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HEPATOPROTECTIVE ACTIVITY OF POLYCARPEA CORYMBOSA

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Abstract:

Aim of study: To evaluate the hepatoprotective activity of *Polycarpea corymbosa* whole plant extract against carbon tetra chloride (CCl_4) –induced hepatotoxicity.

Material and methods: Hepatotoxicity was induced in male wistar rats by administration of CCl_4 (1.25ml/kg/day for 7days). Methanolic extract of whole plant of *Polycarpea corymbosa* were administered to the experimental animals (20 mg/kg/day,p.o.for 7 days). The hepatoprotective effect of these extract was evaluated by the assay of liver function biochemical parameters (alanine aminotranferse, aspartte aminotranferse and alkaline aminotranferse) and histopathological studies of the liver.

Results and Discussion: In methanol extract-treated animals, the toxic effect of CCl_4 as controlled significantly by restoration of the levels of enzymes levels as compared to the normal and the standard drug silymarin-treated groups. Histology of the liver section of the animals treated with the extract showed the presence of normal hepatic cords, absence of necrosis and fatty infiltration, which further support the hepatoprotective activity.

Conclusion: Methanol extract of the whole plant of *P. corymbosa* possesses significant hepatoprotective acivity.

Key words: *Polycarpea corymbosa*, CCl_4. Serum marker enzymes.

1. Introduction:

The liver regulates many important metabolic functions. Hepatic injury is associated with distortion of these metabolic functions (1). Additionally, it is the key organ of metabolism and excretion is continuously and variedly exposed to xenobiotics because of its strategic placement in the body. The toxins absorbed from the intestinal tract gain access first to the liver resulting in a variety of liver ailments. Thus liver diseases remain one of the serious heath problems. Modern medicines have little to offer for alleviation of hepatic diseases and it is chiefly the plant based preparations which are employed for their treatment of liver disorders. But there are not much drugs available for the treatment of liver disorders (2, 3). Therefore, many folk remedies from plant origin are evaluated for its possible antioxidant and hepatoprotective effects against different chemical-induced liver damage in experimental animals. CCl_4-induced hepatotoxicity model is frequently used for the investigation of hepatoprotective effects of drugs and plant extracts. The changes associated with CCl_4-induced liver damage are similar to that of acute viral hepatitis (4, 5). *Polycarpea corymbosa* (Caryophyllaceae). The leaves of this plant are used in Indian traditional medicine system as poultice, warm or cold over boils and inflammatory swellings and given with molasses in the form a pill in treatment of jaundice. While general phytochemical screening, the plant showed good amount of phenolics compounds. Since the plant is used in the treatment of jaundice, as an astringent and inflammatory swellings in traditional medicine and presence of phenolics in the plant inspired us to study its hepatoprotective activity(6).

2. Materials and Methods:

2.1. Collection of plant material:

The whole plant of *P. corymbosa* was collected from khammam district, Andhra Pradesh. The plant was authenticated by comparing with the herbarium voucher specimen deposited at department of botany, Kakatiya University Warangal.

2.2. Drugs and Chemicals:

Silymarin were the gift sample from Micro Labs Ltd., Hosur, India. Thiopentone Sodium (Thiosol) and olive oil were purchased from Neon Labs, Mumbai, Sevenships, Hyderabad, India repectively.The biochemical analytical kits (Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), were purchased from Merck Specialities Private Limited, Mumbai, India. All other chemicals and solvents used were of analytical grade.

2.3. Preparation of methanolic extract of the whole plant:

The whole plant of *Polycarpea corymbosa* were made free from the adherent foreign material and air dried. Then the air dried material (1kg) was coarsely powdered and macerated with methanol in a round bottom flask for 7-days. The contents of the flask were stirred intermittently to ensure the efficiency of the extraction. After 7-days, they were filtered and concentrated under reduced pressure [Rotavapour, Switzerland]. The so obtained extract was kept in a dessicator to remove moisture and stored properly until used.

