WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 10, 2500-2513. Research Article ISSN 2277– 7105

EVALUATION OF HEPATO-NEPHRO PROTECTIVE ACTIVITY OF ETHANOLIC EXTRACT OF *ABRUS PRECATORIUS* LINN. ROOT AGAINST PARACETAMOL INDUCED TOXICITY IN MALE SPRAGUE DAWLEY RATS

Swapna Kasi Reddy*[1] and Asia Begum[2]

[1]Department of Pharmacognosy, Venkateshwara Institute of Pharmaceutical Sciences Charlapally, Nalagonda.

[2]Department of Pharmacognosy, Vatshyala College of Pharmacy, Bhongir, Nalagonda.

Article Received on
20 Aug 2015,

Revised on 12 Sept 2015,
Accepted on 03 Oct 2015,

***Correspondence for Author**
Swapna Kasi Reddy
Department of Pharmacognosy, Venkateshwara Institute of Pharmaceutical Sciences Charlapally, Nalagonda

ABSTRACT

Liver diseases are amongst the most serious health problems in the world today and hepatocellular carcinoma is one of the world's deadliest cancers. The aim of current study is to evaluate the hepatonephro protective activity of ethanolic extract of *Abrus precatorius* root against paracetamol induced toxicity in Male Sprague Dawley rats.30 male rats were allocated into five groups; Group1-control; Group2- treated orally with paracetamol during last two weeks; Group3-treated with high dose of extract alone; Group4,5-treated with low dose and high dose extract respectively for 4 weeks and administered paracetamol during last two weeks. Clinical, Clinico-pathological and histopathological evaluations were done and paracetamol treated groups were compared with rats receiving no treatment and with rats given high dose of extract alone. The results indicated that oral administration of paracetamol induced severe hepatic and renal injury associated with oxidative stress. The combined treatment of paracetamol with low dose and high dose of extracts results an improvement in all evaluated parameters. This improvement was prominent in group receiving toxicity after pretreatment with high dose of extract. Animals receiving high dose extract alone were comparable to the control group except body weight and food intake which showed significant increase and proved the claim of appetizer activity of root and from histopathological studies it reveals that there were no changes in liver and kidney architecture and proved that extract was non toxic. Our results suggest that

the protective activity of root can be related to antioxidant properties due to the presence of flavonoids.

KEYWORDS: Abrus precatorius, Paracetamol, Hepatotoxicity, Nephrotoxicity, Oxidative stress, Antioxidant, Flavonoids

INTRODUCTION

Herbal medicine is becoming a popular option among many individuals. More and more people are starting to consider the dangerous consequences of subjecting the body to chemicals that are used in prescription and over-the-counter medications.[14] Many natural products have been reported to contain large amounts of antioxidants other than vitamin C, E and carotenoids. These antioxidants play a role in delaying, interrupting or preventing oxidative reactions catalyzed by free radicals.[7] Liver diseases are amongst the most serious health problems in the world today and their prevention and treatment options still remain limited despite tremendous advances in modern medicine. The pathogenesis of hepatic diseases as well as the role of oxidative stress and inflammation and accordingly, blocking or retarding the chain reactions of oxidation and inflammation process could be promising therapeutic strategies for prevention and treatment of liver injury.[12] The liver, unique in its capacity for regeneration following injury, may give rise to malignancies commonly associated with the inflammatory state of advanced fibrosis, or cirrhosis. Kidney disease is a growing global public health issue. Chronic kidney disease (CKD) has a prevalence of over 10% in the general population and this number is increasing by almost 3% per year.[3] Advanced CKD is associated with a more than three-fold increased risk for cardiovascular events and an almost six times increased mortality.[6] Mortality rates of AKI are upto 80% and more than 10% of the survivors eventually develop end stage renal disease (ESRD).[2] Acetaminophen (paracetamol, N-acetyl p- aminophenol; APAP) is a commonly used analgesic and antipyretic agent which, in high doses, causes liver and kidney necrosis in man and animals.

Abrus precatorius L. (Fabaceae) is known as Rosary pea (English) and Guruvenda (Telugu) reported to have antioxidant, anti diabetic activities, used for jaundice, nephritis, and as appetizer.[8] Preliminary chemical tests and TLC analysis revealed the presence of flavonoids, saponins and tannins. Pretreatment with ethanolic extract of root significantly attenuates H_2O_2 induced free radical production and protect against cell death. The aim of current study

was to evaluate the hepatonephro protective activity of ethanolic extact of Abrus precatorius root against paracetamol induced toxicity in rats.

