



HEPATOPROTECTIVE ACTIVITY OF PAPAYA IN ACUTE LIVER INJURY

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Abstract

The liver is the largest organ in the body, contributing about 1/50 of the total body weight, or about 1.5 kg in the average adult human. The liver performs numerous different functions, yet the liver is also a separate organ and numerous of its functions are interrelated with one another. This becomes especially apparent in abnormalities of the liver similar us hepatitis, Jaundice and Cirrhosis.

Waterless splint excerpt of *Carica papaya* (CP) is used as drug against some forms of liver conditions traditionally. The purpose of the study was to estimate and determine the hepatoprotective effect of the waterless splint excerpt of CP in CCl₄ convinced liver damage in rats administered subcutaneously with 75mg/ kg CCl₄ after 48hours. The conditioning of serum alanine aminotransferase(ALT), aspartate aminotransferase(AST), alkaline phosphatase(peak) and the situations of serum malondialdehyde(MDA) and bilirubin were determined in rats administered with 75mg/ kg CCl₄ and rats treated with 200mg/ kg and 400mg/ kg CP before CCl₄ administration.

Key Words: Papaya, Liver, Hepatoprotective, Rats, Administration

Review

The liver is one of the most important organs in the body, performing a abecedarian part in the regulation of different processes, among which the metabolism, stashing, storehouse, and detoxification of endogenous and exogenous substances are prominent. Due to these functions, hepatic conditions continue to be among the main pitfalls to public health, and they remain problems throughout the world. Despite enormous advances in ultramodern drug, there are no fully effective medicines that stimulate hepatic function, that offer complete protection of the organ, or that help to regenerate hepatic cells. Therefore, it's necessary to identify pharmaceutical druthers, for the treatment of liver conditions, with the end of these druthers being more effective and less poisonous. The use of some shops and the consumption of different fruits have played introductory places in mortal health care, and different scientific examinations have indicated

that, in those shops and fruits so linked, their salutary goods can be attributed to the presence of chemical composites that are called phytochemicals. The present review had as its ideal the collecting of data grounded on exploration conducted into some fruits *Carica papaya*, which are consumed constantly by humans and which have demonstrated hepatoprotective capacity, as well as an analysis of a resin (propolis) and some phytochemicals uprooted from fruits, shops, provocations, and algae, which have been estimated in different models of hepatotoxicity. The liver being an important organ is frequently exposed to array of pitfalls. Injury to the liver can lead to deterioration of its functions and may crown in organ failure. The likely threat factors for the development of the liver conditions have been suggested to include pathogenic microorganisms and contagions, hepatotoxins, overdose and duration of medicines, rotundity and malnutrition, alcohol, autoimmune diseases, type- 2 diabetes, and inheritable factors. The conditions of the liver are of public health concern because orthodox remedies for liver conditions produce limited results with attendant side goods. As similar, application of reciprocal and indispensable herbal drug has attracted exploration interest for new presumptive hepatoprotective agents able of upgrading or reversing liver injury with little side goods. Over the times, this hunt has gained motivation with numerous studies fastening on hepatoprotective capabilities of factory medicines. Carbon tetrachloride (CCl₄) is a known hepatotoxic ant in humans and beast models. It has been successfully used in hepatotoxicity exploration as a model and to estimate hepatoprotective agents. With reports on the rise of liver conditions and multitudinous literature reports on shops with implicit hepatoprotective exertion, this review stressed the medium of CCl₄ toxin, the significance, effectiveness, and underpinning mechanisms of herbal factory excerpts on CCl₄- convinced toxin in experimental beast models.

Drug Profile

Carica papaya Linn.(Family Caricaceae) is a imperishable, herbaceous factory, with riotous milky latex reaching to 6 – 10 measures altitudinous. Its standing stem is about 30 cm thick and planed with splint scars. The callow fruit is used traditionally for the treatment of colorful mortal and veterinary conditions including malaria, hypertension, diabetes mellitus, hypercholesterolemia, hostility, intestinal helminthiasis³ and for the operation of sickle cell anaemia⁴. The present study was designed to probe the effect of canted oral boluses(200 and 400 mg/ kg/ day) and the time- course effect of the waterless splint excerpt of *Carica papaya*(CP) in CCl₄ treated rats as a way of validating its folkloric use in treatment of liver conditions. The choice of the excerpt cure range employed in this was grounded on the result attained from the study before conducted.

