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### Assessment of hepatoprotective activity of fruit pulp of *Feronia limonia* (Linn.) against paracetamol induced hepatotoxicity in albino rats

Arshed Iqbal Dar\*, R. C. Saxena and S. K. Bansal

Pest Control & Ayurvedic Research Lab. S.S.L Jain P.G College Vidisha (M.P)

#### ABSTRACT

To evaluate the hepatoprotective effect of the ethanolic extract of fruit pulp of *Feronia limonia* (Linn.) against paracetamol induced hepatotoxicity in albino rats. Albino rats of either sex weighing between 150-200 g were randomly assigned into six groups of six animals each. Group 1-Normal control: The animals were maintained as normal control, which were given distilled water only. Group 2- Induction of hepatotoxicity: The animals received paracetamol 500 mg/kg bw (p.o) at every 72 h for 10 Days. Groups 3 to 5: Animals received ethanolic extract of fruit pulp of *Feronia limonia* at 100, 200 & 300 mg/kg bw/day for 7 days (p.o). Group 6: The animals were treated with Silymarin (100 mg/kg p.o) which served as standard. Groups 3 to 6 were intoxicated with paracetamol (500 mg/kg bw) 1 h before the administration of extract or Silymarin for 10 days. Different hepatic biochemical parameters viz. AST, ALT, ALP, Total Bilirubin, Total cholesterol, Triglycerides & the body weights before & after treatment were evaluated to investigate the hepatoprotective activity. It was observed that in paracetamol intoxicated group; total cholesterol, total bilirubin, triglycerides, AST, ALT, ALP activities were significantly increased as compared to control group. Administration of 300 mg /kg bw of ethanolic extract of *Feronia limonia* L. effectively reduced these pathological damages caused by paracetamol intoxication. In addition to serum parameters treatment of 300 mg / kg bw of ethanolic extract of *Feronia limonia* L. also promotes the body weight in albino rats as shown in table 1 & 2 respectively. In spite of tremendous advances in modern medicine, there are not many effective drugs available that stimulate liver function, offer protection to the liver from damage or help to regenerate hepatic cells. It may be concluded that the ethanolic extract of *Feronia limonia* L. showed hepatoprotective activity against paracetamol induced hepatotoxicity in albino rats. Thus, in future this herbal formulation may be used as a strong hepatoprotective drug.

**Key Words:** - *Feronia limonia* L. hepatoprotective, paracetamol, silymarin.

#### INTRODUCTION

The curative properties of medicinal plants are mainly due to the presence of various complex chemical substances of different composition which occur as secondary metabolites [1, 2]. They are grouped as alkaloids, glycosides, flavonoids, saponins, tannins; carbohydrates & essential oils. Any part of the plant may contain active components [3]. The medicinal action of plants are unique to particular plant species or groups of plants and are consistent with this concept as the combination of secondary products in a particular plant is taxonomically distinct [4]. Arid and semi-arid plants are good sources for the production various types of secondary metabolites which include alkaloids, flavonoids, steroids, phenolics, terpenes, volatile oils, saponins, tannins, lignins and so many other metabolites.

*Feronia limonia* L. (Family Rutaceae) commonly known as Wood Apple or Kaitha & is widely distributed in most tropical & subtropical countries. This plant recently gained a great therapeutically relevance owing to their high coumarins & monoterpenoids content, which is explored for treatment of snake bite [5]. Fruits, leaves & stem bark of *Feronia limonia* L. have been studied for antitumor [6], larvicidal [7] & antimicrobial activity [8]. In India, the fruit is used as a stomachic, diuretic, cardiogenic & tonic to the liver & lungs. Some recent reports identified its use in gastrointestinal disorders. From the traditional knowledge it is very clear that the fruit pulp of *Feronia limonia* L. has the hepatoprotective activity. But still no scientific & methodical investigations have so far been reported in the literature regarding its hepatoprotective activity against paracetamol induced hepatotoxicity in albino rats. This is the reason the present study was undertaken to evaluate the hepatoprotective activity of fruit pulp of *Feronia limonia* L. against paracetamol induced hepatotoxicity in albino rats.

