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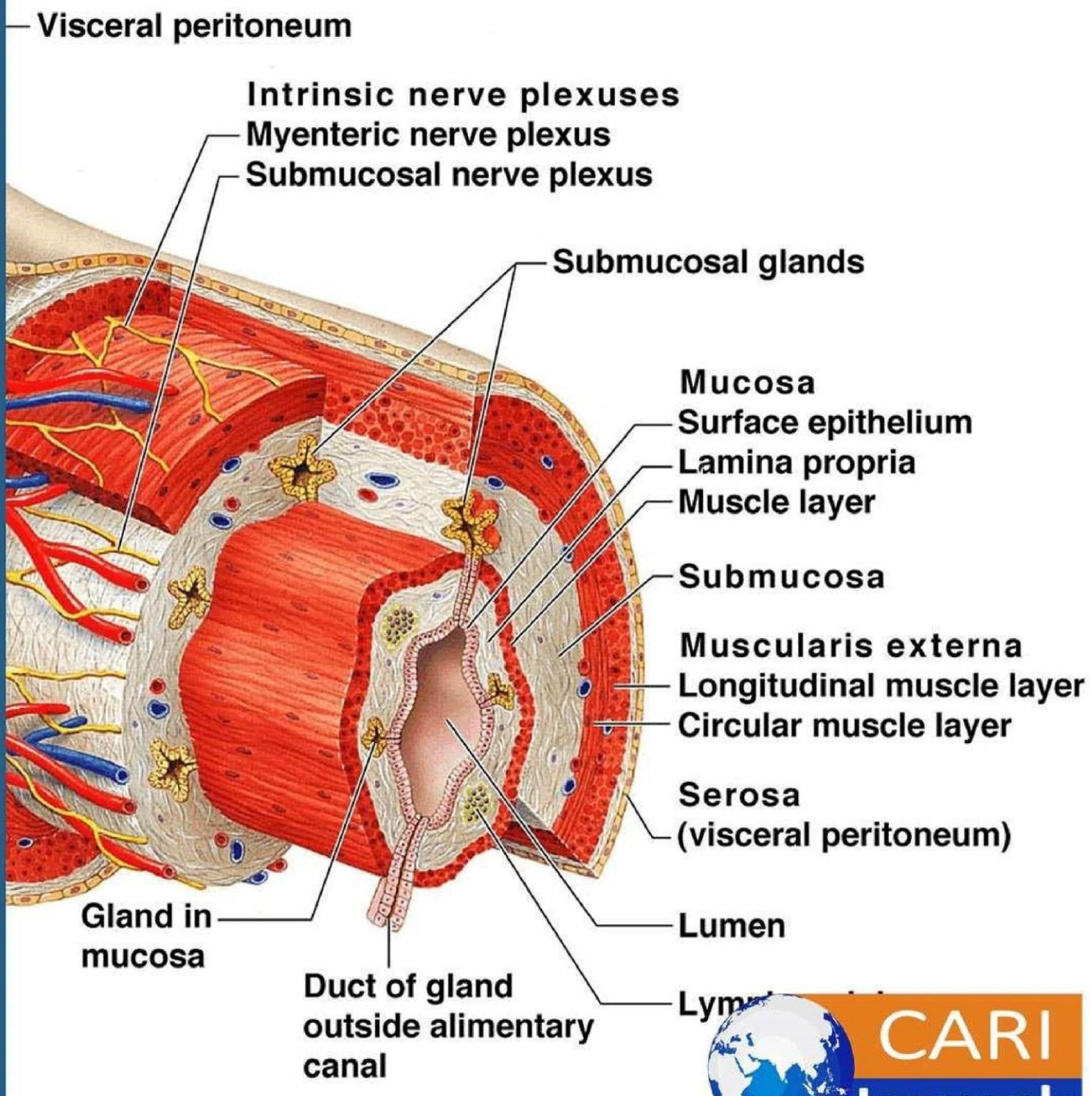

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The Use of Three Medicinal Plants in the Treatment of Hepatotoxicity Induced by Carbon Tetrachloride (Comparative Study)

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Abstract

Purpose: This study investigates the potential hepatoprotective efficacy of three distinct ethanolic plant extracts derived from a common plant family: *Sterculia setigera*, *Mitrogyna inermis*, and *Sonchus oleraceus*. These species were selected based on their established use in traditional medicine for the management of various ailments, including inflammatory diseases, cholera, malaria, tumors, and rheumatism. The objective of this research is to evaluate how these extracts may mitigate chemically-induced hepatotoxicity.

Methodology: The study utilized five experimental groups, each consisting of 10 mice (N=50 total). Hepatotoxicity was established in the subjects by administering carbon tetrachloride at a dose of 0.2 mg/kg body weight. The therapeutic effects were evaluated by the oral administration of the plant extract at dose rates of 200 mg/kg and 400 mg/kg body weight.

Finding: The ethanolic extracts of Sterculia setigera stems, Mitrogina inermis stems, and Sonchus oleraceus leaves contain a hepatoprotective ingredient(s) that protect from carbon tetrachloride-induced hepatic damage. The activity of the tested samples was comparable to that of silymarin, which was used as a reference drug. We found that the high dose (400 mg) of the ethanolic extract of Sterculia setigera, Mitrogina inermis, and Sonchus oleracea significantly reduced the levels of serum alanine aminotransferase (SGPT), serum aspartate aminotransferase (SGOT), and total protein. The administration of CCl4 resulted in a decrease in albumin concentration. Liver toxicity is to blame, as the liver produces the albumin. Treatment with three plant extracts increased albumin levels.

Unique Contribution to Theory, Practice and Policy: The obtained results highlight the importance of isolating the plant's active ingredient responsible for hepatotoxicity treatment.

