The Effect of Alcoholic and Aqueous extract of *Capparis spinosa* leaves on histological and physiological structure in the liver 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. The biochemical parameters included estimating the level of liver enzymes: GGT, ALP, AST, ALT 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 results showed that the peritoneal injection of male rats with lead acetate caused a significant increase at the level of probability ((P≤0.05) in the level of liver enzymes GGT, ALP, AST, ALT and Malone Dialdehyde (MDA), while there was a significant decrease (P≤0.05(in the level of antigens. Total oxidative stress (T-AOX) and glutathione (GSH) in the blood serum compared with the control group The results of groups that were injected with lead acetate intraperitoneally for 30 days and then dosed with alcoholic extract of caper leaves for another 30 days as well as groups that were first dosed with alcoholic extract and aqueous extract showed For caper leaves and after 3 hours, britonia injected with lead acetate showed a significant decrease at the level of probability ((P≤0.05) in the level of liver enzymes GGT, ALP, AST, ALT and malon dialdehyde (MDA) compared with the group that injected Britonia with lead acetate, while the results showed Significant increase in total antioxidants (T-AOX) and glutathione (GSH) compared with the group that was injected with lead acetate intraperitoneally.The results of the study for groups that were dosed with alcoholic extract of caper leaves only showed no significant changes at the level of Tally (P≤0.05) in the level of GGT, ALP, AST, ALT, Malone Dialdehyde (MDA) and total antioxidants (T-AOX) compared with the control group, while the groups dosed with aqueous extract of caper leaves did not show any significant changes at the level of Probability ((P≤0.05) in any of the studied variables compared with the control group. The current study also showed significant histological changes in the liver 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 liver tissues.

Keywords: **lead acetate, capers, liver, ALT, AST, GGT, glutathione, malondialdehyde.**

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1.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

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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 thousand 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)

Capparis spinosa is one of the aromatic perennial plants widely used in the medical field (Rad *et al.,* 2021). It has been used since ancient times in the treatment of many diseases that afflict humans, such as cold, fever, stomach pain, laxative and anti-inflammatoryIt is also one of the plants rich in many bioactive compounds such as quercetin and rutin, which possess antioxidant activity in addition to its activity as an anti-cancer substance (Zhang and Ma, 2018).

2.Aim of the study

1. stimation of indicators of hepatotoxicity in the serum of male rats, including measurement of the level of ALT enzyme, AST enzyme, ALP enzyme and GGT enzyme
2. Estimation of oxidative stress indicators by measuring the level of Malondialdehyde and estimating the level of total antioxidants and glutathione.
3. Study of histological variables in the kidneys.

3.Materials and working methods

1.3 Preparation of alcoholic extract of capers leaves: The alcoholic extract of capers leaves was prepared using the extraction device (Soxhlet), where 50 gm of capers leaves powder were 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 an 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)

2.3 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).

3.3 Preparation of lead acetate: Lead acetate powder was dissolved in physiological solution,

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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).

4.3 Animals used in the study and design of the experiment: (40) males Albino rates of white rats (Sprague Dawley) Rattus norvagegicus were used in this study, their ages ranged between (14-12) weeks, and their weights between (200-170) grams They were placed 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. They were given the standard ration and sufficient water. 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.

5..3 Biochemical tests: The tests included estimating the levels of liver enzymes GGT, ALP, AST, and ALT, 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.

6..3 Histological sections: Histological sections of the Liver 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.

7..3 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.

5. Results

1.5 Analysis of ALT, AST, ALP, GGT

Figure 2, 3, 4, 5 showed that peritoneal injection with lead acetate caused an increase in the concentration of ALT, AST, ALP, GGT compared to the control group, and it decreased in the group treated

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with plant extracts compared to the second group that was injected peritoneally with lead acetate.

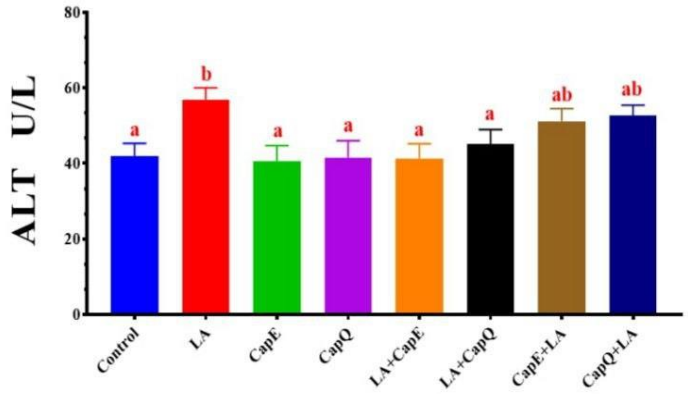

Figure 1: Effect of alcoholic extract and aqueous extract of caper leaf on the concentration of alanine aminotransferase (ALT) in the blood serum of male rats.

