7. Effect of the alcoholic and aqueous extract of Capers leaves on the concentration of malondialdehyde MDA in the serum of male rats

The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group. The different letters indicate the significant difference at the level of probability (0.05 P ≤).

Histological study of the kidneys

Microscopic examination of the histological sections of the kidneys of male laboratory rats in the control group and the group treated with alcoholic extract of capers leaves, and the group treated with aqueous extract of capers leaves showed the normal structural structure of the kidney tissue (image (1), (2) and (3) where the glomeruli appeared in shape and size Normally surrounded by Bowman's capsule, the convoluted urinary tubules appeared as normal. However, the results of the microscopic examination through the histological section of the kidneys in the group injected with lead acetate (picture 4) showed significant histological changes represented by the destruction of the glomerulus (DG), the thickening of the renal vascular wall (TW), its congestion (VC), the shedding of the endothelium (SE) of the urinary tubules, and the infiltration of lymphocytes (LI) and hemorrhage (H), and the results of the histological examination showed the degeneration of the cells of the urinary tubules with the presence of necrotic materials in the cavities of the urinary tubules. While the microscopic examination through the histological section of the kidneys in the group treated with the pathogen and then dosed with alcoholic extract and aqueous extract pictures (5), (6), (7) and (8) showed the presence of histological changes but to a less severe degree compared to the group treated with the pathogen.

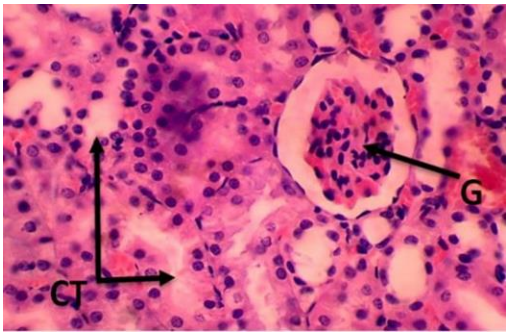
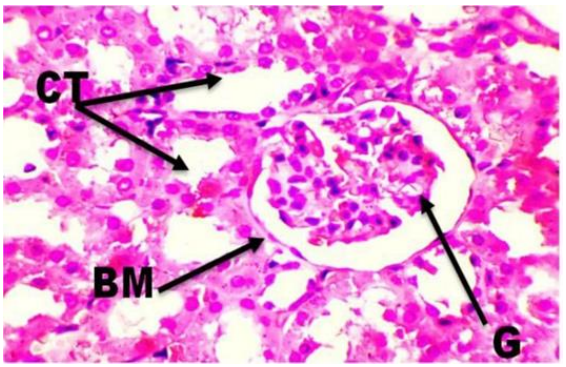


Image 1. Cross-section of the kidneys of the control group showing the normal structure of the glomeruli (G) surrounded by Bowman's capsule (BM) and the convoluted tubules (CT) H&E X40



Picture 2. Cross-section of the alcoholic extract group kidneys showing glomeruli (G) surrounded by Bowman's capsule (BM) and convoluted urinary tubules (CT) H&E X40

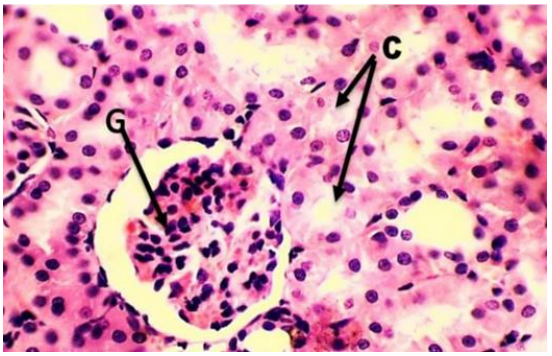
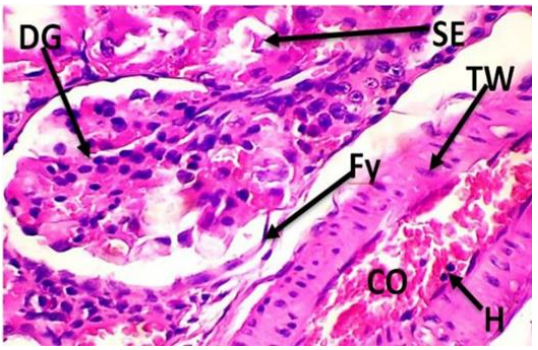
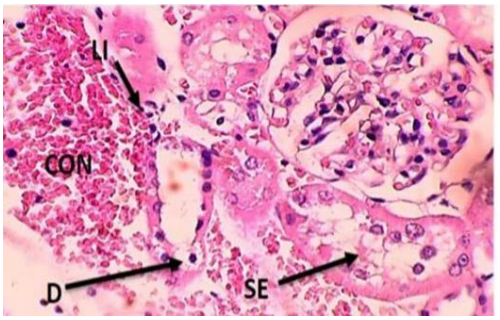


