# Antioxidant and Hepatoprotective effect of Senna leaves (Cassia senna l.) against carbon tetrachloride induced hepatotoxicity in rats

Ahmed A. Amin<sup>1</sup>, Nehal M. Hassan<sup>1</sup> and Alaa O. Aboraya<sup>2</sup>

<sup>1</sup> Nutrition and Food Sciences Dept., Faculty of Home Economics-Helwan University- Egypt

<sup>2</sup> Nutrition Science Faculty – Helwan University – Egypt

#### **Abstract**

The present study was designed to investigate the antioxidant and hepatoprotective effects of Senna leaves on carbon tetrachloride (CCl<sub>4</sub>) induced rats hepatotoxicity. A total of 28 adult male Sprague Dawley albino rats  $(150 \pm 10 \,\mathrm{g})$  were obtained from the Experimental Animals Farm, Helwan, Egypt. The first group (n=7) served as the negative control and received a standard basal diet. The second group (n=21) was intraperitoneally injected with carbon tetrachloride (CCl<sub>4</sub>) at a dose of 1 mL/kg (1:1 in corn oil) for 3 consecutive days to induce hepatotoxicity. Hepatotoxic rats were then subdivided into three groups (n=7 each): a positive control group fed the basal diet only, and two treatment groups receiving the basal diet supplemented with either 1% or 2% of senna leaves. Biological evaluation parameters were determined (IBW, FBW, FER, BWG%) for rats. Blood samples were separated into serum for liver functions determination (ALT, AST and ALP), lipid profile parameters (TC, TG, HDL-C, LDL-C and VLDL-C) and antioxidant parameters determination (MDA and GPx). The increase in IBW, FBW, BWG% and FER were significantly ameliorated by the administration of Senna leaves treatments, compared to hepatotoxicity rats. The results revealed that in CCl<sub>4</sub> group, there were significant increases in ALT, AST, ALP, TC, TG, LDL-C, VLDL-C and MDA, while parameters HDL-C and GPx showed significant decreases. Meanwhile, administration of Senna leaves resulted in a significant decrease in all elevated mentioned parameters and increase in HDL and GPx. Therefore, it could be concluded that Senna leaves have hepatoprotective and antioxidant role.

**Keywords:** Senna leaves, CCl<sub>4</sub> hepatotoxicity, antioxidant, hepatoprotective.

#### INTRODUCTION

Liver plays important metabolic, detoxification, and secretory roles in the body. Liver disease is associated with distortion of these metabolic functions (Chaware et al., 2009). Human continuously exposed to different kinds of chemicals such as food additives, industrial chemicals, pesticides and other undesirable contaminants (Gabele et al., 2003).

Carbon tetrachloride (CCl4) is a common hepatotoxin that is widely used to induce toxic liver injuries (Pereira-Filho et al., 2008). Search for newer drugs continues because the existing synthetic drugs have several limitations (Gandhimathi and Kumar, 2012).

Hepatotoxicity is the term used to describe the functional and structural damage of liver caused by the abuse or misuse of potent medicines and consumption of other hepatotoxic agents; among these agents are alcohol, infections, and chemicals like carbon tetrachloride (Ali et al., 2018). However, excessive intake of these chemicals may still result in oxidative damage to tissue organs by massive production of free radicals, which leads to structural and functional damage to the membrane and eventually causing serious toxicity to hepatocytes (Meng et al., 2018). Moreover, oxidative stress, which is the result of an excess of reactive oxygen species over the antioxidant defenses of the organism, has been considered as a conjoint pathological mechanism and it contributes to initiation and progression of liver injury (Li et al., 2015).

Senna (Cassia senna) is a large genus of around 500 species of flowering plants in the family Leguminosae (Lodha et al., 2010) and is widely distributed throughout Asia including India, Mauritius, China, East Africa, South Africa, America, Mexico, West Indies and Brazil. Cassia species belong to the family Caesalpiniaceae. Caesalpiniaceae is often treated as a sub-family, Caesalpinioideae, of the large family Leguminosae (Deshpande and Bhalsing, 2013).

Cassia senna species are already reported in the ancient ayurvedic literatures and literature survey indicated its use against various skin diseases such as ringworm, eczema, and scabies (Sundaramoorthy et al., 2016). According to ayurveda the leaves and seeds are acrid, laxative, antiperiodic, anthelmintic, ophthalmic, liver tonic, cardiotonic and expectorant. The leaves and seeds are useful in leprosy, ringworm, flatulence, colic, dyspepsia, constipation, cough,

bronchitis, cardiac disorders. The extracts of *Cassia senna* species have been used as a therapy for various skin ailments, rheumatic disease and as laxatives (Singh et al., 2013).

The extract of *Cassia senna* species leaves have been found to possess significant hepatoprotective activity and anti-inflammatory activity. The whole plant is employed in the treatment of impetigo, ulcers, helmenthiasis and as a purgative (Manojlovic et al., 2016).