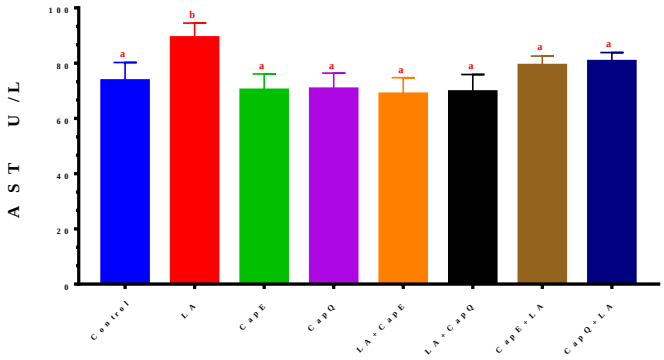

Figure 2: Effect of alcoholic and aqueous extract of capers leaves on the concentration of aspartate aminotransferase (AST) in the serum of male rats.

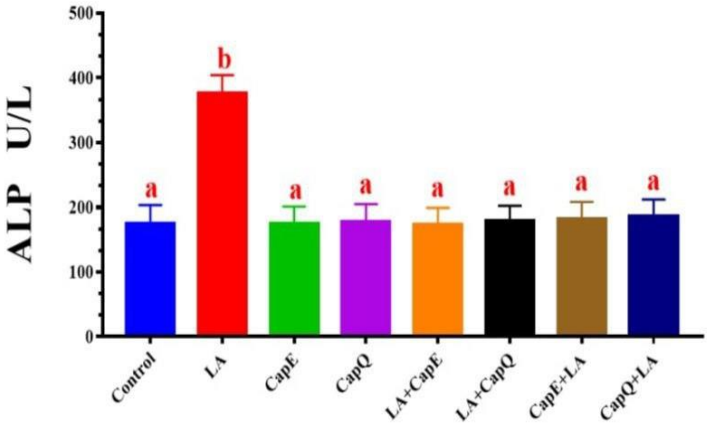

Figure (3): Effect of alcoholic and aqueous extract of capers leaves on the concentration of alkaline phosphatase enzyme ALP in the serum of male rats.

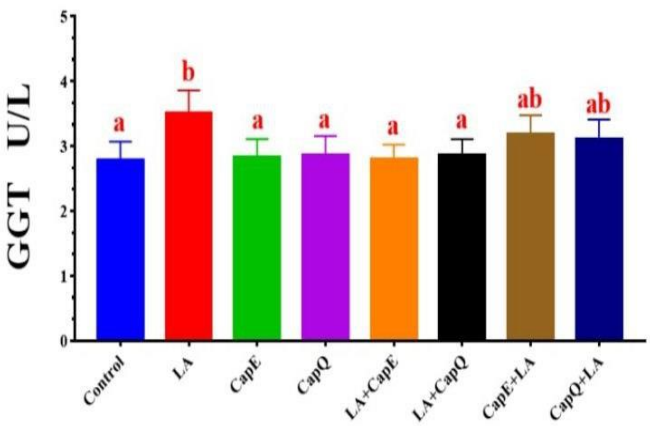

Figure (4): Effect of alcoholic and aqueous extract of capers leaves on the concentration of gamma-glutamyl transferase (GGT) in the blood serum of male rats.

- 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 ≤).

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2. 3. 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.

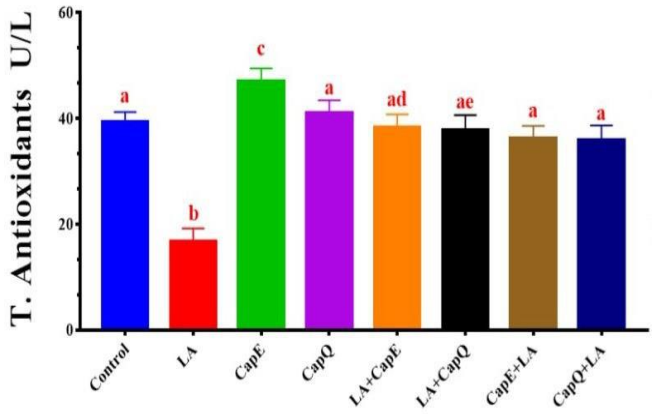


Figure (5): Effect of alcoholic and aqueous extract of capers leaves on the level of total antioxidants (T-AOX) in the blood serum of male rats

