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PHARMACOLOGICAL ASSESSMENT OF *DELONIX REGIA* FLOWERS FOR HEPATOPROTECTIVE ACTIVITY AGAINST PARACETAMOL-INDUCED LIVER TOXICITY

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ABSTRACT

The objective of this study is to assess hepatoprotective activity of ethanolic extract of *Delonix regia* flowers (EEDRF) against Paracetamol induced hepatotoxicity in Rats. The toxicity were induced in rats by paracetamol 2g/kg orally, in four groups of rats (two test, standard and toxic control). Two test groups received EEDRF at doses of 250 mg/kg and 500 mg/kg. Standard group received silymarin (100 mg/kg) and toxic control received only Paracetamol. Control group received only vehicle. On 7th Day animals were sacrificed and liver enzymes like Serum glutamate pyruvate transaminase (SGPT), Serum glutamate oxaloacetate transaminase (SGOT), Serum alkaline phosphatase (ALP), Serum total and direct bilirubin were estimated in blood serum and *invivo* antioxidant enzymes like Tissue Glutathione (GSH), lipidperoxidation(LPO) and superoxide dismutase(SOD) were estimated in tissue homogenate. The ethanolic extract produced significant reduction in SGPT, SGOT, ALP, total and direct bilirubin, LPO levels and significantly increased the depleted GSH and SOD levels as compared with Paracetamol group. This is further confirmed by histopathological studies. The results of the present study reveal that EEDRF has contributed to the reduction of oxidative stress and the protection of liver in experimental animals.

KEYWORDS: *Delonix regia***,** Paracetamol, Silymarin**,** hepatoprotective, Lipid peroxidation.

INTRODUCTION

Liver is one of the prime organ in human body, the chief site for intense metabolism and excretion.[1] So it has a surprising role in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction.[2] The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. Thus, to maintain a healthy liver is a crucial factor for overall health and well being.[3-4] Liver damage ranges from acute hepatitis to hepatocellular carcinoma, through apoptosis, necrosis, inflammation, immune response, fibrosis, ischemia, altered gene expression and regeneration.[5] Liver damage is always associated with cellular necrosis, increase in lipid peroxidation and depletion in the tissue GSH level. In addition serum levels of many biochemical markers like SGOT, SGPT, ALP and bilirubin levels are elevated.[6] Due to the limited prevention and treatment options, liver diseases are considered to be one of the most serious health problems in the World.[7] Exposure of the liver to the free radicals derived from some xenobiotics and drugs leads to oxidative stress, which is recognized to be an important factor responsible for liver injury or be involved in the pathogenesis of liver disorders.[8-9] The common causative agents of liver injuries are toxic chemicals (e.g., CCl_4 aflatoxin etc.), therapeutic agents (e.g., antibiotics, anti-tubercular drugs, NSAIDs etc.), alcohol and microbial agents (e.g., hepatitis virus, leptospira, malarial parasites).[10] Antioxidant is a molecule which terminates the chain reaction by removing the free radical intermediates. Plants and animals maintain complex system of multiple type of antioxidant.[11] Modern medicines have little to offer for alleviation of hepatic diseases and it is chiefly the plant based preparations which are employed for their treatment of liver disorders. But there are not much drug available for the treatment of liver disorders.[12-13]

In recent years, the usage of herbal drugs for the treatment of liver diseases as increased all over the world. The herbal drugs are believed to be harmless and free from serious adverse reactions, as they are obtained from the nature, and are easily available.[10] However there are several herbs/herbal formulations claimed to possess beneficial activity in treating hepatic disorders.[5] Therefore some of the plants origins are tested for its potential hepatoprotective activities in animal models.

The plant *Delonix regia* (family: leguminosae, sub family: fabaceae) some time known as royal Poinciana, may flower plant or Flamboyant. In India it is known as Gulmohar (Hindi

'Gul' means 'Flower' and 'Mohr' is 'coin or stamp' also "Gul" means flower and "Mor" means "Peacock"). It as many branches, broad, spreading, flat crowned deciduous tree and well known for its brilliant display of red-orange bloom, literally covering the tree from May to June.[14]

The present study was performed to assess the hepatoprotective activity of ethanolic extract of *Delonix regia* flowers (EEDRF) against Paracetamol induced hepatotoxicity in Rats.

MATERIALS AND METHODS

Collection of material and preparation of extract: The plant material was collected and the dried powder of flowers were defatted with petroleum ether, chloroform and then extracted with 70% ethanol using soxhlet apparatus.

Animals: *Wistar albino rats* (weighing 150-250g) and *albino mice* (weighing 20-25g) of either sex were used in this study for hepatoprotective activity and acute toxicity studies respectively. The experimental protocol was approved by Institutional Animal Ethics Committee.

Experimental Design[15]

Healthy albino Wistar rats were randomly assigned to 5 different groups having six animals in each group in all the models.