1. MATERIALS AND METHODS

Eight weeks old thirty male Sprague Dawley rats (170–190g) were purchased from Mahaveera Enterprises, Experimental animals, Bagh Umberpait, Hyderabad, Telangana, India. Animals were maintained on standard laboratory diet, and housed in filter-top polycarbonate cages in a room free from any source of chemical contamination, artificially illuminated (12hdark/light cycle) and thermally controlled (25±1◦C) at the Animal House, Nalanda College of Phamacy, Nalgonda. All animals received humane care in compliance with the guidelines of the IAEC (Institutional animal ethical committee) of Nalanda College of Phamacy, Nalgonda. Sacrified animal were disposed as per CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) guidelines.

Abrus precatorius L. is common in forest tracts of India & Burma, ascending in the outer Himalayas was used in the current study.[8] The plant was collected in the month of November to February from the surrounding areas of Nalgonda Dist., Telangana, India. The plant material was identified and authenticated by Mr.Siddulu, Lecturer (Department of Botany) Nagarjuna Government College. (Affiliated to Osmania University) Nalgonda. The specimen was prepared and submitted in the Dept. of Pharmacognosy under the voucher no: Abrus precatorius, Family – Fabaceae, NCOP-NLG/Ph'cog/2011-2012/044.

2. Extraction

Powdered root is extracted with solvent using Soxhlet's apparatus. Initially 20gm of crude powder was taken and packed in a packing paper. This packing was placed in a soxhlet extractor for 24 hrs approximately at the temperature of (30-40^{0}C) and extracted with a solvent ethanol After extraction the extract is subjected to a vacuum rotary evaporator and concentrated extract is obtained along with solvent recovery. The obtained extract is subjected to preliminary phytochemical screening according to the standard procedures mentioned. The studies revealed that the ethanolic extract of root is rich in chemical constituents like flavonoids, saponins, cardiac glycosides, tannins and phenolic compounds which shows effective action against liver and kidney disorders.[9]

3. Experimental Design

After a 1 week acclimatization period, animals were allocated into 5 groups (6 rats/ goup) as shown in table 1 and treated as follows: group (1), untreated control; group (2), treated orally with paracetamol twice a week during last two weeks; group (3), treated orally with high dose (300mg/kg) extract alone; group (4,5), treated orally with low dose (150mg/kg) and high dose (300mg/kg) extract respectively for 4 weeks and administered paracetamol during last two weeks.

Table 1: Experimental groups and their respective treatment

Groups	DOSE	WEEKS			
		1	2	3	4
I) Control	-	-	-	-	-
II) Paracetamol (T)	600mg/kg b.w	-	-	(T) twice a week	(T) twice a week
III) HDE alone	300mg/kg b.w	HDE daily	HDE daily	HDE daily	HDE daily
IV) LDE+T	150mg/kg b.w	LDE daily	LDE daily	LDE daily + (T) twice a week	LDE daily + (T) twice a week
V) HDE +T	300mg/kg b.w	HDE daily	HDE daily	LDE daily + (T) twice a week	LDE daily + (T) twice a week

HDE (High dose of extract), LDE (Low dose of extract), (T) Toxicity, (b.w) Body Weight Body weight and food intake were recorded twice a week throughout the experimental period. One day after the end of experimental period (i.e. day 29, all animals were fasted for 12 h and blood samples were collected via the retro-orbital venous plexus from each animal under diethyl ether anaesthesia.[4] Blood samples were left to clot and the sera were separated by cooling centrifugation (4◦C) at 3000 rpm for 15min and stored at −20 ◦C until analysis. The sera were used for the determination of the following biochemical parameters: Serum glutamate oxalo transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT), Alkaline phosphatase (ALP), Urea, Uricacid, Creatinine, Total protein (TP), Biliubin (Total, Direct, Indirect), Glucose and Nitricoxide. SGOT, SGPT, ALP, total protein kits were purchased from Randex Laboratories (San Francisco, CA, USA). Total and direct bilirubin kits were purchased from Biomerieux, Laboratory of Reagents and Products (Marcy L'Etoile, France). Glucose, nitricoxide (NO), urea, uricacid, creatinine kits were purchased from Biodiagnostics Co. (Cairo, Egypt). Malondialdehyde (MDA) was obtained from Eagle Diagnostics (Dallas, TX, USA). Paracetamol was purchased from Adwic Chemical Co. (Cairo, Egypt). Other chemicals were of the highest purity commercially available.