The plant chemically contains Sennoside A, B, C and D (Singanaboina and Chinna 2018). Further, the phytochemicals are natural bioactive compounds found in plants, including the medicinal plants, fruits, vegetables, flowers, leaves, roots and fibers, and they act as a defense system against diseases, or more accurately protect plants against diseases (Krishnaiah et al., 2009). Some of the most important bioactive phytochemical constituents are the glycosides, alkaloids, flavonoids, tannins, steroids, terpenoids, essential oils and phenolic compounds (Edeoga et al., 2005). Species of Cassia are rich sources of polyphenols, anthraquinone derivatives (Bahorun et al., 2005 and Ayo, 2010), flavonoids and polysaccharides. These biologically active chemical substances, known as secondary metabolites in medicinal plants, form the foundations of modern prescription drugs (Deshpande and Bhalsing, 2013). This study would be conducted to investigate the antioxidant and hepatoprotective effects of Senna leaves (Cassia senna l.) on CCL4 induced hepatotoxicity in rats.

### **Materials And Methods**

## Materials

- Leaves of Senna would be obtained from Pharmacy Farm, Cairo University, Egypt.
- 2. Carbon tetrachloride CCl4 and chemical kits would be obtained from El-Gomhoriya Pharm, Cairo, Egypt.
- 3. Casein, cellulose, sucrose, choline chloride, D-L methionine, vitamins and minerals constituents would be purchased from El-Gomhoriya Pharm.Cairo, Egypt.

#### Methods

#### **Preparation of Basal Diet:**

The basal diet would be included protein (14%), fat (5%), mineral mixture (3.5%), vitamin mixture (1%), cellulose (5%), sucrose (10%), choline chloride (0.2%) and the remainder will be Corn starch. These constituents will be thoroughly mixed and formulated according to (Reeves et al., 1993).

#### **Induction of hepatotoxicity in rats:**

Carbon tetrachloride (CCl<sub>4</sub>)-induced acute hepatotoxicity in rats. Intraperitoneal injection of male albino rats with CCl4 1mL/kg, (1:1) mixture with corn oil for 3 days increased serum alanine transaminase, aspartate transaminase, and alkaline phosphatase activities as well as total bilirubin, triglycerides and total cholesterol levels. This is in addition to the disrupted histology (karthikeyan and Deepa, 2010).

#### **Experimental design:**

Adult male albino rats Sprague Dawley Strain (28 rats) will be housed in well aerated cages under hygienic condition in lab of Agricultural Research Center-Giza. They will be left for one week as adaptation period and they will be allowed to feed standard laboratory food and water. After this week the rats would be divided into two main groups, as follows:

<u>The first main group</u>: Negative control group, rats (n=7) will be fed on basal diet

<u>The second main group</u>: Hepatotoxic group, rats (n=21), would be injected 1 ml CCl<sub>4</sub>/kg b.w. (karthikeyan and Deepa, 2010). After 24h from injection for 3 days, rat from each group would be taken to measure liver function to be sure that all rats had liver injury. After liver injury rats will be divided as follow: -

**Subgroup** (1) Hepatotoxic rats (positive control group), animals will be fed on basal diet only.

**Subgroup (2)** Hepatotoxic rats would be fed on basal diet supplemented with (1% Senna leaves powder per kg of basal diet).

**Subgroup (3)** Hepatotoxic rats would be fed on basal diet supplemented with (2% Senna leaves powder per kg of basal diet).

#### **Biological Evaluation**

**Determination of FI, IBW, FBW and Percent of BWG:** Feed intake will be recorded daily, and animals will be weighed at the beginning and twice a week throughout the experimental period. Body weight gain% and feed efficiency ratio will be calculated at the end of the experiment according to the method of **(Chapman et al., 1959)**.

# **Biochemical Assessments**

Evaluation of Lipid Profile: Serum levels of total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-c), and low density lipoprotein cholesterol (LDL-c) were determined using trading reagent kits (Biomed diagnosis, Egypt) as referred by Zollner and kirsch (1962), Vassault et al., (1986), Hostmark et al., (1991), Friadwald et al., (1972) and Young, (2001), respectively. While, very low-density lipoprotein cholesterol (VLDL-C) was measured using the following formula: VLDL-c (mg/ dL) = TG/5

Evaluation of Liver Functions: The serum activity of Alanine transaminase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP) enzymes and gammaglutamyl (GGT) was colorimeters quantified utilizing kits (Diamond Co, Hanover, Germany) in line with the instructions of Young (1997) for AST and ALT assay, Sherwin (1984) for ALP assay and Dufour et al., (2000) for GGT assay. The biometrics were quantified using a spectrophotometer (Hum star 200, automatic biochemistry analyzer, Germany) adjusted at 505 for ALT, AST and ALP, and 510 nm for GGT.

Serum levels of total protein (TP), albumin (Alb), total bilirubin (TBL) and direct (DBL) were quantified colorimetrically using a spectrophotometer (Hum star 200, automatic biochemistry analyzer, Germany) as mentioned by **Tietz** (1994), Young (2000), Henry (1991) and Burtis and Ashwood (1999), respectively.