2.4 Maintenance of animals:

Wistar albino rats weighing 150-200 g were purchased from Mahaveera agencies, Hyderabad, India with a prior permission from our institutional animal ethical committee and used for the studies. The animals were housed in standard polypropylene cages, and maintained under standard laboratory

conditions (12:12 hour light and dark cycle; at an ambient temperature of 25 ± 50C; 35- 60% of relative humidity). The animals were fed with standard rat pellet diet and water ad libutum.

2.5. Acute toxicity study:

The acute toxicity studies were carried out as per stair case method (10) Fifty male rats were divide into five groups of 8 each and were administered with doses of the extracts orally (100, 150, 200, 250 and 300 mg/kg). Mortality was noticed upto 200 g/kg, whereas, 100% mortality was in the dose of 300 mg/kg. The LD50 of the extracts was found to e 250 mg/kg body weight. One-tenth of this dose selected as the therapeutic dose for the evaluation. (7).

2.6. In vivo hepatoprotective activity:

Four groups of animal's containing six each were used for the study. The animals from Groups I served as the control and received the vehicle 1% gum tragacanth at a dose of 1 ml /kg/day of p.o. or 7 days. Groups II received CCl_4 1.25 ml/kg/bw. p.o. on the 7 day. GroupsIII-IV received extract (25 mg/kg/bw p.o.) and standard drug silymarin (50 mg/kg/bw p.o.) daily for 7 days and after two hours of administration received CCl_4 1.25 ml/kg/bw. p.o. (8)

2.6.1. Assessment of hepatoprotective activity

All animals are killed on day 8 under light ether anaesthesia. The blood samples were collected separately by carotid bleeding into sterilized dry centrifuges tubes and allowed to coagulate for 30 min at 37^0C. The clear serum was separated at 2500 rpm for 10 min and biochemical investigation were carried out to assess liver function viz., alanine aminotransfersae, aspartate aminotransferase and alkaline phosphatase

2.7. Hepatoprotective activity:

Their percentage protection was calculated by using following formula.

$$\text{Percentage protection} = \left\{1 - \frac{T - V}{C - V}\right\} \times 100$$

Where "T" is the mean value of test group (extract /standard), "C" is the mean value of toxic group (CCl_4) alone and "V" is the mean value of control group (vehicle treated animals) (9).

2.8. Statistical analysis:

The data obtained were analyzed by one-way of variance (ANOVA) followed by student–Newman-keul multiple comparision test for the significant interrelation between the various groups using Graph pad prism-4 computer software. $P<0.05$ was considered to be significant**.**

2.9 Histopathology:

After draining the blood samples, liver samples were excised, washed with normal saline and processed separately for histological observations. Initially, the materials were fixed in 10% buffered neutral formalin for 48 h and then taken with bovine solution for 6h. Paraffin sections were taken at 5 mm thickness. Processed in alcohol-xylene series and were stained with alum hematoxylin and eosin (17). The sections were examined microscopically for histopathological changes.

3 Results:

3.1. Effect on biochemical parameters (prophylactic study):

The administration of CCl_4 to the animals resulted in a marked increase in serum alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase. The toxic effect of CCl_4 was controlled in the animals treated with the methanolic extract by the way of restoration of the levels of the liver function biochemistry similar to that of standard drug silymarin (Table 1 and Fig 1).

Table 1. Effect of PC against CCl_4 induced liver damage (prophylactic study)..

Design of treatment	Dose (mg/kg)	AST U/L	ALT U/L	ALP U/L
Control	--	131±.98	45.3±0.84	160.6±3.79
CCl_4	1.25 ml/kg	217.3±4.5	341.5±3.8	388.6±18.25
Silymarin+CCl_4	50 mg/kg	138.0±2.17**	81.3±9.10*	218.6±5.47**
Methanolic extract+CCl_4	25 mg/kg	115.2±1.16*	83.4±5.79*	292.6±5.32*

N= 6 animals in each group, *P <0.001; **P <0.01 when compared with control. Values are expressed as mean±SEM.