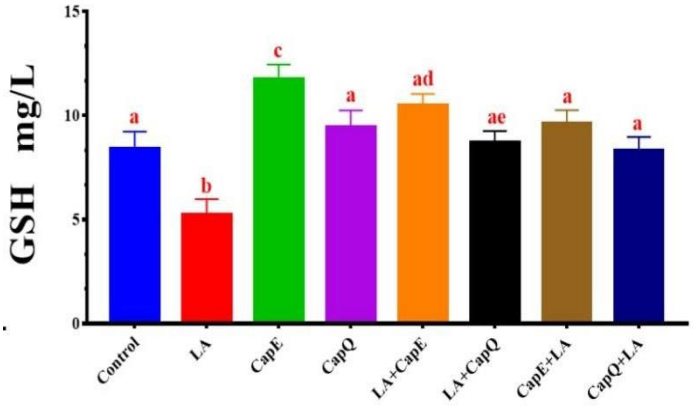


Figure (6): Effect of alcoholic and aqueous extract of capers leaves on the activity of glutathione (GSH) in the serum of male rats.

- 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 ≤).

Malone Dialdehyde MDA Analysis

Figure 8 showed a significant increase in lipid peroxidation (MDA) in the intraperitoneal lead acetate injected group compared with the control group, while it decreased in the alcoholic extract and aqueous extract of capers leaf compared to the intraperitoneal lead acetate injected pathogen group.

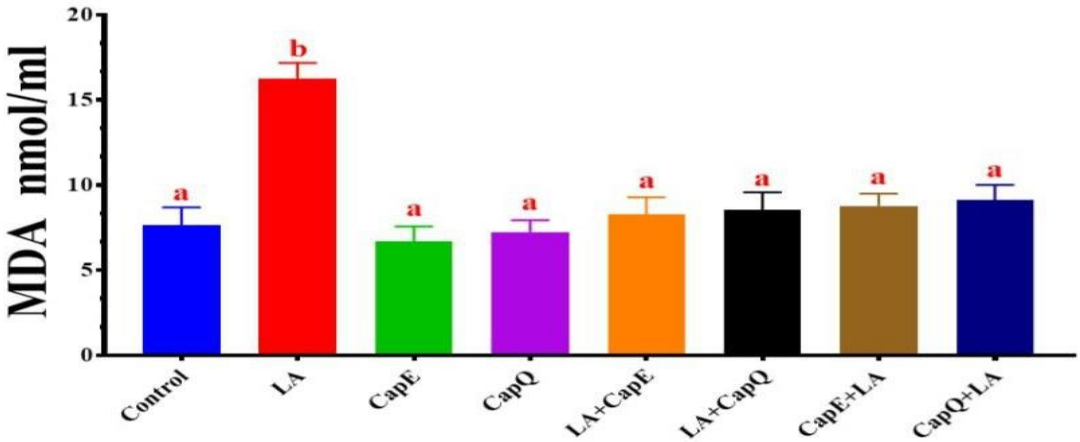
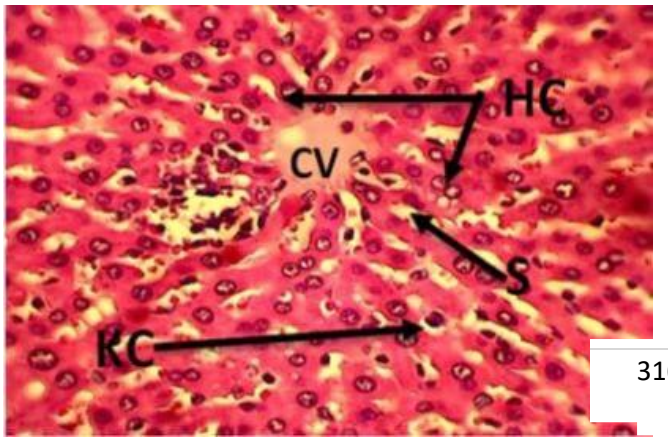


Figure (7): Effect of the alcoholic and aqueous extract of Capers leaves on the concentration of malondialdehyde MDA in the serum of male rats.