## MATERIALS AND METHODS

### 2. Experimental Design

#### 2.1. Plant Collection

The fruits of *Feronia limonia* used for the present study were collected from Vidisha district of MP in India. The fruit of the plant was identified, confirmed & authenticated by Prof. P. N. Srivastav, Department of Botany, S.S.L Jain P.G College Vidisha (MP). The herbarium specimen of the plant was kept in Herbarium of Pest Control & Ayurvedic Drug Research Lab. S.S.L Jain P.G College Vidisha, (MP). The fruits pulps were shade dried & pulverized.

#### 2.2. Preparation of Extract

The extraction of shade dried powder material of the plant was carried out by soxhlet apparatus using different solvents according to increasing order of polarity viz. n-hexane, Pet-ether, Chloroform, Ethyl acetate, Ethanol & distilled water. The extracts thus obtained were dried under reduced pressure yielding 4.24%, 2.98%, 0.4%, 1.42%, 1.25%, & 2.34% respectively.

#### 2.3. Animal model

Albino rats weighing between 150-200 g, bred in Animal House of Pest Control & Ayurvedic Drug Research Laboratory, were used for the study. The animals were procured & housed in the animal house maintained under standard hygienic conditions, at a temperature of  $25 \pm 1$  °C with  $50 \pm 10\%$  relative humidity & with a 12: 12 hr light / dark cycle. Food pellets (Hindustan lever Ltd. Mumbai, India) & tap water were provided *ad libitum*. Studies were performed in accordance with the CPCSEA guidelines. The animals were divided into six groups of six animals in each group. Group 1 served as normal control which received distilled water only. Group 2 served as paracetamol control & received paracetamol at a dose of 500 mg/kg bw (p.o) at every 72 h for 10 Days. Groups 3 to 5 received ethanolic extract of the fruit pulp of *Feronia limonia* at 100, 200 & 300 mg/kg bw/day for 7 days (p.o). Group 6 served as standard control & received Silymarin (100 mg/kg p.o). Groups 3 to 6 were intoxicated with paracetamol (500 mg/kg bw) 1 h before the administration of extract or Silymarin for 10 days.

#### 2.4. Biochemical investigation

Rats of all groups were anaesthetized using anesthetic ether, & blood collected by retro orbital puncture & biochemical parameters like ALT, AST, ALP, Total Bilirubin, Total Cholesterol, & Triglycerides were estimated. The animals were sacrificed by overdose of ether & autopsied [9]. Livers from all animals were removed, washed with ice cold saline, weighed. Small piece of liver tissue was collected & preserved in 10% formalin solution for histopathological studies. Livers of some animals were homogenized with ice-chilled 10% KCl solution & centrifuged at 2000 rpm for 10 min.

