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Research Article

Hepatoprotective Activity of *Polyalthia longifolia* Leaves against Paracetamol Induced Hepatotoxicity in Rats

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Abstract: The present study was conducted to assess the hepatoprotective activity of ethanolic leaf extract of *Polyalthia longifolia* against paracetamol induced liver damage in rats. The ethanolic leaf extract of *Polyalthia longifolia* (400mg/kg) was administered orally to the animals with hepatotic damage induced by paracetamol (3gm/kg). Silymarin (25mg/kg) was given as reference standard. All the test drugs were administered orally by suspending in 0.5% Carboxy methyl cellulose solution. The plant extract was effective in protecting the liver against the injury induced by paracetamol in rats. This was evident from significant decrease in serum enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin. It was concluded from the result that the ethanolic leaf extract of *Polyalthia longifolia* possesses hepatoprotective activity against paracetamol induced hepato toxic in rats.
Keywords: *Polyalthia longifolia*, Paracetamol, Hepatoprotetive, Hepatotoxicity

INTRODUCTION

Hepatic damage is still a worldwide health problem. Unfortunately, conventional or synthetic drugs used in the treatment of liver diseases are inadequate and sometimes can have serious side effects [1]. In the absence of a reliable liver protective drug in modern medicine there are a number of medicinal preparations in Ayurveda recommended for the treatment of liver disorders [2]. In view of severe undesirable side effects of synthetic agents, there is growing focus to follow systematic research methodology and to evaluate scientific basis for the traditional herbal medicines that are claimed to possess hepatoprotective activity. *Polyalthia longifolia* cv. *pendula* (Annonaceae) is native to the drier regions of India and is locally known as "Ashoka" and is commonly cultivated in India, Pakistan, and Sri Lanka. *P. longifolia*, although an ornamental tree, finds its reference in Indian medicinal literature owing to its popular Hindi name Ashoka. Ashoka (Latin name: *Saracaasoka* (Roxb) De Wilde) is also a Sanskrit name in Ayurveda of a drug used for the treatment of uterine disorders [3]. The Annonaceous plants are well known as folk medicines for the treatment of septic infections, coughing, hepatomegaly, hepatospleenomegaly, diarrhea, and cancers[4]. Pharmacologic studies on the bark and leaves of this plant display effective skin disease, antimicrobial activity[5], cytotoxic function[6] and hypotensive effects [7].

The study was conducted to evaluate the traditional use of *Polyalthia longifolia* as hepatoprotective against paracetamol induced hepatotoxicity in rats.

MATERIAL AND METHODS

Plant material

The leaves of *Polyalthia longifolia* were collected from outskirts of Erode, in the month of May. The leaves of *Polyalthia longifolia* were identified and authenticated by the botanist, Botanical Survey of India, Agricultural University, Coimbatore. The (voucher no:92/614) specimen had been deposited in the herbarium for future reference.

Preparation of extract

100 g of powdered drug was soaked in 250 ml of 95% ethanol solution for 24 h followed by cold maceration for further 48 h with occasional shaking. The mixture was filtered using muslin cloth followed by removal of excess of solvent by means of rotatory evaporator. The dried extract was used for the study.

Animals

Male Wistar Albino rats weighing between 150–220 g were used for the study. The animals were obtained from animal house of Nandha College of Pharmacy, Erode, India. On arrival the animals were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at a temperature of 24 ± 2^{o}C and relative humidity of 30–70 %. A 12:12 light: dark cycle was followed. All animals were allowed free access to water and fed with standard commercial pelleted rat chaw (Hindustan Lever Ltd, Mumbai). All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (688/2/C-CPCSEA) and were in accordance with the guidelines of the CPCSEA.

Hepatoprotective Activity

A total of 24 animals were equally divided into 4 groups of six each. Group – I served as normal control received 0.5% (CMC) carboxy methyl cellulose solution (1 ml/kg) once daily for 3 days. Group – II served as paracetamol control, administered with paracetamol (3gm/kg) as single dose on day 3. Group – III received, *Polyalthia longifolia* extract (200 mg/kg) once daily for 3 days. Group – IV served as reference control, received Silymarin (25mg/kg) once daily for 3 days. Group III and IV received paracetamol (3gm/kg) as single dose on day 3, thirty minutes after the administration of *Polyalthia longifolia* and Silymarin respectively. All the test drugs and paracetamol were administered orally by suspending in 0.5% CMC solution. After 48h of paracetamol feeding, the blood was collected by direct cardiac puncture under light ether anesthesia and serum was separated for the estimations of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) [8, 9] and bilirubin [10].

