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Hepatoprotective Activity of *Capparis decidua* Aqueous and Methanolic Stems Extracts Against Carbon Tetrachloride Induced Liver Histological Damage in Rats

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ABSTRACT

In this study, hepatoprotective effect of aqueous and methanolic extracts of *Capparis decidua* stems were evaluated against carbon tetrachloride induced liver damage in rats. Simultaneous oral administration of both extracts (200, 400 mg kg^{-1}) with CCl_4 in paraffin oil (1:9 v/v) at a dose of 0.2 mL kg^{-1} for 10 days covered the liver fatty changes induced by the hepatotoxic compound observed in the intoxicated control rats. Slight to mild changes in hepatocytes were observed in rats dosed by aqueous extract of *C. decidua* stems and higher dose of methanolic extract, whereas the lower dose of methanolic extract revealed more severe lesions than the higher dose. The results were compared with the hepatoprotective effect of the standard drug silymarin.

Key words: Hepatoprotective activity, *Capparis decidua*, rats, CCl_4

INTRODUCTION

Capparis decidua belongs to the family Capparaceae and locally known as Altoundob (Elamin, 1990). This plant is widely used in the treatment of various ailments mainly among the local population as anthelmintic, analgesic, aphrodisiac, carminative, diaphoretic, emmenagogue and laxative (Rahman *et al*., 2004). The bark of *C. decidua* has been used by people in the treatment of cough, asthma and inflammation; roots are used in fever and buds in the treatment of boils (Satyanarayana *et al*., 2008). The water extract of the green stems of *C. decidua* is used as a bathe for jaundice (El-Ghazali, 1986).

A large number of plants and formulations have been claimed to have hepatoprotective activity. Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity. In India, more than 87 plants are used in 33 patented and proprietary multi-ingredient plant formulations (Handa *et al*., 1986).

In an earlier study, Ali *et al*. (2009) investigated the hepatoprotective effect of the aqueous and methanolic extracts of *C. decidua* in rats against CCl_4 induced hepatotoxicity and the results indicated that the plant can be exploited for future hepatoprotective drug. In this respect, previous studies also showed that other species of the genus *Capparis*, e.g., *C. spinosa* have potential protective activity against liver damage (Gadgoli and Mishra, 1995).

Pharmacological studies of the extracts of *C. decidua* were found to have anti-inflammatory and antipyretic effects (Ageel *et al.*, 1986), antioxidant (Yadav *et al.*, 1997), hypoglycemic and hypolipidemic (Modak *et al.*, 2007; Chahlia, 2009), anthelmintic, antibacterial and antifungal activities (Satyanarayana *et al.*, 2008) and CNS depressant and anticonvulsant activities (Goyal *et al.*, 2009).

Various substances are known to cause liver and kidney damage and one of them is carbon tetrachloride (CCl_4), which is a well known hepato and nephrotoxin. Within the body, CCl_4 breaks down to highly toxic trichloromethyl (CCl_3) and trichloromethyl peroxyl (CCl_3O_2) free radicals by cytochrome P450 enzyme and causes damage to hepatocytes (Abraham *et al.*, 1999).

The aim of the present study was to investigate the protective effect of aqueous and methanolic extracts of *C. decidua* stems against carbon tetrachloride induced liver damage in rats.

MATERIALS AND METHODS

Collection and identification of the plant: *Capparis decidua* stems were collected from Arkaweit area in southern Khartoum, during May 2004 and dried at room temperature. The plant was identified by the botanists in Medicinal and Aromatic Plants Research Institute.

Preparation of the extract: Aqueous extract was prepared by infusion method and dried using freeze drier apparatus and the yield percentage was 6.94%. Methanolic extract was also prepared by using soxhlet extractor and the yield percentage was 12.61% (Harborne, 1973).