After the collection of blood samples all animals were sacrificed and samples from liver and kidney tissues (approximately 0.05–0.1 g) were homogenized in phosphate buffer (pH7.4) to give 20% w/v homogenate.[11] This homogenate was centrifuged at 1700rpm and 4 ◦C for10min; the supernatant was stored at −20 ◦C until analysis. This supernatant (20%) was used for the determination of lipid peroxidation was expressed as nmol malondialdehyde (MDA)/gtissue.[13] The homogenate was further diluted to give 5% homogenate (w/v) and used for the estimation of Lactate dehydrogenase(LDH), Reduced glutathione (GSH).

Samples of the liver and kidney from all animals were fixed in 10% neutral formalin and paraffin embedded. Sections (5µm thickness) were stained with hematoxylin and eosin (H&E) for the histological examination.

4. Statistical analysis

Experimental data were expressed as mean ± SD. The difference between experimental groups was compared by One – way Analysis of Variance (ANOVA) followed by Dunnet Multiple comparison test (control vs test) using the software Graph Pad Instat. The differences were considered to be statistically significant when $P<0.01$ or $P<0.05$.

All the results were expressed as mean ± SD for six observations in each group.

5. RESULTS

The results indicated in (Table 2) showed that animals treated with HDE alone showed the significant increase in the food intake and body weight till the last week when compared to control group. Animals pretreated with LDE and HDE for the first 2 weeks had showed the increase in food intake and body weight. After administration of toxicity they showed slight changes in their food intake and body weights but not reduced much during the last two weeks. This improvement was pronounced in the animals pretreated with HDE.

Table 2: Group mean food intake, body weight

Groups	Food intake (g)				Body weight (g)			
	Weeks				Weeks			
	I	II	III	IV	I	II	III	IV
Control	19.42 ± 0.4025	19.68 ± 0.3114	19.48± 0.4764	19.8 ± 0.2	182.6 ± 2.793	182.8 ± 1.924	200.8 ±0.836	200.2 ±0.836
Toxicity	19.36 ± 0.2302^{ns}	19.66 ± 0.4159^{ns}	17.6 ± 0.3937**	16.8 ± 0.1581**	172.2 ± 2.49**	192.4 ± 1.949**	211 ± 1.000**	180.4 ± 1.14**
HDE alone	24.3 ± 0.7583**	34.52 ± 0.5020**	34.3 ± 0.4472**	34.54± 0.313**	204.2 ± 3.033**	224.6 ± 3.209**	222.4 ± 1.949**	229.6 ± 1.14**
LDE+T	23.8 ±	34.3 ±	29.6 ±	27.36±	184 ±	182.8 ±	200.6 ±	204.4 ±

	1.304 **	0.8367**	0.8944**	0.3782**	2.646^{ns}	2.168^{ns}	2.302^{ns}	1.342*
HDE+T	24.54 ± 0.8649**	34.42 ± 0.4266**	29.9 ± 0.5477**	27.48 ± 0.4817**	182.4 ± 2.51^{ns}	202.4± 1.517**	200.4 ± 0.547^{ns}	201 ± 1.225^{ns}

Within the column means with superscript with different letters are significantly different at **p<0.01, *p<0.05, ns (non significant) (n=6).

The results indicated in (Table 3) showed that the paracetamol administered group had showed decrease in liver and kidney weights. Moreover the animals treated with HDE alone resulted in more or less similar weights as control group. Animals pretreated with LDE and HDE alone for first 2 weeks before paracetamol administration showed a significant improvement in liver and kidney weights. This improvement was pronounced in the animals pretreated with HDE.