Keywords: *Sterculia Setigera, Mitrogina Inermis, Sonchus Oleraceus, Silymarin, SGPT, SGOT, carbon tetrachloride, albumin*

1- Introduction:

The liver is a central, multifunctional organ vital for physiological homeostasis, orchestrating key processes including metabolism, immunity, and detoxification. Its critical roles encompass the filtration of systemic blood, production of bile salts essential for lipid digestion, and acting as a primary site for vitamin storage (Ward and Daly 1999). Consequently, the maintenance of hepatic integrity is indispensable for overall health. Despite its regenerative capacity, the liver's role as the main biotransformation center renders it continuously susceptible to injury. Hepatotoxicity can arise from cumulative exposure to environmental toxins and the therapeutic use or abuse of various agents, particularly over-the-counter and prescription pharmaceuticals (Sharma et al., 1991; Subramonium and Pushpander, 1999). Furthermore, infectious agents such as the hepatitis virus, *Leptospira*, and malarial parasites are significant microbial causes of liver damage (Subra and Puch 1999), and prolonged regimens involving specific antibiotics, such as antituberculosis drugs, present a recognized clinical risk for iatrogenic liver toxicityThe indication of drug-induced hepatotoxicity varies, from asymptomatic elevation of liver enzymes such as ALT (Alanine amino transaminase) and AST (Aspartate amino transaminase) to failure of hepatic function. These two conditions may lead to hepatic toxicity. People use a variety of drugs to treat liver disorders (Owoabi et al., 2007; Reitman and Frankel, 1957). Drug-induced liver disorders are one of the most common and serious adverse drug reactions (Miguel et al. 2012). We should use these drugs with caution. Misdiagnosis and inappropriate treatment may reduce the efficacy of these drugs.

Plants are the most important source of traditional medicine for their cheaper availability and few or no side effects (Karim et al., 2011). They are considered to be potential sources of development of alternative therapeutics (Cox and Balick, 1994). The ethnobotanical approach in collaboration with traditional healers can be a rich source of drug discovery since herbal treatment of various diseases is widespread in Africa (Ozioma, 2019). Investigation of natural remedies is of enormous interest to produce new drugs. Some naturally occurring chemical compounds can serve as models of drugs (Mathady et al., 2008).

Researchers widely use carbon tetrachloride (CCl4) to study the hepatoprotective effects of drugs and plant extracts. It hurts the liver by either making covalent bonds between reactive intermediates and cell parts or by speeding up the lipid peroxidation process started by free radical intermediates. It causes intracellular and intramembranous lipid destruction (Naziroglu et al., 1999). CCl4 can hurt the liver by creating reactive free radicals that can attach to large molecules in cells and break them down into nucleic acid, protein, and lipid products (Shana and Dalton, 2009). CCl4 can also induce centrilobular steatosis, apoptosis, and necrosis. If the damage continues, the liver will progress to fibrosis and cirrhosis. Sudan, with its uniquely climatic conditions, possesses a huge wealth of flora, cultivated or wild. These plants have found their way into the realm of folk medicine. Experimental animal models test numerous folk medicines of plant origin for their potential and hepatoprotective effects on liver damage.

We conducted the present study to compare the hepatoprotective activity of the ethanolic extract of Sterculia setigera stem bark, Mitrogyna inermis, and Sonchus oleracea against carbon

tetrachloride-induced toxicity in rats. Sterculia setigera, a savanna tree in the family Sterculiaceae, is widespread in tropical Africa. Some African countries, like Burkina Faso, use the stem bark of S. setigera as a traditional remedy to treat various diseases. In Sudan, people use the plant for food, preparing salads from the leaves and a coffee-like drink from the seeds. Some studies reported the antibacterial as well as antifungal activities of *S. setigera* (Sharma and Sharma, 2009).

In West Africa, Mitrogina inermis is well-known. The family Rubiacees includes Mitrogina inermis, which has garnered widespread attention for its biological activity in treating various diseases like cholera, malaria, and others (Ouerdraego et al., 2007). Additionally, people use it to treat fever, high blood pressure, dysentery, wounds, and epilepsy (Burkill, 1985). People use the leaves of M. inermis to treat rheumatism, weakness, and fatigue.

Sonchus oleraceus is a flowering plant of the family Asteraceae. Europe, western Asia, and Africa all experience its widespread. The plant is located in Damzein City, Sudan. Folk medicine employs it to treat gastrointestinal tract disorders, tumors, and inflammatory diseases (Alothman et al., 2018). Traditional medicine uses it to treat numerous ailments related to the kidney, lungs, and liver. Khan et al. (22014) illustrated Sonchus Asper-'s hepatoprotective activity and found it to be very active. McDowell et al. (2011) studied the antioxidant activity of *S. oleraceus*.

2-Material and methods:

2.1 Animals:

Albino rats were used. Fifty rats of both sexes weighing 100- 150g were obtained from the central veterinary research laboratory, in Khartoum Sudan. They were housed in cages under standard environmental conditions where the temperature was 22± 2°C and applied with free access to food and water.

2.2 Plant material:

Stercula setigera bark was used. It was obtained from Alnohod City, Sudan. The tree is often found on hills, poor and little deep soil. Its color is greyish. The stem bark of the plant was collected, dried, and grinned. The powder was weighed and kept for preparation of extract.

Mitragyna inermis was collected from South Sudan, Zalengy city. The stem bark was used in this study. It grows in the wet tropical biome. The stem was dried, grinned and the powder was weighed and prepared for extraction.

Sonchus Oleraceus was collected from Hag Yousif in Khartoum Bahri city. The leaves of the plant were dried at room temperature, weighed, and prepared for extraction.

All three plants were authenticated by the botanist in the Medicinal and Aromatic Plants Research Institute.