# **Evaluation of Malondialdehyde and Activities of Antioxidant Enzymes:**

The principal method for the determination of oxidative stress was depending on colorimetric by quantifying thiobarbituric acid (TBA) reactivity as malondialdehyde (MDA) in a spectrophotometer adjusted at 534 nm according to the described method by **Ohkawa** *et al.*, (1979).

The activities of antioxidant enzymes glutathione peroxides (GPx) was determined as referred by the commercial testing kits (Cayman Practice ELISA Kits). The serum activity of GPx was checked according to the kit's instruction manual as mentioned by **Beutler** *et al.*, (1963) and **Paglia and Valentine.**, (1967) using spectrophotometrically at 405 nm and 340 nm.

<u>Statistical Analysis:</u> Data were assessed statistically according to the computerized SPSS package program (SPSS 22.00 software for Windows) by one-way analysis of variance (ANOVA). The gained data was stated as Mean  $\pm$  SD, and the significant difference between means was estimated at p<0.05.

#### **Results and Discussion**

#### **Results**

Effect of Senna leaves on FI, FBW, BWG and BWG (%) in rats with hepatotoxicity: The current results in Table 1 revealed that untreated hepatotoxicity rats (positive) have a significant (P<0.05) decrease in FI compared to that of healthy rats (negative rats). In contrast, hepatotoxicity rats fed on basal diet supplemented with (1% and 2% Senna leaves) had significant increase changes in FI compared to that of the positive rats and had a significant decrease, compared to the negative group.

Regarding body weight, the tabulated results showed that hepatotoxicity rats fed on basal diet had a significant (P<0.05) decrease in IBW, FBW and BWG%, compared to that of the normal rats fed on basal diet. Incorporated, the hepatotoxicity rats fed on basal diet supplemented with (1% and 2% Senna leaves) caused significant increase (P<0.05) in IBW, FBW and BWG%, compared to the positive control rats. On other hand, the result revealed that hepatotoxicity rats fed on basal diet had a significant (P<0.05) increase in FER compared to that of the normal rats fed on basal diet while, the hepatotoxicity rats fed on basal diet supplemented with (1% and 2% Senna leaves) caused significant increase (P<0.05) in FER compared to the positive control rats. The increase in IBW, FBW, BWG% and FER were significantly ameliorated by the administration of Senna leaves treatments, compared to hepatotoxicity rats.

Table (1): Effect of Senna leaves on FI, FBW, FER and BWG (%) in rats with hepatotoxicity

Parameters	Parameter as Mean ± SD					
	FI	IBW	<b>FBW</b>	FER	BWG (%)	
Groups	<b>(g)</b>	<b>(g)</b>	(g)			
Negative group	20.25	190.2±4.55a	219.0±4.88 <sup>a</sup>	$3.16\pm0.24^{a}$	$15.14\pm1.10^{a}$	
Positive group	15.50	195.0±2.85a	196.5±2.95 <sup>b</sup>	$0.21\pm0.03^{d}$	$0.76\pm0.14^{d}$	
1 % Senna leaves	18.25	202.2±3.49a	216.75±3.44 <sup>a</sup>	$1.77\pm0.20^{bc}$	$7.18\pm0.80^{bc}$	
2 % Senna leaves	19.00	204.0±3.48 <sup>a</sup>	216.25±3.70 <sup>a</sup>	$1.43\pm0.10^{c}$	$6.00\pm0.36^{c}$	

Means with different letters in each row are significantly differs at p< 0.05; FI: Food Intake; IBW: Initial body weight; FBW: Final body weight; FER: Feed efficiency ratio; BWG%: Change in body weight gain%.

Effect of Senna leaves on TC, TG, LDL-c, HDL-c and VLDL-c in rats with hepatotoxicity: In the case of the serum lipid profile, the parameters of serum TC, TG, LDL-c, HDL-c, and VLDL-c levels were used to check the effect of Senna leaves on hepatotoxicity rats. The results in Table 2 revealed that hepatotoxicity rats fed on basal diet had a significant (P<0.05) increase in the serum concentrations of TC, TG, LDL-c, HDL-c, and VLDL-c, and a decrease in HDL-c levels, compared to that of the normal rats fed on a normal basal diet. In contrast, the administration of Senna leaves caused a significant amendment in the serum levels of the above parameters, as compared to hepatotoxicity rats fed on basal diet alone (positive rats). The rate of improvement in the serum levels of TC, TG, LDL-c, and VLDL-c was more evident with the administration of 2% Senna leaves, while serum HDL-c, levels were improved in treated groups with same level 2% Senna leaves.