#### 2.5. Histological investigation

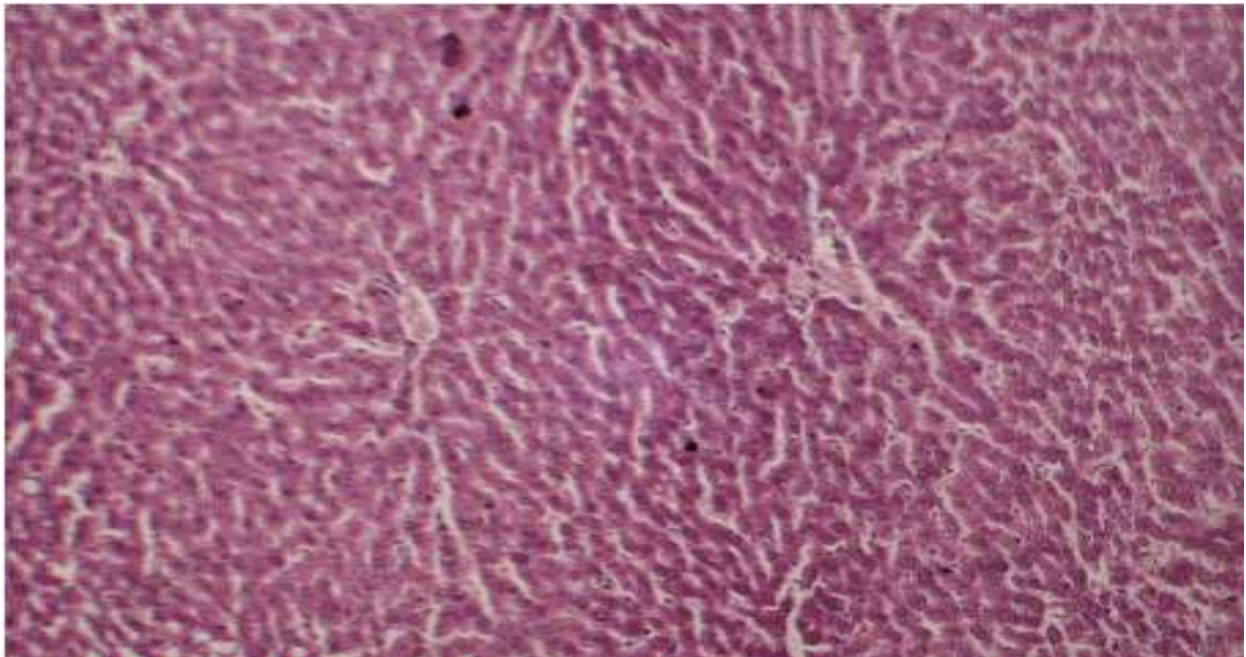
Liver slices fixed for 48 h in 10% formosaline were processed for paraffin embedding & sectioned at 5µm following the standard microtechnique. Sections were stained with Haematoxylin & Eosin & mounted in Canada balsam. Light microscopic examination of the sections was then carried out & micrographs produced using **Olympus BX-60 photographic microscope** at Jawaharlal Nehru Cancer Hospital & Research Centre. Bhopal.



