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PROTECTIVE ACTIVITY OF *SEMECARPUS ANACARDIUM* FRUIT EXTRACTS AGAINST PARACETAMOL INDUCED HEPATIC DAMAGE IN WISTAR RATS

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ABSTRACT

The objective of the present investigation of hepatoprotective activity of various Fruit extract of *Semecarpus anacardium* in paracetamol induced liver damage model in Wistar rats. Liver damage was produced by paracetamol (2gm/kg, p. o.) in 1% CMC. The Plant extracts (200mg/kg, p. o.) were administered every 24 hrs for seven days, while standard group received N-acetyl l- cysteine. At the end of the study the marker enzymes in serum were analyzed. The aqueous as well as alcoholic extract showed significant hepatoprotective activity and efficacy of alcoholic extract was almost comparable to that of N-acetyl l-cysteine.

INTRODUCTION: Herbal medicines have recently attracted much attention as alternative medicines useful for treating or preventing life style related disorders and relatively very little knowledge is available about their mode of action. There has been a growing interest in the analysis of plant products which has stimulated intense research on their potential health benefits. The liver, because of its strategic anatomical location, is exposed to many kinds of xenobiotics and therapeutic agents.

Moreover, the rapidly increasing morbidity and mortality rates from liver diseases are largely attributable to the repeated chemical insult either from drug abuse or from environmental pollution. Unfortunately so far, in the modern era of medicine there is no specific treatment to counter the life threatening impact of these dreaded conditions [1, 2], though N- acetyl l-cystine can reverse the pathology due to paracetamol induced injury. Several plants have been investigated and reported to possess antioxidant property and hepatoprotective activity e.g., *Baliospermum montanum* [3], *Ocium sanctum* [4], *Tamarindus indica* [5] etc.

Similarly *Semecarpus anacardium* (Marking Nut) is a widely distributed plant throughout India, and is a popular folk medicine. The nuts are having anti-inflammatory activity, immunosuppressant activity [6, 7], Fruit extract has reported to have anticancer activity [8]. However hepatoprotective activity of *Semecarpus anacardium* fruits (false fruit) has not been scientifically investigated. Therefore, the present study is planned to investigate the effect of aqueous as well as other extracts of *Semecarpus anacardium* fruit in paracetamol induced liver damage in Wistar rats.

MATERIALS AND METHODS:

Preparation of *Commelina benghalensis* Extract: *Semecarpus anacardium* fruits were collected from local market of Belgaum city in the month of January were identified and authenticated by the taxonomist Dr. Harsha Hegde and the herbarium (voucher number-RMRC 470) has been preserved at Regional Medical Research Centre (Belgaum). Shade dried fruits were powdered to moderately coarse grade.

Petroleum ether, chloroform, alcohol & aqueous extracts of fruits were obtained by using soxhlet extractor. The extraction was continued for 12 cycles or until the solvent in the thimble has cleared. After evaporating the solvent, the dark brown semisolid extract was kept in an air tight container at 40c for future use. Suspensions of each extract were freshly prepared using 0.1% Tween 80, for experimental use.

Animals: The complete course of the experiment was carried out using healthy adult male Wistar rats obtained from registered breeders (Venkateshwara Enterprises) Bangalore and were maintained at the Animal House of the Institution. They were fed on commercial laboratory animal feed (Amrut brand, Sangli) and tap water *ad lib*. The rats weighing between 120-150 gm were housed for about a week for acclimatization with natural 12:12 hr light- dark cycle. The animals were

starved overnight with tap water *ad lib* prior to the day of experimentation. Ethical clearance was obtained from Institutional Animal Ethics Committee constituted as per CPCSEA guidelines.

Acute Toxicity Study: Acute toxicity studies were carried out for all the extracts as per OECD guideline 425 [9] in Swiss mice weighing 25 to 30 gm by administering a dose 2000 mg/kg orally. The groups were almost continuously observed for mortality and behavioural changes during first 24 hr and then daily for a fortnight. The oral LD_{50} was found to be more than 2000 mg/kg.

Drugs used and their Doses: In four groups (n=6, in each) of animals Alcoholic, aqueous, petroleum ether & chloroform extracts of fruits were administered with the dose of 200 mg/kg body wt. Fifth group received Liv- 52 5ml/kg body wt. [10]. While sixth group received N-acetyl L- cystine (Lobe chem.) 100 mg/kg body wt., seventh group and eighth group received equivalent volume of 1% CMC, Paracetamol 2gm/kg body wt. in 1% CMC was administered to all seven groups on fifth day [11]. All the treatments were administered orally.

Methodology: All the treatments were given for a total period of 7days, on the eighth day all the rats were anaesthetized by halothane to withdraw cardiac blood and the animals were sacrificed by over anaesthesia to dissect out liver for histopathological studies. Blood was allowed to coagulate for 30 min and serum was separated by centrifugation at 2500 rpm, to estimate alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein and bilirubin content [12].