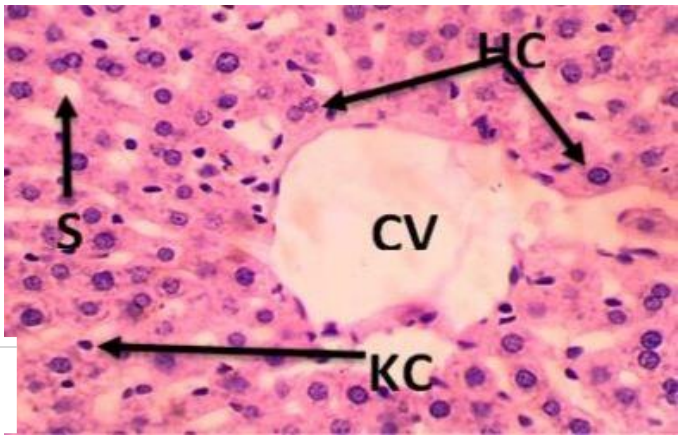
- The values expressed in each row mean the mean ± standard deviation, and the number of rats/5 in the group.
- The different letters indicate the significant difference at the level of probability (0.05 P ≤).

4. 3. Histological study of the liver

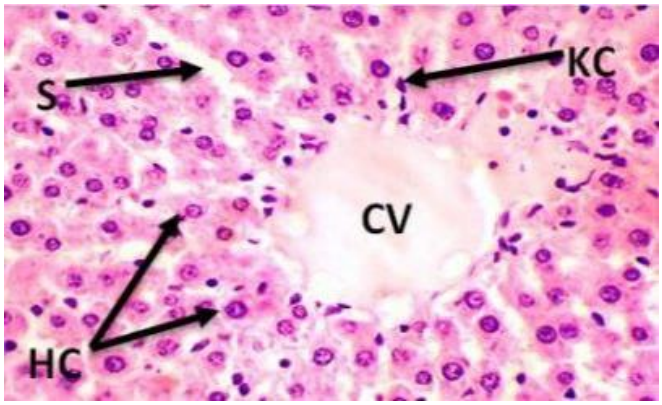
Microscopic examination of the histological sections of the Liver of male laboratory rats in the control group and the group treated with alcoholic extract of capers leaves, and the group treated with aqueous extracts of capers leaves showed the normal structural structure of the liver tissue. Picture (1), (2) and (3) Hepatocytes are shown in normal shape and size, arranged in a radial pattern from the center of the lobule containing the central vein (CV) towards the circumference of the lobule. Some cells contain more than one nucleus, interspersed with sinusoids blood with a small number of Kupffer cells, While the results of our histological study through histological sections in the liver of a group of male rats that were injected peritoneally with lead acetate (Picture 4) showed significant histological changes represented by thickening of the walls of hepatic veins (TW), degeneration of hepatocytes (D) and condensation of nuclei (PN) of some of them with infiltration of cells Lymphocytic (LI) with amyloid protein deposition (AM) and presence of fibroblasts (Fy) when compared with the control group The results of microscopic examination of liver tissue in the group treated with lead acetate and then dosed with alcohol extract showed the normal pattern. Pictures (5) show blood vessels and hepatocytes with their normal size, shape and alignment on the radial, while the group treated with lead acetate and then dosed with aqueous extract showed minor histological changes. Picture (6) represented thickening of the wall of the central veins TW and degeneration of hepatocytes (D) with edema compared to the group exposed to lead acetate. The microscopic examination of the liver tissue in the group treated with alcoholic extract and then injected peritoneally with lead acetate, as well as the group treated with aqueous extract and then intravenously injected with lead acetate Picture(7),(8) showed less severe histological changes compared with the nurse group with lead acetate



Picture (1): Cross section of the liver of the control group showing the central blood vessels (CV), hepatocytes (HC) and their radial arrangement, and the sinusoids (S) with the presence of KC cells H&E X40.



Picture (2): Cross section of the liver of the alcoholic extract group showing the central blood vessels (CV), hepatocytes (HC) and their radial arrangement, and the sinusoids (S) with the presence of KC cells H&E X40. H&E X40.



Picture (3):transverse section of the liver of the aqueous extract group showing the central blood vessels (CV), hepatocytes (HC) and their radial arrangement, and the sinusoids (S) with the presence of KC cells H&E X40.

