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Research Article

Hepatoprotective Activity of *Gymnosporia emerginata* (Willd) and *Marsedenia volubillis* (Linn.F) Stapf Against Paracetamol Induced Hepatotoxicity in Rats

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ABSTRACT

The present study was conducted to evaluate the hepatoprotective activity of methanolic extracts of *Gymnosporia emerginata & Marsedenia volubillis* against paracetamol induced liver damage in rats. The methanolic extracts of G*ymnosporia emerginata* (300mg/kg) *and Marsedenia volubillis* (500 mg/kg) was administered orally to the animals with hepatotoxicity induced by paracetamol (3 gm/kg). Silymarin (25 mg/kg) was given as reference standard. All the test drugs were administered orally by suspending in 1% Tween-80 solution. The plant extract was effective in protecting the liver against the injury induced by paracetamol in rats. This was evident from significant reduction in serum enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and bilirubin. It was concluded from the result that the methanolic extract *Gymnosporia emerginata* and *Marsedenia volubillis* possesses hepatoprotective activity against paracetamol induced hepatotoxicity in rats.

Keywords: *Gymnosporia emerginata* and *Marsedenia volubillis*, Paracetamol, Hepatoprotective and Hepatotoxicity

INTRODUCTION

Liver disease 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

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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. *Gymnosporia emerginata* commonly known as "Thorny staff tree[3]**"** is a Decidecious tree, scandent shrub or small tree which grows endemically in seshachalam hill ranges, seshatheertham and kumaradhara theertham in Tirumala, India,belonging to the family*"Celastraceae"*.It contains Emarginatine G, F, Triterpenes, Sesqueterpenes alkaloids. It possess wide-reaching pharmacological actions, including anti-oxidant, anti-cancer, anti-asthmatic, anti-neoplastic, antimicrobial, anti-viral, antidote, anti-pyretic, cardio tonic, anti-inflammatory, diuretic and in the treatment of skin diseases like eczema, colitis and psoriasis.

Marsedenia volubillis is commonly known as "Green wax flower*"* which belongs to the family "Asclepiadaceae*"*is a Climbing and woody shrub. It contains β sitosterol, Kaempherol-3-galactoside and glycosides. It is reported for its antioxidant, antimicrobial and wound healing activity. Ethno medically, the leaves and stem bark of this plant were used by tribal for skin diseases, obesity[4] and in the management of cancer [5]. The study was conducted to establish the traditional use of *Gymnosporia emerginata and Marsedenia volubillis* as hepatoprotective against paracetamol induced hepatotoxicity in rats.

MATERIALS AND METHODS

Animals: Male wistar rats weighing between 150-220gm were used for this study. The animals were obtained from NIN, Hyderabad, India. 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°C and relative humidity of 30-70 %. A 12:12 light:day cycle was followed. All animals were allowed to free access to water and fed with standard commercial pelleted rat chaw. All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (IAEC) and were in accordance with the guidelines of the CPCSEA (No. 1447/po/a/11/CPCSEA).

Plant Materials: The fresh plants of *Gymnosporia emerginata and Marsedenia volubillis* were collectedfrom Sri Venkateshwara University, Tirupati, Andhra Pradesh, India, in June 2010[6].The plant was identified by a Botanist, Dr. K. MadhavaChetty, Assistant professor, Department of Botany and voucher specimen was deposited in Sri Venkateshwara University, Department of Botany and a copy has been preserved for the future reference at the herbarium of the institute TRRCP. After authentication, the plants were cleaned and shade dried and milled into coarse powder by a mechanical grinder.

Table 1: Effect of *Gymnosporia emerginata and Marsedenia volubillis* on serum marker enzymes (ALT, AST, ALP) and Total bilirubin on paracetamol induced hepatotoxicity in rats.

Group	Dose	ALT (µ/l)	AST (µ/l)	ALP(µ/l)	TB(µ/l)
Control	-	60 ±3.55	53.68±1.5	26.67±1.94	0.4±0.009
Paracetamol control	-	123.8 ± 3.89*	85.62±2.13*	110.5±6.04*	2.47±0.35*
MEGE	300mg/kg	43.5 ±1.78**	63.18±3.64**	46.5±3.11**	0.3±0.012**
MEMV	500mg/kg	42.33±2.15**	59.05±3.56**	23.67±2.18**	0.318±0.019**
Silymarin	25mg/kg	37.67±2.47	51.87±1.3	18.33±0.55	0.321±0.017*

*MEGE, Methanolic Extract of Gymnosporia emerginata, MEMV, Methanolic Extract of Marsedenia volubillis, Values are expressed as mean ± SEM for six rats in each group. *P<0.01 when compared to control. **P<0.01 when compared to paracetamol. @P<0.01 when compared to Silymarin.*

Preparation of Extract: The coarse powder plant material was defatted with petroleum ether (60-80°C) in a soxhlet extraction apparatus and marc wasextracted with methanol (1000 mL).Overnight, at room temperature with constant stirring. The extract was filtered and the filtrate was concentrated at 30°C under reduced pressure in a rotary evaporator. The crude extract was dissolved in 1% Tween 80 to required concentrations and used for the experiments.

