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RESEARCH ARTICLE

HEPATOPROTECTIVE ACTIVITY OF *Premna serratifolia* Linn. ON EXPERIMENTAL LIVER DAMAGE IN RATS

Muthukumaran, P*. and Pattabiraman, K.

[1]Meenakshi Chandrasekaran Arts and Science College, Pattukkottai 614 601, Thanjavur, Tamilnadu, India
[2]Department of Siddha Medicine, Faculty of Science, Tamil University, Vakaiyur, Thanjavur - 613 010, Tamilnadu, India.

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The aqueous extract of *Premna serratifolia* Linn (Verbenaceae), was tested for hepatoprotective activity against carbon tetrachloride- and paracetamol-induced hepatotoxicity in rats. *Premna serratifolia* Linn (Verbenaceae), exhibited significant hepatoprotective activity by reducing carbon tetrachloride- and paracetamol-induced change in bio-chemical parameters that was evident by enzymatic examination. The plant extract may interfere with free-radical formation, which may conclude in hepatoprotective action. Acute toxicity studies revealed that the L [D.sub.50] value is more than the dose of 4 g/kg body wt.

Key words: *Premna serratifolia* Linn (Verbenaceae), Carbontetrachloride; Paracetamol

INTRODUCTION

Premna serratifolia Lin., is having an important place in such cardiovascular medicinal herbs (Yoganarasimhan, 2000) and its synonym is *Premna integrifolia* Lin. It is known as "Munney" in Tamil, "Agnimantha" in Ayurveda and used as cardiotonic, antibiotic, anti hyperglycemic (Natkarni, 1976). It is widespread throughoutMicronesia and tropical Asia. Root forms an ingredient in well known Ayurvedic formulation "Dasamula" for variety of affections (Anonymous, 1972). It has shown anticoagulant activity (Gopaland Purushothaman, 1984) and the decoction exhibited anti inflammatory and antiarthritic activity (Rathore *et al*., 1977). However, its cardiotonic activity has not been investigated still now. Hence it was considered to evaluate the cardio active potential and its mechanism of action. Preliminary phytochemical studies revealed the presence phytochemicals like flavanoids, alkaloids, triterpenoids in the alcoholic extract. The present study was carried out to determine the effect of the aqueous extract of the herb on experimental liver damage induced by carbon tetrachloride and paracetamol.

***Corresponding author:** muthubabi_p@yahoo.co.in*

MATERIALS AND METHODS

Plant material : The leaves of *Premna serratifolia* Linn (Verbenaceae), used in this study were collected from Madurai, Tamil Nadu, during the month of March-April where a voucher specimen has been preserved for future identification. The leaves were shade dried and powdered. Two hundred grams of the powdered leaves were extracted with distilled water and filtered. The filtrate was dried by vacuum rotary evaporation to yield a solid residue of 12.4 g (yield, 6.2%).

***Animals* :** Wistar albino rats (150-200 mg each) of either sex, maintained under standard animal housing conditions (12 h light and dark cycle), were used for all sets of experiments performed on eight rats each. The rats were allowed standard laboratory feed and water ad libitum.

Acutetoxicity: The leaf extract was administered to the test groups in graded doses ranging up to 4 g/kg body wt. and the rats were observed for signs of toxicity and mortality for 48 h afterward (Jayasekar *et al.*, 1997).

Hepatoprotective activity

Carbon tetrachloride-induced experimental liver damage : The aqueous extract of *Premna serratifolia* Linn (Verbenaceae), leaf extract at doses of 100 mg and 200 mg/kg body wt. and silymarin at a dose of 100 mg/kg body wt. were administered orally to rats of the respective groups three times at 12 h intervals. Control animals received vehicle. Carbon tetrachloride diluted with liquid paraffin (1:1) was administered in a dose of 1 ml/kg body wt. for 2 days to all animal groups except for control (Rao and Mishra, 1998). Animals of the untreated group received only C[Cl.sub.4], to assist assessing the severity of toxicity produced by carbon tetrachloride administration. After 36 h of carbon tetrachloride treatment, blood was collected from all groups of rats by puncturing the retro-orbital plexus. Serum was separated by centrifugation at 2500 rpm at 37[degrees]C for 15 min and analyzed for various biochemical parameters.

Paracetamol-induced experimental liver damage : In case of paracetamol-induced hepatotoxicity, the *Premna serratifolia* Linn (Verbenaceae), leaf extract (at doses of 100 and 200 mg/kg body wt.) and silymarin (100 mg/kg) were given orally to respective groups once daily for 3 days. On the third day, paracetamol at 3 g/kg body wt. was administered to all groups except for control, 30 min after the respective treatment with *Premna serratifolia* extract, silymarin and vehicle (Rao and Mishra, 1997). One group received only paracetamol to assist in assessing the severity of toxicity produced by paracetamol at 3 g/kg body wt. After 48 h of paracetamol administration, blood was collected from all groups, including control, and serum was separated and analyzed for various biochemical parameters as in the case of carbon tetrachloride-induced liver damage.

Assessment of liver functions: Biochemical parameters, such as serum glutamic oxaloacetate Transaminase, serum glutamic pyruvate transaminase (Reitman and Frankel, 1975), alkaline phosphate (Kind and King, 1972), total bilirubin, direct bilirubin (Mally and Evelyn, 1937) and liver glutathione (Ellman, 1959), were analyzed according to the standard method.