Factory excerpt Fresh leaves of *C. papaya* were collected in December 2022 from botanical theater, Department of drugstore GRDIMT, Dehradun. The leaves of *C. papaya* were linked and authenticated by Dr. Arvind Negi of the Department of drugstore GRDIMT, Dehradun.

Aim & Objectives

The leaves were sorted to exclude any dead matter and other unwanted patches. The leaves were air-dried for 2 weeks and also base into fine greasepaint using pestle and mortar. An aggregate of 200g of the ground greasepaint was soaked in 1 L of distilled water for 48 hours at room temperature. The admixture was filtered into 500 ml conical beaker with Watman sludge paper. The filtrate was dried at a temperature of 30°C for 10 hours, which counted 20.5g.

Experimental Beast Young adult manly Wistar rats, importing between 120 and 150 g were used for this study. The rats were allowed two weeks of adaptation under standard laboratory conditions. The rats were maintained on standard rat feed and drinkable water ad libitum. The experimental rats were all handled in strict compliance with transnational guidelines as specified by the CPCSEA. Experimental Design An original study was conducted to determine the cure range of the waterless leaves excerpt of *Carica papaya* to be used for the studies. Thirty five (35) rats were divided into five (5) groups of seven (7) rats each. Group I served as normal control; Group II served as CCl₄ Control, Group III served as CCl₄ 200mg/ kg/b.w *Carica papaya* splint excerpt, Group IV served as CCl₄ 400mg/ kg/b.w *Carica papaya* splint excerpt, and Group V served as CCl₄ silymarin(100mg/ kg/b.w)

Plan of Work

Experimental induction of CCl₄ hepatotoxicity Rats were divided into five groups, each group conforming of six creatures. Group I(control) creatures were administered a single cure of water(1 mL/ kg,p.o.) daily for 7 days and entered liquid paraffin(1 mL/ kg,s.c.) on day 4 and 5. Group II(CCl₄) entered water(1 mL/ kg body weight,p.o.) Formerly daily for 7 days and entered CCl₄ liquid paraffin (11, 2 mL/ kg body weight,s.c.) on day 4 and 5. Test groups creatures (Groups III- IV) were administered orally on a cure of 200mg/ kg and 400 mg/ kg of the waterless excerpt, independently, formerly daily. Group V entered standard medicine silymarin(100 mg/ kg,p.o.) Formerly daily for 7 days. The Groups III – V creatures were administered contemporaneously CCl₄ liquid paraffin (11, 2 mL/ kg body weight,s.c.) on day 4 and 5 after 30 min of administration of the excerpt and silymarin. Creatures were offered 48 h after the last treatment. Blood was collected, allowed to clot and serum was separated at 2500 rpm for 15 min and biochemical examinations were carried out. Liver was deconstructed out and used for histopathological studies. Determination of Labels of Liver Damage the rats were offered 48h post administration of CCl₄ at a cure of 75mg/ kg under anesthesia using petroleum ether. The separated serum was estimated for colorful biochemical parameters; aspartate aminotransferase(AST) 7, alanine transaminase(ALT) 8, serum alkaline phosphatase(peak) 8, malondialdehyde(MDA) 9 and total bilirubin¹⁰. Histological Studies The liver towel was deconstructed out and fixed in 10 formalin, dehydrated in gradational ethanol ⁸⁰, cleared in xylene and bedded in paraffin. Sections were prepared and also stained with hematoxylin and eosin (H and E) color for photo microscopic observation, including cell necrosis and adipose change. Quantitative determination of Phytochemicals Quantitative determination of phytochemicals was carried out for total

phenolics¹¹, flavonoids¹², alkaloids¹¹ tannins¹³, and saponins¹⁴. Statistical analysis all results were expressed as means \pm SD for each group. Data were analyzed statistically with pupil's t-test using SPSS programme. P values of lower than 0.05 ($P < 0.05$) were considered significant.

