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HEPATOPROTECTIVE ACTIVITY OF FERONIA ELEPHANTUM FRUIT EXTRACT AGAINST PARACETAMOL INDUCED HEPATIC DAMAGE IN WISTAR RATS

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ABSTRACT

The objective of the present investigation is to elucidate hepatoprotective activity of Methanolic Fruit extract of *Feronia elephantum* in paracetamol induced liver damage in Wistar rats. Liver damage was produced by paracetamol (2gm/kg,p.o.) in 1% CMC. The Plant extract (200mg/kg, p.o.) was administered every 24 hrs for seven days, while standard group received N-acetyl l-cystine. At the end of the study the marker enzymes in serum were analysed.The methanolic extract showed significant hepatoprotective activity and efficacy of extract was almost comparable to that of N-acetyl l-cystine.

Keywords: *Feronia elephantum;* Hepatoprotective; N-acetyl l-cystine; Paracetamol

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 eg. *Baliospermum montanum* [3], *Ocium sanctum* [4], *Tamarindus indica* [6] etc. Similarly *Feronia elephantum* is a widely distributed plant throughout India, and is a popular folk medicine. The fruit pulp of the plant has been reported in traditional medicine as a curative for various ailments such as diarrhea, pruritis, impotence, dysentery, heart disease, vomiting, and anorexia, and has also been used for the treatment of asthma and tumors, as a liver tonic and peptic ulcer [6]. Hetropolysaccharide from *Feronia elephantum* has reported to have anticancer activity [7]. However hepatoprotective activity of *Feronia elephantum* fruits has not been scientifically investigated. Therefore, the present study is planned to investigate the effect of methanolic extract

of *Feronia elephantum* fruit in paracetamol induced liver damage in Wistar rats.

Materials and methods

Preparation of *Feronia elephantum* Extract:

Feronia elephantum fruits were collected from Sangli city in the month of April were identified and authenticated by Prof. and the herbarium (voucher No.) has been preserved at R.L.S.College (Belgaum). Shade dried fruits were powdered to moderately coarse grade. Methanolic extract of fruits was obtained by using soxhlet extractor. The extraction was continued for 12 cycles or until the solvent in the thimble was clears. After evaporating the solvent, the greenish brown semisolid extract was kept in an air tight container at 40^0c for future use. Suspensions of extract was 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 g were housed for about a week for acclimatization with natural 12:12hr 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 [8] in Swiss mice weighing 25 to30gms by administering a dose 2000 mg/kg orally. The groups were almost continuously observed for mortality and behavioral changes during first 24hr and then daily for a fortnight. The oral LD50 was found to be more than 2000mg/kg.

Drugs used and their Doses:

In first group (n=6, in each) of animals methanolic extract of fruit was administered with the dose of 200mg/kg b.w. Second group received Liv52 5ml/kg b.w [9], while third group received N-acetyl L-cystine (Lobe chem.)100mg/kg b.w., fourth group and fifth groups received equivalent volume of 1%CMC, Paracetamol 2gm/kg b.w in 1% CMC was administered to all groups except fifth group (Normal Control) on fifth day [10]. 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 overanesthesia 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 billirubin content [11].

Statistical analysis:

The results were analysed by ANOVA followed by Tukey's multiple comparison 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, billirubin and significantly decreased total protein content as compared to negative control(not challenged with paracetamol) animals. The animals treated with methanolic extract, Liv52 and Nacetyl L-cystine showed significant reduction in all the biochemical parameters. Methanolic extract, Liv52 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)

Table No.1: Effect of *Feronia elephantum* in paracetamol induced Hepatotoxicity

Biochemical Parameters

Treatment/ groups	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 #
Methanolic Extract	148.3 ±2.19 ***	118.3 ± 1.12 ***	5.48 ± 0.12 ***	0.65 ± 0.01 ***	0.14± 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.

# $p<0.001$ considered significant as compared to Normal control group.

Discussion

Findings of the present study clearly indicate that methanolic extract of *Feronia elephantum* showed significant Hepatoprotective activity against paracetamol induced hepatic injury. 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. 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 triterpines. [12, 13]. *Feronia elephantum* fruit have been reported to contain flavanoids, sterol and glycosides in addition to alkaloids, tannins, saponnins etc. Hepatoprotection offered by *Feronia elephantum* extract could be attributed to these constituents. Since antioxidants have been reported to posses Hepatoprotective activity [14]. The present study was not aimed to elucidate hepatoprotective mechanisms of *Feronia elephantum* extract. In order to confirm their antioxidant potential and to identify various enzymes involved in generating oxygen free radicals further studies are essential.

REFERENCE

1. Chatterjee TK.Herbal Options. Calcutta: Books and Allied (P) Ltd; 2000:155.
2. Handa SS, Kapoor VK. International book of Pharmacognosy. New Delhi: Vallabh Prakashan; 1989:125.
3. Wadekar Raju Ratan, Supale Radhika Sachin, Tewari Kunal Mahesh, et al. Screening of roots of Baliospermum montanum for Hepatoprotective activity against paracetamol induced liver damage in albino rats. *Int J Greenpharmacy* 2008:220-223
4. Chattopadhay R.R.Sarkar S.K, Ganguly S.,et al.Hepatoprotective activity of Ocimum sanctum leaf extract against paracetamol induced hepatic damage in rats.*Indian J Pharmacol* 1992; 24: 163-165.
5. Pimple B.P., Kadam P.V., Badgujar N.S., et al, Protective effect of Tamarindus indica Linn against paracetamol induced Hepatotoxicity in rats. *Indian J Pharm Sci* 2006; 68:32-5.
6. Anurag Mishra, Sandeep Arora, Rajiv Gupta, Manvi, Rajesh Kumar Punia and Ashish Kumar Sharma. Effect of *Feronia elephantum* (Corr) Fruit Pulp Extract on Indomethacin-induced Gastric Ulcer in Albino Rats. Tropical Journal of Pharmaceutical Research 2009;8(6):509-514.
7. Saima Y,Das AK,SarkarKK et al,An antitumor pectic polysaccharide from Feronia limonia.*Int J Biol Macromol* 2000:27;233-235.
8. OECD Guidelines for Testing Chemicals, Guidelines 423, acute oral toxicity: Acute toxic class method. Paris: 1996.
9. Jalalpure S.S. Patil M.B, Prakash N.S, et al.Hepatoprotective activity of the fruits of Piper longum Linn. *Indian J Pharm Sci*.2003, 64(4):363-66.
10. Dhawan B.N, Patnaik G.K, Kulshreshtha D.K, et al,Absence of Hepatoprotective activity in Laqotis cashmitiana an adulterant to Picorohiza kurrooa. *Indian J Pharmac*,1991.23:121-2
11. Reitman S, Frankel S. A Colorimetirc method for the determination of serum glutamic oxaloacetate and glutamic pyruvic transaminase. *J Clin Pathol* 1957; 28:28-56.
12. Ali S.A., Al-Amin T.H, Mohamed A.H, et al.Hepatoprotective activity of aqueous and methanolic extracts of Capparis deciduas stem against carbon tetrachloride induced liver damage in rats. *J Pharmac toxicol* 2009.4:167-172.
13. Sultana Sarwat, Perwaiz Shahid, Iqbal Mohamed et al, Crude extracts of Hepatoprotective plants, Solanum nigrum and Cichorium intybus free radical-mediated DNA damage. *J Ethnopharm*, 1995.45.3:189-192.
14. Helieh S.Oz,Craig J.Mc Clain et al , Diverse antioxidants protect against acetaminophen hepatotoxicity, *J Biochem Mol Toxicol*,18,6:361-368.