Evaluation of Hepatoprotective Activity of *Tecoma stans* Flowers

[1]S. Kameshwaran, [1]A.R. Kothai, [2]C. Jothimanivannan and [2]R. Senthilkumar

[1]Department of Pharmacology, Swamy Vivekanandha College of Pharmacy, Thiruchengode, Tamil Nadu, India
[2]Department of Pharmaceutical Chemistry, Swamy Vivekanandha College of Pharmacy, Thiruchengode, Tamil Nadu, India

ABSTRACT

Objective: *Tecoma stans* is a plant with a diversity of ethnic medicinal uses along with antioxidant activity. Hence, we have intended to screen hepatoprotective activity with ethanolic (EETS) extract of flowers of *Tecoma stans*. **Methods:** Powder of flower petals extracted with ethanol and it was subjected for phytochemical screening to categorize the different phytoconstituents. Hepatoprotective activity of the extract was studied against the liver injury induced by paracetamol, carbon tetrachloride, thioacetamide and chronic liver damage induced by carbon tetrachloride in rats. **Results:** The extract significantly reduced the elevated serum levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin. EETS at the dose of 500 mg kg^{-1}, p.o. prevented the increase in liver weight when compared to hepatoxin treated control while the extract at the dose 250 mg kg^{-1} was ineffective except in the paracetamol induced liver damage. In the chronic liver injury induced by carbon tetrachloride, EEPG at the dose of 500 mg kg^{-1}, p.o. was found to be more effective than the extract at the dose of 250 mg kg^{-1}, p.o.. Histological examination of the liver tissues supported the hepatoprotection. **Conclusion:** It is concluded that both extracts of flowers of *Tecoma stans* possesses good hepatoprotective activity.

Keywords: *Tecoma stans*, hepatoprotective activity, carbon tetrachloride, paracetamol, thioacetamide

INTRODUCTION

Liver is one of the largest organs in human body and the chief site for intense metabolism and excretion. So, it has a surprising role in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction[1]. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. Thus, to maintain a healthy liver is a crucial factor for overall health and well being. But it is continuously exposed to environmental toxins and abused by poor drug habits and alcohol and prescribed and over-the-counter drug which can eventually lead to various liver ailments like hepatitis, cirrhosis and alcoholic liver disease[2,3]. Liver disease is still a worldwide health problem. Unfortunately, conventional or synthetic drugs used in the treatment of liver diseases are inadequate and sometimes can have serious side effects[4]. In the absence of a reliable liver protective drug in modern medicine there are a number of medicinal preparations in ayurveda recommended for the treatment of liver disorders[5]. In view of severe undesirable side effects of synthetic agents, there is growing focus to follow systematic research methodology and to evaluate scientific basis for the traditional herbal medicines that are claimed to possess hepatoprotective activity.

Tecoma stans (Common name: Yellow bell) is also known as Yellow Trumpet bush and belongs to the family Bignoniaceae. It is an erect ornamental plant and is a branched, slightly hairy or nearly smooth shrub 2-4 m in height. The leaves are opposite, odd-pinnate and up to 20 centimeters in length with 5-7 leaflets. The leaflets are lanceolate to oblong-lanceolate, 6-13 centimeters long, pointed at both ends and toothed on the margins. The trumpet-shaped flowers are yellow, faintly scented and occur in short, dense, terminal clusters. The calyx is green, 5-7 millimeters long and 5-toothed. Flowering can begin as early as April and continue into the fall (autumn). The leaves of *T. stans* contain the alkaloids tecomine and tecostamine, potent hypoglycaemic agents when given intravenously. Anthranilic acid is responsible for its antidiabetic activity and the roots exhibit a powerful diuretic and vermifuge activity[6]. Tecoma is not toxic and is used in Latin America as a remedy for diabetes also for feeding cattle and goats in Mexico[7]. A literature survey shows that there are no reports from India regarding the hepatoprotective activity of ethanolic extract of *T. stans* flowers so, the present study was carried out to investigate the heparoprotective activity of ethanolic flower extract of *Tecoma stans*.

Corresponding Author: S. Kameshwaran, Department of Pharmacology, Swamy Vivekanandha College of Pharmacy, Thiruchengode, Tamil Nadu, India Tel: +91-9488031588

MATERIAL AND METHODS

Collection of plants and preparation of extract: The flowers of *Tecoma stans* were collected in the month of May 2011 from Rasipuram (Namakkal District) Tamil Nadu. An herbarium specimen of the plant was deposited in the Department of Pharmacognosy. The plant was identified by Dr. G.V.S. Murthy, Joint Director of the Botanical Survey of India, Southern circle, TNAU Campus, Coimbatore, who authenticated the plant from information available in the literature. The flower petals were dried in the shade and then powdered and 100 g of the dried powder was extracted with ethanol using a soxhlet apparatus. The solvent was removed under reduced pressure and controlled temperature using a rotary flash evaporator. Phytochemical screening of the extracts revealed the presence of tannin, flavonoids, phenols, alkaloids, steroids, triterpenes and saponins.