Table: 3 Group mean of Liver and Kidney weights

Groups	Liver weight(g)	Kidney weight(g)
Control	7.414 ± 0.003	0.9738 ± 0.003
Toxicity	5.399 ± 0.003**	0.7236 ± 0.002**
HDE alone	7.118 ± 0.002^{ns}	0.9462 ± 0.001**
LDE + T	6.389 ± 0.002**	0.868 ± 0.009**
HDE +T	6.987 ± 0.002**	0.9362 ± 0.003**

Within the column means with superscript with different letters are significantly different at **p<0.01, ns = non significant (n=6)

Liver function tests (LFTs) and Kidney function tests (KFTs) are a group of blood tests can help to show liver and kidney condition. The results indicate that the animals treated with paracetamol showed a significant increase in all biochemical parameters (SGOT, SGPT, ALP, urea, Glucose, uric acid, nitric oxide, creatinine, bilirubin) tested and significant decrease in serum total protein. However, animals treated HDE alone showed a significant decrease in SGOT, ALP, urea, Glucose, uricacid, nitricoxide and significant increase in serum total protein when compared to control group. Animals pretreated with LDE for 2 weeks before paracetamol administration showed significant decrease in uric acid, SGOT, and bilirubin levels and significant improvement in serum total protein when compared to toxicity group. But the animals pretreated with HDE for 2 weeks before the intoxication with paracetamol showed a significant decrease in all the tested parameters and significant increase in serum total protein towards the control group (Table 4).

The results also indicated that treatment with paracetamol resulted in a significant increase in MDA (Table 5) and significant decrease in antioxidant levels like LDH and GSH (Table 6).

Treatment with HDE alone resulted in a significant decrease in MDA and significant increase in LDH and GSH in liver and kidney. Animals pretreated with LDE and HDE alone for first 2 weeks before paracetamol administration showed a significant improvement in MDA, LDH and GSH of liver and kidney towards the control levels. This improvement was significantly more pronounced in the animals pretreated with HDE.

Table 4: Group mean of Serum biochemical parameters

Serum Parameters	Groups				
	Control	Toxicity	HDE alone	LDE +T	HDE+T
SGOT (U/ml)	61.4 ± 0.547	181.8 ± 1.304**	61 ± 1.225ns	70.6 ± 1.517**	67.2 ± 1.304**
SGPT (U/ml)	38.41 ± 0.006	173.84 ± 0.043**	36.56 ± 0.011**	80.31 ± 0.001**	55.34 ± 0.022**
ALP (U/ml)	60.8 ± 0.003	218.2 ± 0.11**	58.04 ± 0.015**	113.3 ± 0.02**	99.5 ± 0.001**
Total protein (µmol/mg protein)	0.0081± 0.0001	0.0029 ± 0.0001ns	0.0087± 0.0001*	0.0047± 0.0001ns	0.0083± 0.0001*
Nitric oxide (µmol/L)	2.838 ± 0.001	19.72 ± 0.001**	2.034 ± 0.025**	12.22 ± 0.011**	10.55 ± 0.02**
Creatinine(mg/dl)	0.804 ± 0.011	4.16 ± 0.151**	0.83 ± 0.012ns	2.848 ± 0.01**	1.866 ± 0.015**
Uric acid (mg/dl)	2.624 ± 0.019	4.626 ± 0.015**	2.028 ± 0.017**	3.648 ± 0.022**	3.116 ± 0.002**
Urea (mg/dl)	65 ± 2.345	141.8 ± 0.83**	57.2 ± 2.168**	77 ± 1.581**	70.2 ± 0.83**
Glucose (mg/dl)	50.7 ±0.44	122.7 ± 0.36**	48.62 ± 0.37*	78.1 ± 1.817**	62 ± 1.581**
Total bilirubin (mg/dl)	0.554 ± 0.001	0.832 ± 0.001**	0.552 ± 0.002ns	0.663 ± 0.001**	0.594 ± 0.001**
Direct bilirubin (mg/dl)	0.155 ± 0.005	0.281 ± 0.001**	0.131 ± 0.001**	0.228 ± 0.013**	0.181 ± 0.001**
Indirect bilirubin (mg/dl)	0.405 ± 0.001	0.552 ± 0.001**	0.425 ± 0.001**	0.445 ± 0.001**	0.415 ± 0.002**

Within the column means with superscript with different letters are significantly different at **p<0.01, ns = non significant (n=6)

Table: 5 Group mean of MDA, LDH and GSH levels in liver and kidney

Groups	MDA (µ mol/g tissue)		LDH (µMoles/mg tissue)		GSH (µMoles/mg tissue)	
	Liver	Kidney	Liver	Kidney	Liver	Kidney
Control	15.62 ± 0.2387	13.34 ± 0.2702	114.14± 1.6	22.48± 0.4481	310.15± 2.056	20.354± 0.2027
Toxicity	37.908 ± 0.027**	27.56 ± 0.251**	29.093± 1.646**	7.88± 0.1924**	205.09± 3.584**	10.194± 0.117**
HDE alone	15.1 ±	9.56 ±	77.648	23.06±	308.71±	28.448±