The toxicity were induced in rats by paracetamol 2g/kg orally, in four groups of rats (two test, standard and toxic control). Two test groups received EEDRF at doses of 250 mg/kg and 500 mg/kg. Standard group received silymarin (100 mg/kg) and toxic control received only Paracetamol. Control group received only vehicle. On 7th Day animals were sacrificed and liver enzymes like Serum glutamate pyruvate transaminase (SGPT), Serum glutamate oxaloacetate transaminase (SGOT), Serum alkaline phosphatase (ALP), Serum total and direct bilirubin were estimated in blood serum after centrifugation and *invivo* antioxidant enzymes like Tissue Glutathione (GSH), lipidperoxidation(LPO) and superoxide dismutase(SOD) were estimated in tissue homogenate. The tissue is stored in 10% formalin and preceded for histopathology to evaluate the details of hepatic architecture in each group microscopically.

RESULTS

Paracetamol treated rats showed a significant increase in serum marker enzymes like SGPT, SGOT, ALP, total bilirubin, direct bilirubin, LPO levels and there is marked depletion of tissue GSH and SOD levels when compared with control. Silymarin and 70% ethanolic extract pretreated rats showed significantly decreased levels of serum marker enzymes, restoration of tissue GSH and SOD and inhibition of lipid peroxidation levels when compared with the hepatotoxicants treated rats. The effects are statistically significant in a dose dependent manner. The histopathological studies confirm the results. The results are summarized in table 1 and 2 and Fig 1-5.

Table 1: Effects of 70% EEDRF on biochemical markers in paracetamol induced hepatotoxicity

Treatment	Biochemical parameters Mean ± SEM				
	SGOT U/L	SGPT U/L	ALP IU/L	Total Bilirubin mg/dl	Direct Bilirubin mg/dl
Negative Control (1ml vehicle)	192.21±8.03	80.65±2.83	266.93±08.96	0.84±0.06	0.15±0.007
Positive Control Paracetamol (2 g/kg p.o.)	274.0±0.67	234.8±0.48	401.4±1.16	2.60±0.05	0.84±0.024
Paracetamol + Standard (Silymarin) (2 g/kg p.o.+ 100 mg/kg p.o.)	96.34±3.85***	104.94±4.83***	133.48±3.95***	0.88±0.02**	0.35±0.026***
Paracetamol + 70% ethanolic extract (2 g/kg p.o. + 250 mg/kg p.o.)	143.28±21.13***	183.46±17.70**	243.25±7.01***	2.05±0.39**	0.38±0.10***
Paracetamol+ 70% ethanolic extract (2 g/kg p.o. + 500 mg/kg p.o.)	138.4±12.52***	166.5±8.69***	201.33±9.13***	1.58±0.44**	0.36±0.049***

Values are the mean ± S.E.M. of six rats/ treatment.

Significance *P <0.05, **P <0.01 and *** P<0.001, compared to paracetamol treatment.

Table 2: Effect of EEDRF on tissue GSH, lipid peroxidation and Superoxide dismutase in paracetamol induced hepatotoxicity in rats

Groups	Tissue GSH Absorbance Mean ± SEM	Lipid peroxidation Absorbance Mean ± SEM	Superoxide dismutase Absorbance Mean ± SEM
Negative Control (1ml vehicle)	0.371 ± 0.039	0.171 ± 0.039	0.551 ± 0.088
Positive Control Paracetamol (2 g/kg p.o.)	0.152 ± 0.017	0.615 ± 0.041	0.279 ± 0.023
Paracetamol + Standard (Silymarin) (2 g/kg p.o. + 100 mg/kg p.o.)	0.299 ± 0.018***	0.204 ± 0.018**	0.540 ± 0.044**
Paracetamol + 70% EEDRF (2 g/kg p.o. + 250 mg/kg p.o.)	0.201 ± 0.018***	0.502± 0.030***	0.387 ± 0.023***
Paracetamol + 70% EEDRF (2 g/kg p.o. + 500 mg/kg p.o.)	0.247 ± 0.012***	0.397 ± 0.030***	0.438 ± 0.020***

Values are the mean ± S.E.M. of six rats /treatment.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ as compared to positive control.