Animals: Wister rats (100-150 g) of both sexes were used in these experiments and they were housed under standard environmental conditions like, ambient temperature ($25°\pm1°C$), relative humidity ($55\pm5\%$) and a 12/12 h light dark cycle. Animals had free access to a standard pellet diet and water. All animal experiments were carried out in accordance with the guidelines of CPCSEA. The animal ethical committee of the institute gave its approval to conduct the animal experiments (approval No. 1158/ ac/07/CPCSEA).

Pharmacological studies

Acute hepatitis models: Paracetamol (PCM) induced hepatotoxicity:

* The liver was damaged using PCM ($1 g kg^{-1}$, p.o.) diluted with sucrose solution (40% w/v)
* The animals were divided into 5 groups of 6 each. The animals were then subjected to either one of the following treatments for 9 days:

Group 1: Distilled water ($1 mL kg^{-1}$, p.o.)
Group 2: Distilled water for 9 days+PCM ($1 mL kg^{-1}$, p.o.) on ninth day
Group 3: Silymarin ($100 mg kg^{-1} day^{-1}$, p.o.) for 9 days+PCM ($1 g kg^{-1}$, p.o.) on ninth day
Group 4: EETS ($250 mg kg^{-1} day^{-1}$, p.o.) for 9 days+PCM ($1 g kg^{-1}$, p.o.) on ninth day
Group 5: EETS ($500 mg kg^{-1} day^{-1}$, p.o.) for 9 days+PCM ($1 g kg^{-1}$, p.o.) on ninth day

Food was withdrawn 12 h before PCM administration to enhance the acute liver damage in animals of groups 2, 3, 4 and 5. The animals were sacrificed 24 h after the administration of PCM. Blood samples were collected and the serum was used for assay of marker enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and serum bilirubin. The liver was immediately isolated and washed with normal saline, blotted with filter paper and weighed. The liver was then subjected to histopathological examination[8].

Carbon tetrachloride (CCl₄) induced acute hepatotoxicity: The CCl_4 was diluted with liquid paraffin (1:1) before administration. The animals were divided into 5 groups of 6 each. The animals were then subjected to either one of the following treatments for 9 days:

Group 1: Distilled water ($1 mL kg^{-1}$, p.o.)
Group 2: Distilled water for 9 days+CCl_4 ($1 mL kg^{-1}$, p.o.) on ninth day
Group 3: Silymarin ($100 mg kg^{-1} day^{-1}$, p.o.) for 9 days+CCl_4 ($1 mL kg^{-1}$, p.o.) on ninth day
Group 4: EETS ($250 mg kg^{-1}$/day, p.o.) for 9 days+CCl_4 ($1 mL kg^{-1}$, p.o.) on ninth day
Group 5: EETS ($500 mg kg^{-1} day^{-1}$, p.o.) for 9 days+CCl_4 ($1 mL kg^{-1}$, p.o.) on ninth day

Food was withdrawn 12 h before carbon tetrachloride administration to enhance the acute liver damage in animals of groups 2, 3, 4 and 5. The animals were sacrificed 24 h after the administration of CCl_4. Blood samples were collected and the serum was used for assay of marker enzymes such as aspartateaminotransferase(AST),alanine aminotransferase (ALT), alkaline phosphatase (ALP) and serum bilirubin. The liver was immediately isolated and washed with normal saline, blotted with filter paper and weighed. The liver was then subjected to histopathological examination[9].

Thioacetamide (TAA) induced liver necrosis: The Liver Damage was induced by using TAA ($100 mg kg^{-1}$, s.c.) which was prepared in distilled water (2% solution) 12 the animals were divided into 5 groups of 6 each. The animals were then subjected to either one of the following treatments for 9 days:

Group 1: Distilled water ($1 mL kg^{-1}$, p.o.)
Group 2: Distilled water for 9 days+TAA ($1 mL kg^{-1}$, p.o.) on ninth day
Group 3: Silymarin ($100 mg kg^{-1} day^{-1}$, p.o.) for 9 days+TAA ($100 mg kg^{-1}$, s.c.) on ninth day
Group 4: EETS ($250 mg kg^{-1} day^{-1}$, p.o.) for 9 days+TAA ($100 mg kg^{-1}$, s.c.) on ninth day
Group 5: EETS ($500 mg kg^{-1} day^{-1}$, p.o.) for 9 days+TAA ($100 mg kg^{-1}$, s.c.) on ninth day

Food was withdrawn 12 h before TAA administration to enhance the acute liver damage in animals of groups 2, 3, 4 and 5. The animals were sacrificed 24 h after the administration of TAA. Blood

samples were collected and the serum was used for assay of marker enzymes such as Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and serum bilirubin. The liver was immediately isolated and washed with normal saline, blotted with filter paper and weighed. The liver was then subjected to histopathological examination[10].