Statistical analysis

Results were expressed as mean ± SEM. The data were analyzed by using one way analysis of variance (ANOVA) followed by Dunnet's t test. P values < 0.05 were considered as significant.

RESULTS

Table 1: Effect of *Polyalthia longifolia* on serum enzyme and bilirubin in Paracetamol induced hepatic damage in rats

Groups	Drug Treatment	Serum Enzymes (IU/L)			Bilirubin mg/dl
		ALT	AST	ALP	
I	Vehicle Control (0.5%) CMC	48.20± 2.66***	122.42± 5.69***	62.41± 2.22***	0.98± 0.06***
II	Paracetamol Control (3gm/kg)	186.35± 8.47	278.46± 12.53	301.08± 9.36	2.96± 0.27
III	*Polyalthia Longifolia* (200mg/kg)	120.38± 5.96**	188.62± 5.18**	164.62± 7.06**	1.66± 0.09***
IV	Silymarin (25mg/kg)	62.71± 43.54***	174.52± 7.33**	89.23± 6.12***	1.26± 0.07***

Values are in Mean ± SEM; (n = 6), *p < 0.05,**p < 0.01, *** p < 0.001 Vs Paracetamol Control

The results of hepatoprotective activity of ethanolic leaf extract of *Polyalthia longifolia* on Paracetamol treated rats are shown in Table 1. The hepatic enzymes ALT, AST, ALP and bilirubin in serum was significantly (P <0.001) increased in paracetamol treated animals when compared to control. The ethanolic leaf extract of *Polyalthia longifolia* treatments significantly reversed the levels of ALT, ASP, ALT ((P < 0.01) and bilirubin(P < 0.001) when compared to paracetamol alone treated rats. Silymarin (25 mg/kg) treated animals also showed significant decrease in ALT, ALP, bilirubin (P<0.001) and AST (P<0.01) levels when compared to paracetamol alone treated rats.

DISCUSSION

Paracetamol hepatotoxicity is caused by the reaction metabolite N-acetyl-p-benzo quinoneimine (NAPQI), which causes oxidative stress and glutathione depletion. It is a well-known antipyretic and analgesic agent, which produces hepatic necrosis at higher doses [11]. Paracetamol toxicity is due to the formation of toxic metabolites when a part of it is metabolized by cytochrome P-450. Introduction of cytochrome [12] or depletion of hepatic glutathione is a prerequisite for paracetamol induced hepatotoxicity [13].

Normally, AST and ALP are present in high concentration in liver. Due to hepatocyte necrosis or abnormal membrane permeability, these enzymes are released from the cells and their levels in the blood increases. ALT is a sensitive indicator of acute liver damage and elevation of this enzyme in non hepatic diseases is unusual. ALT is more selectively a liver paranchymal enzyme than AST [14]. Assessment of liver function can be made by estimating the activities of serum ALT, AST, ALP and Bilirubin which are enzymes originally present higher concentration in cytoplasm.

When there is heaptopathy, these enzymes leak into the blood stream in conformity with the extent of liver damage [15]. The elevated level of these entire marker enzymes observed in the group II, paracetamol treated rats in this present study corresponded to the extensive liver damage induced by toxin. The reduced concentrations of ALT, AST and ALP as a result of plant extract administration observed during the present study might probably be due to its anti oxidant property which was already reported [16].

Bilirubin is one of the most useful clinical clues to the severity of necrosis and its accumulation is a measure of binding, conjugation and excretory capacity of hypatocyte. Decrease in serum bilirubin after treatment with the extract in liver damage induced by paracetamol, indicated the effectiveness of the extract in normal functional status of the liver.

CONCLUSION

The results of above study concludes, that the ethanolic extract of *polyalthia longifolia* has protects the liver damage induced by paracetamol in rats. The probable mechanism of action may be due to its antioxidant property and further studies required on this to prove its exact mechanism of action as hepatoprotective.

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