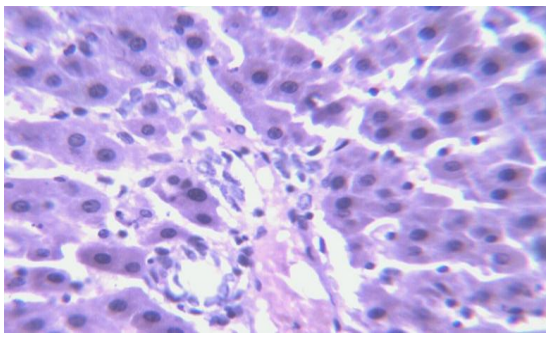

Fig. No. 1: Liver architecture of Normal Control

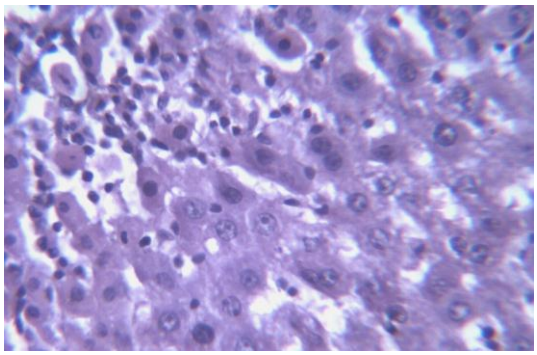

Fig. No. 2: Liver architecture of PCM treatment

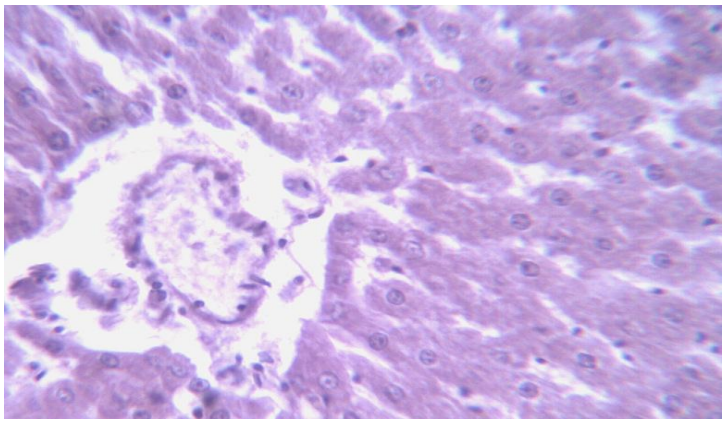

Fig. No. 3: Liver architecture of PCM + 100 mg/kg Silymarin treatment

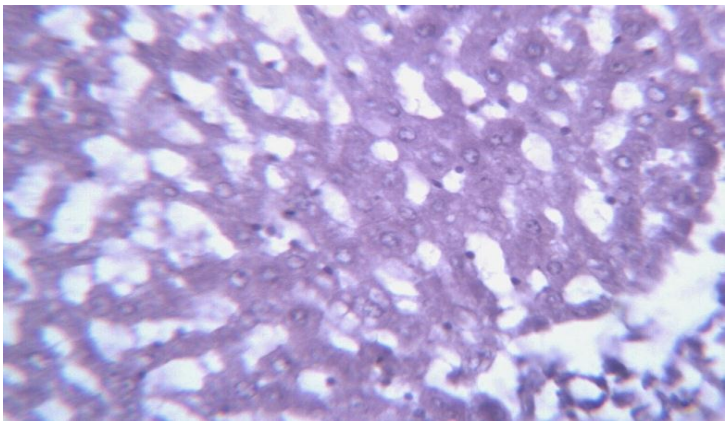

Fig. No. 4: Liver architecture of PCM + 250mg/kg EEDRF.

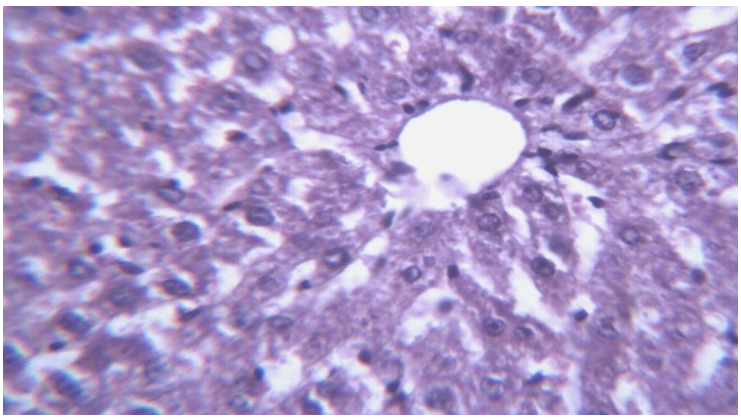

Fig. No. 5: Liver architecture of PCM + 500mg/kg o

DISCUSSION

It was reported that many mechanisms are involved in paracetamol induced hepatotoxicity, showing that the toxicity is mediated by CYP450 (CYP2E1) metabolism of paracetamol to NAPQI (N-acetyl p-benzo-quinine-amine) which is covalently binds to critical proteins leading to inactivation of these proteins, especially after GSH depletion.[16]

In the present study the pre-treatment with extract was found to significantly reverse the paracetamol rise in the biochemical parameters like SGPT, SGOT, ALP, total and direct bilirubin level, thereby demonstrating the membrane stabilizing activity of the extract. The activities of all biochemical properties were all most brought down to normal suggesting the membrane stabilizing effect of the extract.

In case of in-vivo antioxidant enzymes, EEDRF showed significant reduction in LPO levels and significantly increased the depleted GSH and SOD levels as compared with Paracetamol group. So this has contributed to the reduction of oxidative stress as showed hepatoprotective in experimental rats. The results obtained from the present investigation suggest, ethanolic extract of *Delonix regia* flowers possess significant preventive effects against Paracetamol induced hepatotoxicity in Rats. Further, preliminary phytochemical investigation revealed that the test extract showed presence of flavonoids, tannins, alkaloids, saponins and glycosides. Thus, it revealed that the hepatoprotection offered by titled plant extract may be due to its flavonoid content.

CONCLUSION

It may conclude that the flowers of the *Delonix regia* possesses profound hepatoprotective activity by preventing alterations in serum marker enzyme activity and cellular damage due to its antioxidant potential.

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