Influence of Carica Papaya Linn Extracts on Paracetamol and Thioacetamide Induced Hepatic Damage in Rats
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Citation

Abstract
The Carica papaya Linn (Family Caricaceae) has been used for summer heat syndrome as home remedy in Japan and China, and it has recently been used to treat Paracetamol and Thioacetamide Induced Hepatic Damage in Rats in India. So we investigate the pharmacological effect of Carica papaya extracts (CPE). We examined the effect of CPE on rat models of paracetamol (PCM) and thioacetamide (TAA) induced hepatic damage. Wistar strain albino rats were prophylactically treated with three dose of CPE (100, 250 and 500mg/kg, p.o) for 10 days and subsequently liver damage was induced. Hepatoprotective potential was evaluated by measuring biomarkers and this is mainly due to the presence of vitamin C.

INTRODUCTION
Papaya, Carica papaya L., (Caricaceae) is one of the major fruit crops cultivated in tropical and sub-tropical zones. It is the first fruit tree to have its genome deciphered\(^1\). The milky sap of an unripe papaya contains a complex proteolytic enzyme called Papain. The crude extract consists of two crystallized enzymes called 'papain' and 'chymopapain'. The enzyme is similar to pepsin and hence it helps to digest protein in the body\(^2\). It is therefore used to relieve indigestion. Papain can induce asthma and rhinitis and the related enzyme carpaine can cause paralysis, numbing of the nerve centers and cardiac depression. Papain is also applied topically (in countries where it grows) for the treatment of cuts, rashes, stings and burns. Fruit of C. papaya is a rich source of vitamin C\(^3\). 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\(^4\). The administration of vitamin C after TAA intoxication led to decrease the severe biochemical, hematological and histopathological changes\(^5\).

The present investigation was designed to evaluate the effects of Carica papaya extracts (CPE) on Paracetamol (PCM) and Thioacetamide (TAA)-induced hepatic damage. The rats with hepatic damage caused by TAA and PCM were chosen as animal models for this study, because TAA is used to induce hepatic encephalopathy.

MATERIALS AND METHODS
PREPARATION OF C. PAPAYA PLANT EXTRACT
The fruits of C. papaya were brought from a local market in Warangal city, Andhra Pradesh, India. The ripen fruits of C. papaya were cut into small pieces, shade dried under sunlight and powdered. To prepare aqueous extract, 100 g of powdered fruits of papaya were taken and mixed with 1 liter of distilled water in a conical flask and kept for 48 hours with occasional shaking and stirring. Then filtration through fine cloth and kept for further 24 hours followed by re-filtration 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 200 g of powdered fruits of papaya were suspended in 2 liters 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 liters of 90% ethanol for 48 hours and being filtered, kept for another 24 hours with ethanol followed by re-filtration 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.
ANIMALS
Adult Wistar strain albino rats (weighing, 150-200 g) were used for the study. Animals were supplied by Animal House Facility of Guru Nanak Institute of Pharmacy, Ibrahimpatnam, Hyderabad, A.P., India (Ref. No: 1374/ac/10/CPCSEA) and kept under standard laboratory conditions in polypropylene cages in 12-h light/dark cycle at 25 ± 2°C. Animals were provided with standard pellet diet (Lipton, India) and water ad libitum. All the procedures carried out on animals were approved by Institutional Animal Ethics Committee (JHAEC).

PARACETAMOL (PCM) INDUCED HEPATIC DAMAGE
The animals were divided into six groups (n=6) and treated for 10 days orally. The animals of Group I and II were treated with vehicle for 10 days. Group III animals received silymarin (100 mg/kg, p.o) as standard drug. The groups IV, V and VI animals were given low (250 mg/kg, p.o), medium (500 mg/kg, p.o) and high dose (1000 mg/kg, p.o) of Carica papaya extracts (CPE). On 11th day, PCM (2 g/Kg, p.o.) suspended in sucrose solution (40% w/v) was administered in 3 divided doses to animals of groups II, III, IV, V and VI. Food was withdrawn 12 hr before PCM administration to enhance the acute liver toxicity. Animals were sacrificed 48 hr after the administration of PCM. Blood samples were collected and the serum was used for determinations of activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) and serum bilirubin levels (Total and direct). The liver was immediately isolated and washed with normal saline, blotted with filter paper and weighed. Liver tissue homogenate (LTH) was prepared in sucrose solution (0.25 M) and used for estimation of endogenous marker enzymes and biological antioxidants viz., superoxide dismutase (SOD) and catalase activities. The liver was then subjected to histopathological examination.

THIOACETAMIDE (TAA) INDUCED HEPATIC TOXICITY
The animal groupings and treatment was similar to that used in PCM induced liver damage. Single dose of TAA (100 mg/kg, s.c) diluted with distilled water (2% solution) was administered on 10th day to animals of groups II, III, IV, V and VI and the animals were sacrificed 48 hr after administration of TAA. Biochemical estimations were carried out in serum and LTH as mentioned above in PCM model.

RESULTS
PARACETAMOL INDUCED LIVER TOXICITY
After 48 hr of administration of PCM, the serum levels of ALT, AST, ALP and bilirubin were markedly increased when compared to normal control. Pretreatment with low dose of Carica papaya extracts (CPE) medium dose (250 mg/kg, p.o), higher dose (500 mg/kg, p.o) and silymarin significantly reduced the levels of these biochemical markers compared to PCM control (P<0.001). Similarly, there was significantly high level of these biomarker enzymes in LTH of animals pretreated with low and medium dose of Carica papaya extracts (250 and 500 mg/kg, p.o) and silymarin compared to PCM control (Table-1). Pretreatment with medium and high doses CPE (250 and 500 mg/kg, p.o) and silymarin also attenuated the increase in the liver weight observed after PCM intoxication (Table-1). The activities of SOD and catalase in LTH were significantly increased in animals pretreated with all the three doses of CPE (100, 250, 500 mg/kg) and silymarin when compared to PCM control. Histopathological studies revealed that PCM induced centrilobular necrosis and mild hydropic degeneration. Prophylactic administration of medium and high doses of CPE (250 and 500 mg/kg, p.o) and silymarin reduced hydropic degeneration of liver cells when compared to PCM control.

THIOACETAMIDE INDUCED LIVER INJURY
The effects observed in this model were almost similar to that observed in PCM induced hepatotoxicity. The medium (250 mg/kg, p.o) and high doses dose of CPE (500 mg/kg, p.o) were effective in reducing TAA induced damage (Table 2). Histopathological studies revealed that TAA produced cloudy swelling surrounding central vein, hydropic degeneration and coagulative necrosis. The hydropic degeneration was reduced by silymarin and medium and high dose of CPE (250 and 500 mg/kg, p.o).

Figure 1
Table 1: effect of Silymarin and extracts (CPE) on ALT, AST, ALP, bilirubin levels and liver wet weight in Paracetamol (PCM) induced acute liver injury in rats
that fruits of Carica papaya extracts possess hepatoprotective activity. The exact constituent(s) responsible for this effect cannot be explained with the present data. It is speculated that hepatoprotective activity of Carica papaya extracts may be due to the presence of Vitamin C.

ACKNOWLEDGMENTS

The authors are thankful to the Director and Principal, SRL Institute of Pharmaceutical Sciences, Kakatiya University, Kummarigudem Road, Madikonda, Kizipet, Warangal, Andhra Pradesh, India, and Department of Pharmacology, Guru Nanak Institute of Pharmacy, Ibrahimpatnam, Hyderabad, A.P., India for providing laboratory facilities and financial support.

References

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