	0.235**	0.3847**	±2.644**	0.658^{ns}	2.34^{ns}	0.4388**
LDE+T	22.2 ± 0.2449**	20.44 ± 0.3782**	41.797± 3.049**	15.452± 0.2841**	212.74± 4.371**	19.18± 0.3346**
HDE + T	18.14 ± 0.016**	18.64 ± 0.2408**	48.975± 2.386**	18.64± 0.3786**	251.89± 3.256**	20.248± 0.2061^{ns}

Within the column means with superscript with different letters are significantly different at $^{**}p<0.01$, $^{*}p<0.05$, ns (non significant) (n=6)

The histological examination of liver sections in the control rat or those treated with HDE alone, showed the normal hepatocytes architecture and the central vein, no inclusion and no infiltration (Fig. 1a). Liver sections of animals treated with paracetamol showed showing vacuolation, mononuclear inflammatory cells dissecting the parenchyma, damaged hepatocytes are seen as eosinophilic spot, damaged and collapsed blood vessel is seen with rough margins. Severe infiltration (inf) is evident (Fig. 1b). The examination of liver section of rat pretreated with LDE then paracetamol showed massive vacuolar degeneration and mononuclear inflammatory cells around the portal tract(Fig. 1c); however, rat pretreated with HDE then paracetamol showed minimal damaged area around the central vein (Fig. 1d).

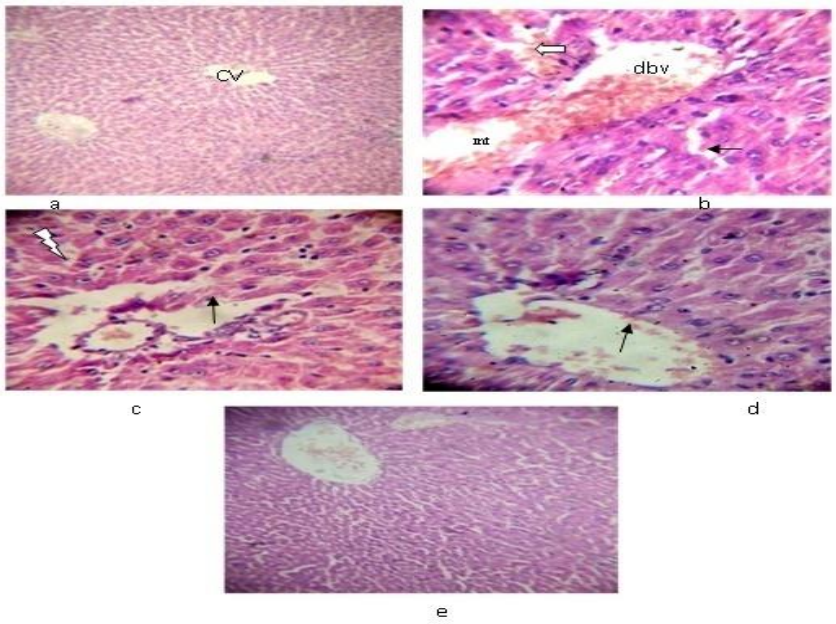

Fig No: 1 Photomicrograph of liver section

A photomicrograph of liversection a) control rat showing the normal histology of the liver radiating cords of hepatocytes around the central vein indicates well organized histoarchitecture. No inclusion and no infiltration, b) rat treated with paracetamol showing vaculation(arrows), mononuclear inflammatory cells dissecting the parenchyma, damaged hepatocytes are seen as eosinophilic spots (double headed arrows), damaged and collapsed blood vessel (dbv) is seen with rough margins. Severe infiltration (inf) is evident c) rats

pretreated with LDE then paracetamol showing massive fatty degeneration ( ) and mononuclear inflammatory cells around the portal tract (arrows), d) rat pretreated with HDE then paracetamol showing minimal damaged area around the central vein (arrows) e) rats treated with HDE alone showing normal liver architecture as control group (H&E. ×400)

