Hepatoprotective Effects of 50% Ethanolic Extract of *Ficus hispida* Linn Against CCl4 Induced Hepatotoxicity in Rats

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**Abstract:** The hepatoprotective effect of 50% ethanolic extract of *Ficus hispida* L (Moraceae) by carbon tetrachloride (CCl4) induced liver damage in rats. The 50% ethanolic extract of *Ficus hispida* was studied for their hepatoprotective effects on CCl4 induced liver damage on Wistar albino rats. The degree of protection was measured by physical changes (liver weight), biochemical (SGPT, SGOT, ALP, total bilirubin, albumin and decreases in total protein). Pretreatment with extract significantly prevented the physical, biochemical changes induced by CCl4 in the liver. The effects of extract of *Ficus hispida* were comparable to that of standard drug, Silymarin. These results indicated that the *Ficus hispida* could be useful in preventing chemically induced acute liver injury. The present study, it can be concluded that, the 50% ethanol extracts of *Ficus hispida* possesses significant hepatoprotective activity.

**Key words:** Carbon Tetrachloride · Hepatoprotective · *Ficus hispida*

**INTRODUCTION**

Liver diseases are the most serious ailment and are mainly caused by toxic chemicals (Excess consumption of alcohol, high doses of paracetamol, carbon tetrachloride, chemotherapeutic agents, peroxidised oil, etc). Carbon tetrachloride is one of the most commonly used hepatotoxins in the experimental study of liver diseases since the changes associated with CCl4 induced liver damage is similar to that of viral acute hepatitis [1]. Carbon tetrachloride is metabolically activated by the cytochrome P-450 dependent mixed oxidease in the endoplasmic reticulum to form trichloromethyl free radical (CCl3) which combined with cellular lipids and proteins in the presence of oxygen to induce lipid per-oxidation [2]. In spite of the tremendous advances made in allopathic medicine, no effective hepatoprotective medicine is available. Herbal medicines are believed to be much safer and proved elixir in the treatment on various ailments. Though the medicinal plants which have been used in the treatment of liver disorders many of them are yet to be proved scientifically. Therefore, there is a need for identification of such plants for scientific pharmacological investigation [3]. In spite of the tremendous advances made in allopathic medicine, no effective hepatoprotective medicine is available. Plant drugs are known to play a vital role in the management of liver diseases. There are numerous plants and polyherbal formulations claimed to have hepatoprotective activities. In India, more than 87 medicinal plants are used in different combinations in the preparation of 33 patented herbal formulations [4-7].

Liver damage is associated with cellular necrosis, increase in tissue lipid peroxidation and depletion in the tissue GSH levels. In addition serum levels of many biochemical markers like SGOT, SGPT, triglycerides, cholesterol, bilirubin, alkaline phosphatase are elevated.

*Ficus hispida* (FH) Linn belongs to the family Moraceae moderate sized tree, up to the level of 3.0 m, with spreading branches and many aerial roots. It is widely distributed throughout India, Srilanka, Myanmar, Southern region of the Republic of China, New Guinea, Australia and Andaman Islands in damp localities, as well as grows in secondary forests, open lands and river banks up to 1200 m in altitude [8]. FH is used by the maaiba indigenous medicine -man of Manipur) as an indigenous traditional medicine. All parts of the plant have been reported to be bitter, cooling, astrigent, antisydentric, psoriasis, anemia, piles, jaundice and hemorrhage. The fruit acts as a coolant and tonic. The juice obtained from the fig is taken with jaggery as a mild purgative. A mixture of honey and its juice is a good antihemorrhage [9] the root and leaves are of particular interest from a medicinal
point of view as an antidiarrhoeal [10] and cardio protective [11] among others. The current study was undertaken to evaluate the antiulcer activity of FH methanolic extract by aspirin induced gastric ulcer, till now no pharmacological evaluation has been done on FH especially in root for its anti-ulcer activity. This prompted us to pursue the activity and examine for their efficacy as well as to determine their possible mechanism of action.

**MATERIALS AND METHODS**

**Plant Material:** Leaves of *Ficus hispida* was collected in and around shevaran hills, Salem, Tamilnadu India in the month of September 2009 and identification done by Professor (Dr) P. Jayaraman, Plant Anatomy research Centre, Chennai, India. The voucher specimen of *Ficus hispida* (FH/92/09) has been preserved in our laboratory for further collection and reference. The leaves were dried under shade, powdered with a mechanical grinder and pass through sieve no 40 and were extracted with 50% ethanolic 48 h using soxhlet apparatus. The solvent was removed from the extract under reduced pressure by using rotary vacuum evaporator.