Table (2): Effect of Senna leaves on TC, TG, LDL-c, HDL-c and VLDL-c in hepatotoxicity rats

Parameters	TC	TG	HDL-C	LDL-C	VLDL-C
Groups	(mg/dl)	(mg/dl)	(mg/dl)	(mg/dl)	(mg/dl)
Negative group	184.45±1.54 <sup>g</sup>	$96.50 \pm 1.19^{f}$	$60.50\pm1.70^{ab}$	104.65±0.83	19.30±0.23 <sup>f</sup>
Positive group	241.77±1.31a	153.50±1.44 <sup>a</sup>	37.75±1.10°	173.32±1.22	30.70±0.28 <sup>a</sup>
1 % Senna leaves	217.80±1.18 <sup>b</sup>	143.97±1.35 <sup>b</sup>	58.50±1.04 <sup>b</sup>	130.51±1.81	28.79±0.27 <sup>b</sup>
2 % Senna leaves	207.72±1.24 <sup>cd</sup>	125.32±1.29 <sup>d</sup>	59.50±1.32ab	123.16±2.01	25.06±0.25 <sup>d</sup>

Means with different letters in each row are significantly differs at p< 0.05; **TG:** Triglycerides; **TC:** Total Cholesterol; **LDL**: Low Density Lipoprotein; **HDL**: High Density Lipoprotein; **VLDL-C:** Very Low-Density Lipoprotein Cholesterol.

Effect of Senna leaves on AST, ALT and ALP in hepatotoxicity rats: The tabulated results in Table (3) outlined that untreated rats with (CCL<sub>4</sub>) had a significant increase in the serum activity of AST, ALT and ALP enzymes, compared to the normal rats. Whilst the treated rats by the oral administration of Senna leaves caused significant (P<0.05) reductions in the serum activity of AST, ALT and ALP enzymes, compared to hepatotoxicity rats. The significant improvement in the activities of liver enzymes (AST, ALT and ALP) were reported in hepatotoxicity rats treated with 2% Senna leaves.

rais.			
Parameters	ALT (u/L)	AST (u/L)	ALP (u/L)
Groups			
Negative group	18.25±1.85 <sup>e</sup>	21.50±1.32 <sup>f</sup>	81.14±0.53 <sup>e</sup>
Positive group	40.05±1.06 <sup>a</sup>	41.75±0.85 <sup>a</sup>	117.00±1.08 <sup>a</sup>
1 % Senna leaves	29.52±0.84 <sup>b</sup>	34.99±0.91 <sup>bc</sup>	97.98±1.22 <sup>b</sup>
2 % Senna leaves	23.81±0.68 <sup>cd</sup>	$31.70\pm0.65^{d}$	83.14±1.77 <sup>e</sup>

Table (3): Effect of Senna leaves on AST, ALT and ALP hepatotoxicity rats.

Means with different letters in each row are significantly differs at p< 0.05; **AST:** Aspartate Aminotransferase; **ALT**: Alanine Aminotransferase; **ALP**: Alkaline Phosphatase.

Effect of Senna leaves on MDA and GPx in hepatotoxicity rats: Table 4 represents the results of lipid peroxidation as indicated by serum MDA level and activity of GPx in normal rats, untreated hepatotoxicity-rats and treated hepatotoxicity-rats with the oral administration of Senna leaves. In comparison to normal rats, untreated hepatotoxicity rats (positive rats) have a significant increase (P<0.05) in serum levels of MDA and decrease in serum activities of GPx. However, oral administration of Senna leaves in (1% and 2%) encourages a significant (P<0.05) decrease in serum MDA level and increase in the activity of GPx enzymes compared to the positive control group. The good result in serum concentration of MDA and activity of antioxidant enzymes was shown in the hepatotoxicity group that treated by 2% Senna leaves as compared to the other treated group.

Table 4: Effect of Senna leaves on MDA and GPx in hepatotoxicity rats.

Parameters	GPx	MDA
Groups	(u/ml)	(u/ml)
Negative group	87.50±1.19 <sup>a</sup>	$36.30\pm0.35^{d}$
Positive group	49.98±1.57 <sup>e</sup>	83.67±1.42 <sup>a</sup>
1 % Senna leaves	76.50±1.04°	46.31±1.08°
2 % Senna leaves	85.75±0.85 <sup>ab</sup>	36.97±0.47 <sup>d</sup>

Means with different letters in each row are significantly differs at p< 0.05; **MDA**: Malondialdehyde and **GP**x: Glutathione Peroxidase.

#### **Discussion**

The liver is the main organ for metabolizing and excreting foreign substances. Organ dysfunction, membrane damage, and liver degeneration invariably follow as a result of liver cell exposure to high quantities of hazardous compounds (Firdous & Fayed, 2021). Exposure to xenobiotics and pollutants in the environmental, such as alcohol, thioacetamide, carbon tetrachloride, paracetamol, and paracetamol, can cause damage to the liver by generating reactive oxygen species (ROS), which is one of the main reasons for these diseases (Salim & Abdel-Alim, 2024). Carbon tetrachloride (CCl4) is a known hepatotoxicant in humans and animal models. It has been successfully used in hepatotoxicity research as a model and to appraise hepatoprotective agents (Ugwu & Suru, 2021). Currently, modern medicine and conventional modern drugs are used to treat liver diseases. However, these drugs such as Ursodiol, silymarin still have many adverse effects which include diarrhea, constipation, dizziness, fullness and pains in the stomach and back (Hamzah et al., 2021). Senna is a small herb belonging to the Cassia genus of the Caesalpiniaceae family which is a subfamily of Leguminosae (or Fabaceae). Cassia has more than 350 species around the world, many of which play a significant role in treating various diseases (Thaker et al., 2023). The synergistic mechanism behind the chemical substances of Cassia species makes them more beneficial. In the folk medicinal history, these plants are used as a laxative and purgative agent. In the Ayurveda system of medicine, they are used to cure headaches and fever. They exhibited pharmacological activities at large scale such as antiinflammatory, antitumor, anti-plasmodial, antioxidant, hypoglycemic, hyperglycemic, and antimutagenic (Khurm et al., 2021).