Statistical analysis : The mean value [±] SEM was calculated for each parameter. Results were statistically analyzed by student's' test (Snedecor and Cochran, 1967). $P < 0.01$ indicates significant differences between group means.

Table 1. Effect of an aqueous extract of *Premna serratifolia* leaves on carbon tetrachloride-induced hepatotoxicity in rats

Design of treatment	SGOT	SGP	ALKP	T. Bil	D. Bil	GSH
Control	127.43±2.33	62.16± 1.78	139.74±6.21	1.01±0.20	0.18±0.01	10.64±0.76
Carbon tetra-chloride	823.45±7.31(a)	27.00± 8.20 (a)	438.61±8.21(a)	3.66±0.38(a)	1.60±0.30(a)	6.72±0.54(a)
Silymarin	152.22±3.10(b)	65.34±2.00 (b)	163.81±4.28(b)	0.96±0.05(b)	0.24±0.02(b)	8.81±0.64(b)
P.serratifolia (100 mg/kg body wt.)	363.41±8.21(b)	288.41±5.16(b)	266.52±7.68(b)	1.96±0.22(b)	0.72±0.04(b)	8.08±0.52(b)
P.serratifolia (200 mg/kg body wt.)	291.76±6.98(b)	212.56±6.78(b)	232.91±6.28(b)	1.66±0.56(b)	0.52±0.04(b)	8.66±0.33(b)

Values are mean [±] S.E.; n = 8; (a) $p < 0.01$ compared to control;
(b) $P < 0.01$ compared to carbon tetrachloride.

Table 2. Effect of an aqueous extract of *Premna serratifolia* leaves on paracetamol-induced hepatotoxicity in rats

Design of treatment	SGOT	SGPT	ALKP	T. Bil	D. Bil	GSH
Control	112.69±6.18	48.06±2.63	122.36±6.13	1.04±]0.16	0.23±0.02	10.38± .89
Paracetamol	376.22±3.0(a)	294.28±3.18(a)	338.31±1.50(a)	3.66±0.20(a)	0.80±0.04(a)	3.91±0.76(a)
Silymarin	118.66±12.34(b)	46.08± 1.18(b)	93.2±3.72 (b)	1.07±0.08(b)	0.26±0.01(b)	8.02±0.42(b)
P.serratifolia (100 mg/kg body wt.)	271.24± 4.24 (b)	65.14± 6.10(b)	173.09±5.09(b)	1.63±0.17(b)	0.40±0.04(b)	7.22±0.61(b)
P.serratifolia (200 mg/kg body wt.)	253.21± 6.24 (b)	62.41± 5.14(b)	161.22±4.75(b)	1.44±0.16(b)	0.36±0.02(b)	7.88±0.44(b)

Values are mean [±] S.E.; n = 8; (a) $p < 0.01$ compared to control;
(b) $P < 0.01$ compared to paracetamol.

RESULTS

The aqueous leaf extract of *Premna serratifolia* Linn (Verbenaceae), was found to be practically nontoxic

when administered orally to rats and its L [D.sub.50] value was found to be higher than 4 g/kg body wt. Administration of carbon tetrachloride and paracetamol to rats caused significant liver damage, as evidenced by the altered serum biochemical parameters. Pretreatment of rats with *Premna serratifolia* Linn (Verbenaceae), aqueous extract exhibited marked protection against carbon tetrachloride- and paracetamol-induced hepatotoxicity, which is shown in Tables 1 and 2, respectively. The aqueous extract of *Premna serratifolia* Linn (Verbenaceae), showed significant hepatoprotective activity against carbon tetrachloride and paracetamol, comparable with the standard silymarin.

DISCUSSION

Hepatic cells appear to participate in a variety of enzymatic metabolic activities and both carbon tetrachloride and paracetamol produced marked liver damage at the given doses as expected (Roderick *et al.*, 1989; Kenneth *et al*., 1992). Administration of carbon tetrachloride elevated the serum levels of SGOT, SGPT, ALKP and bilirubin significantly, due to its enzymatic activation of C[Cl.sub.3] free radical, which in turn alters the structure and function of liver cells (Singh *et al.*, 1998). Pretreatment with *Premna serratifolia* Linn (Verbenaceae), aqueous extract showed a dose-dependent protection against the injurious effects of carbon tetrachloride that may result from the interference with cytochrome [P.sub.450] resulting in the hindrance of the formation of hapatotoxic free radicals (Sharma *et al.*, 1994; Nadeem *et al.*, 1997). Paracetamol in larger doses produces liver necrosis after undergoing bio-activation to a toxic elcctrophile, N-acetyl-p-benzo-quinone-imine (NAPQI)by cytochrome [P.sub.450] monooxygenase (Dahlin *et al*., 1984). NAPQI binds to macromolecules and cellular proteins, and also oxidizes lipids and alters homeostasis of calcium after depletion of glutathione. Pretreatment with aqueous *Premna serratifolia* extract restored the depleted GSH Concentration near normalcy and also brought down the elevated levels of SGOT, SGPT, ALKP and bilirubin. These biochemical restorations may be due to the inhibitory effects on cytochrome [P.sub.450] or/and promotion of its glucuronidation (Wesley *et al.*, 1992; Gilman *et al.*, 1992). Further studies are in progress to isolate the active constituents and also to evaluate the exact mechanism of action.

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