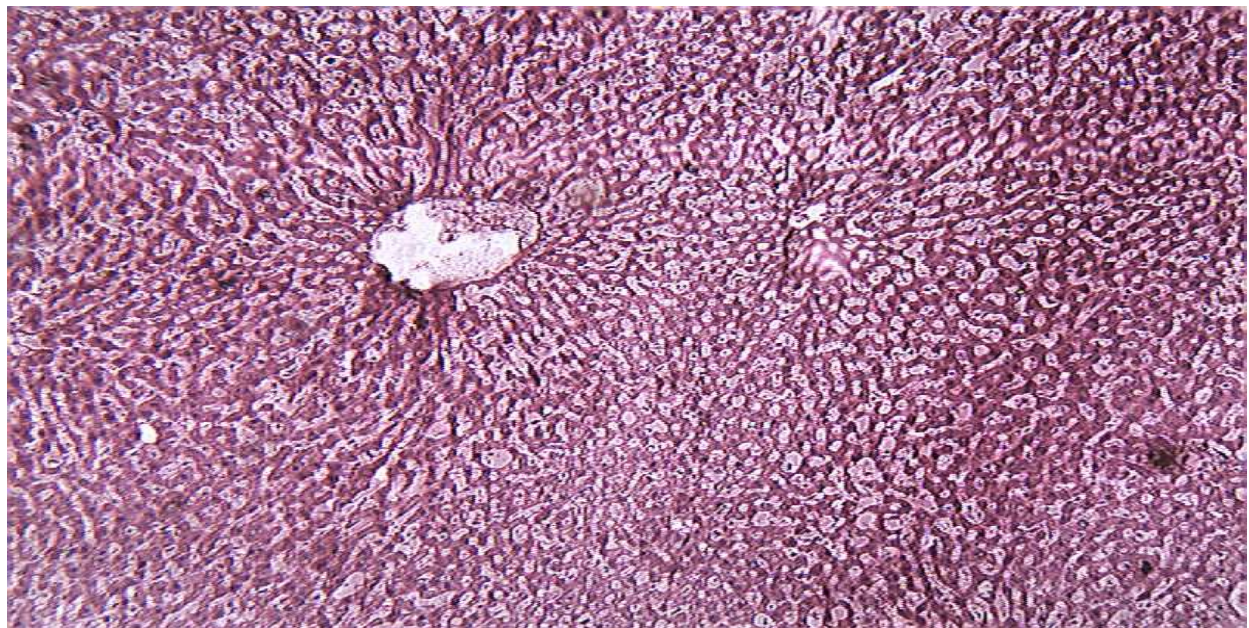
### 2.6. Statistical Analysis

Numerical data obtained from this study were expressed as the mean value  $\pm$  standard error of mean. Differences among the control & treatment groups were determined using statistical package (**Graph Pad Instant**). A probability level of less than 5% ( $p < 0.05$ ) was considered significant.