Phytochemical constituents: Methanolic extract of Sophora interrupta was found to contain Matrine, Oxymatrine type of Alkaloids, Flavonoids, Saponins and Polysaccharides and methanolic extract of Holoptela integrefolia found to contain Carbohydrates, Proteins, and Amino acids, Steroids, Glycosides, Alkaloids, Tannins and Phenolics through literature.

Hepatoprotective Activity: A total of 30 animals were equally divided into 5 groups of six each. Group- I served as normal control received 1% Tween-80 (1 ml/kg) once daily for 3 days. Group- II served as paracetamol control, administered with paracetamol (3 gm/kg) as single dose on day 3. Group- III and IV received, *Gymnosporia emerginata* (300 mg/kg) *and Marsedenia volubillis* (500 mg/kg) once daily for 3 days. Group- V served as reference control, received Silymarin (25 mg/kg) once daily for 3days. Group-III, IVand V received paracetamol (3 gm/kg) as single dose on day 3, thirty minutes after the administration of *Gymnosporia emerginata and Marsedenia volubillis and Silymarin respectively. All the test drugs and* paracetamol were administered orally by suspending in 1% Tween-80 solution . After 48h of paracetamol feeding, the blood was collected by retro orbital artery bleeding under light ether

anesthesia and serum was separated for the estimations of Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP) and Bilirubin[7].

STATISTICAL ANALYSIS

The values were expressed as mean ± SEM. The statistical analysis was carried out by one way analysis of variance (ANOVA) followed by Dunnet's't' - test. P values <0.001 were considered significant.

RESULT

The results of hepatoprotective activity of methanolic extract of *Gymnosporia emerginata and Marsedenia volubillis* on Paracetamol treated rats are shown in Table I. The hepatic enzymes ALT (123.8 ± 3.89), AST (85.62 ±2.13), ALP (110.5 ± 6.04) and bilirubin (2.47 ± 0.35) in serum was significantlyincreased in paracetamol treated animals when compared to control. The methanolic extract of *Gymnosporia emerginata and Marsedenia volubillis* treatments significantly reversed the levels of ALT (43.5 ±1.78; 42.33±2.15), AST (63.18±3.64; 59.05±3.56) ALP (46.5±3.11; 23.67±2.18) and bilirubin (0.3±0.012; 0.318±0.019) when compared to paracetamol alone treated rats. Silymarin (25 mg/kg) treated animals also showed significant decrease in ALT (37.67 ± 2.47), AST (51.87 ± 1.3), ALP (18.33 ± 0.55) and bilirubin (0.321 ± 0.017) levels when compared to paracetamol alone treated rats.

DISCUSSION

Paracetamol hepatotoxicity is caused by the reaction metabolite N-acetyl-p-benzoquinoneimine (NAPQI), which causes oxidative stress and glutathione depletion. It is a well-known antipyretic and analgesic agent, which produces hepatic necrosis at higher doses[8]. Paracetamol toxicity is due to the formation of toxic metabolites when a part of it is metabolized by cytochrome P-450. Introduction of cytochrome[9] or depletion of hepatic glutathione is a prerequisite for paracetamol induced hepatotoxicity [10.] 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 parenchymal enzyme than AST[11].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 hepatopathy, these enzymes leak into the blood stream in conformity with the extent of liver

damage [12]. 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 concentration of ALT, AST and ALP as a result of plant extract administration observed during the present study might probably be due in part to the presence of flavonoids. Liver protective herbal drugs contain a variety of chemical constituents like phenols, coumarins, lignin's, essential oil, monoterpenes, carotenoids, glycosides, flavonoids, organic acids, lipids, alkaloids and xanthines [13]. 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 hepatocyte. Decrease in serum bilirubin after treatment with extract in liver damage induced by paracetamol, indicated the effectiveness of the extract in normal functional status of the liver.

CONCLUSION

The methanolic extract of *Gymnosporia emerginata and Marsedenia volubillis* extract has shown the ability to maintain the normal functional status of the liver. From the above preliminary study, we conclude that the methanolic extract of *Gymnosporia emerginata and Marsedenia volubillis*, is proved to be one of the herbal remedies for liver ailment.

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