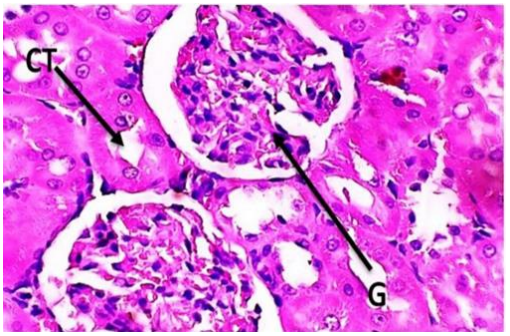
Image 3. Cross-section of the kidneys of the aqueous extract group showing glomeruli (G) surrounded by Bowman's capsule (BM) and convoluted urinary tubules (CT) H&E X40



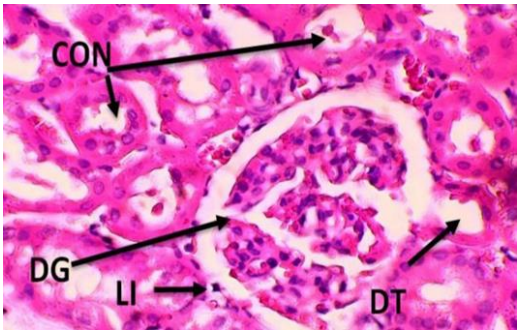
Picture 4. Cross-section of the lead acetate group kidneys showing glomerulosclerosis (DG), renal vascular wall thickening (TW), congestion (VC), urinary tubule endothelial dissection (SE), lymphocyte infiltration (LI), and hemorrhagic (H) H&E X40



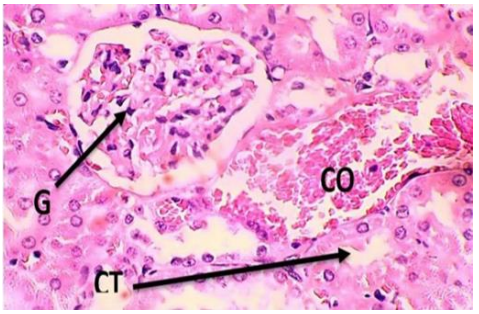
Picture 5. Cross-section of the kidneys of the lead acetate group and alcoholic extract showing necrosis of the lining (SE) of the urinary tubules and degeneration (D) of some of its cells with congestion (CON) and infiltration of lymphocytes (LI) H&E X40



Picture 6. Cross-section of the kidneys of the lead acetate and aqueous extract group showing glomeruli (G) and convoluted (CT) urinary tubules (CT) H&E X40



Picture 7. Cross-section of the kidneys of the alcoholic and lead acetate group showing glomerular (DG) and some urinary (DT) damage with infiltration of lymphocytes (LI) H&E X40



Picture 8. Cross-section of the kidneys of the aqueous extract and lead acetate group showing glomeruli (G) and convoluted urinary tubules (CT) with congestion (CON) of renal blood vessels H&E X40

Discussion

The group that was injected with lead acetate intraperitoneally had a significant increase in the biochemical indicators of kidney function, which include urea, creatinine, uric acid and total protein. Large amounts of urea (Guliński, 2021) or it may be as a result of the formation of free radicals resulting from the peritoneal injection of lead acetate that leads to the oxidation of proteins and amino acids, which results in an increase in the concentration of urea in the blood serum of

animals exposed to oxidative stress as a by-product (Xia *et al.,* 2021). Or perhaps due to the breakdown of renal nephrons as a result of the high toxicity of lead acetate (Chakraborty *et al.*, 2013). As for the cause of the rise in creatinine level, it may be due to the chronic complications that occur in some organs, including the kidneys, as a result of exposure to lead acetate, which causes oxidative stress. Functional cell lining of the glomerular capillary vessels, which leads to an increase in the concentration of creatinine in the blood and a decrease in its amount excreted with urine, resulting in an increase in the level of urea and creatinine (Eom *et al.,* 2020).

The high concentration of uric acid may be attributed to the increase in the formation of purine bases, which are the main component of the formation of uric acid, which may result from the digestion of nucleic acids due to exposure to lead (Braga *et al.*, 2020), and (Johnson *et al.*, 2005) indicated that the high concentration of uric acid Uric acid is a result of a decrease in the rate of renal filtration of uric acid, and thus an increase in its concentration in the blood, and then its deposition in the joints and kidneys, causing chronic kidney inflammation. As for the high concentration of total protein, it is probably due to the renal and hepatic damage caused by the effect of lead acetate (Mohammed *et al.*, 2019). As for the decrease in the level of vital indicators of kidney function in groups treated with alcoholic extract and aqueous extract, it may be due to the activity of the active compounds of capers, such as flavonoids, phenols and glycosides, which have great potential to scavenge free radicals from the body such as (OH•,1O2,O2-•) and reduce Oxidative damage to renal cells and glomeruli and an increase in glomerular filtration rate. It is noteworthy that giving the alcoholic extract of caper leaves to the pathogenic groups by injecting them intraperitoneally with lead acetate had somewhat better results compared to the pathogenic groups with lead acetate and given the aqueous extract of caper leaves (Tlili *et al.,* 2017).