Experimental procedure: Thirty five adult male Wister albino rats were used; the animals were grouped randomly into 7 groups of 5 rats each. Group I served as normal control and received only the vehicle liquid paraffin at a dose rate of 0.2 mL/kg/day i.p. for 10 days. Group II served as intoxicated control given CCl_4 at a dose rate of 0.2 mL/kg/day i.p. in liquid paraffin (1:9) for 10 days. Group III served as hepatoprotective drug control when the rats were given CCl_4 at a dose rate of 0.2 mL/kg/day i.p. in liquid paraffin (1:9) for 10 days and at the same time received orally silymarin suspended in 5% *Acacia mucilage* at a dose of 100 mg/kg/day. Group IV, V, VI and VII rats were given CCl_4 at a dose rate of 0.2 mL/kg/day i.p. in liquid paraffin (1:9) for 10 days. In addition group IV received simultaneous oral administration of aqueous extract of *C. decidua* stems at a dose of 200 mg kg^{-1}, group V was given 400 mg kg^{-1} of aqueous extract of *C. decidua* stems orally, group VI received 200 mg kg^{-1} of methanolic extract of *C. decidua* stems orally and group VII rats were dosed with 400 mg kg^{-1} of methanolic extract of *C. decidua* stems orally.

Histopathological studies: The animals were sacrificed by decapitation under anaesthesia and post-mortem examination was performed. Small pieces of livers were collected in 10% neutral buffered formal saline for histopathological study. Section 5-6 μ were cut and stained by haematoxyline and eosine.

RESULTS

Post-mortem investigations of CCl_4 group showed severe generalized fatty change, petechial haemorrhages and week adhesions in all lobes of the liver. Petechial haemorrhages and slight fatty change in the livers were seen in standard drug group and rats dosed with 200 and 400 mg kg^{-1} aqueous extract of *C. decidua* stems. In rats that received 200 mg kg^{-1} of methanolic

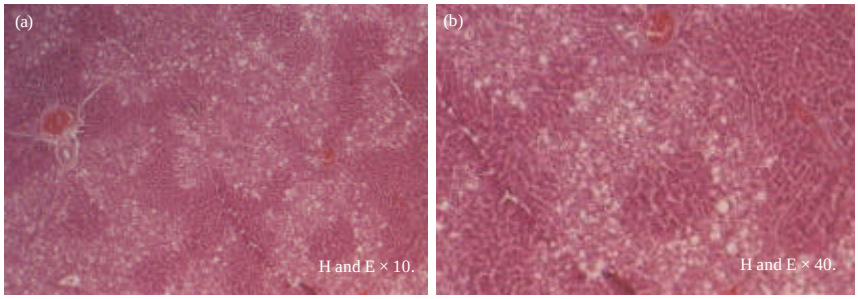

Fig. 1: (a, b) Liver section, CCl_4 group, showing diffuse areas of vacuolar degeneration and centrilobular necrosis with mononuclear cell infiltration

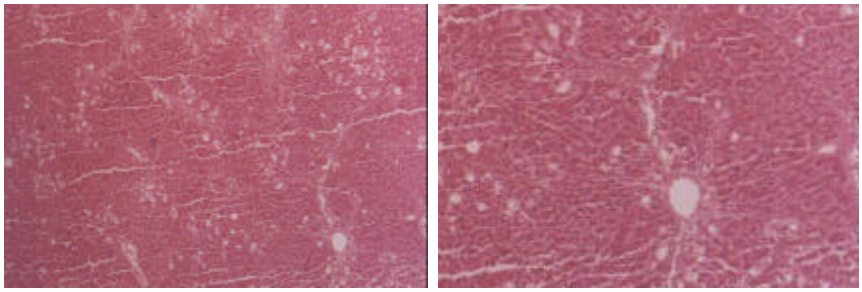

Fig. 2: (a, b) Liver section, standard drug group, showing mild hepatocyte vacuolation

extract also showed fatty change and petechial haemorrhages, similarly, petechial haemorrhages and slight fatty change were observed in the liver of rats receiving the higher dose. No significant changes were observed in control group except slight congestion.

Histopathological examination of CCl_4 group (II) demonstrated significant changes in the livers which included diffuse vacuolar degeneration, mainly centrilobular, swelling of hepatocytes and congestion of hepatic veins and sinusoids (Fig. 1a, b).

In standard drug group (III) mild to moderate changes were noticed. Hepatocytes contained small single or multiple cytoplasmic vacuoles, mainly at the periphery of the lobules. Hepatocyte swelling and congestion were also observed (Fig. 2a, b).

Group IV (200 mg kg^{-1} aqueous extract of *C. decidua* stems) showed very little changes. However some hepatocytes appeared swollen with fragmentation or dissolution of cytoplasm. The mild vacuolations had a patchy distribution (Fig. 3a, b).