Chronic toxicity induced by CCl₄: The animals were divided into 5 groups of 6 rats each and treated as follows [11]:

Group 1: Distilled water (1 mL kg⁻¹, p.o.) for 8 weeks (control)

Group 2: CCl_4 (1 mL kg⁻¹, p.o.) weekly twice for the 8 weeks

Group 3: Silymarin 100 mg kg⁻¹ day⁻¹, p.o., for 8 weeks+CCl_4 (1 mL kg⁻¹, p.o.) weekly twice for 8 weeks

Group 4: EETS (250 mg kg⁻¹, p.o.) for 8 weeks+CCl_4 (1 mL kg⁻¹, p.o.) weekly twice for 8 weeks

Group 5: EETS (500 mg kg⁻¹, p.o.) for 8 weeks+CCl_4 (1 mL kg⁻¹, p.o.) weekly twice for 8 weeks

Food was withdrawn 12 h before carbon tetrachloride administration to enhance the acute liver damage in animals of groups 2, 3, 4 and 5. The animals were sacrificed 24 h after the administration of CCl_4. Blood samples were collected and the serum was used for assay of marker enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and serum bilirubin. The liver was immediately isolated and washed with normal saline, blotted with filter paper and weighed. The liver was then subjected to histopathological examination.

Statistical analysis: The statistical significance was assessed using one way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison test. The values are expressed as mean±SE and $p = 0.05$ were considered significant.

RESULTS

Carbon tetrachloride induced acute hepatotoxicity: The dose of EETS (500 mg kg⁻¹ p.o.) and silymarin (100 mg kg⁻¹, p.o.) produced a significant reduction in serum marker enzymes ($p = 0.001$). EETS at the dose of (250 mg kg⁻¹, p.o.) also produced a significant reduction in ALT, AST, ALP and serum bilirubin when compared to CCl_4 treated group but it was less effective. Administration of CCl_4 produced a non-significant increase in liver weight. Silymarin

and the EETS at dose of 250 mg kg⁻¹, p.o. did not affect the liver weight when compared to CCl_4 treated control, whereas EETS at the dose of 500 mg kg⁻¹, p.o. showed a significant reduction in the liver weight ($p = 0.05$) when compared with CCl_4 treated group (Table 1). Histological examination of the liver tissue from CCl_4 treated animals revealed that CCl_4 had produced profound inflammation and congestion especially in the sinusoids. Hydropic degeneration and steatosis in the periportal region was also observed. Pretreatment of animals with silymarin, EETS (250 mg kg⁻¹, p.o.) and EETS (500 mg kg⁻¹, p.o.) reduced the inflammation, degenerative changes and steatosis (Fig. 1).
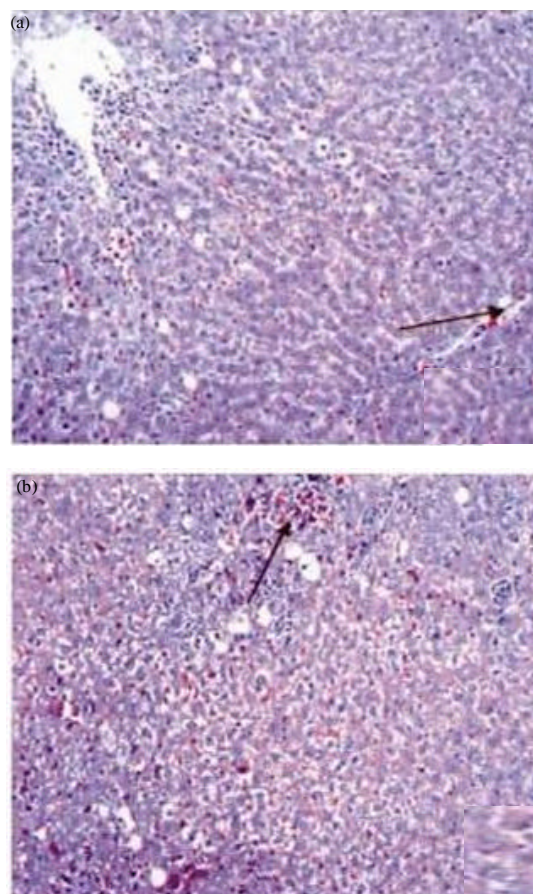

Fig. 1(a-b): Effect of EETS on acute liver injury induced by CCl_4 (a) CCl_4 treated control: profound inflammation and congestion (b) CCl_4+extract: Reduced inflammation degenerative changes and steatosis