## RESULTS AND DISCUSSION

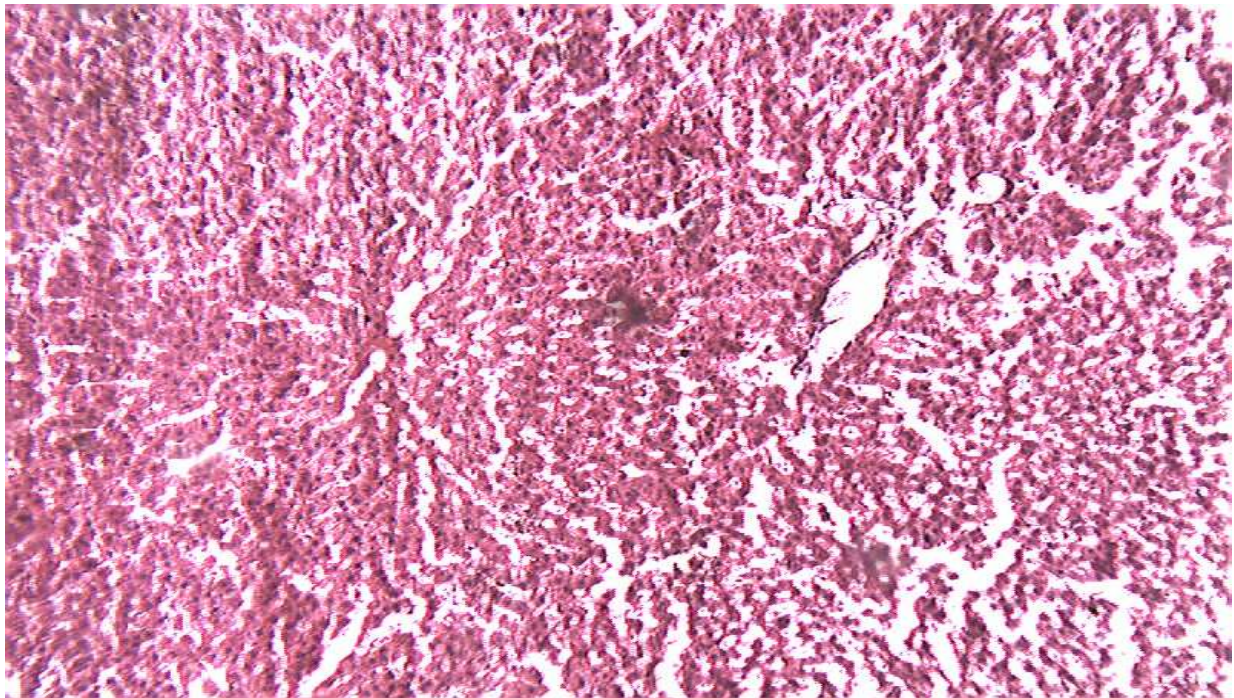


**Fig. A. Normal Control**

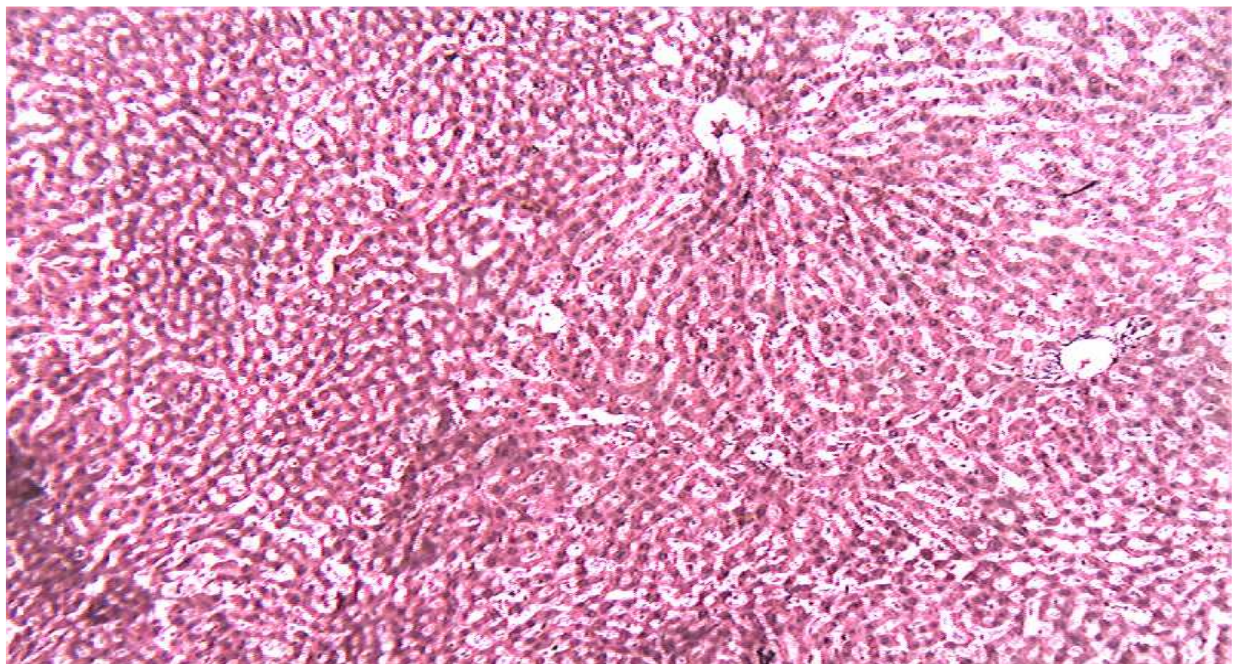


**Fig. B. Paracetamol treated**





**Fig. C.** Treated with 90% ethanolic extract of *Feronia limonia* L.



**Fig. D.** Treated with Silymarin

**Fig. E.** Effects of Ethanolic extract of fruit pulp of *Feronia limonia* L. on the body weight (before & after treatment) in albino rats.