Our results showed that positive control group showed a significant reduction in FBW (compared to the negative control) and a decrease in BWG% and FER, which could indicate a condition that inhibited growth or weight gain. These results showed improved FBW and BWG%, with a decrease in FER compared to the negative control, suggesting moderate weight gain but possibly less efficient food utilization than some other groups. In line with (Shaily et al., 2023) reported that CCl4 group significantly ( $P \le 0.05$ ) reduced FBW compared to the control group. Mice which were treated with Senna Alexandrina leaf powder supplementation with CCl4 administration did not show any kind of significant reduction of final body weight compared to the CCl4 group. control + SA group reduced a significant amount of final body weight compared to the CCl4 group. While, no significance was found between

CCl4 and control group in food intake. Also, no significant difference was found between CCl4 + SA and CCl4 group in food intake. However, the control + SA group increased the food intake level significantly compared to the CCl4 group.

The results in the thesis showed that, positive control group showed significant increase in total cholesterol (TC), triglycerides (TG), LDL-c, and VLDL-c compared to the negative control group. The treatment group with 2% Senna leaves showed the most favorable lipid profile with a significant reduction in TG, LDL, and VLDL levels, along with slightly lower total cholesterol compared to other treatment groups. This accumulated with (Bellassoued et al., 2021) reported that in CCl4 induced intoxicated rats, the plasma lipid levels cholesterol, triglycerides and LDL increased as compared to the control group, also a significant decrease in the HDL-Ch level. Treatment with MECA alone did not cause any significant change in lipid profile. However, rats pre-treated with MECA exhibited a marked reversal of the serum lipid profile cholesterol, triglycerides and LDL compared to toxic control. Moreover, HDL-Ch level significantly increased as compared to the CCl4 group. As well (Sakr et al., 2011) aimed to investigate the effect of basil on Ccl4-induced hepatotoxicity and apoptotic in albino rats, reported that administration of CCl4 to rats caused significant increase in cholesterol, triglycerides and LDL compared with animals of control groups. Animals treated with both CCl4 and O. basilicum extract showed reduction in their sera level of cholesterol and triglycerides in comparison of those given CCl4.

Our thesis showed that positive control group showed a significant increase in ALT, AST, and ALP compared to the negative control group, indicating liver stress or damage. The official group treatment with 1 Senna leaves showed a reduction in liver function markers, but ALT and AST were still higher than in the negative control. This accompanied with (Bellassoued et al., 2021) aimed to investigate the preventive effects of methanol fraction from Cassia angustifolia leaf extract (MECA), associated with its phytochemical content, on CCl4-induced hepatic toxicity in adult rats, reported that compared to the control group, the CCl4-intoxicated rats showed a significant (p < .001) increase in the AST, ALT and ALP levels. Although treatment with MECA alone did not cause any significant change in these biomarkers compared to

control. Pre-treatment with MECA for 15 days restored AST, ALT and ALP levels as compared to CCl4 group. Furthermore (Shaily et al., 2023) aimed to determine whether administering Senna alexandrina leaf supplementation to CCl4-induced mice reduced hepatic inflammation, fibrosis, and oxidative stress, reported that CCl4 increased plasma levels of ALP, ALT, and AST significantly compared to the control group. Mice which received both CCl4 and leaf powder supplementation of Senna alexandrina showed reduced ALP, AST, and ALT plasma levels significantly compared to mice that only received CCl4. The control + SA group reduced ALP, ALT, and AST plasma significantly compared to the CCl4 group. Similarly, (Nkechi et al., 2020) investigated the hepatoprotective potential of the aqueous extract of Senna mimosoides leaves on Wistar albino rats, reported that there was a significant increase in AST, ALT and ALP serum level of rats in CCl4 compared to the normal control, S. mimosoides aqueous extract caused a significant decrease in the activity of these enzymes (AST, ALT and ALP) when compared to CCl4 group. In this thesis showed that negative control group had normal levels of GPX and MDA than positive control group that showed a significant decrease in GPX levels and a significant increase in MDA indicating a high level of oxidative stress or damage. The group treatment with 2% Senna leaves had the highest GPX levels and the lowest MDA levels. This agreement with (Sarhan et al., 2019) reported that compared with normal control rats, MDA was significantly increased in CCl4 injected rats, while GPx was significantly decreased, concerning to OBE administered rats when compared with normal control rats showed significant decreases in GPx activities in 1st check point while non-significant changes in 2nd check points. and a significant increase in the level of MDA were observed in 1st and 2<sup>nd</sup> check points, also revealed significant increases in GPx and significant decrease in MDA when compared with CCl4 injected rats in 1st check point. Moreover (Bellassoued et al., 2021) reported that a significant decrease in the level GPx in the CCl4 treated rats compared with controls. Pre-treatment with MECA highly improved the antioxidant status in the liver tissue compared to CCl4-treated group. The MECA group showed no noticeable variation in the activities of enzymatic and non-enzymatic compared with the control one. Furthermore (Shaily et al., 2023) reported that mice which received only CCl4 showed an elevated level of MDA concentration significantly compared to mice that only took normal laboratory