Table 1: Effect of silymarin, EETS on serum ALT, AST, ALP, bilirubin levels and liver wet weight in CCl_4 induced acute liver injury in rats

Parameters	Vehicle control	CCl_4 control	CCl_4+silymarin 100 mg kg⁻¹	CCl_4+EETS 250 mg kg⁻¹	CCl_4+EETS 500 mg kg⁻¹
ALT (IU L⁻¹)	72.3±5.020	379.41±2.000ᵃ	057.39±2.77***	016.67±4.20**	060.13±7.640*
ASP (IU L⁻¹)	186.26±7.70	642.23±2.200ᵃ	205.28±6.23***	151.50±13.8**	572.51±43.11ⁿˢ
ALP (IU L⁻¹)	398.14±6.40	749.42±3.300ᵃ	407.89±5.23***	488.59±9.90**	540.12±79.24***
Serum Bilirubine (mg dL⁻¹)	000.25±0.43	001.47±0.120ᵃ	000.28±0.01***	000.26±0.10***	000.26±0.410***
Liver wt. g 100 g⁻¹ of b.wt.	003.29±0.04	003.59±0.283ᵇ	003.89±0.04ⁿˢ	002.89±0.12*	003.19±0.010ⁿˢ

Values are Mean±SE from 6 animals in each group, p-values, a: 0.001, vs. Vehicle control, b: 0.05, vs. vehicle control, ns>0.05, *: 0.05, **: 0.01, ***: 0.001 vs, CCl_4 treated control

Table 2: Effect of silymarin, EETS on serum ALT, AST, ALP, Bilirubin levels and liver wet weight in paracetamol (pcm) induced acute liver injury in rats

Parameters	Vehicle control	CCl_4 control	CCl_4+silymarin 100 mg kg⁻¹	CCl_4+EETS 250 mg kg⁻¹	CCl_4+EETS 250 mg kg⁻¹
ALT (IU L⁻¹)	72.84±6.190	383.12±75.00ᵃ	10074.89±4.200***	086.92±18.94***	098.26±2.51***
ASP (IU L⁻¹)	36.11±7.790	642.22±31.04ᵃ	0167.36±5.490***	178.24±8.040***	170.49±5.11***
ALP (IU L⁻¹)	18.21±6.730	749.51±36.26ᵃ	0322.41±6.950***	338.12±39.90***	624.32±89.7ⁿˢ
Serum bilirubine (mg dL⁻¹)	26.00±0.075	001.54±0.230ᵃ	000.23±0.049***	030.32±0.120***	000.48±0.01***
Liver wt. g 100 g⁻¹ of b.wt.	12.00±0.260	004.54±0.259ᵃ	003.14±0.020***	002.25±0.019ⁿˢ	018.00±0.042*

Values are Mean±SE from 6 animals in each group, p-values: a= 0.001 vs. vehicle control, ns>0.05, *: 0.05, **: 0.01, ***: 0.001 vs. PCM treated control
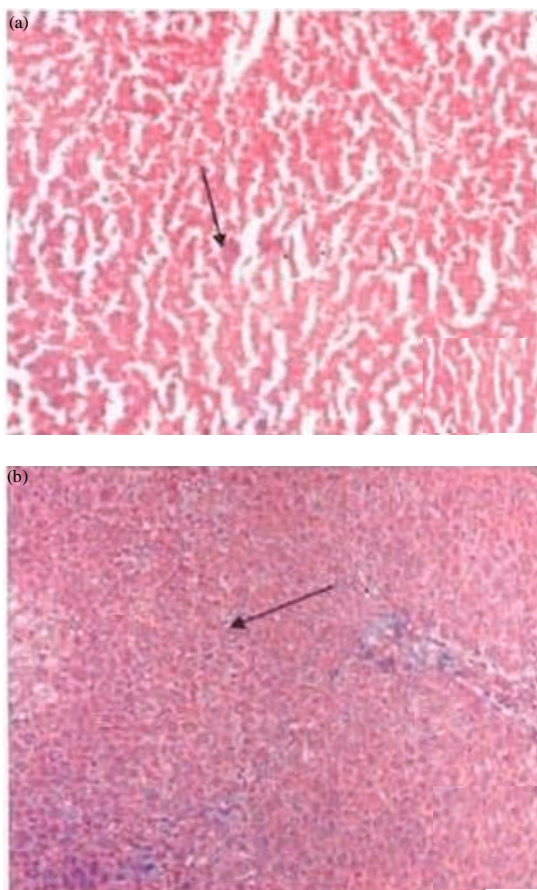

Fig. 2(a-b): Effect of EETS on paracetamol induced acute liver injury (a) Paracetamol treated control: severe congestions, hydropic degeneration pyknosis and occasional necrosis (b) Paracetamol+extract: mild degeneration and no pyknosis