**Phytochemical Analysis:** The 50% ethanolic extract of *Ficus hispida* was subjected to identify the presence of various phytoconstituents viz. alkaloids (Dragendroffs test), steroids and terpenoids (Leibermann Burchard test), tannin and phenolic compounds (ferric chloride test), flavonoids (Shinoda test), amino acids (Ninhydrin test), etc. by usual methods prescribed in standard texts [12, 13].

**Experimental Animals:** Wistar albino rats (150-200 g) used in the present studies. The animals were fed with standard pellet diet (Hindustan lever Ltd. Bangalore) and water ad libitum. All the animals were acclimatized for a week before use. The animals were received the drug by oral gavages tube. The laboratory conditions duly undertaken by registered veterinary practitioner.

**Chemicals:** All the chemicals and solvents were of analytical grade and were procured from Ranbaxy Fine Chemicals Ltd., Mumbai, India. The standard drug silymarin was obtained as gift sample from Micro Lbs, India. Standard kits for SGOT, SGPT, ALP and bilirubin were obtained from Span Diagnostics Ltd., India.

**Toxicity Studies:** Healthy Wistar albino rats of either sex weighing 150-200 g maintained under standard laboratory conditions were used for acute oral toxicity test according to Organization for Economic Co-operation and Development guidelines 423 (OECD, 1996). A total of three animals were used which received a single oral dose of (2000 mg/kg) of 50% ethanolic extract. After administration of extract the food was withheld for further 3-4 h. Animals were observed individually at least once during first 30 min after dosing, periodically during first 24 h (with special attention during the first 4 h) and daily thereafter for period of 3 days.

**Ccl4 Induced Hepatotoxicity Rat:** The rats were divided into seven groups of 6 animals (n = 6) in each [14]

**Group I:** Received water (5 ml/kg. p.o) for 9 days once daily and served as normal control.

**Group II:** Received water (5 ml/kg. p.o) for 9 days once daily and carbon tetra chloride (CCl4)1 ml/kg in 50% v/v olive oil, s.c. on 7th day.

**Group III:** Received standard drug silymarin (25 mg/kg. p.o.) for 9 days once daily and carbon tetra chloride (CCl4) 1 ml/kg in 50% v/v olive oil, s.c. on 7th day.

**Group IV and V:** Received 50% ethanolic extract of *Ficus hispida* (200 and 400 mg/kg) 9 days once daily and carbon tetra chloride (CCl4)1 ml/kg in 50% v/v olive oil, s.c. on 7th day.

**Assessment of Hepatotoxicity:** After 48 h of carbon tetrachloride administration, the blood was obtained from animals by puncturing retro orbital plexus. The blood samples were allowed to clot for 45 min at room temperature. The serum was separated by centrifugation at 2500 rpm at 30°C for 15 min and utilized for the estimation of various biochemical parameters including SGOT and SGPT, serum bilirubin and serum protein. After collection of blood samples, the animals were sacrificed under deep ether anesthesia and their livers were excised immediately and washed with ice cold saline and a 10% homogenate prepared in phosphate buffer (pH 7.0). The homogenate was centrifuged at 3000 rpm for 15 min at 4°C and the supernatant was used for the estimation glutathione and lipid per oxidation [15, 16].

**Statistical Significance:** The results of the study were expressed as mean ± SEM, n = 6. ANOVA was used to analyze and compare the data, followed by Dunnett’s test for multiple comparisons.
Table 1: Effect of 50% ethanolic extract of *Ficus hispida* on biochemical parameters viz SGPT, SGOT, ALP in CCl4 induced hepatotoxicity in rats

<table>
<thead>
<tr>
<th>Treatment/Dose</th>
<th>SGPT (IU/L)</th>
<th>SGOT (IU/L)</th>
<th>ALP (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>55.60±7.131</td>
<td>110.03±9.72</td>
<td>86.07±4.79</td>
</tr>
<tr>
<td>CCl4 (1ml/kg i.p)</td>
<td>172.30±7.67</td>
<td>227.91±14.36</td>
<td>133.56±6.79</td>
</tr>
<tr>
<td>Ethanolic extract of <em>Ficus hispida</em> (200mg/kg)</td>
<td>92.35±5.01*</td>
<td>146.24±9.25**</td>
<td>97.98±7.69</td>
</tr>
<tr>
<td>Ethanolic extract of <em>Ficus hispida</em> (400mg/kg)</td>
<td>70.00±3.82**</td>
<td>116.75±10.73**</td>
<td>89.77±5.74**</td>
</tr>
<tr>
<td>Silymarin (100mg/kg)</td>
<td>67.35±4.40**</td>
<td>126.59±4.17**</td>
<td>87.30±4.40**</td>
</tr>
</tbody>
</table>

Values are expressed in Mean ± SEM of 6 rats in each group. *p<0.01, **p<0.001 when compared with respective CCl4 treated group.