chow food. Mice which were part of receiving both CCl4 and leaf powder supplementation of Senna alexandrina reduced MDA concentration significantly compared to mice that only received CCl4. Similarly, (Nkechi et al., 2020) reported that intoxication with CCl4 depleted the plasma levels of GPx activity of the Wistar Albino rats as compared to those of the control group. There was a dose-dependent significant increase in the plasma levels of GPx activity of the Wistar Albino rats on administration of aqueous extract of Senna mimosoides, also MDA values showed a dose-dependent significant decreases when compared to CCl4 group.

#### **Conclusion**

Our study demonstrated that Senna leaves exert beneficial effects in mitigating carbon tetrachloride (CCl<sub>4</sub>)-induced hepatotoxicity in rats. Supplementation with 2% Senna leaves significantly improved liver function markers (ALT, AST and ALP), lipid profiles (TC, TG, HDL- c, LDL-c and VLDL-c), and antioxidant status (increased GPX, decreased MDA), approaching values observed in the negative control group. The 2% Senna leaves group consistently showed the most pronounced protective effects across all measured parameters, including improved body weight gain and feed efficiency ratio. These findings suggest a synergistic hepatoprotective and antioxidant potential of Senna leaves when used particularly at higher concentrations.

#### REFERENCES

Ali, M., Khan, T., Fatima, K. Ali, Q., Ovais, M., Khalil, A. T., Ullah, I., Raza, A., Shinwari, Z. and Idrees, M. (2018): "Selected hepatoprotective herbal medicines: evidence from ethnomedicinal applications, animal models, and possible mechanism of actions". PhytotherapyResearch; 32(2): pp. 199–215.

**Ayo, R. G. (2010):** "Phytochemical constituents and bioactivities of the extracts of Cassia nigricans Vahl: A review", Journal Medicinal Plants Research; Vol. 4(14), pp. 1339-1348.

Bahorun, T., Neergheen, V. S and Aruoma, O. I. (2005): "Phytochemical constituents of Cassia fistula", Afr. J. Biotechnol.; Vol. 4(13), pp. 1530-1540.

**Bellassoued, K., Hamed, H., Ghrab, F., Kallel, R., Van Pelt, J., Makni Ayadi, F., & Elfeki, A. (2021):** Antioxidant and hepatopreventive effects of Cassia angustifolia extract against carbon tetrachloride-induced hepatotoxicity in rats. Archives of Physiology and Biochemistry, 127(6), 486–496.

**Beutler E., Duron O. and Kelly BM. (1963):** Improved method for the determination of blood glutathione .j.Lab .clin .med; 61:882-888.

**Burtis A. and Ashwood R. (1999):** editors. Tietz Textbook of Clinical Chemistry, 3rd ed. Philadelphia, PA: WB Saunders.1169.

**Chapman D. G., GastillaR. and Campbell J. A. (1959):** Evaluation of protein in foods: 1- AMethod for the determination of protein efficiency ratio. Can. J. Biochem. Phys; 37:679-86.

Chaware, V., Joshi, Y. and Biyani, K., (2009): Hepatoprotective activity of Hydroalcoholic extract of Momordica charantia Linn. leaves against Carbon tetra chloride induced Hepatopathy in Rats 1, 355-358.

**Deshpande, H. A. and Bhalsing, S. R. (2013):** Recent advances in the phytochemistry of some medicinally important Cassia species: A REVIEW. Int. J. Pharm. Med. & Bio. Sc;. 2(3): 2-21.

Dufour DR., Lott JA., Nolte FS., Gretch DR., Koff RS. and Seeff LB.(2000)

: Diagnosis and monitoring of hepatic injury. I. Performance characteristics of laboratory tests. Clin Chem; 46:2027-2049.

Edeoga, H. O., Okwu, D. E. and Mbaebie, B. O. (2005): "Phytochemical constituents of some Nigerian medicinal plants", Afr. J.Biotechnol.; Vol. 4(7), pp. 685-688.

Firdous, S. M., & Fayed, M. A. A. (2021): Effects of Medicinal Plants on Carbon Tetrachloride-Induced Liver Injury: A Review.

Friedewald W.T., Levy R.I. and Fredrickson D.S. (1972): Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem.; 18:499–502.

Gandhimathi, R. and Saravana Kumar, A., (2012): Effect of Malachra capitata (L.) extracts on biogenic amines concentrations in rat brain after induction of seizure. International Journal of Pharmacy 2, 54-58.

Hamzah, R. U., Busari, M. B., Ankewo, E., Mohammed, H. A., Yahaya, A. M., & Akomolafe, A. P. (2021): Hepatoprotective effect of methanol extract of Senna occidentalis seeds in carbon tetrachloride induced hepatotoxic rats. Biokemistri, 33(4), 259–272.