Paracetamol induced hepatotoxicity: After 48 h of administration of PCM, the serum levels of ALT, AST, ALP and bilirubin were markedly increased. Pretreatment with EETS (500 mg kg⁻¹, p.o.) and silymarin significantly reduced the levels of biochemical markers when compared to PCM treated group (p = 0.001). Pretreated with EETS (250 mg kg⁻¹, p.o.) did not show significant effect when compared with the PCM control. Pretreatment with EETS (250 mg kg⁻¹, p.o.) and silymarin significantly reduced the increase in the liver weight seen after PCM intoxication (Table 2). PCM produced severe congestion of blood vessels, mild hydropic degeneration, pyknosis of nucleus and occasional necrosis. Silymarin reduced the pyknosis of hepatocytes when compared to PCM treated control. Animals treated with both lower and higher dose of EETS showed mild hydropic degeneration and there was no pyknosis or congestion (Fig. 2).

Thioacetamide induced liver necrosis: A significant difference in serum biochemical markers was observed between normal and TAA treated group (p = 0.001). Pretreatment of animals with EETS 500 mg kg⁻¹, p.o. and 250 mg kg⁻¹, p.o. and silymarin significantly reduced the levels of AST, ALT and ALP (p = 0.001). EEPG at the dose of 500 and 250 mg kg⁻¹, p.o. did not affect serum bilirubin levels. TAA induced acute toxicity increased the weight of liver significantly (p = 0.01). EETS at the dose of 500 mg kg⁻¹, p.o. and silymarin prevented the increase in liver weight that was observed in TAA treated group, EETS at the dose of 250 mg kg⁻¹, p.o. did not produce any significant decrease in liver weight (Table 3). Histological examination showed perilobular hepatocyte necrosis, inflammation and congestion with cytoplasmic vacuolation in TAA treated control animals. In silymarin treated animals, mild inflammation and mild necrosis of hepatocytes with cytoplasmic vacuolation was noted. Animals treated with lower dose showed periportal

Table 3: Effect of silymarin, EETS on serum ALT, AST, ALP, bilirubin level and liver weight in thioacetamide (taa) induced acute liver injury in rats

Parameters	Vehicle control	CCl_4 control	CCl_4+silymarin 100 mg kg^{-1}	CCl_4+EETS 250 mg kg^{-1}	CCl_4+EETS 500 mg kg^{-1}
ALT (IU L^{-1})	72.25±5.26	336.71±32.44[a]	101.52±4.21***	032.31±7.89***	132.15±7.71***
ASP (IU L^{-1})	187.46±5.41	438.31±10.69[a]	185.41±8.29***	237.18±15.4***	175.48±7.25***
ALP (IU L^{-1})	400.40±5.84	769.74±23.87[a]	418.36±5.11***	479.25±7.85***	380.45±13.5***
Serum bilirubine (mg dL^{-1})	000.27±0.06	000.25±0.110[b]	000.23±0.65[ns]	000.31±0.07[ns]	00.11±0.04[ns]
Liver wt. g 100 g^{-1} of b.wt.	003.11±0.12	004.17±0.960[c]	003.28±0.21*	002.75±0.12***	03.43±0.04[ns]

Values are Mean±SE from 6 animals in each group, p-values: a = 0.001 vs. vehicle control, ns >0.05, *: 0.05, **: 0.01, ***: 0.001 vs.thioacetamide control

Table 4: Effect of silymarin, -EETS on serum ALT, AST, ALP, bilirubin levels and liver wet weight in CCl_4 induced chronic liver injury in rats

Parameters	Vehicle control	CCl_4 control	CCl_4+silymarin 100 mg kg^{-1}	CCl_4+EETS 250 mg kg^{-1}	CCl_4+EETS 500 mg kg^{-1}
ALT (IU L^{-1})	049.71±2.030	320.4±17.1100[a]	127.14±6.990***	238.66±15.00***	329.95±8.420[ns]
ASP (IU L^{-1})	119.90±4.520	617.82±15.400[a]	476.63±19.01***	422.22±15.50***	504.61±26.10[ns]
ALP (IU L^{-1})	424.87±13.30	745.27±22.800[a]	545.47±18.01***	613.16±13.90***	651.91±25.04*
Serum bilirubine (mg dL^{-1})	000.351±0.02	000.768±0.048[a]	000.530±0.02***	000.681±0.03***	000.951±0.04[ns]
Liver wt. g 100 g^{-1} of b.wt.	002.83±0.110	003.83±0.2000[a]	002.94±0.280*	002.87±0.281	003.45±0.077[ns]