2.3 Preparation of extract:

All three plants were subjected to the same extraction procedure according to the method described by Harborn 1984. 300 g of each plant sample was extracted by soaking in 80% ethanol for about seventy-two hours with daily filtration and evaporation. The solvents were evaporated under reduced pressure to obtain dry material using a rotatory evaporator apparatus. The yield percentages were calculated as follows:-Weight of extract x 100

Weight of sample.

Fig. (1) Sonchus oleraceus

Fig.(2) Sterculia setigera stem

Fig.(3) Mitragyna Inermis tree

2.4 Experimental design:

For each experiment, we divided 50 rats into 5 groups of 10. The experiment employed carbon tetrachloride to induce hepatotoxicity.

Group A was given only food and water to serve as a negative control.

Group B was treated as induction control by being given a single intraperitoneal dose of 0.2 mg/kg body weight of carbon tetrachloride (CCl4).

Group C was given CCl4 together with silymerin, which was used as a standard drug for the treatment of hepatotoxicity.

Group D was given CCl4 together with 200 mg/kg BW of the plant extract.

Group E was given CCl4 together with 400 mg/kg BW of the plant extract.

Blood samples were obtained from the ocular vein before starting the experimental dosing and then on days 5 and 10. Serums were analyzed for the activities of AST, ALT, and ALP and the concentration of metabolic indicators, total protein, albumin, and bilirubin.

After 10 days, the rats were dissected, and liver tissues were fixed in 10% neutral formalin and processed for histopathology.

2.5 Biochemical analysis:

The activity of AST, ALT, and ALP was measured by commercial kits (Randox Laboratories LTD., U.K.). Serum albumin, total protein, and bilirubin were determined by a colorimetric method using commercial kits (Randox Laboratories LTD (U.K.).

2.6 Statistical analysis:

We expressed values as mean SD using the one-way analysis of variance (ANOVA) in SPSS version 10.0.

2.7 Standard drug:

One of the most common products used for hepatoprotection is silymerin, which is flavonolignans from the milk thistle (Silybum marianum) plant. Silymarin consists of four flavonolignan isomers, namely Silybin, Silydianin, isosilybin, and Silchristin. Silymarin offers excellent protection in various toxic models of experimental liver diseases in laboratory animals (Gillessen and Schmidt, 2020).

3. Results:

3.1 Sample extracts:

Sterculia setigerd, Sonchus oleraceus, and Mitragyna inermis were extracted with ethanol, and the yield percentages are calculated and shown in Table 1.

Table: (1) The yield of ethanolic extract of Sterculia setigerd stem, Sonchus Oleraceus leaves and Mitragyna Inermis stems

Sample	Tested material	Weight (g)	Extract	Yield %
Sterculia Setigerd	Stems	16.5	Ethanol	5.5
Sonchus Oleraceus	Leaves	36.9	Ethanol	12.3
Mitragyna Inermis	Stems	16.5	Ethanol	5.5

3.2 Phytochemical screening

Phytochemical screening for the active constituents of Sterculia setigerd, Mitragyna inermis, and Sonchus oleraceus was carried out using the methods described by Harborne (1984), Martinez & Valencia (1999- 2003), Sofowora (1993), with many few modifications.

Table: (2) Result of phytochemical screening Sterculia Setigerd stems, Sonchus Oleraceus leaves and Mitragyna Inermis stems.

Test	Sonchus oleraceus	Sterculia setigerd	Mitragyna inermis
Alkaloids	-	-	-
Sterols	+++	-	+
Triterpenes	+++	+	-
Flavonoids	+	++	++
Saponins	-	+	+++
Cumarins	+	-	+
Tannins	+	+++	+
Anthraquenones	-	-	-
Cyanogenic	-	-	-

All these parts of plants have no anthraquinone, Cyanogenic and Alkaloids

Key: + Trace ++ Moderate ++ High - Negative

3.3 Hepatoprotective experiment:

We tested the ethanolic extract of Sterculia setigerd stems, Sonchus oleraceus leaves, and Mitragyna inermis stems for hepatoprotective activity against CCL4-induced hepatotoxicity in experimental laboratory animals (Wister albino rats).

3.4 Aspartate transaminase (GOT):

Administration of CCL4 resulted in an increase in the group's GOT concentration compared to the control group. We noticed the elevation on day 10. Treatment with extracts of either S. setigera, M. inermis, or S. oleraceas resulted in a decrease in the concentration of GOT with the three plant extracts and returned to the normal level at the end of the experiment.

3.5 Alanine transaminase (GPT):

When compared to the control group, Group B, which received 0.20 mg/kg bw intraperitoneal of CC4, showed an increase in the level of GPT. On day 10, the increase was high (10.15 ± 0.01 with S. setigera, 10.25 ± 0.01 with M. inermis, and 10.15 ± 0.01 with S. oleraceas).

The administration of the three plant extracts resulted in a decrease in the concentration of GPT, which returned to normal at the end of the experiment. The values were 8.1±0.1 with S. setigera, 9.48 ± 0.04 with M. inermis, and 8.40 ± 0.57 with S. oleraceas.

3.6 Albumin:

Following CCL4 injection into the rats, the concentration of albumin decreased slightly. The decrease was noticed on day 10 of the experiment (1.12± 0.04 with S. setigera, 1.82± 0.04 with M. inermis, and 1.98 ± 0.24 with S. oleraceas). After the plant extracts were administered, the concentration of albumin increased but remained within the normal values found in the control group.

Compared to Mitrogyna inermis and Sonchus oleraceas, S. setigera produced a better result.