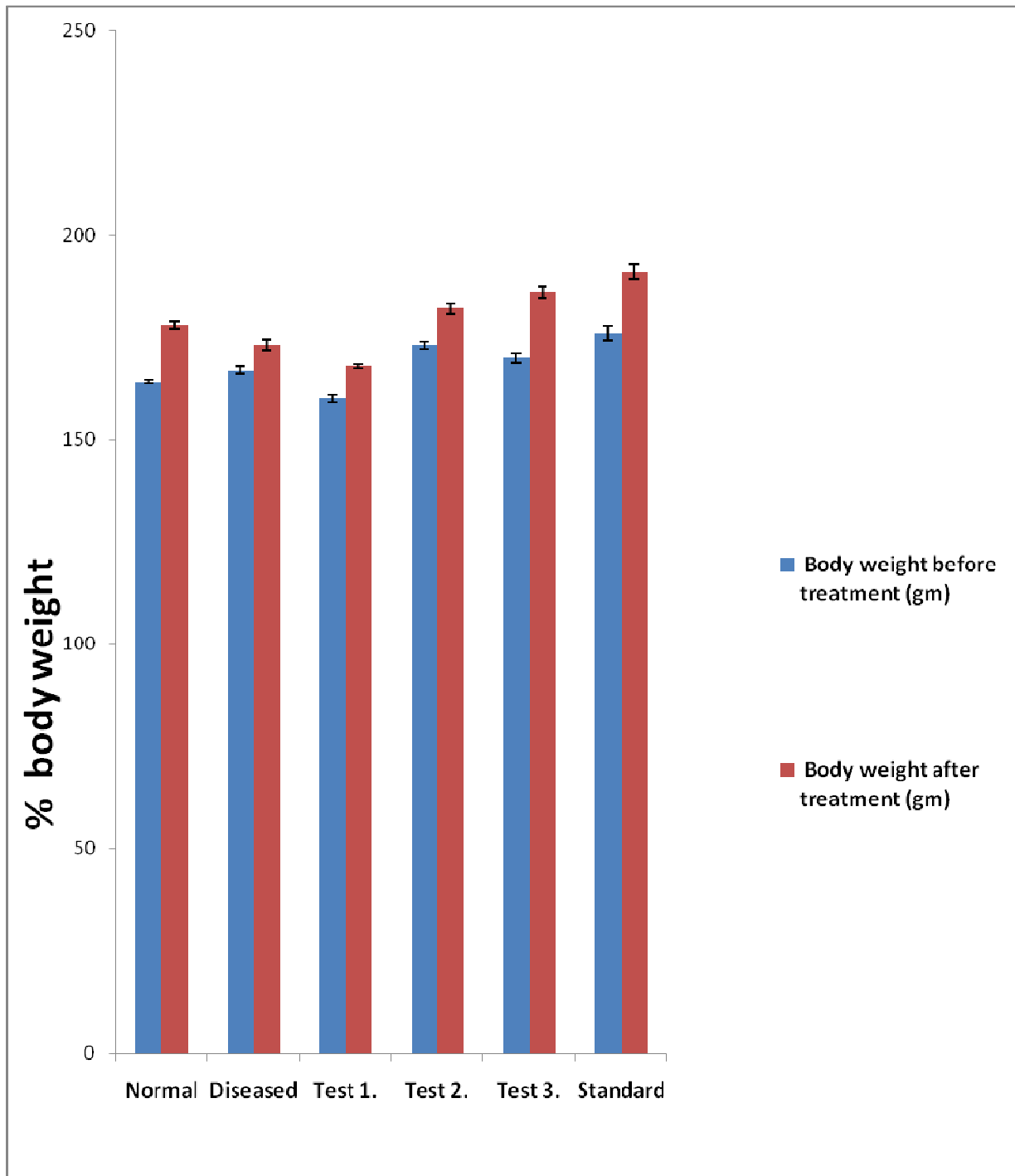
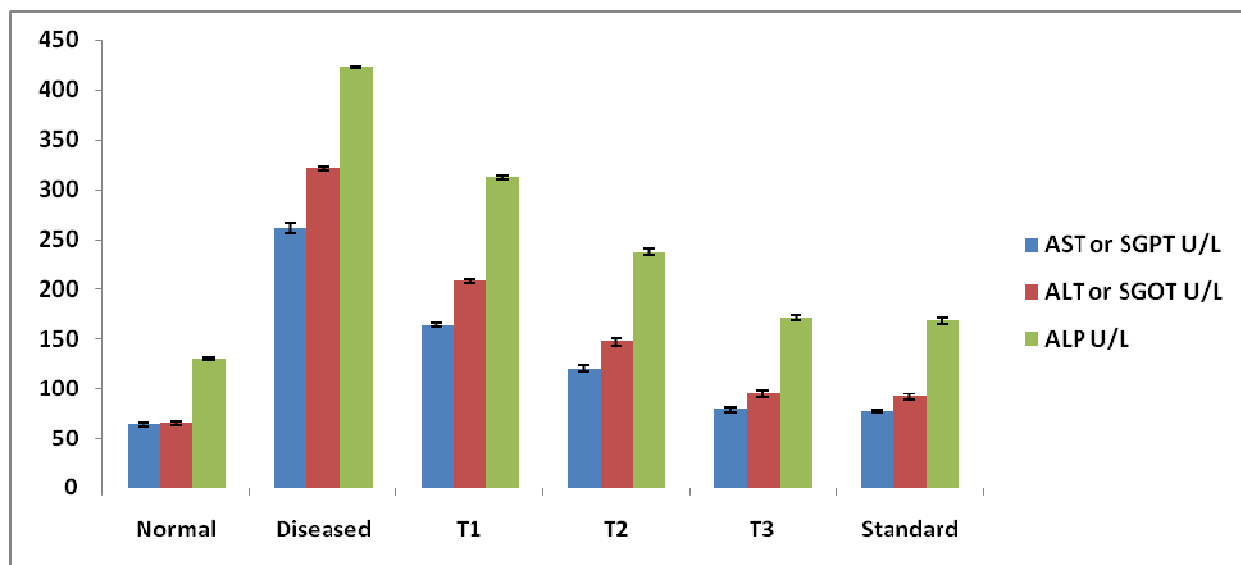