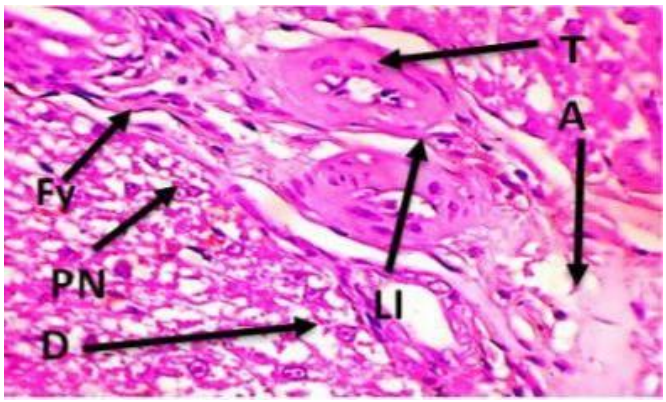


Image (4):Cross section of the liver of the lead acetate group showing thickening of the hepatic venule wall (TW), degeneration of hepatocytes (D) and condensation of nuclei (PN) some of them with infiltration of lymphocytes (LI) with deposition of amyloid protein(AM) and the presence of fibroblasts (Fy) H&E X40.

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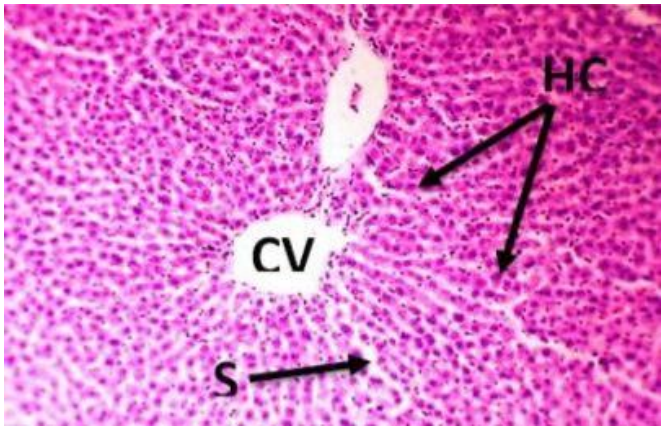
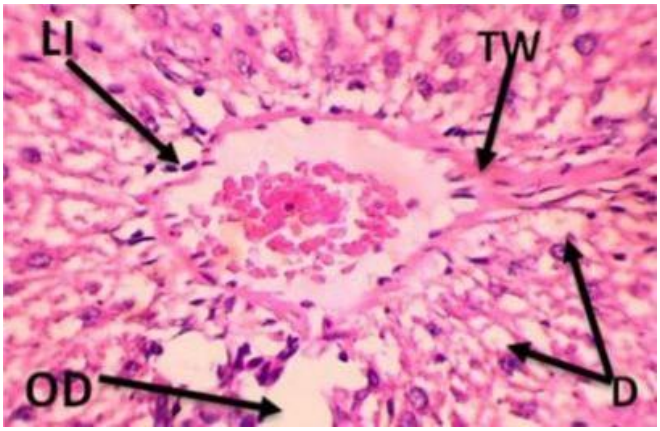
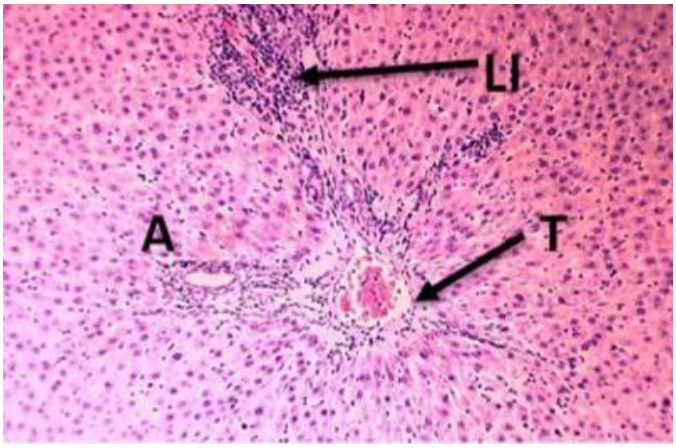


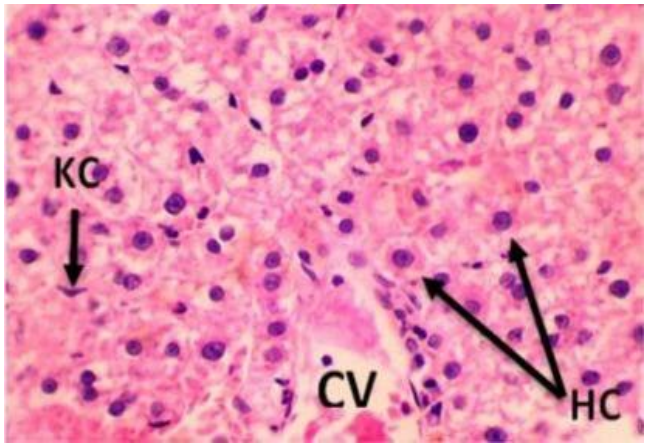
Picture (5): Cross section of the liver of the lead acetate group and alcoholic extract showing central blood vessels (CV), hepatocytes (HC), their radial arrangement, and sinusoids (S) H&E X10.