The histological examination of kidney sections of control rat or those treated with HDE alone showed normal renal tubular brush borders and intact glomeruli, No evidence of congestion or inflammation was observed in the sinusoid. (Fig. 2 a,e). The kidney sections in rats treated with paracetamol showed interstitial haemorrhage (H) and some tubular damaged and glomular tufts, tubular brush-borders loss, interstitial oedema (O), glomerular hypercellularity (H), necrosis of epithelium (N) and inflammatory cells infiltration. The kidney tubules were obliterated with pyknosis in the epithelial cells lining (Fig. 2b). The kidney of rat pretreated with LDE then paracetamol showed intertubular infiltration, cloudy swelling, cellular debris in their lumen and necrosis in the kidney tubules with interstional mononuclear cellular infiltration (Fig. 2c). However, kidney sections of rat pretreated with HDE then paracetamol showing cellular swelling and fatty degeneration (FD) of most of renal tubules, attenuated necrosis, reduced inflammatory cells and improved tubule and glomeruli architecture (Fig. 2d).

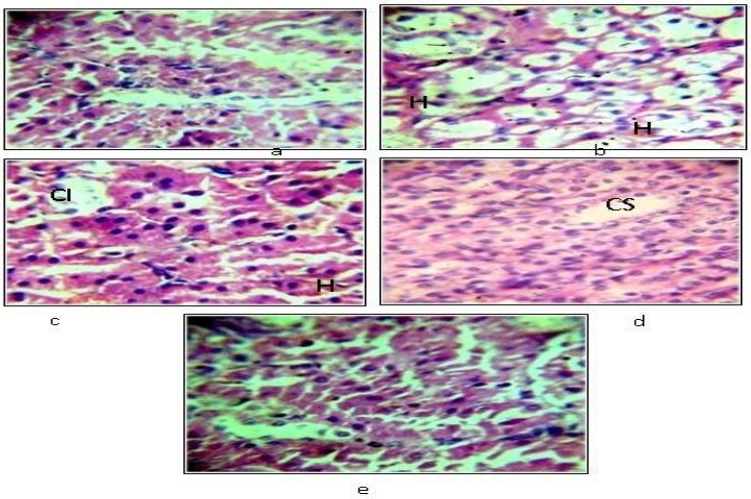

Fig no: 2 Photomicrograph of kidney sections

A photomicrograph in the kidney of (a) control rat showing the normal renal tubular brush borders and intact glomeruli, No evidence of congestion or inflammation was observed in the sinusoid. (b) rat treated with paracetamol showing interstitial hemorrhage (H) and some tubular damaged and glomular tufts (*), tubular brush-borders loss, interstitial oedema (O), glomerular hypercellularity (H), necrosis of epithelium (N) and inflammatory cells infiltration. (c) rat pretreated with LDE then paracetamol showing intertubular infiltration,

cloudy swelling(CS), cellular debris in their lumen, necrosis (N) in the kidney tubules with interstional mononuclear cellular infiltration (CI) and (d) rat pretreated with HDE then paracetamol showing cellular swelling and fatty degeneration (FD) of most of renal tubules, attenuated necrosis, reduced inflammatory cells and improved tubule and glomeruli architecture. e) rats treated with HDE alone showing normal morphology of kidney as control group. (H&E. ×400)

6. DISCUSSION

In the present study, we evaluated the protective effects of ethanolic extract of Abrus precatorius Linn root against the hepato-nephrotoxicity induced by paracetamol in male Sprague Dawley rats. In our study, treatment with paracetamol resulted in a significant decrease in body weight, food intake, liver and kidney weights and these results were in agreement with those reported in the previous literature.[5] A significant increase in serum ALT, AST, ALP, urea, creatinine, uricacid, glucose, bilirubin and nitric oxide as well as MDA in liver and kidney levels accompanied with a significant decrease in total protein and TAC in liver and kidney were found in animals treated with paracetamol alone. These results may indicate degenerative changes and hypofunction of liver and kidney as well as hepatic cell necrosis which increase the release of these enzymes in the blood stream. Ingestion of paracetamol significantly increased NO suggesting that paracetamol preferentially affects macrophage functions. These results clearly showed that paracetamol has a harmful and stressful influence on the hepatic and renal tissues consistent with those reported in the previous literature.[1,5]

