Effect of Dried Fruits of Carica papaya Linn on Hepatotoxicity

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Received April 26, 2002; accepted July 23, 2002

Ethanol and aqueous extracts of Carica papaya has been evaluated for its anti hepatotoxic activity. The ethanol and aqueous extracts of Carica papaya showed remarkable hepatoprotective activity against CCl4 induced hepatotoxicity. The activity was evaluated by using biochemical parameters such as serum aspartate amino transferase (AST), alanine phosphatase, total bilirubin and gamma glutamate transpeptidase (GGTP). The histopathological changes of liver sample was compared with respect to control.

Key words Carica papaya; CCl4; hepatoprotective activity

In traditional medicines, various herbal preparations are being used for treating liver disorders. In the absence of an effective treatment in modern medicine, efforts are being made to find out suitable herbal drugs. In previous work we have reported the hepatoprotective activity of Moringa oleifera,1 Caseria esculenta2 and Orthosiphon thymiflorus3 against paracetamol induced hepatotoxicity. The present study was taken up to evaluate the effects of ethanol and aqueous extracts of the dried fruits of Carica papaya Linn against CCl4 induced hepatotoxicity.

Carica papaya (Family: Caricaceae) is a short lived, fast growing woody large herb to 10 or 12 feet in height. The green fruit contains papain similar to pepsin, pulp of the fresh fruit contains a caoutchoung like substance, a soft yellow green fruit contains papain similar to pepsin, pulp of the growing woody large herb to 10 or 12 feet in height. The alkaloid named carpaine and glucoside named carposide. A properly ripened papaya is juicy, sweetish and somewhat like a cantaloupe in nature. The fruits contain papain which helps in digestion and is used to tenderize meat.5 It also used to reduce enlarged spleen and liver.

MATERIALS AND METHODS

Materials The fruits of Carica papaya were collected in and around Salem District in the month of June and it was identified in the Botany department, National College, Trichirappalli found to comply with all specifications of the taxon.

The fruits of C. papaya were cut into small pieces, shade dried and powdered. The course powder was subjected to continue hot extraction in a soxhlet by using ethanol (95% v/v). Aqueous extract was prepared by maceration process. The ethanol was removed by distillation under reduced pressure. These extracts were suspended in 5% acacia and used for the present experiments.

The LD50 values of ethanol and aqueous extracts of fruits of C. papaya were determined by Miller and Tainter method.5

Animals Male albino rats were procured from Perundurai Medical College, Perundurai and bred in the college animal house. They were fed on commercial diet (Hindustan lever, Bangalore) and water ad libitum during the experiments. The room temperature was maintained at 25±1°C.

Four groups (I—IV) comprising each of six animals weighing between 140—180 g were selected. Group I served as control and received 0.2 ml of Gum acacia daily for seven days orally. Groups II rats were similarly treated as group I. Groups III and IV were treated with ethanol and aqueous extracts of C. papaya at a dose of 250 mg/kg respectively for 7 d.

On the seventh day carbon tetrachloride (1.25 ml/kg; p.o.7) was administered 30 min after the last dose to all rats except rats in group I. After 36 h, all the rats were sacrificed under light ether anesthesia, blood was collected in sterile centrifuge tube and allowed to clot. Serum was separated by centrifuging at 2500 rpm for 15 min and used for the estimation of biochemical parameters such as serum aspartate amino transferase (AST),8 serum ALT,8 alkaline phosphatase,9 total bilirubin10 and gamma glutamate transpeptidase.11

After the animals were sacrificed, the abdomen was cut and opened. The liver was removed. The ratio of wet liver weight per 100 g of animal body weight was calculated. The liver preserved in neutral buffered formalin and were processed for paraffin embedding, following the standard microtechnique.12 5 µ section of the livers, stained with alum haemotoxylin and eosin were observed microscopically for the histopathological studies.

RESULTS

The LD50 value of ethanol and aqueous extracts of C. papaya were found to be 2426.37 and 2516.53 mg/kg, respectively.