3.7 Total protein:

Compared to the control group, induced hepatotoxicity with carbon tetrachloride resulted in an increase in the concentration of total protein in the rats injected with CCL4. On day 10, we observed a significant increase. The amount of total protein in the blood dropped when different amounts of plant extract were given. It went back to normal with three plant extracts (8.10 ± 0.11 with S. setigera, 9.48 ± 0.04 with M. inermis, and 8.40 ± 0.57 with S. oleraceas).

3.8 Billirubin:

The group (B) that received CCL4 showed an increase in bilirubin concentration compared to the negative control group (A). The increase was found to be high on day 10 when it reached 3.90 ± 0.03. Administration of the plant extracts decreased the concentration of bilirubin, especially with a high dose of three plant extracts. The best value was found at the end of the experiment, where it was 3.50 ± 0.65 with S. setigera, 1.01 ± 0.13 with M. inermis, and 2.25 ± 0.21 with S. oleraceas.

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Table (3): Effect of Sterculia setigera stem, Mitrogyna inermis stem, and Sonchus oleracea leaves ethanolic extract administered simultaneously with CCL4 on total protein (mean±S.E.) in rats.

Group	Sterculia setigera			Mitrogyna inermis			Sonchus oleaceous		
	Day o	Day 5	Day10	Day 0	Day 5	Day10	Day 0	Day 5	Day10
A	7.40±0	7.50±0.02	7.30±0.1	7.40±0.2	7.50±0.02	7.30±0.01	7.40±0.00	7.50±0.00	7.30±0.01
B	7.30±0.19	9.70±0.01	10.15±0.01°	7.30±0.11	9.70±0.01	10.25±0.01	7.20±0.01	9.70±0.03	10.15±0.03°
C	7.20±0.00	10.20±0.01	10.90±0.03*	7.20±0.01	10.20±0.02	8.90±0.01*	7.30±0.01	10.20±0.00°	6.90±0.01
D	8.00±0.7	7.00±0.30	8.10±0.11°	6.72±0.42	11.40±0.09	9.25±0.06	7.75±0.35	10.50±0.28	8.40±0.57°°
E	8.00±0.70	7.00±0.30	8.10±0.11**	6.70±0.42	12.20±0.02	9.48±0.04**	7.75±0.35	10.50±0.28	8.40±0.57°

A (control +), B (control -), C(standard drug), D (low dose), and E(high dose). The difference was found to be significant (°P<0.05, (°°P<0.01) when compared with group B (control -), and significant (*P<0.05, (**P<0.01) when compared with group C (standard drug).

Table (4): Effect of Sterculia setigerastem, Mitrogyna inermis stem, and Sonchus oleraceas leaves ethanolic extract administered simultaneously with CCL4 on Total Bilirubin (Mean±S.E)) in rats.

Group	**Sterculia setigera**			**Mitrogyna inermis**			**Sonchus oleraceaus**		
	Day o	Day 5	Day10	Day 0	Day 5	Day10	Day 0	Day 5	Day10
A	1.20±0.00	1.10±0.00	0.96±0.00	1.20±0.00	1.10±0.00	0.96±0.00	1.15±0.03	1.10±0.00	0.96±0.00
B	1.20±0.00	2.80±0.02	3.90±0.03$^{\circ\circ}$	1.20±0.00	2.80±0.00	3.90±0.03°	1.24±0.02	3.35±0.03	3.90±0.03$^{\circ\circ}$
C	1.30±0.01	2.90±0.02	3.40±0.02	1.30±0.01	2.90±0.02	1.40±0.00*	1.30±0.01	2.90±0.021	2.40±0.02*
D	0.90±0.10	0.70±0.34	0.85±0.03*	1.04±0.08	3.00±0.28*	1.04±0.02*	0.87±0.24	4.21±0.21	2.27±0.34$^{\circ\circ}$
E	0.90±0.10	0.70±0.34	0.85±0.03*	1.04±0.08	3.00±0.28	1.01±0.13**	0.87±0.24	4.21±0.21	2.25* ±0.21

A (control +), B (control -), C(standard drug), D (low dose), and E(high dose). The difference was found to be significant ($^{\circ}P<0.05$, ($^{\circ\circ}P<0.01$) when compared with group B (control -), and significant ($^{*}P<0.05$, ($^{**}P<0.01$) when compared with group C (standard drug).

Table (5): Effect of Sterculia setigerastem, Mitrogyna inermis stem, and Sonchus oleraceas leaves ethanolic extract administered simultaneously with CCL4 on Aspartate transaminase AST (SGOT) (Mean±S.E) in rats.

Group	Sterculia setigera			Mitrogyna inermis			Sonchus oleraceaus		
	Day o	Day 5	Day10	Day 0	Day 5	Day10	Day 0	Day 5	Day10
A	12.00 ±0.00	11.50±0 .05	12.00±0 .00	12.00±0 .00	12.10±0 .00	12.20±0 .00	12.00±0 .00	12.00±0 .00	12.00±0 .00
B	11.10 ±0.02	14.00±0 .02	17.00±0 .00$^{\circ\circ}$	11.50±0 .05	13.20±0 .02	15.20±0 .02°	11.50±0 .05	13.20±0 .02	15.20±0 .00°
C	9.70± 0.03	14.00±0 .02	16.10±0 .01$^{\circ\circ}$	10.20±0 .00	13.20±0 .02	11.30±0 .01**	10.20±0 .00	13.20±0 .02	11.30±0 .01*
D	10.06 ±0.70	10.04±0 .72	10.48±0 .60**	10.45±0 .64	12.65±0 .21	11.95±0 .07**	11.40±0 .57	17.30±0 .41	12.00±0 .00
E	10.06 ±0.70	10.04±0 .72	10.48±0 .60	10.45±0 .64	12.65±0 .21	11.95±0 .07*	11.40±0 .57	17.30±0 .41	11.00±0 .05**

A (control +), B (control -), C(standard drug), D (low dose), and E(high dose). The difference was found to be significant ($^{\circ}P<0.05$, ($^{\circ\circ}P<0.01$) when compared with group B (control -), and significant ($^{*}P<0.05$, ($^{**}P<0.01$) when compared with group C (standard drug).