**Henry d. (1991):** Clinical Diagnosis and Management by Laboratory Methods, 18th Edition, W.B. Saunders, Philadelphia, PA.

Hostmark A., Berg J., Osland A., Simonsen S. and Vatne K. (1991): Lipoprotein-related coronary risk factors in patients with angiographically defined coronary artery disease and controls: improved group separation by indexes reflecting the balance between low-and highdensity lipoproteins. Coronary Artery Dis, 2(6): 679-84.

**Karthikeyan, M. and Deepa, k. (2010):** Hepatoprotective effect of premnacorymbosa (Bum f.) Rottl. & wild leaves extract on CCL4 induced hepatic damage in wistar albino rat. Asian Pac. J. trop. Med., 3(1): 17-20.

- Khurm, M., Wang, X., Zhang, H., Hussain, S. N., Qaisar, M. N., Hayat, K., Saqib, F., Zhang, X., Zhan, G., & Guo, Z. (2021): The genus Cassia L.: Ethnopharmacological and phytochemical overview. Phytotherapy Research, 35(5), 2336–2385.
- Krishnaiah, D., Devi, T., Bono, A. and Sarbatly, R. (2009): "Studies on phytochemical constituents of six Malaysian medicinal plants", Journal of Medicinal PlantsResearch; Vol. 3 (2), pp. 067–072.
- Li, C., Yi, L.-T., Geng, D., Han, Y.-Y. and Weng, L.-j., (2015): Hepatoprotective effect of ethanol extract from Berchemia lineate against CCL4- induced acute hepatotoxicity in mice. Pharmaceutical biology 53, 767-772.
- Lodha, S. R., Joshi, S. V., Vyas, B. A., Upadhye, M. C., Kirve, M. S., Salunke, S. S., Kadu, S. K. and Rogye, M. V. (2010): "Assessment of the antidiabetic potential of Cassia grandis using an in vivo model", J Adv PharmTechnol Res.; Vol. 1(3), pp. 330-333.
- Manojlovic, I., Bogdanovic-Dusanovic, G., Gritsanapan, W. and Manojlovic, N. (2006): Isolation and identification of anthraquinones of caloplacacerina and cassia species. Chemical Pap; 60(6):466-68.
- Meng, X., Li, Y., Li, S., Gan, R. Y. and Li, H. B. (2018): "Natural products for prevention and treatment of chemical-induced liver injuries". Comprehensive Reviews in Food Science and Food Safety; 17(2): pp. 472–495.
- Nkechi, N. F., Chinenye, N. C., Nmaduka, N. J., & Chiletugo, N. O. F. (2020): Research Article Hepatoprotective Effect of Senna mimosoides Aqueous Leaf Extract Against Carbon Tetrachloride Induced Hepatotoxicity in Albino Rats.
- Okhawa H., Ohishi N. and Yagi K. (1979): Assay for lipid peroxides in. animal tissues by thiobarbituric acid reaction. Anal Biochem; 95:351-358.
- **Paglia D.E. and Valentina W.N.(1967):** Studies on the quantitative and qualitative characterization of erythrocyte glutathione per-oxidase. J Lab Clin Med;70:158–69.
- Pereira-Filho, G., Ferreira, C., Schwengber, A., Marroni, C., Zettler, C. and Marroni, N., (2008): Role of N-acetylcysteine on fibrosis and oxidative stress in cirrhotic rats, Arq. Gastroenterol 45, 156–162.
- **Reeves P., Nielsen F. and Fahmy G. (1993):** AIN-93. Purified diets for laboratory rodents: Final reports of the American Institute of Nutrition adhoe 9 wriling committee of reformulation of the AIN-76 A Rodent Diet. J. Nutr., 123: 1939-1951.
- Sakr, S. A., El-Abd, S. F., Osman, M., Kandil, A. M., & Helmy, M. S. (2011): Ameliorative effect of aqueous leave extract of Ocimum basilicum on CCl4-induced hepatotoxicity and apoptosis in albino rats. J. Am. Sci, 7(8), 116–127.
- Salim, N., & Abdel-Alim, M. (2024): Hepatoprotective Effect and Antioxidant Effects of Sonchus Oleraceus Leaves Extract Against Carbon Tetrachloride (CCl4) Induced hepatotoxicity in Albino Rats. Egyptian Journal of Chemistry.

Sarhan, H., Farid, A., & Mostafa, K. (2019): Hepatoprotective and antioxidant effects of Ocimum basilicum extract in CCl4-induced rats hepatotoxicity compared with silymarin. Benha Veterinary Medical Journal, 36(2), 282–292.

Shaily, S. D., Paul, S., Kawser, M., Chowdhury, F. I., Das, P., Nayan, S. I., Amena, I. J., Mondal, P., Dina, S. S., & Sharmin, N. (2023): Senna alexandrina leaf powder supplementation prevents hepatic inflammation and fibrosis in CCl4-induced Swiss albino mice. Clinical Nutrition Open Science, 51, 136–148.