Group V (400 mg kg^{-1} aqueous extract of *C. decidua* stems) showed mild to moderate vacuolar changes with hepatocyte swelling and fragmentation or lysis of cytoplasm. These vacuolar changes appeared more peripherally in the lobules (Fig. 4a, b).

In group VI (200 mg kg^{-1} methanolic extract of *C. decidua* stems) mild to moderate vacuolations were also observed in hepatocytes. Distinct interlobular tissue and mononuclear cell infiltration in parenchyma and portal areas were observed. Most cells showed small vacuolations (Fig. 5a, b).

In group VII (400 mg kg^{-1} methanolic extract of *C. decidua* stems), mild to moderate vacuolar degeneration was observed with no definite pattern. Some hepatocytes exhibited cytoplasmolysis. Others appeared swollen with pyknotic nuclei. Distortion of lobular pattern, areas of sinusoidal congestion and small aggregates of mononuclear cells in parenchyma were also seen (Fig. 6a, b).

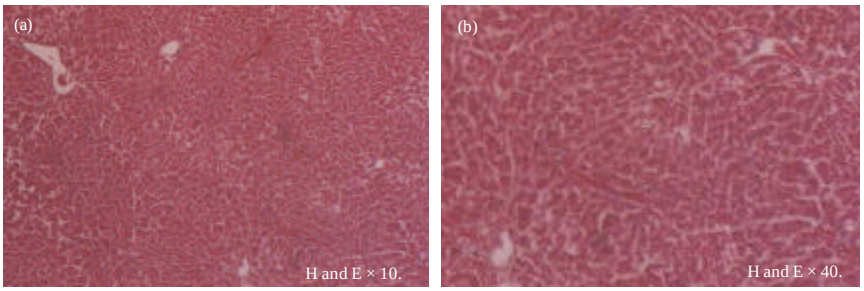

Fig. 3: (a, b) Liver section, rats treated with 200 mg kg^{-1} *C. decidua* stems aqueous extract showing mild hepatocyte swelling

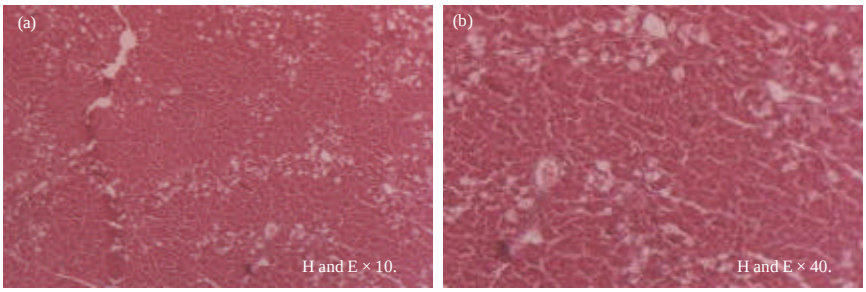

Fig. 4: (a, b) Liver section, rats received 400 mg kg^{-1} *C. decidua* stems aqueous extract showing mild vacuolar degeneration

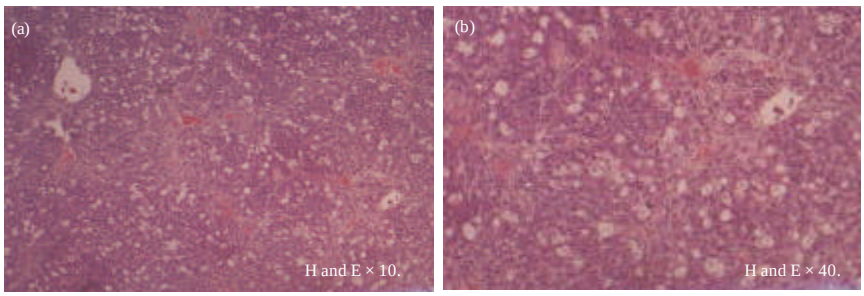

Fig. 5: (a, b) Liver section of 200 mg kg^{-1} *C. decidua* stems methanolic extract showing vacuolar degeneration and mononuclear cell infiltration in parenchyma and portal areas