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Table (6) Effect of Sterculia setigera stems, Mitrogyna inermis stem, and Sonchus oleraceas leaves ethanolic extract administered simultaneously with CCL4 on Alanine Transaminase ALT (SGPT): (Mean±S.E) in rats.

Group	**Sterculia setigera**			**Mitrogyna inermis**			**Sonchus oleraceaus**		
	Day o	Day 5	Day10	Day 0	Day 5	Day10	Day 0	Day 5	Day10
A	11.20 ±0.00	11.50±0 .05	12.00±0 .00	11.20±0 .00	11.50±0 .05	12.00±0 .00	11.20±0 .00	11.50±0 .05	12.00±0 .00
B	11.10 ±0.02	14.00±0 .02°	17.02±0 .30$^{\circ\circ}$	11.10±0 .02	14.00±0 .02	17.00±0 .00$^{\circ\circ}$	11.10±0 .02	14.00±0 .02	17.00±0 .00°
C	9.70± 0.03	14.00±0 .02	16.10±0 .01*	9.70± 0.03	14.05±0 .21	10.10±0 .01**	9.70± 0.01	14.00±0 .02	16.10±0 .01*
D	2.06± 0.07	2.21± 0.70	10.88±0 .06$^{\circ\circ}$	10.40±0 .57	14.05±0 .21	12.45±0 .06$^{\circ\circ}$	9.06± 0.70	11.08±0 .60	12.28±0 .60°
E	2.06± 0.07	2.21± 0.70	10.20±0 .02*	10.40±0 .57	14.00±0 .02	12.45±0 .06**	8.06± 0.70	11.08±0 .60	12.28±0 .60*

A (control +), B (control -), C(standard drug), D (low dose), and E(high dose). The difference was found to be significant ($^{\circ}P<0.05$, ($^{\circ\circ}P<0.01$) when compared with group B (control -), and significant ($^{*}P<0.05$, ($^{**}P<0.01$) when compared with group C (standard drug).

Table (7): Effect of Sterculia setigerastem, Mitrogyna inermis stem, and Sonchus oleraceas leaves ethanolic extract administered simultaneously with CCL4 on Albumin : (Mean±S.E) in rats.

Group	**Sterculia setigera**			**Mitrogyna inermis**			**Sonchus oleraceaus**		
	Day o	Day 5	Day10	Day 0	Day 5	Day10	Day 0	Day 5	Day10
A	2.46±0.02	2.46±0.02	2.50±0.04	2.24±0.01	2.24±0.01	2.50±0.04	2.42±0.02	2.50±0.04	2.32±0.03
B	2.24±0.01	1.52±0.03	1.52±0.04°	2.25±0.02	2.21±0.01	1.82±0.04°	2.42±0.02	2.12±0.02	1.98±0.24°
C	2.46±0.02	2.46±0.02	2.42±0.02	2.50±0.04	2.12±0.02	2.40±0.01	2.44±0.04	2.42±0.02	2.44±0.04
D	2.12±0.02	2.12±0.02	2.12±0.02°°	2.14±0.01	2.15±0.02	2.18±0.04°°	2.21±0.01	2.15±0.02	2.18±0.04°
E	2.28±0.24	2.44±0.04	2.52±0.02**	2.24±0.01	2.32±0.03	2.42±0.02°	2.24±0.01	2.24±0.01	2.42±0.02°

A (control +), B (control -), C(standard drug), D (low dose), and E(high dose). The difference was found to be significant (°P<0.05, (°°P<0.01) when compared with group B (control -), and significant (*P<0.05, (**P<0.01) when compared with group C (standard drug).