Materials & Methods

The quantitative phytochemical analysis of the waterless splint excerpts of *Carica papaya*, revealed the presence of some potent bioactive composites (Tables 1). Still, the presence of these phytochemicals conferred the hepatoprotective and anti-inflammatory goods of *Carica papaya* observed in the CCl₄ convinced liver damaged groups. As the medicinal effect of the shops is due to the phytochemicals present. Carbon tetrachloride (CCl₄) is one of the most generally used hepatotoxins in the experimental study of liver conditions. It's laboriously metabolized in the body apkins to its largely reactive halogenated metabolites (. CCl₃ and. Cl) and its metabolic activation is accompanied by the release of reactive oxygen species (ROS) 15. The reactive metabolites and the free revolutionaries released latterly affect in the induction of lipid peroxidation leading to array of organ venom similar as hepatotoxicity, nephrotoxicity, neurotoxicity, cardio toxicity and hematotoxicity^{16, 17}. In detecting liver damage by CCl₄ the determination of enzyme situations similar as AST, ALT is largely used. Necrosis or membrane damage releases the enzyme into rotation and hence it can be measured in the serum. Elevated situations of serum enzymes are reflective of cellular leakage and loss of functional integrity of cell membrane in liver¹⁸. Serum peak and bilirubin situations on other hand are related to the function of hepatic cell. Increase in serum position of peak is due to increased conflation, in presence of adding biliary pressure.

Table 1

Quantitative phytochemical ingredients (g/ 100g) of waterless excerpt of the splint of *Carica papaya*

SAMPLE

Flavonoids.42 \pm 0.011 (g/ 100g)

Alkaloids1.36 \pm 0.480 (g/ 100g)

Total Phenolics2.25 \pm 0.051 (g/ 100g)

Tannins.54 \pm 0.03(g/ 100g)

Values are presented as mean \pm Standard divagation. All values are of triplet determination

Table 2

Effect of *Carica papaya* waterless splint excerpt on some biochemical parameters of liver in rats

GROUPS ALT(IU/ L) AST(IU/ L) peak(IU/ L) MDA(μ M) Total Bilirubin(mg/ dl)

Group I.36 \pm 7.67ALT(IU/ L) 58 \pm 7.14 AST(IU/ L) 144 \pm 9.65peak(IU/ L) 0.12 \pm 0.05MDA(μ M) 0.540.07) Total Bilirubin(mg/ dl)

Group II 125 ± 26.37 , 157 ± 28.35 , 421 ± 27.58 , 0.40 ± 0.10 , 2.25 ± 0.33

Group III 105 ± 10.21 , 131 ± 13.10 , 350 ± 13.11 , 0.32 ± 0.01 , 1.84 ± 0.16

Group IV 106 ± 9.00 , 117 ± 11.04 , 300 ± 14.01 , 0.29 ± 0.10 , and 1.43 ± 0.15

Group V 88 ± 11.10 , 104 ± 12.81 , 200 ± 19.22 , 0.25 ± 0.11 , 0.97 ± 0.05

Values are presented as mean \pm Standard deviation. a represents a largely significant at $p < 0.05$) increased in MDA position in CCl₄ convinced liver damage groups (Table 2).

This signifies increased product of reactive oxygen species. This agrees with the former findings that CCl₄- convinced liver damage is associated with the release of reactive oxygen species¹⁵. But administration of 200 and 400mg/ kg/b.w of CP drop the position of MDA to near normal (Table 2). The result can be further verified with histopathological studies. The histopathological examination easily reveals the peri-portal adipose change characterized by vacuolated hepatocytes around the portal tract from rat treated with 75mg/ kg CCl₄.

Summary of Work Done

The CCl₄ also showed to produce expansive vascular degenerative changes and centrilobular necrosis in hepatocytes of those rats treated with 75mg/ kg CCl₄ only. But treatment with 200mg/ kg and 400mg/ kg boluses of Carica papaya excerpt showed that the hepatic cells are analogous to those of normal control group, with group IV, showing maximum hepato-defensive effect, in discrepancy to group which entered CCl₄ only (Figure 3). This is also nearly analogous to group that entered 100mg/ kg silymarin (Figure 4). It has been reported that dwindling the metabolic activation of carbon tetrachloride, forestallment of generation of reactive oxygen species and scavenging of generated free revolutionaries or by combination of these are important mechanisms in the protection against CCl₄- convinced hepatic lesion^{20, 21}. therefore, grounded on the result attained, it's suggested that the excerpt may ply its hepato-defensive goods either by dwindling the metabolic activation of carbon tetrachloride, or by acting as a chain- breaking antioxidant for scavenging free revolutionaries or by a synergistic combination of these goods.

Therefore, in conclusion, Carica papaya waterless splint excerpt can be considered to be an effective hepato-defensive agent as it brings near to normality the damage caused by CCl₄ to hepatic function. Hence the excerpt can be used in polyherbal phrasings to give a synergistic effect with other hepato-defensive medicines and thereby precluding the process of inauguration and progress of hepato- cellular conditions.

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