**Sherwin J. E. (1984):** Liver function. In: kaplan LA, PESCE AJ, eds. Clinical chemistry, theory, analysis, and correlation. St Louis: Mosby; 1984:420-438.

**Singanaboina, K. and Chinna, V. (2018):** Pharmacognosy of Cassia angustifolia Leaf Grown in Differently Treated Soils. Int.J.Curr.Microbiol.App.Sci; 6: 2580-2589.

**Singh, S., Singh, S. K. and Yadav, A. (2013):** A Review on Cassia Species: Pharmacological, Traditional and Medicinal Aspects in Various Countries. American Journal of Phytomedicine and Clinical Therapeutics; ISSN 2321 –2748.

Sundaramoorthy, S., Gunasekaran, S., Arunachalam, S. and Sathiavelu, M. (2016): A Phytopharmacological Review on Cassia Species. J. Pharm. Sci. & Res.; Vol. 8(5): 260-264.

Thaker, K., Patoliya, J., Rabadiya, K., Reddy, N. R. R., & Joshi, R. (2023): Senna (Cassia angustifolia Vahl.): A comprehensive review of ethnopharmacology and phytochemistry. Pharmacological Research-Natural Products, 1, 100003.

**Tietz W. (1994):** Specimen Collection and Processing; Sources of Biological Variation in Textbook of Clinical Chemistry, 2nd Ed. Philadelphia; W.B. Saunders.

Ugwu, C. E., & Suru, S. M. (2021): Medicinal plants with hepatoprotective potentials against carbon tetrachloride-induced toxicity: a review. Egyptian Liver Journal, 11, 1–26.

Vassault A., Grafmeyer D., Naudin C.I., Dumont G., Bailly M., Henny J., Gerhardt M. and Georges P. (1986): Ann Biol Clin.,44(N686):45.

**Young D. S. (2001):** Effects of Disease on Clinical Laboratory Tests, 4<sup>th</sup> Edition Washington, DC: AACC Press.

**Young S. (1997):** Effects of Preanalytical Variables on Clinical Laboratory Tests, 2nd Edition, AACC Press, Washington, D.C.

**Young S. (2000):** Effects of Drugs on Clinical Laboratory Tests, fifth edition, AACC Press, Washington, D.C.

**Zöllner N. and Kirsch K. (1962):** Colorimetric Method for Determination of Total Lipids. Journal of Experimental Medicine, 135, 545-550.

# التأثير الوقائي الكبدي والمضاد للأكسدة لأوراق السنا (Cassia senna l) ضد السمية الكبدية المستحدثة برابع كلوريد الكربون في الفئران الملخص العربي

صممت هذه الدراسة للتحقق من التأثيرات المضادة للأكسدة والوقاية الكبدية لأوراق السنا على التسمم الكبدي لدى الفئران التي تم حقنها برابع كلوريد الكربون .(CCl4) تم الحصول على ٢٨ فأر من ذكور فئران سبراغ داولي ألبينو البالغين (١٥٠ ± ١٠ جم) من مزرعة حيوانات التجارب بحلوان في مصر. المجموعة الأولى (ن-٧) كانت بمثابة المجموعة الضابطة السلبية وتلقت نظاماً غذائياً أساسياً قياسياً. المجموعة الثانية (العدد = ۲۱) تم حقنها داخل الصفاق بمركب رابع كلوريد الكربون (CCl<sub>4</sub>) بجرعة ١ مل/كجم (١:١ في زيت الذرة) لمدة ٣ أيام متتالية لتحفيز تسمم الكبد. ثم قسمت الفئران المصابة بالتسمم الكبدي إلى ثلاث مجموعات (ن=٧ لكل منها): مجموعة ضابطة إيجابية تتغذى على النظام الغذائي الاساسي فقط، ومجموعتان تم معالجتهما حيث تتلقيان النظام الغذائي الاساسي مضافاً إليه إما ١٪ أو ٢٪ من أوراق السنا. وتم تحديد معايير التقييم البيولوجي (وزن الجسم الأول(IBW) ، وزن الجسم الاخير (FBW) ، معدل الاستفادة من الغذاء (FER) ، نسبة الزيادة في وزن الجسم للفئران (BWG%). وتم فصل عينات الدم للحصول على سيرم الدم لتحديد وظائف الكبد ALT و AST و(ALP ، ومعدل الدهون VLDL-C ،LDL-C ،HDL-C ،TG ،TC وتحديد مضادات الأكسدة MDA و GPx وكشفت النتائج أنه في مجموعةCCI4 ، كانت هناك زبادات كبيرة في ALT و AST و TC و TC و TG و LDL-C و VLDL-C و MDA ، في حين أظهرت المؤشرات الاخرى HDL-Cو GPx انخفاضًا كبيرًا. وفي الوقت نفسه، أدى تناول أوراق السنا إلى انخفاض كبير في جميع المؤشرات المذكورة سابقا وزيادة في HDL و GPx. ولذلك، يمكن أن نستنتج أن أوراق السنا لها دور وقائي للكبد كمضاد للأكسدة.

الكلمات المفتاحية: أوراق السنا، السمية الكبدية لـ CCl4، مضادات الأكسدة، وقاية الكبد.