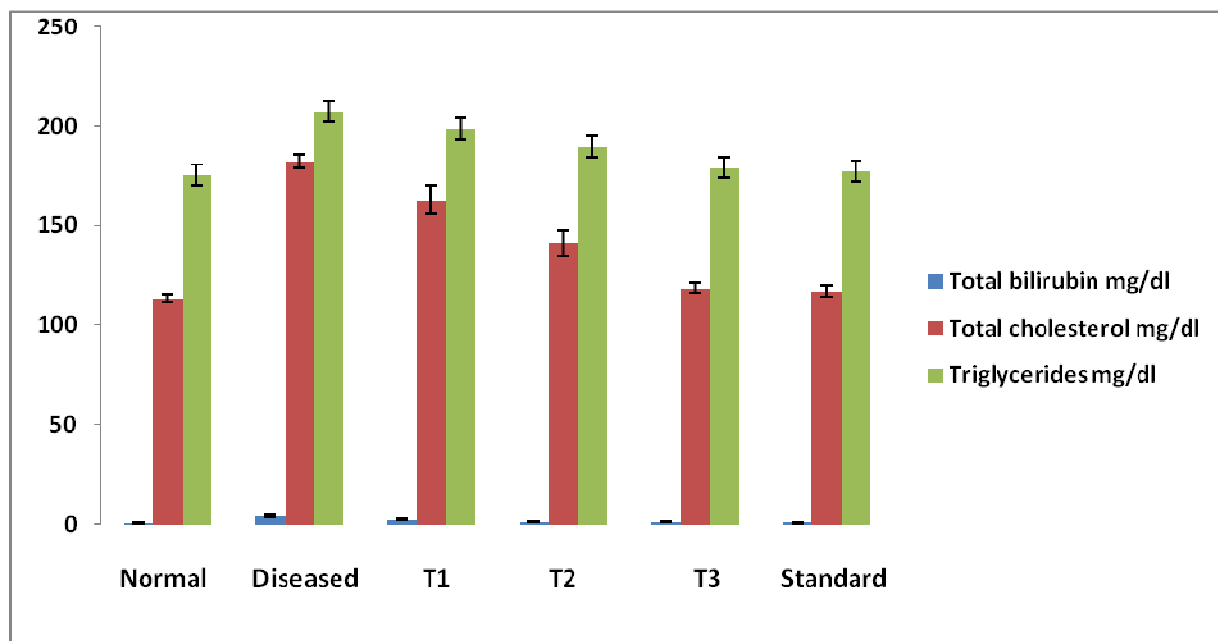