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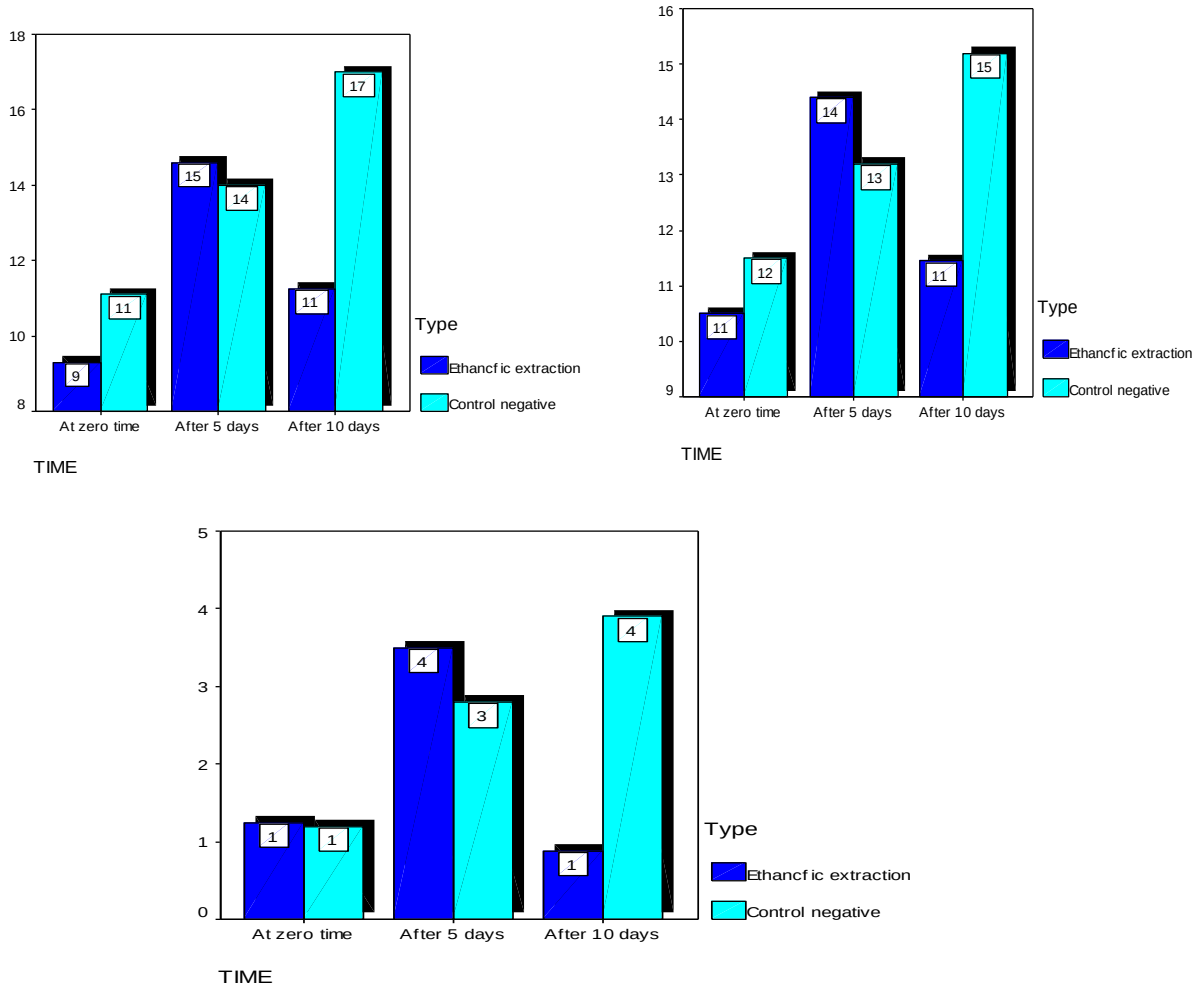
Fig(4): Effect of *Sterculia Setigerd* stems ethanolic extract administered simultaneously with CCL_4 on serum ALT, AST, and Total bilirubin levels in rats



Fig(5): Effect of *Sonchus Oleraceus* leaves ethanolic extract administered simultaneously with CCL_4 on serum ALT, AST, and total bilirubin levels in rats