Table 2: Effect of 50% ethanolic extract of *Ficus hispida* on biochemical parameters viz total protein, albumin and total bilirubin in CCl4 induced hepatotoxicity in rats

<table>
<thead>
<tr>
<th>Treatment/Dose</th>
<th>Total protein (g/dl)</th>
<th>Total albumin (g/dl)</th>
<th>Total bilirubin (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.54±0.65</td>
<td>4.22±0.431</td>
<td>0.53±0.02</td>
</tr>
<tr>
<td>CCl4 (1ml/kg i.p)</td>
<td>2.01±0.43</td>
<td>1.03±0.211</td>
<td>1.75±0.11</td>
</tr>
<tr>
<td>Ethanolic extract of <em>Ficus hispida</em> (200mg/kg)</td>
<td>6.70±0.37***</td>
<td>3.19±0.613***</td>
<td>1.07±0.14***</td>
</tr>
<tr>
<td>Ethanolic extract of <em>Ficus hispida</em> (400mg/kg)</td>
<td>8.25±0.40***</td>
<td>4.20±0.41***</td>
<td>0.59±0.10***</td>
</tr>
<tr>
<td>Silymarin (100mg/kg)</td>
<td>6.59±0.29***</td>
<td>4.30±0.370***</td>
<td>1.00±0.10***</td>
</tr>
</tbody>
</table>

Values are expressed in Mean ± SEM of 6 rats in each group. *p<0.01, **p<0.001 when compared with respective CCl4 treated group.

RESULTS

Preliminary phytochemical studies revealed the presence of various phytochemicals including alkaloids, glycosides, steroids, flavonoids, saponin, tannin and phenolic compounds, terpenoids, carbohydrates, gums and mucilage in 50% ethanolic extract was found to be nontoxic up to a dose of 2000 mg/kg. CCl4 caused significant elevation of serum liver enzymes and bilirubin. Treatment with 50% ethanolic extract of *Ficus hispida* (200 and 400 mg/kg) caused significant hepatoprotective effect was almost comparable to that of silymarin, the known hepatoprotective agent (Tables 1 and 2).

DISCUSSION

The liver can be injured by many chemicals and drugs. In the present study, CCl4 was selected as a hepatotoxicant to induce liver damage, since it is clinically relevant. CCl4 produces a constellation of dose related deleterious effects in the liver. CCl4 produces a constellation of dose related deleterious effects in the liver. Carbon tetrachloride is one of the most commonly used hepatotoxins in the experimental study of liver diseases since the changes associated with CCl4 induced liver damage is similar to that of viral the liver, CCl4 is activated by microsomal oxidizing acute hepatitis. Liver is the most important organ, which plays a pivotal role in regulating various physiological processes in the body. It is involved in several vital functions, such as metabolism, secretion and storage. It has great capacity to detoxicate toxic substances and synthesize useful principles Therefore; damage to the liver inflicted by hepatotoxic agents is of grave consequences [17]. During hepatic damage, cellular enzyme like SGOT, SGPT, ALP and serum bilirubin present in the liver cell, leak into the serum resulting to increase in concentration. Histological changes such as steatosis (fatty changes in hepatocytes) and perivenular fibrosis were observed in CCl4 control group. Both extracts prevented these histological changes, further indicating their hepatoprotective activity. All the histological changes observed were in correlation with the biochemical and functional parameters of the liver.

CONCLUSION

It can be concluded that the 50% ethanolic extract of *Ficus hispida* have significant hepatoprotective on CCl4 induced hepatic damage in rats, as evidenced by the biochemical parameters. These results revealed that the hepatoprotective effect of extract of *Ficus hispida* may be due to its ability to block the bioactivation of toxicant and its potent antioxidants activity and/or by scavenging the free radicals and inhibiting lipid peroxidation. Further study will deal with isolation and characterization the active principles in these extracts.

REFERENCES


