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Protective effect of dried fruits of *Carica papaya* on hepatotoxicity in rat

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Abstract

Aqueous and ethanol extracts of *Carica papaya* has been evaluated for its hepatoprotective activity in rats. The aqueous and ethanol extracts of *C. papaya* showed significant hepatoprotection against carbon tetrachloride induced hepatotoxicity. The protective activity was evaluated by using biochemical parameters such as serum bilirubin, serum alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase. The histopathological changes of liver were compared with control.

Introduction

Despite tremendous development in the field of medical science, liver diseases are still the threatening problems to our health. Virus related liver diseases are important causes of morbidity and mortality in Bangladesh. HBV and HCV are emerging as important etiological factor for such disease in Bangladesh (Ahmed, 2005). Viral hepatitis has become a menace to public health in Asia and Africa, making development of inexpensive control measures urgent (Al-Qarawi et al., 2001). The absence of an effective treatment in modern medicine has made it urgent to search for suitable herbal drugs for treating hepatic disorders. The hepatoprotective activity of *Moringa oleifera* (Ruckmani et al., 1998), *Cocculus hirsutus* (Thakare et al., 2009), *Caseria ecsulenta* (Jayakar et al., 1999), *Trianthema decandra* (Balamurugan and Muthusamy, 2008) and *Phyllanthus niruri* (Iqbal et al., 2007) have been described.

Carica papaya Linn (Family:Caricaceae) is a short, fast growing large herb. The green fruit contains papain similar to pepsin, pulp of the fresh fruit contain a soft yellow resin, fat, albuminoid sugar and pectin. Leaves contain an alkaloid called carpaine and a glucoside named carposide (Samson, 1986). *C. papaya* is commonly cultivated and planted in Bangladesh for its edible fruits, also grows naturally in Waste Lands. Fruit of *C. papaya* is a rich source of vitamin C. It also contains vitamin E, pectin and carotinoids. Fruits, latex and juice of *C. papaya* are digestive and have been reported to be used in dyspepsia, intestinal irritation, habitual constipation and chronic diarrhea. The fruit is also useful in treating bleeding piles and enlarged spleen and liver (Ghani, 2003). To combat the increasing liver diseases in Bangladesh, it is essential to explore our plant resources to develop an effective hepatoprotective agent for the benefit of our people. The present study was chosen to investigate the effect of dried fruits of *C. papaya* on hepatotoxicity (Rajkapoor et al., 2002) with giving emphasis on comparative efficacy of aqueous and ethanol extracts of *C. papaya* used in both studies which may be helpful for determination of active principle in future.

Materials and Methods

The fruits of *C. papaya* was brought from a local market in Dhaka city. The preparation of the aqueous and ethanol extracts were performed in the Department of Chemistry of Dhaka University. The green fruits of *C.*

Table I

Effects of pretreatment with Carica papaya on mean serum bilirubin, ALT, AST and ALP levels in CCl_4 treated rats

Groups	Serum bilirubin (mg/dL)	Serum ALT (u/L)	Serum AST (u/L)	Serum ALP (u/L)
Normal control	0.5 ± 0.6	40.3 ± 3.7	54 ± 2.7	276 ± 27.0
CCl_4 treated	0.7 ± 0.0[a]	525 ± 35.7[c]	265 ± 6.2[c]	425 ± 15[c]
CCl_4 treated control for *C. papaya*	0.7 ± 0.0	530 ± 34.9	260 ± 10.3	426.7 ± 19.1
C. papaya (aqueous extract)	0.6 ± 0.0[NS]	194.3 ± 12.9[c]	203.3 ± 9.5[b]	295.3 ± 15.7[c]
C. papaya (ethanol extract)	0.7 ± 0.0[NS]	273.3 ± 25.6[c]	213.3 ± 18.4[NS]	334.3 ± 13.7[b]

N = 6 rats in each group, [a]p<0.05, [b]p<0.01, [c]p<0.001 when compared to control group. Values are expressed as mean ± SE

papaya were cut into small pieces, shade dried and powdered. To prepare aqueous extract, 200 g of powdered fruits of papaya were taken and mixed with 1500 mL of distilled water in a conical flask and kept for 24 hours with occasional shaking and stirring. Then filtration through fine cloth and kept for further 24 hours followed by refiltration by vacuum pump. Then the whole extract was concentrated with rotary vacuum evaporator under low temperature. Then the extract was put into freeze dryer to make it powder. Finally the extract was stored in refrigerator. To prepare ethanol extract 180 g of powdered fruits of papaya were suspended in 3 L of petroleum ether and kept in refrigerator overnight for removing all the fatty substances. The supernatant was discarded by filtration with fine cloth and the residue was kept open to dry out the petroleum ether by air. Then the residue material was mixed with 2.5 liters of 90% ethanol for 24 hours and being filtered, kept for another 24 hours with ethanol followed by refiltration by vacuum pump. Then the whole extract was concentrated with rotary vacuum evaporator. Then the extract was put into freeze dryer to make it powder. Finally the extract was stored in refrigerator