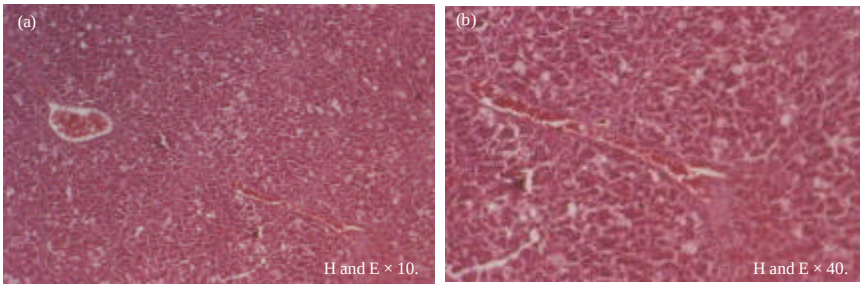

Fig. 6: (a, b) Liver section of 400 mg kg^{-1} *C. decidua* stems methanolic extract showing mild vacuolar degeneration and mild hepatocyte swelling

DISCUSSION

The present study was performed to identify the hepatoprotective activity of *C. decidua* stems in rats against CCl_4 induced liver damage. The plant has been used in different traditional medical practices (Rahman *et al.*, 2004; Al-Yahya, 1986; El-Ghazali *et al.*, 1997).

Many folk remedies from plant origin are tested for its potential antioxidant and hepatoprotective liver damage in experimental animal model. Carbon tetrachloride induced hepatotoxicity model is widely used for the study of hepatoprotective effects of drugs and plant extracts (Ahsan *et al.*, 2009).

In this study, histopathological examination demonstrated that CCl_4 induces diffuse centrilobular degeneration and congestion of hepatic veins and sinusoids and this is in agreement with the results of Ozbek *et al.* (2004) and Gupta *et al.* (2004).

Administration of aqueous and methanolic extracts of *C. decidua* stems with CCl_4 remarkably masked severe hepatic lesions induced by hepatotoxic compound. The activity of the tested extracts was comparable to that of silymarin used as a reference drug.

Furthermore, the results of the present study indicated that the aqueous extract of *C. decidua* stems possesses higher activity than the methanolic extract, especially in the lower dose, probably related to the more polar phytoconstituents.

However, CCl_4 hepatotoxicity depends on the reductive dehalogenation of CCl_4 catalysed by the cytochrome P-450 in the liver cells endoplasmic reticulum leading to the generation of an unstable complex $CCl\bullet_3$ radical (Gupta *et al.*, 2004), which is reported as a highly reactive species. These free radicals attack microsomal lipids leading to its peroxidation and also covalently bind to microsomal lipids and proteins. These results in changes of structures of the endoplasmic reticulum and other membrane, loss of metabolic enzyme activation, reduction of protein synthesis and loss of glucose-6-phosphatase activation, leading to liver injury (Azri *et al.*, 1992).

Concurrent treatment with aqueous and methanolic extracts of *C. decidua* stems and CCl_4 minimized the liver damage induced by CCl_4 which indicates that this plant has antihepatotoxic effect, probably due to its antioxidant properties (Gupta *et al.*, 2004). The plant contains high concentration of vitamin C (Duhan *et al.*, 1992; AL-Yahya, 1986), which is an important dietary, water soluble antioxidant and has been reported to decrease the adverse effect of Reactive Oxygen Species (ROS) and Nitrogen Species generated *in vivo* in animals (Halliwell and Gutteridge, 1999; Adams, 2001).

The preliminary phytochemical screening of the powdered plant showed positive results for the presence of flavonoids, cyanogenic glycosides and triterpenes which are antioxidants and may be responsible of the hepatoprotective property of the plant as suggested by earlier studies (AL-Yahya, 1986; Evans, 2002; Duhan *et al.*, 1992; Pattanayak and Priyashree, 2008).

In conclusion, these results have clearly indicated potential effect of *Capparis decidua* stems as a hepatoprotective against carbon tetrachloride-induced hepatic damage in rats.

Moreover, our results indicate that the aqueous extract of *C. decidua* had higher activity than the methanolic extract and this is probably related to the more polar phytoconstituents.

Further investigations are required to determine the exact phytoconstituent(s) responsible for hepatoprotective effect *C. decidua*.

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