Values are Mean±SE from 6 animals in each group, p-values: a = 0.001 vs. vehicle control, ns >0.05, *: 0.05, **: 0.01, ***: 0.001 vs. CCl_4 control
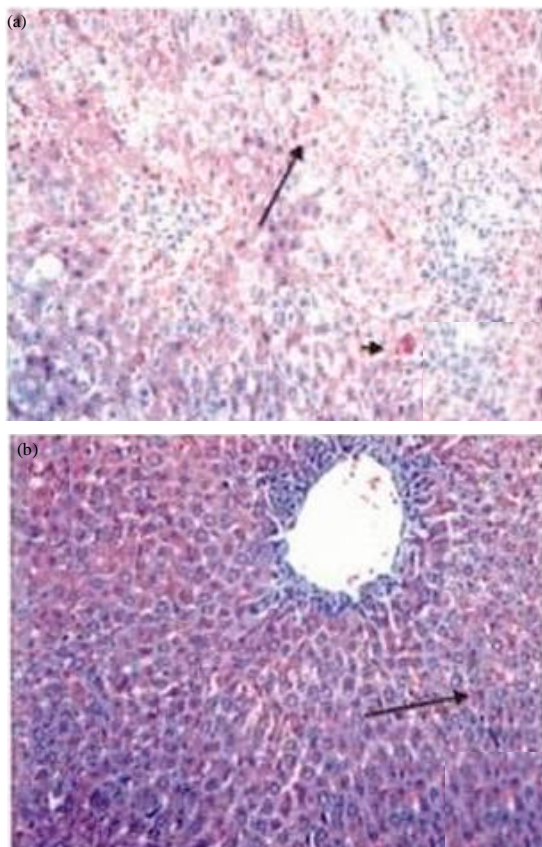

Fig. 3(a-b): Effect of EETS on thioacetamide induced acute liver damage (a) Thioacetamide treated control: arrow-Perilobular hepatocyte necrosis, inflammation and congestion; arrow head: cytoplasmic vaccoulation (b) thioacetamide+extract: mild inflammation and no necrosis
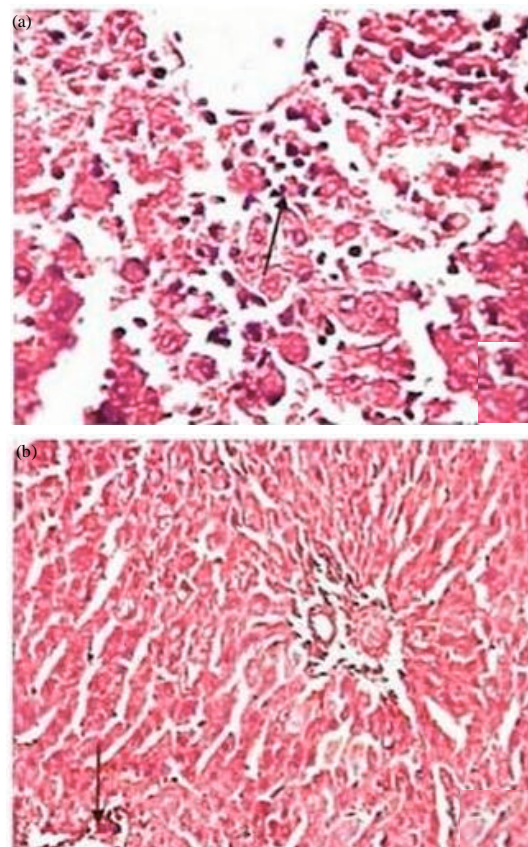

Fig. 4(a-b): Effect of EETS on CCl_4 induced chronic liver damage (a) CCl_4 treated control: fatty changes, mild congestion, connective tissue and cirrhosis (b) CCl_4 +extract: degenerative changes

necrosis and those treated with higher dose showed mild inflammation and no necrosis (Fig. 3).

Chronic hepatitis induced by CCl_4: A significant difference in biochemical markers, ALT, AST, ALP and bilirubin was observed between normal and CCl_4 treated group (p = 0.001). Comparative analysis between

different groups revealed that EETS (500 mg kg^{-1}, p.o.) and silymarin (100 mg kg^{-1}, p.o.) have similar activity (p = 0.001), whereas EETS (250 mg kg^{-1}, p.o.) did not prevent the increase in biochemical markers. Pretreatment with EEPG (500 mg kg^{-1}; p.o.) and silymarin significantly prevented the increase in liver weight, observed after intoxication with CCl_4. EETS (250 mg kg^{-1}; p.o.) did not produce any significant reduction in liver weight (Table 4). Liver sections from CCl_4 treated control animals showed moderate degree of fatty changes, mild congestion, connective tissues, proliferation and cirrhosis. It also showed focal areas of coagulating necrosis. Formation of pseudolobular with fibrosin was also observed. Further, there were evidences of regenerating hepatocytes. In silymarin treated animals, there were fewer amounts of necrosis and regeneration. There were mild congestions, mild fatty changes and mild connective tissue proliferation. Animals treated with EETS (250 mg kg^{-1}, p.o.) showed congestion vessels and moderate degree of fatty changes, connective tissue and cirrhosis. EETS at the dose of (500 mg kg^{-1}, p.o.) reduced the degenerative changes compared to CCl_4 treated animals (Fig. 4).