Rattns norvigicus rats of either sex were procured from the animal house of ICDDR'B, Dhaka. The rats were 8 to 10 weeks old, healthy and weighing between 140 to 180 g. The rats were well accommodated in metallic cages (6 rats in each cage), at room temperature, in the animal house which was maintained in properly hygienic condition and well ventilated. The rats were fed with pelleted food (10 to 15 g/rat/day). Proper cleaning measures were taken regularly.

Adult rats of either sex were used for the present study. The rats were divided into five groups, each group comprising of 6 rats, treated for 7 days and sacrificed on 8th day. For convenience, the experiment was divided into two parts: Experiment II and I. Experiment II was designed to demonstrate the hepatotoxic effects of CCl4 on normal rats. The rats of Group A and B were fed with normal diet and 2 mL distilled water orally for 7 days. Group B was given CCU at the dose of 1.3 mL/kg/day orally on 7th day and both groups were sacrificed on 8th day of experiment. In experiment I, Group C received normal diet; 2 mL distilled water each rat per day orally for 7 days. Group D received normal diet; 250 mg/kg aqueous extract of *C. papaya* in a volume of 2 mL of distilled water each rat per day orally for 7 days. Group E received normal diet, 250 mg/kg ethanol extract of *C. papaya* in a volume of 2 mL of distilled water each rat per day orally for 7 days. On the seventh day CCl_4 (1.3 mL/kg/day orally) was administered to all the rats of each group and sacrificed on 8th day of experiment. On average, 3 mL blood from each rat was collected by cardiac puncture for the estimation of serum bilirubin, ALT, AST, and ALP levels of the rats by enzymatic colorimetric method. Livers were collected to see the histological changes.

Results

Experiment I resulted in elevated level of biochemical parameters in CCl_4-treated group indicating the hepatotoxic effects of carbon tetrachloride. In Experiment II, the decrease in mean serum bilirubin level in the aqueous and ethanol extract of *C. papaya* pretreated group was not significant. The decrease in mean serum ALT level in the aqueous extract of *C. papaya* pretreated group was highly significant ($p<0.001$; Table I). The decrease in mean serum ALT level in the ethanol extract of *C. papaya* pretreated group was highly significant ($p<0.001$). The decrease in mean serum AST level in the aqueous extract of *C. papaya* pretreated group was significant ($p<0.01$). The decrease in mean serum AST level in the ethanol extract of *C. papaya* pretreated group was not significant ($p<0.01$). The decrease in mean serum ALP level in the aqueous extract of *C. papaya* pretreated group was highly significant ($p<0.001$). The decrease in mean serum ALP level in the ethanol extract of *C. papaya* pretreated group was significant ($p<0.01$).

Histological examination of the liver sections pretreated with extracts of *C. papaya* showed remarkable reduction

in necrosis and degenerative changes against carbon tetrachloride.

Discussion

In hepatotoxicity, the most important mechanism of cell injury by carbon tetrachloride involves the formation of reactive free radicals and subsequent lipid peroxidation. The free radicals produced locally cause auto oxidation of the polyenoic fatty acids present within the membrane phospholipids. There oxidative decomposition of the lipid is initiated and organic peroxides are formed after reacting with oxygen (Kumar et al., 1992). The lipid peroxidative degradation of biomembranes induced by carbon tetrachloride causes hepatotoxicity which is evidenced by an elevation in the serum marker enzymes namely AST, ALT, ALP and total bilirubin (Kaplowitz et al., 1986).

In this study, the aqueous and ethanol extracts of *C. papaya* decreased the carbon tetrachloride induced elevated levels of the enzymes like serum ALT, AST and ALP which were statistically significant compared to control group. It was also found that aqueous extract of *C. papaya* showed more significant hepatoprotection than that of ethanol extract. This finding may indicate the dominant anti-oxidant effect of vitamin C which is richly contained in *C. papaya.* Histological examination of the liver sections pretreated with extracts of *C. papaya* showed remarkable reduction in necrosis and degenerative changes against carbon tetrachloride (data not shown). The finding of this study is in agreement with that of the study of the effect of dried fruits of *C. papaya* Linn on hepatoxicity (Rajkapoor et al., 2002) although they have demonstrated a more complete recovery. The variation could be due to different animal models used.

Conclusion

This study shows the hepatoprotective effect of *C. papaya* on carbon tetrachloride-induced hepatotoxicity in experimental rats.

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Conflict of Interest

Authors declare no conflict of interest

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