Fig. F. Effects of 90% Ethanolic extract of fruit pulp of *Feronia limonia* L. on biochemical markers in paracetamol induced hepatotoxicity in albino rats.

(A)



(B)



The present studies were performed to assess the hepatoprotective activity in rats against paracetamol as hepatotoxin to prove its claims in folklore practice against liver disorders. The extent of hepatic damage is assessed by histological evaluation & the level of various biochemical parameters in circulation. Paracetamol (N-acetyl-p-aminophenol) is a widely used analgesic & antipyretic drug & is safe when used in therapeutic doses. However, over dosage of paracetamol is known to be hepatotoxic & nephrotoxic in man & in experimental animals [10]. At lower doses, about 80% of ingested paracetamol is eliminated mainly as sulfate & glucuronide conjugates before oxidation & only 5% is oxidized by hepatic cytochrome P450 (CYP2E1) to a highly reactive & toxic electrophile i-e N-acetyl-p-benzoquinimine (NAPQI). After over dosage of paracetamol the glucuronidation & sulfation routes become saturated & as a consequence, paracetamol is increasingly metabolized into NAPQI [11]. In the present study the



damage of liver due to paracetamol over dosage was confirmed by elevated levels of biochemical parameters like AST, ALT, ALP, Serum bilirubin, total cholesterol, serum triglycerides. This is due to the fact that hepatic cells possess a variety of metabolic activities & contain a host of enzymes. SGPT, SGOT found in higher concentration in cytoplasm & SGPT particularly in mitochondria. In liver injury the transport function of hepatocytes is disturbed, resulting in the leakage of plasma membrane [12], thereby causing leakage of such enzymes leading to the increased serum levels of them. Treatment with 90% ethanolic extract of *Feronia limonia* decreased the elevated levels of AST, ALT which may be a consequence of the stabilization of plasma membrane as well as repair of hepatic tissue damage caused by paracetamol (Fig. F-A). This may be supported by a view that the healing of hepatic parenchyma & regeneration of hepatocytes [13]. Serum ALP & bilirubin levels on the other hand are related to the function of hepatic cell. Increased in serum ALP level is due to increased synthesis in presence of biliary pressure [14]. The extract shows dose dependent significant reduction in serum ALP & bilirubin, indicating an improvement in the secretory mechanism. Total cholesterol & serum triglycerides level also increased in paracetamol induced liver damage. Total cholesterol level increased may be due to the inhibition or destruction of triglycerides secretory mechanism by liver. 90% ethanolic extract of *Feronia limonia* significantly reduced the level of total cholesterol & serum triglycerides (Fig. F-B). Histological examination of the liver sections reveals that the normal liver architecture was disturbed by hepatotoxins intoxication which shows apoptotic hepatocytes & congested central veins (Fig. B). Treatment of rat with 90% ethanolic extract of *Feronia limonia* exhibit regenerative changes like normal appearance of hepatic cells with nucleus, less vacuolization & fatty change supplements the protective effect of the extract (Fig. C). However the results strongly suggest an initiation of the process of liver regeneration, which is also evident from the various biochemical parameter results. (Fig. E) showed the promotion of body weights after the treatment of 90% ethanolic extract of fruit pulp of *Feronia limonia* in albino rats.

The preliminary phytochemical studies revealed the presence of flavonoids in ethyl extract of *Feronia limonia* L. Various flavonoids have been reported for their hepatoprotective activity [15]. So the hepatoprotective effect of *Feronia limonia* L. may be due to its flavonoids content.

### CONCLUSION

In conclusion, the result of this study demonstrated that 90% ethanolic extract of *Feronia limonia* L. (300 mg/kg bw) shows significant hepatoprotective activity against paracetamol induced hepatotoxicity in albino rats. Hence the present study justified the traditional use of *Feronia limonia* L. in treatment of liver diseases.

### Acknowledgements

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