DISCUSSION

Liver cirrhosis, a critical stage in chronic liver diseases with high morbidity and mortality, may be caused by viral infection, tissue-immune-mediated damage, toxic agents, obstructive jaundice, gene abnormalities or alcohol and non-alcohol steatohepatitis[12], one of the major functions of the liver is detoxification of xenobiotics and toxins[13]. In many cases reactive oxygen species are produced during detoxification[14].

The ethanolic extract of *Tecoma stans* flowers showed superior hepatoprotective activity when administered at dose of 500 mg kg^{-1} orally, at the dose of 250 mg kg^{-1}, p.o. did not show hepatoprotective result in chronic hepatic damage induced by CCl_4. The effect shaped by the EETS was alike to silymarin (100 mg kg^{-1}, p.o.), a well known hepatoprotective agent. Liver damage induced by CCl_4 is commonly used model for the screening of hepatoprotective drugs[15]. The CCl_4 is converted into reactive metabolite, halogenated free radical by hepatic cytochrome P450s[16]. Which in turn covalently binds to cell membrane and organelles to elicit lipid peroxidation with subsequent tissue injury[17,18]. Drugs posessing antioxidant activity is effectual in treating CCl_4 induced hepatotoxicity. The CCl_4 induced a significant raise in liver weight which is due to blocking of secretion of hepatic triglycerides into the plasma[19]. Silymarin and EETS (250 mg kg^{-1}, p.o.) did not avert the increase of liver weight, whereas EETS (500 mg kg^{-1}, p.o.) barred the increase of liver weight in rats.

Paracetamol hepatotoxicity is caused by the reaction metabolite N-acetyl-p-benzo quinoneimine (NAPQI) which causes oxidative stress and glutathione depletion. It is a well-known antipyretic and analgesic agent which produces hepatic necrosis at higher doses[20]. Paracetamol toxicity is due to the formation of toxic metabolites when a part of it is metabolized by cytochrome P-450. Introduction of cytochrome[21] or depletion of hepatic glutathione is a prerequisite for paracetamol induced hepatotoxicity[22,4]. Depletion of GSH causes the remaining quinone to bind to cellular macromolecules leading to cell death[23]. The anti-hepatotoxic actions of EETS (500 mg kg^{-1}, p.o.) were substantiated by significant attenuation of the increased levels of serum enzymes in rats intoxicated with PCM. Drugs having antioxidant activity are also effective in treating paracetamol induced hepatotoxicity by scavenging the free radicals produced by PCM metabolism, thereby preventing the liver induced by both PCM metabolite and due to depletion of glutathione. Extract of *Tecoma stans* might posses the anti oxidant activity and this activity may be responsible for its effect in PCM induced hepatotoxic model. The PCM induced a significant increase in liver weight which is due to the blocking of secretion of hepatic triglyceridesintotheplasma .EETS at the dose of 250 and 500 mg kg^{-1}; p.o.) prevented the increase in liver weight of rats pretreated with PCM

TAA interferes with the movement of RNA from the nucleus to the cytoplasm which may cause membrane injury. A metabolite of TAA (S-oxide) is responsible for hepatic injury[24]. Pre treatment with EETS (250 and 500 mg kg^{-1}, p.o.) significantly reversed the elevated serum enzyme markers in animals treated with TAA. This effect may also be due to antioxidant effect of *Tecoma stans* which may neutralize the reactive metabolite of TAA.

The ethanolic extract of *Tecoma stans* flowers showed significant hepatoprotective activity in CCl_4 induced acute and chronic liver damage, PCM induced liver damage and TAA induced liver necrosis. Activity may be due to the phaytoconstituents present in the both extracts as well as the anti oxidant nature of the plant. Further, studies to characterize the active principles and to elucidate the mechanism of action are in progress.

REFERENCES

1. Ward, F.M. and M.J. Daly, 1999. Hepatic Disease. In: Clinical Pharmacy and Therapeutics, Walker, R. and C. Edward (Eds.). Churchill Livingstone, New York, pp: 195-212.
2. Sharma, A., K.K. Chakraborti and S.S. Handa, 1991. Anti-hepatotoxic activity of some Indian herbal formulations as compared to silymarin. Fitoterapia, 62: 229-235.
3. Subramonium, A. and P. Pushpangadan, 1999. Development of Phytomedicines for liver diseases. Indian J. Pharmacol., 31: 166-175.