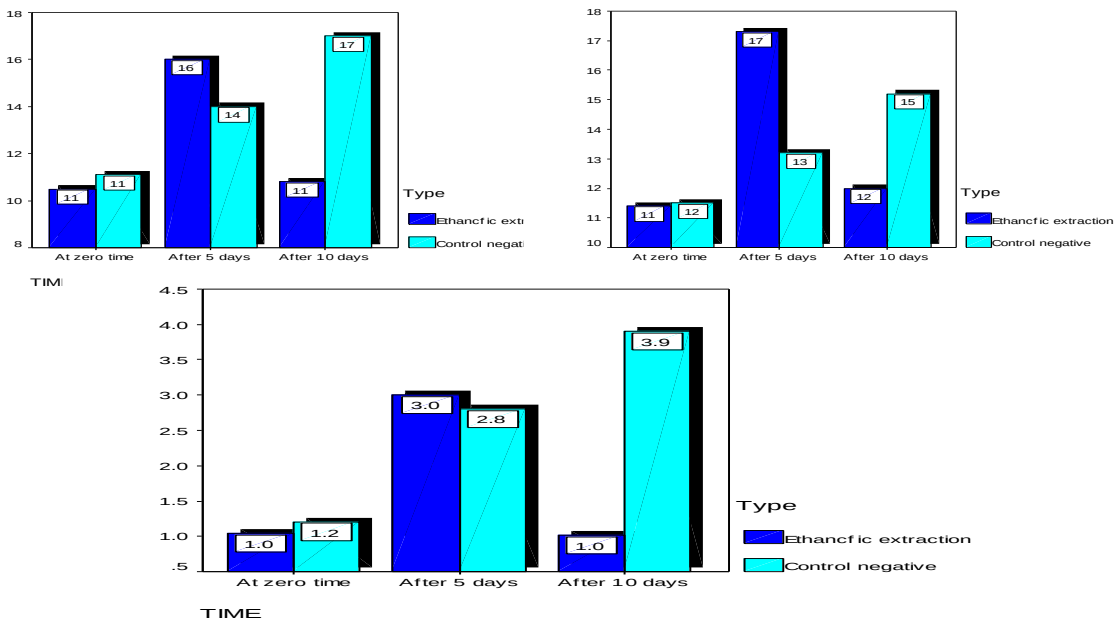


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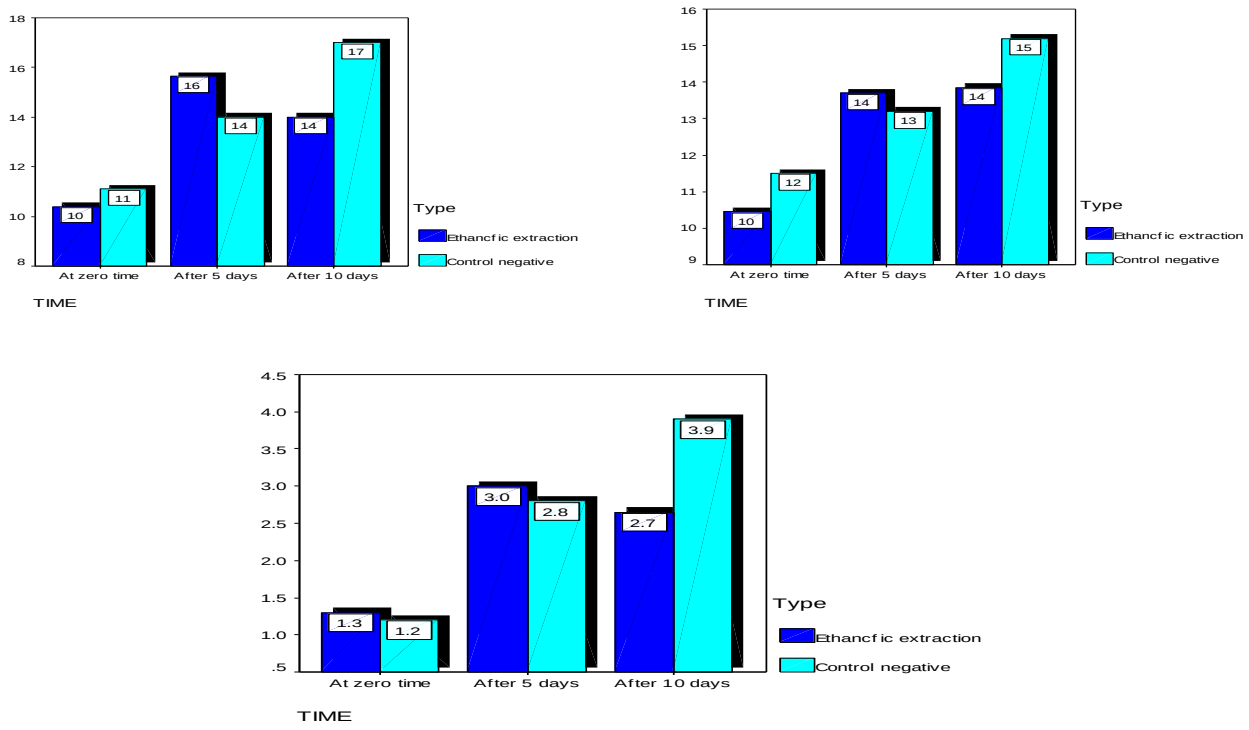
Fig (6): Effect of *Mitragyna Inermis* ethanolic extract administered simultaneously with CCL_4 on serum ALT, AST, and total bilirubin levels in rats



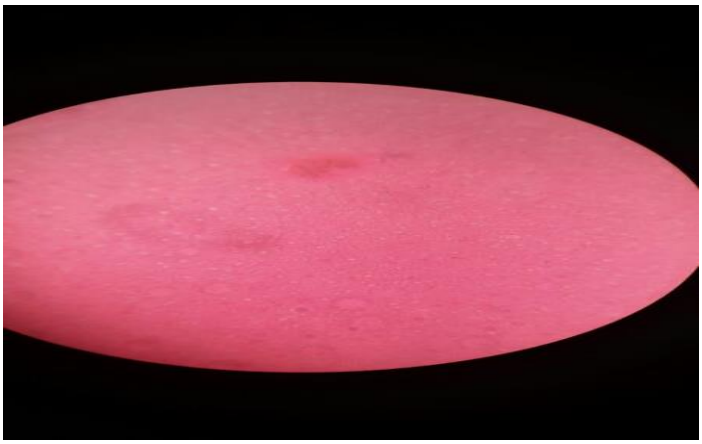
3.9 Histopathological changes:

At the end of toxicological studies, all vital organs of rats' livers were subjected to microscopic examination and compared with control animals. Figure displays the histopathological sections from the experiment. The histopathological results of the ethanolic extract of the S. *Setigera* plant are better and stronger when compared to the ethanolic extract of the M. *Inermis* and *S. Oleraceus* plants. Group A (control) exhibited normal hepatic cells, each with well-defined cytoplasm, prominent nucleus, some cell-fragmented nuclear, and nucleus well-brought-out central vein.

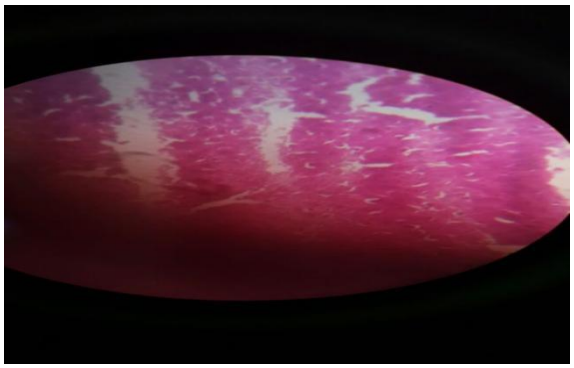
Group B (CCL_4) showed total loss of hepatic architecture with centrilobular hepatic necrosis, fatty changes, vacuolization and congestion of sinusoids, crowding of central vein, and apoptosis. Group C (standard drug) exhibited normal hepatic cells; the cytoplasm was pale and granular, with the same vacuolation appearance, and some cells had fragmented nuclei.

Group D and E dose rate (200 and 400 mg/kg) cloudy swelling necrosis, few hepatocytes immediately adjacent to the central vein in the affected area, and tissue damage and necrosis were of less extent in this group than the CCl4 group. The periphery of the central vein displayed minimal tissue degeneration. No derangement was observed at hepatocyte cords, especially in group E. The ethanolic extract of *S. Setigera* showed very potent hepatoprotective activity at a dose rate of 400 mg/kgbwt.

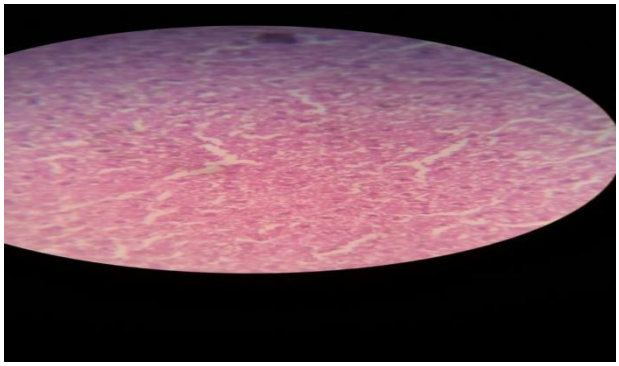
Fig (7) Histopathological changes in the livers of rats given ethanol extract of *Sterculia Setigera* stem simultaneously with CCL4.