The results of biochemical parameters revealed to the elevation of enzyme level in CCl4 treated group indicating that CCl4 induces damage to the liver (Table 1). Liver tissue rich in both transaminase increased in patients with acute hepatic diseases, AST which is slightly elevated by cardiac necrosis is a more specific indicator of liver disease.13 A significant reduction was (p<0.001) observed in AST, alanine amino transferase (ALT), alkaline phosphatase (ALP), total bilirubin and gamma glutamate transpeptidase (GGTP) levels in the groups treated with ethanol and aqueous extracts of C. papaya. The enzyme levels were almost restored to the nor-
metabolite, trichloromethyl radical. 14) These activated radicals brown and enlarged in CCl₄ intoxicated rats but it was normal.

Table 2. Effect of Ethanol and Aqueous Extracts of Dried Fruits of C. papaya on CCl₄ Treated Rats

<table>
<thead>
<tr>
<th>Design of treatment</th>
<th>Dose (mg/kg)</th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
<th>ALP (U/L)</th>
<th>Total bil. (mg%)</th>
<th>GGTP (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>—</td>
<td>131.5 ± 1.98</td>
<td>45 ± 0.8</td>
<td>195.66 ± 10.63</td>
<td>0.70 ± 0.03</td>
<td>123.0 ± 4.10</td>
</tr>
<tr>
<td>CCl₄</td>
<td>1.25 ml/kg</td>
<td>217.33 ± 4.5</td>
<td>341.0 ± 3.8</td>
<td>408.0 ± 19.25</td>
<td>1.2 ± 0.07</td>
<td>257.33 ± 5.31</td>
</tr>
<tr>
<td>Ethanol extract + CCl₄</td>
<td>250</td>
<td>140.0 ± 1.70*</td>
<td>67.0 ± 5.79*</td>
<td>299.60 ± 6.70*</td>
<td>0.90 ± 0.03*</td>
<td>133.33 ± 3.46*</td>
</tr>
<tr>
<td>Aqueous extract + CCl₄</td>
<td>250</td>
<td>126.0 ± 2.0*</td>
<td>48.0 ± 0.02*</td>
<td>246.0 ± 5.30*</td>
<td>0.93 ± 0.01*</td>
<td>113.40 ± 2.41*</td>
</tr>
</tbody>
</table>

n=6 animals in each group. *p<0.001; **p<0.05 when compared to CCl₄. Values are expressed as mean±S.D.

DISCUSSION

Carbon tetrachloride is one of the most commonly used hepatotoxins in the experimental study of liver diseases. The hepatotoxic effects of CCl₄ are largely due to its active metabolite, trichloromethyl radical.¹⁴ These activated radicals bind covalently to the macromolecules and induce peroxidative degradation of membrane lipids of endoplasmic reticulum rich in polyunsaturated fatty acids. This leads to the formation of lipid peroxides. This lipid peroxidative degradation of biomembranes is one of the principal cause of hepatotoxicity of CCl₄.¹⁵ This is evidenced by an elevation in the serum marker enzymes namely AST, ALT, ALP, total bilirubin and GGTP.

The efficacy of any hepatoprotective drug is dependent on its capacity of either reducing the harmful effect or maintaining the normal hepatic physiology which has been disturbed by a hepatotoxin. The extracts decreased the CCl₄ induced elevated levels of the enzymes in groups III and IV, indicates the production of structural integrity of hepatocyctic cell membrane or regeneration of damaged liver cells by the extracts.

Histopathological examination of the liver section of the rats treated with toxin showed intense centrallobular necrosis and vascuolisation. The rats treated with extracts along with toxicant showed sign of protection against these toxicants to considerable extent as evident from formation of normal hepatic cards and absence of necrosis and vacoules.

Decrease in serum bilirubin after treatment with the extract in liver damage indicated the effectiveness of the extracts in normal functional status of the liver. So, the result of present investigation indicates that the ethanol and aqueous extracts of C. papaya possess good hepatoprotective activity. The hepatoprotective mechanism of this herbal drug as well as active principles are not known. Further investigation are required to characterise the active hepatoprotective principle and its mechanism of action.

REFERENCES