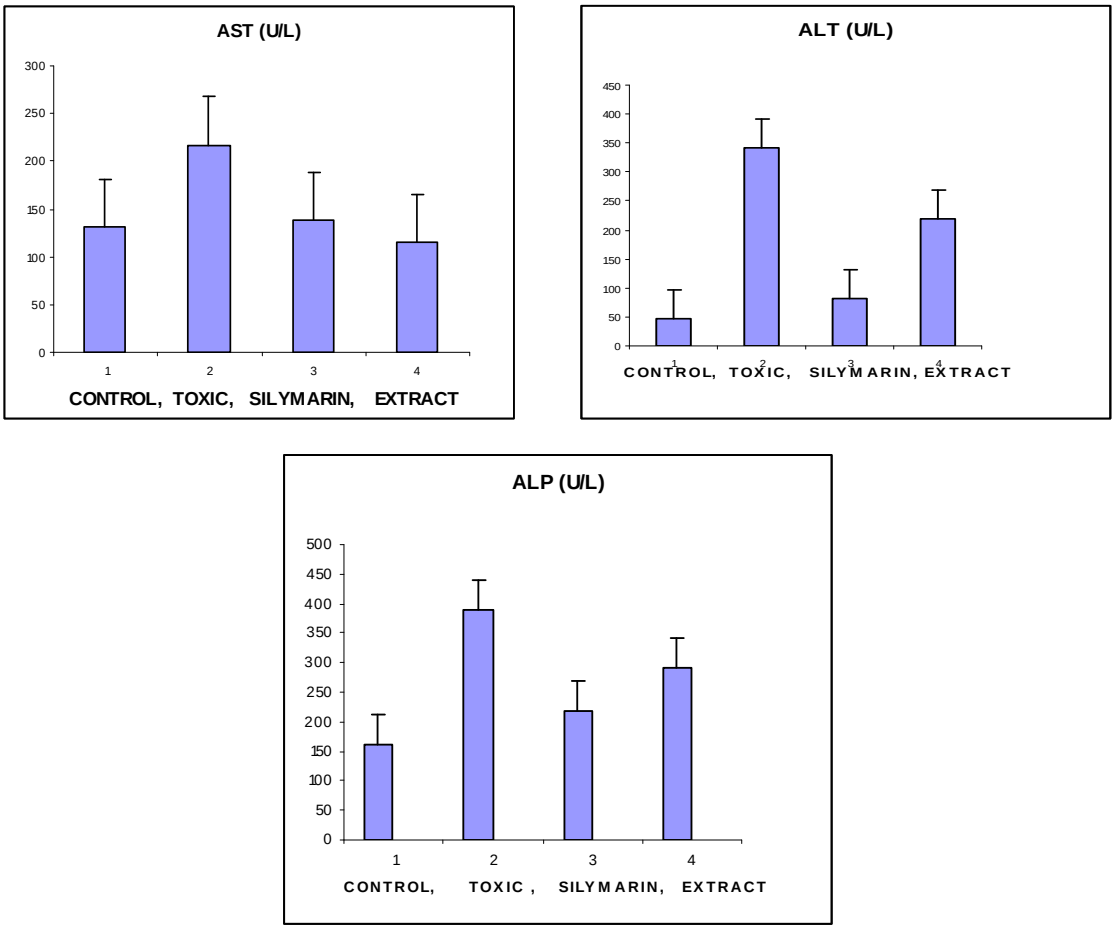
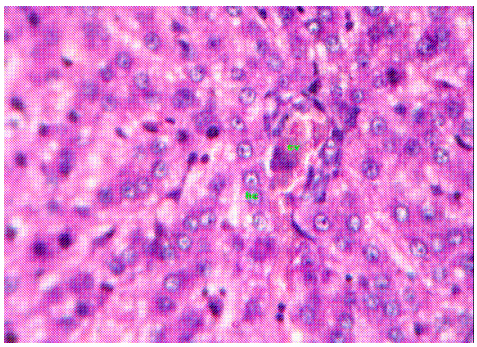


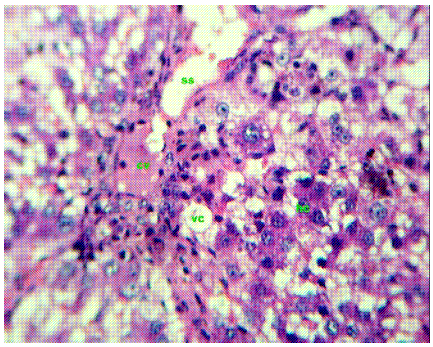
Fig.1. Effect of PC on serum biochemical parameters against CCl_4 (1.23 ml/kg/bw/p.o.) induced liver damage (prophylactic study) representation of aspartate aminotransferase, alanine aminotranferase and alkaline phosphatase.