Picture (6): Cross section of the liver of the lead acetate group and aqueous extract showing central venous wall thickening (TW) and hepatocyte degeneration (D) with lymphocyte infiltration (LI) and edema (OD) H&E X40.



Picture (7): Cross-section of the liver of the alcoholic and lead acetate group showing thickening of the hepatic vein wall (TW) with amyloid deposition (AM) and lymphocyte infiltration (LI) H&E X10.



Picture (8): Cross section of the liver of the group of aqueous extract and lead acetate showing the central vein (CV) and the arrangement of hepatocytes (HC) around the veins with the presence of KC cells H&E X40.

Discussion

The peritoneal injection of lead acetate led to an increase in the level of liver enzymes ALT, AST, ALP, GGT. The reason for the increase in liver enzymes ALT, AST may be attributed to the exacerbation of the damage to the liver tissues that contain the largest proportion of these enzymes due to the damage caused by the treatment with lead acetate Which leads to the production of free radicals that affect the effectiveness of hepatocytes, especially the cell membranes, as lead acetate is a toxic substance that binds directly with the cell membrane, causing fat peroxidation, causing changes in the structure and function of the membrane by increasing its permeability, allowing the spread of liver enzymes in the blood (Choudhury and Panda, 2004) or the cause may be due to necrosis of liver cells that occurs as a result of exposure to lead acetate, causing cancerous infiltration or cirrhosis of the liver that leads to the leakage of these enzymes into the blood (Al-Hamdani and Rashid, 2012). As for the high level of ALP enzyme, it may be due to the body's inability to excrete it through the bile duct due to its blockage as a result of damage caused by exposure to lead acetate in hepatocytes (Saukkonen *et al*., 2006). As for the high level of GGT concentration, it is likely

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that it is due to oxidative damage, damage to hepatocytes and the rapid release of these enzymes into the blood circulation after the rupture of the plasma membrane of hepatocytes (Tatli Seven *et al*., 2021). . The present results are in agreement with several previous studies (Al-Megrin *et al.,* 2019; Mohammed *et al*., 2019; Sabeeh and Taher, 2015). Caper plant extracts reduce the level of liver enzymes, and the reason for this is that caper plant extracts have the ability to improve liver enzyme levels because they contain a high percentage of flavonoids, alkaloids and glucosinolates, which enhance the antioxidant system in the body and neutralize the effects of lead (Sharaf *et al*., 2000).

The cause of peritoneal injection of lead acetate is significant damage to the liver tissue. The reason for these tissue changes may be due to the oxidative stress caused by the injection of lead acetate, the toxicity of which lies in the formation of free radicals that interact with the phosphorylated lipids of the membranes of hepatocytes, causing lipid peroxides, which causes serious changes represented in Decreased mitochondrial membrane vitality and breakdown of lysosomes membranes to the stage of cell necrosis (Abdel-Moneim *et al*., 2015).

Histological examination showed that the groups treated with the pathogen were then treated with caper plant extracts an improvement in the histological picture of the liver tissue The reason for the improvement in the histological picture in the groups that were dosed with extracts of capers leaves is due to the fact that they contain many effective chemical compounds, especially phenolic compounds and flavonoids, which are antioxidants that neutralize oxidative damage by scavenging free radicals and preventing fat peroxidation (Yashin *et al.*, 2017). Microscopic examinations of liver tissue have demonstrated the hepatoprotective role of alcoholic and aqueous extract of capers leaves, and this role can be related to their ability to scavenge active radicals, increase their antioxidant activity and inhibit lipid peroxidation, where active types of oxygen are one of the most important causes of acute hepatotoxicity resulting from exposure to acetate. Lead and this has been confirmed by many studies (Albarracin *et al*., 2012; Kelsey *et al*., 2010)

Conclusions

Intraperitoneal injection of lead acetate to male rats led to a significant increase in the level of liver enzymes ALT, AST, ALP, GGT 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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