Statistical analysis: The results were analysed by ANOVA followed by Dunnet's Posthoc test and $p \leq 0.05$ was considered as significant.

RESULTS: The groups treated with Paracetamol alone (positive control) showed significantly elevated level of ALT, AST, bilirubin and significantly decreased total protein content as compared to negative control(not challenged with paracetamol) animals. The animals treated with aqueous, alcoholic extract, Liv- 52 and N-acetyl L- cystine showed significant reduction in all the biochemical parameters. Aqueous, alcoholic extract, Liv- 52 though significantly lowered all the biochemical parameters as compared to only paracetamol treated group but failed to restore them to the normal level. In contrast, N- acetyls L-cystine restored the biochemical parameter to the normal level (Table 1).

DISCUSSION: Findings of the present study clearly indicates that both water and alcoholic extracts of *Semecarpus anacardium* showed significant hepatoprotective activity against paracetamol induced hepatic injury. Alcoholic extract appears to be better than aqueous extract since it significantly elevated total serum protein in contrast to aqueous extract. No similar reports could be traced in available literature. As expected N- acetyl L- cystine, a specific antidote for paracetamol hepatotoxicity totally restored the hepatic histology except sinus congestion.

TABLE 1: EFFECT OF *SEMECARPUS ANACARDIUM* IN PARACETAMOL INDUCED HEPATOTOXICITY

TREATMENT/GROUPS	BIOCHEMICAL PARAMETERS				
	AST (IU/L)	ALT (IU/L)	TOTAL PROTEIN (g/dl)	BILIRUBIN (mg/dl)	
				TOTAL	DIRECT
	MEAN ± SEM				
Normal	146.2 ± 1.26	92.25 ± 1.25	8.59 ± 0.17	0.42 ± 0.02	0.13 ± 0.05
Paracetamol Control	206.1 ± 6.48 #	172.4 ± 2.40 #	3.64 ± 0.16 #	0.89 ± 0.02 #	0.18 ± 0.02 #
Alcoholic Extract	155.3 ±3.09 ***	122.4 ± 2.32 ***	5.37 ± 0.14 ***	0.66 ± 0.01 ***	0.13± 0.01 ***
Aqueous Extract	189.3 ± 1.23**	157.02 ± 1.62**	5.32 ± 0.12	0.89 ± .01**	0.14 ± 0.01**
Chloroform Extract	211.8 ± 1.42	163.08 ± 1.92	4.36 ± 0.16	0.98 ± 0.01	0.17 ± 0.01
Pet. Ether	227.02 ± 4.90	169.07 ± 2.60	4.37 ± 0.17	0.96 ± 0.01	0.18 ± 0.01
Liv 52	150.8 ± 1.35 ***	123.3 ± 1.25 ***	5.60 ± 0.17 ***	0.79 ± 0.01 ***	0.13 ± 0.01***
N- acetyl L- Cystine	133.0±2.42***	153.8±1.79***	5.54±0.15***	0.61±0.02***	0.15±0.01***

ANOVA: *** p<0.001 considered significant as compared to Paracetamol control group
Students T test #; p<0.001 considered significant as compared to Normal control group. *** p<0.001 ** p<0.01

It is well known that N- acetyl L- cystine replenishes the glutathione stores of liver and prevents binding of the toxic metabolite to other cellular constituents, similarly Liv- 52 which contains the various herbal plants mainly *Capparis spinosa, Cichorium intybus, Solanum nigrum, Terminalia arjuna, Cassia occidentalis and Achillea millefolium* shows the hepatoprotective activity by the virtue of their antioxidant property and this is due to the presence of flavanoids, cynogenic glycosides and triterpenes [13,14]. *Semecarpus anacardium* fruit have been reported to contain bhiwanols, Biflavanoids semecarpuflavone, jeediflavanone) sterol and glycosides in addition to alkaloids, tannins, saponins etc., [15]. Jeediflavanone have been reported to posses' antioxidant activity [16], Hepatoprotection offered by *Semecarpus anacardium* extracts could be attributed to these constituents. Since antioxidants have been reported to posses Hepatoprotective activity [17], phytochemical analysis of alcoholic extract had flavonoids, sterols, aqueous extract showed the presence of flavonoids, while chloroform and pet. Ether extract showed only presence of carbohydrates and glycosides and no flavonoids and sterols, probably extracts in providing hepatoprotection.

The present study was not aimed to elucidate hepatoprotective mechanisms of *Semecarpus anacardium* extracts. In order to confirm their antioxidant potential and to identify various enzymes involved in generating oxygen free radicals further studies are essential.

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