3.2. Histopathology:

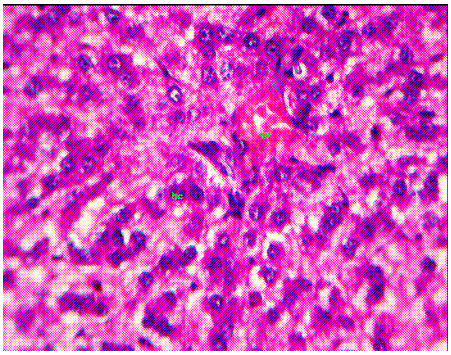
The histological profile of the control animas showed normal hepatocytes (fig 2) Group II showed intense centrilobular necrosis, fatty change and lymphocyte infiltration. The sections of liver taken from the animals treated with standard silymarin showed the hepatic architecture, which was similar to that of control. The animal's treated with methanolic extract exhibited significant liver protection against the toxicant as evidenced by the presence of normal hepatic cords, absence of necrosis, less lymphocyte infiltration.



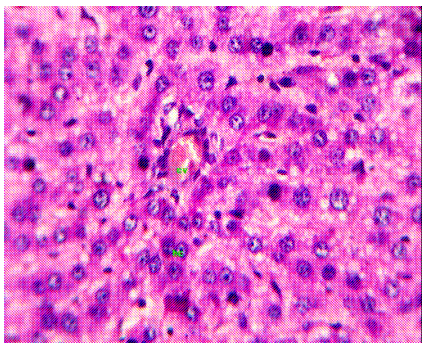
Normal rat liver section



CCl_4 treated liver section



Silymarin+CCl_4 treated liver section



PC+CCl_4 treated liver section

Fig 2. **Normal rat liver** showing central vein, hepatic cells, sinusoidal space, **CCl_4** treated showing fatty change, centrilobular necrosis, lymphocyte infiltration, dilatation of sinusoidal spaces, **Silymarin+CCl_4** treated liver section showing reduced sinusoidal space, less derangement of hepatic cells and **PC+CCl_4** treated liver section showing reduced sinusoidal space, less centrilobular necrosis, less fatty change.

4. Discussion:

The CCl_4 has been used as a tool to induce hepatotoxicity in experimental animals. (10, 11).This toxic chemical caused per oxidative degradation in the adipose tissue resulting in fatty infiltration of the hepatocytes. The increase in the levels of serum enzymes AST, ALT and ALP was the clear indication of cellular leakage and loss of functional integrity of the cell membrane (12). Administration of methanolic extract of *P.corymbosa* showed significant hepatoprotective activity, which was comparable to that of standard silymarin. These findings can further corroborated with histopathological studies. The histopathological examination clearly reveals that the hepatic cells, fatty change, lymphocyte infiltration in PC (25mg/kg/bw.p.o) group in contrast to group which received CCl_4. Phytochemical analysis revealed that the methanolic extract of the plant was found to contain flavonoids and phenolic compounds further it has been reported that the flavonoid constituents of the plant possess antioxidant properties (13) was found to be useful in the treatment of liver damage (14). The administration of hepatoprotective drugs may induce the hepatocytes to resist the toxic effect of CCl_4. The results indicate that the methanolic extract of *P.corymbosa* has significant hepatoprotective activity. This may probably due to the content of flavonoids. The earlier investigation have screened the hepatoprotective acivity of the flavonoid compound, rutin (15) isolated from the *Artemisia scoparia*, which is also claimed to have free radical scavenging and antilipid peroxidant activities against CCl_4 induced hepatic toxicity.

Conclusion:

In view of the hepatoprotective potential of the extract of leaves of the plant, a comprehensive investigation on it is required to isolate the active fractions/chemicals, to elucidate the mechanism of action, to evaluate its efficacy and toxicity in other models for developing it as a safe and effective herbal hepatoprotective drug.

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