Paracetamol is one of the most extensively studied hepatonephro toxicants and the mechanism by which it causes toxicity is well documented. At lower doses, about 80% of ingested paracetamol is eliminated mainly as sulfate and glucoronide conjugates before oxidation and only 5% is oxidized by cytochrome P_{450} (CYP2E1) to highly reactive and toxic electrophile i.e. N-acetyl-p-benzoquineimine (NAPQI). After over dosage of paracetamol the glucoronidation and sulfation routes become saturated and as a consequence, paracetamol is increasingly metabolized into NAPQI. Semiquinone radical, one- electron reduction metabolite of NAPQI mediates the cytotoxic effects of NAPQI. Production of this toxic semiquinone radical is catalyzed by the micrososmal cytochrome P450 reductase. These semiquinone radicals, in turn, can bond directly with cellular macromolecules to produce toxicity or alternatively, the radical can be reoxidized back to their original quinines by

donating one electron to molecular oxygen under aerobic conditions. This donation of one electron then generates reduced oxygen radical species and hydroxyl radical. Both semiquinone and oxygen radical are known to be responsible for cytotoxic effects observed with quinines.[10]

In the present study TAC was found to decline significantly in rats treated with paracetamol. It is well known that TAC plays an important role in the elimination of ROS derived from the peroxidative process in liver tissues. Taken together, the increased level of MDA and the decreased in TAC may be attributed to free radical formation which initiated chain reactions of direct and indirect bond formation with cellular molecules (nucleic acids, proteins, lipids and carbohydrates) impairing crucial cellular processes that may ultimately culminate in extensive cell damage and death.[5]

In the current study, When toxicity had been administered the overdose leads to hepatic and renal necrosis therefore it causes decrease in food intake and body weight. But when treated with HDE alone had shown a significant increase in food intake and body weight, where as in groups pretreated with LDE and HDE of extract had shown significant improvement in food intake and body weight even after administration of toxicity this was much pronounced in the group pretreated with HDE. These results suggested that root was proven for appetizer activity.

An elevation in the levels of the serum marker enzymes is generally regarded as one of the most sensitive index of the hepatic and renal damage. Assessment of liver and kidney function can be made by estimating the activities of serum AST, ALT and ALP, which are enzymes originally present in higher concentration in cytoplasm, when there is hepatopathy and nephropathy, these enzymes leak into blood stream in confirmity with the extent of liver damage.

In the present study administration of paracetamol treated rats showed an increase in the levels of SGOT, SGPT, ALP, urea, creatinine, uricacid, glucose, bilirubin and nitric oxide as well as MDA in liver and kidney levels accompanied with a significant decrease in total protein and TAC in liver and kidney when compared with control rats. Oral administration of HDE alone had shown a more or less similar value as control group, where as in groups pretreated with LDE and HDE then administration of toxicity had shown significant

improvement in all the parameters. This improvement was much more pronounced in the group pretreated with HDE.

The histopathological study of structure and chemical composition of tissues of animals are related to their function. The primary aim is to understand how tissues are organized at all structural levels, including the molecular and macromolecular, the entire cell and intercellular substances and the tissues and organs. Paracetamol is a popular over-the counter analgesic and antipyretic that is safe and effective at therapeutic doses. The histopathological studies support the biochemical findings. The paracetamol treated rats showed fatty changes, necrosis, vacuoles, space formation and loss of cell boundaries in liver. Hemorrhage, cellular infiltration, cloudy swelling, glomerular tufts are found in kidney. Pretreatment with LDE and HDE before intoxication in rats brought back the above-mentioned changes in liver and kidney to near normal. The best results were achieved when the animals pretreated with HDE.

In the current study, the treatment with extract were found to be the most effective in the protection of the liver and the kidney injuries resulted from the administration of paracetamol. This may be due to the cumulative effects of the antioxidant constitutes (Flavonoids) of these agents. This treatments succeeded to normalize most of the parameters tested, significantly decreased the oxidative stress markers and significantly increased the antioxidant capacity of the body. In this concern, several reports suggested potential drug–herbal interactions.

Oral administration with HDE alone showed the results comparable with control rats where both liver and kidney tissue more or less restore the normal histological and histochemical pictures. Hence from the results it was concluded that plant was non-toxic.

7. CONCLUSION

It could be concluded from the present results that Abrus precatorius root protect against the severe paracetamol induced hepatic and renal toxic effects. Our results suggest that the protective activity of root can be related to antioxidant properties due to the presence of flavonoids, tannins and phenolic compounds and it was proven as non toxic and best Anti hepato-nephroprotective agent and appetizer.

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