The reason for the decrease in the level of the antioxidants T-AOX, GSH in the group that injected intraperitoneally with lead acetate can be attributed to the increase in the formation of free radicals, in particular ROS and the occurrence of oxidative stress, causing the oxidation of glutathione due to its antioxidant activity and then converting it to the oxidized form represented by GSSG disulfide. Which is considered toxic and works to stimulate other types of free radicals (Lamidi *et al.*, 2021), and the levels of total antioxidants and glutathione increased in groups treated with alcoholic extract and aqueous extract of caper leaves. Caper leaves possess many effective chemical compounds, especially phenolic compounds, flavonoids, tannins, and vitamins E, C, which have a major role in inhibiting and removing free radical reactions (Mansour *et al.,* 2016). Eliminate damage caused by free radicals (Neha *et al.*, 2019).
As for the indicators of oxidative stress, represented by Malone Dialdehyde (MDA), there was a significant increase in the group that was injected with lead acetate peritoneally. The reactions of free radicals as a result of having double bonds, and MDA is produced from the oxidation of these acids through the reactions of free radicals in the process of lipid peroxidation (Kabel, 2014). -acyl-CoA oxidase, which starts the oxidation of fatty acids, which in turn leads to an increase in the production of endogenous hydrogen peroxide, which contributes to the process of lipid peroxidation of the cell membrane. The results of the current study showed a

decrease in the level of MDA in groups treated with plant extracts. The results of (Abdel-Salam *et al.,* 2009) agree with the current results, as it was shown that capers extracts have an effect on the toxicity caused by lead acetate in a For mice, it is highly effective in reducing MDA levels due to its high content of flavonoids, alkaloids, lipids and glucosinolates that may enhance the antioxidant system in the body and neutralize the effects of lead.

Microscopic examination through the histological section of the kidneys in the lead acetate-injected group showed significant histological changes represented by glomerulosclerosis (DG) damage glomerulus, renal vascular wall thickness (TW) thickness, VC vascular congestion, necrosis of the urinary tubule endothelium (SE) and infiltration of lymphocytes (LI) infiltration Leucocytic and (H) hemorrhage. As the results of histological examination showed the degeneration of the cells of the urinary tubules with the presence of necrotic materials in the cavities of the urinary tubules, the histological changes in the kidneys can be attributed to the oxidative stress caused by intraperitoneally injecting rats with lead acetate, which leads to stenosis. In the blood vessels of the kidneys, which negatively affects their functions and causes an increase in the level of nitrites in the urine and serum.

An increase in nitrites causes pathological changes in the kidneys, constriction of blood vessels, generation of free radicals, the generation of fat peroxidation and destruction of the renal tubules. These histological changes are consistent with the current results that showed an increase in urea levels. And creatinine in the blood serum of male rats treated with lead acetate. The concentration of lead rises only when half of the nephron is destroyed or completely destroyed (Khan *et al.*, 2015), and injecting male laboratory rats with lead acetate leads to vascular constriction in the kidneys, resulting in ischemic blood loss, which leads to damage in the number of kidneys. of cell membranes (Offor *et al.*, 2017; Sanchez, 2018), lead directly affects the functioning of the renal tubules, causing damage to these tubules and resulting in a type of urine containing amino acids causing high blood pressure with increased levels of urea and creatinine in the blood (Amin *et al.*, 2021). As for the results of the microscopic examination of the kidneys of the groups treated with caper plant extracts, they showed improvement and minor histological changes compared to the pathogenic group injected with lead acetate intraperitoneally.

Conclusions

Intraperitoneal injection of lead acetate to male rats led to a significant increase in the level of urea, creatine, uric acid, total protein and malondialdehyde (MDA), while it caused a significant decrease in the concentrations of antioxidants, as the activity of total antioxidants (T-AOX and GSH glutathione enzyme) decreased in comparison with the control group. Also, treatment with alcoholic extract and aqueous extract of capers leaves caused the reversal of all the values of the studied biochemical variables resulting from exposure to oxidative stress towards normal values or close to them, which makes it possible to use it alone to reduce oxidative stress or to prevent it and in the end use it as a preventive antagonist.

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