4. Rao, G.M.M., C.V. Rao, P. Pushpangadan and A. Shirwaikar, 2006. Hepatoprotective effects of rubiadin, a major constituent of *Rubia cordifolia* Linn. J. Ethnopharmacol., 103: 484-490.

5. Chatterjee, T.K., 2000. Medicinal Plants with Hepatoprotective Properties. In: Herbal Options. 3rd Edn. Calcutta Books and Allied (P) Ltd., pp: 135.

6. Khare, C.P., 2007. Indian Medicinal Plants and Illustrated Dictionary. Springer Science Publishers, New Delhi, India.

7. Susano Hernandez, R., 1981. Especies arboreas forestalessusceptibles de aprovecharse como forraje. Ciencia. Forestal., 6: 31-39.

8. Minamide, Y.Y., T.T. Horie and S.S. Awazu, 1992. High molecular weight protein aggregates formed in the liver of paracetamol treated rats. J. Pharm. Pharmacol., 44: 932-934.

9. Matsuda, H., K. Samukawa and M. Kubo, 1991. Anti-hepatitic activity of ginsenoside Ro. Planta Medica, 57: 523-526.

10. Ahmed, A., K. Pillai, S. Ahmed, D. Balani, A. Najmi and R. Marwah, 1999. Evaluation of hepatoprotective potential of jingrine of Thioacetamide induced liver damage in rats. Indian J. Pharmacol., 31: 416-521.

11. Mclean, E.K., A.E.M. Mclean and P.M. Sutton, 1969. Instant cirrhosis. An improved method for producing cirrhosis of the liver in rats by simultaneous administration of carbon tetrachloride and phenobarbitone. Br. J. Exp. Pathol., 50: 502-506.

12. Heidelbaugh, J.J. and M. Bruderly, 2006. Cirrhosis and chronic liver failure: Part I. Diagnosis and evaluation. Am. Fam. Physician, 74: 756-762.

13. Mitra, S.K., M.V. Venkataranganna, R. Sundaram and S. Gopumadhavan, 1998. Protective effect of HD-03, a herbal formulation, against various hepatotoxic agents in rats. J. Ethnopharmacol., 63: 181-186.

14. Jeong, T.C., H.K. Gu, J.I. Park, H.I. Yun, H.C. Kim, C.S. Ha and J.K. Roh, 1999. Pretreatment of male BALB/c mice with α-ionone potentiates thioacetamide-induced hepatotoxicity. Toxicol. Lett., 105: 39-46.

15. Slater, T.F., 1965. Biochemical Mechanism of Liver Injury. Academic Press, London, UK.

16. Packer, J.E., T.F. Slater and R.L. Willson, 1978. Reactions of the carbon tetrachloride-related peroxy free radical (CCl_3O_2.) with aminoacids: pulse radiolysis evidence. Life Sci., 23: 2617-2620.

17. Brattin, W.J., Jr. E.A. Glende and R.O. Recknagel, 1985. Pathological mechanisms in carbon tetrachloride hepatotoxicity. J. Free Radic. Biol. Med., 1: 27-38.

18. Prabakan, M., R. Anandan and T. Devaki, 2000. Protective effect of *Hemidesmus indicus* against rifampicin and isoniazid induced hepatotoxicity in rats. Fitoterapia, 71: 55-59.

19. Aniya, Y., T. Koyama, C. Miyagi, M. Miyahira, C. Inomata, S. Kinoshita and T. Ichiba, 2005. Free radical scavenging and hepatoprotective actions of the medicinal herb, *Crassocephalum crepidioides* from the Okinawa Islands. Biol. Pharm. Bull., 28: 19-23.

20. Boyd, E.H. and G.M. Bereczky, 1966. Liver necrosis from paracetamol. Br. J. Pharmacol., 26: 606-614.

21. Dahlin, D.C., G.T. Miwa, A.Y. Lu and S.D. Nelson, 1984. N-acetyl-p-benzoquinone imine: A cytochrome P-450-mediated oxidation product of acetaminophen. Proc. Natl. Acad. Sci. USA., 81: 1327-1331.

22. Moron, M.S., J.W. Depierre and B. Mannervik, 1979. Levels of glutathione, glutathione reductase and glutathione *S*-transferase activities in rat lung and liver. Biochem. Biophys. Acta, 582: 67-78.

23. Gupta, A.K., H. Chitme, S.K. Dass and N. Misra, 2006. Hepatoprotective activity of *Rauwolfia serpentina* rhizome in paracetamol intoxicated rats. J. Pharmacol. Toxicol., 1: 82-88.

24. Udem, S.C., I. Madubunyy, J.O.A. Okoye and S.M. Anika, 1997. Anti-hepatotoxic effects of the ethanolic extracts of *Combretum dolichopetalum* root bark and *Morinda lucida* leaf. Fitoterapia, 68: 21-25.