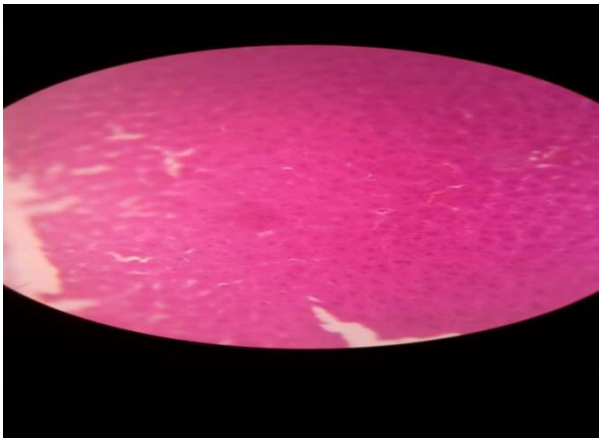
Group A showed a normal histopathological appearance



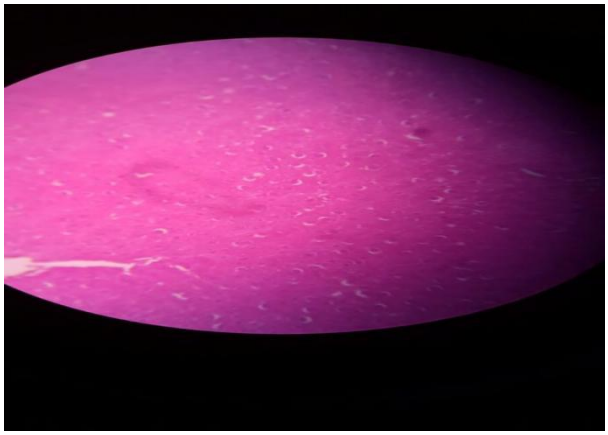
GroupB. CCL4 group



Group C standard drugs group



Group D liver section (200mg/kg)



Group E liver section (400mg/kg)

4. **Discussion:**

The liver is the largest gland and vital organ in the body because of its role in bile production, excretion, and metabolism of fats, proteins, and carbohydrates. It also plays an important role in the storage of glycogen, vitamins, and minerals. Microbial agents, such as the hepatitis virus and material parasites, expose the liver to toxicity (Subra and Puch 1999). Drug-induced liver disorders are one of the most common and serious adverse drug interactions (Miguel et al. 2012). CCl4 is one of the most commonly used hepatotoxins in experimental studies of liver diseases (Dohnson and Kroening, 1998). This study used Ccl4 to induce hepatotoxicity in rats, administering it intraperitoneally at a dose rate of 0.2 ml/kg BW.

Aspartate aminotransaminase (AST) and Alanine transaminase (ALT) are metabolic enzymes. High levels of these enzymes in the blood show that liver cells are dying and there is inflammation. On day 10 of the experiment, we observed an increase in these enzymes in the group that received carbon tetrachloride. Plant extracts were administered at dose rates of 200 and 400 mg/kg body weight, resulting in a gradual decrease in both AST and ALT concentrations until the end of the experiment. The extract of S. setigera (10.48 ± 0.66) had the best result for AST concentration, compared to M. enermis (11.40 ± 0.75) and S. oleraceas (11.0 ± 0.05). The concentration of ALT was 10.20 ± 0.02 with S. setigera, 12.45 ± 0.06 with Mitrogyna inermis, and 12.28 ± 0.06 with S. oleraceas. The damaged liver released the hepatic enzymes, elevating their levels in the serum. Following liver injury, the cytoplasmic area of the cell will release these enzymes (Recknagel et al. 1989; Brent and Rumack 1993). These findings agreed with those of Sharma et al. (2009), who used curcumin as a natural product to produce hepatotoxicity.

The administration of CCl4 resulted in a decrease in albumin concentration. The liver's production of albumin is the cause of this toxicity. Treatment with the extracts of the three plants resulted in increased levels of albumin, and the effect was more pronounced at higher concentrations of the plant extracts. The most effective plant extract was S. setigera compared to the standard drug (Sylmerin).

Day 10 of the experiment marked the increase in protein concentration following the administration of CCl4. The accumulation of protein in the body due to insufficient liver function may be the cause of this increase (Johnson et al. 1998). Administration of plant extracts resulted in a decreased concentration of total protein, which returned to the normal level at the end of the experiment. A high concentration of the three plant extracts yielded the best results. S. setigera plant extract gave better results when compared with M. inermis and S. oleraceas.

After the administration of CCl4, the concentration of bilirubin increased, and the increase became noticeable on day 10. Following the treatment with plant extracts, the level of bilirubin decreased till the end of the experiment. The best result was found also with S. Setigera (0.85± 0.03), followed by M. inermis (1.01 ± 0.13), and then Sonchus oleraceas (2.25±0.21). The presence of chemical compounds in S. setigera, which is responsible for treating liver disorders, may explain the best result.

5. **Conclusion:**

We conclude that a variety of Sudanese medicinal plants exhibit hepatoprotective activity against carbon tetrachloride toxicity in animal models. The activity depends on the concentration of plant extract. Sudanese herbs may offer novel alternatives to treat liver disorders.

Data Availability

The data used to support this study are included in the paper. However, data are available from the corresponding author upon responsible request.

Conflicts of Interest

The author declare that there is no conflict of interest regarding the publication of this paper.

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