Hepatoprotective Activity of Carica Papaya and Ficus Bengalensis Latex against Paracetamol Induced Hepatotoxicity in Rats

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***Abstract*— Objectives: The aim of the present study was to evaluate the hepatoprotective activity of Carica Papaya latex and Ficus bangelensis latex against Paracetamol induced hepatotoxicity in rats.**

Method: Paracetamol (3g/kg.b.w) was used to induced hepatotoxicity in rats. Salymarin (100mg/kg)was used as a standard drug for present study. Silymarin and Carica Papaya Latex at the dose 400mg/kg/b.w. per oral and Ficus bangelenesis latex at dose 300mg/kg/b.w. per oral were given for 10 days followed by single administration of Paracetamol 3mg/Kg b.w. per oral 1hour after Caraca Papaya Latex , Ficus Bengalasis and Silymarin administration for 10 days. On 10 days blood samples were collected from the animals for biochemical analysis and liver were subjected to histopathological examination.

***Result and Discussion*: The degree of protection was measured by using bio-chemical parameters like serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), Bilirubin (BRN), Alkaline phosphate (ALP) and total protein. The decreased levels of SGOT, SGPT, ALP, Bilirubin and increased levels of total protein parameters in treated rats were an indication of the hepatoprotective activity of Carica papaya latex and Ficus bengalenesis latex. Silymarin (100 mg/kg) a well known hepatoprotective drug used for comparision exhibited significant activity (<0.05). Conclusion: The both plants latex were completely prevented the toxic effect of Paracetamol on the above serum parameter. Significant hepatoprotective activity of both plant latex were reported. Carica papaya latex was found to be more protective effect as compare to Ficus bengalenesis latex.**

***Keywords*— Carica Papaya, Ficus Bengalensis, Hepatoprotective, Paracetamol, Silymarin.**

I. INTRODUCTION

Liver is a vital organ human body which is maintained the Metabolic reactions in the human body but unnecessary food habits, consumed impure drinks may be bring problems in functioning of the liver consumed more number of drugs can cause damage the liver and Liver Architecture, like junk food intake of alcohols. Damage of liver can elevated levels of serum enzymes like Bilirubin, SGPT and SGOT[1].

Drug induced liver damage has been identified a leading cause of Hepatic dysfunction. The mechanism of hepatic injury in most of the cases of drug induced liver injury remains unknown. Few mechanisms are suggested direct injury to hepatocytes by the drugs [2].

Paracetamol is one of the widely used antipyretics with few side effects when taken in therapeutic doses[3]. Hepatotoxicity is a common toxic effect with over dose of paracetamol[4]. Thus present study was conducted to evaluation of hepatoprotective effect against paracetamol induced hepatotoxicity in rats.

Carica Papaya belongs to family Caricaceae. It is fast growing herb. The pulp of fresh fruit containing soft yellowish resin, pectin , fat, and albuminoid sugar also. Green fruit contains pepsin and papain. The Carica Papaya leaves contain Glucoside, it is known as Carposide and alkaloid, it is k known as Carpain[5].

Carica Papaya seed contains proteins, lipid fiber, it also contain minerals like phosphorus and calcium[6]. It has been reported muscles relaxant and sedative properties [7]. Seed extracts of Carica Papaya posses bacteriocidal activity against Escherischia Coli, Bacillus cereus, staphylococcus [8].

Ficus Bengalensis linn belong to family Moraceae. Plant is distributed all over India. It grows in road sides for shades and gardens[9]. It also reported inhibit the lipid per oxidation[10]. It also used in Ayurveda for the treatment of disease like piles, dysentery and diarrhea[13],[14]. Fruit extracts of Ficus Bengalensis linn was reported antitumor activity in potato disc bioassay. The plant also reported hypoglycemic activity[11],[12].

The bark extract of Ficus Bengalensis posses anti-inflammatory activity[17].

A. Material and Methods - Plant materials

Carica Papaya and Ficus Bengalensis were collected from Mathura, Uttar Pradesh. The authentication and identification was done by (Prof.) Dr. D.K. Singh, Department of Botany, KR (PG) College , Mathura, Uttar Pradesh.

B. Carica Papaya Latex Collection

Latex was collected locally in early morning 7:00 to 8:00 am, as the flow of latex is low during the day. Collection was done by making a 1-2 mm deep vertical incisions on the skin of

unripe fruit. But mature fruit. The latex was then dried at room temperature till it became crumbly and non-sticky. The dried latex was triturated using a mortar and pestle.. It was stored at 4-8 ºC until use.

C. Ficus Bengalensis Latex Collection

Latex was collected locally in early morning 7:00 to 8:00 am, as the flow of latex is low during the day. Collection was done by making a 1-2 mm deep vertical incisions on the skin. Latex was extracted by maceration process (48h) in methyl alcohol after defatted with petroleum ether at (72h) at room temperature. The extracted was dried by rotatory evaporator under reduced pressure[15]. The dried latex was triturated using a mortar and pestle. It was stored at 4-8^{0}C until use.

D. Phytochemical studies

Phytochemical analyses was carried out on Carica Papaya Latex and Ficus Bengalensis Latex for the detection of various phytochemicals by following standard methods described in practical pharmacognosy by Trease and Evans.

E. Phytochemical Screening

Phytochemicals are chemical compounds that occur naturally in plants. The term is generally used to refer to those chemicals that may affect health, but are not established as essential nutrients. The presence of tannins, alkaloids, flavonoids, general test for glycosides (reducing sugars), anthraquinones, sterols and saponins were tested by simple qualitative methods (Trease and Evans, 1989).

F. Animals

Albino rats of either sex (Wister strain) weighing 150-200g and female albino mice weighing 20-25g were used in this study. Animals were used from animal house of Sanjay College of Pharmacy, Mathura, U.P.

The animals were acclimatized for ten days under laboratory conditions. They were housed in polypropylene cages and maintained at 27 ºC ± 2 ºC , relative humidity 65 ± 10% under 12 hours light/ dark cycle. The animals were fed with rodent pellet diet (Gold Mohur Lipton India Ltd.) and water *ad libitum.*

Ethical clearance for performing the experiments on animals was obtained from the Institutional Animal Ethics Committee (IAEC) and registration number 1334/a/10/CPCSEA of Sanjay College of Pharmacy, Mathura, Uttar pradesh.

G. Toxicity study - Determination of acute toxicity LD_{50}

The acute toxity for Carica Papaya Latex and Ficus bengalensis latex were determined in female albino mice. The animals were fasted overnight prior to the experiment, fixed dose method of OECD guideline No. 420; (Annexure 2d)of CPCSEA was adopted for this purpose. Group of three mice were taken for each test dose and 1/10th of LD_{50} cut off value of test latex selected as screening dose for Hepatoprotective activity.

II. PARACETAMOL INDUCED HEPATOTOXICITY

Group 1- Serve as control

Group 2- Received Paracetamol(3 g /kg .)- P.O.

Group 3 Received) Paracetamol(3 g /kg .) and carica papaya latex (400mg/kg) P.O. .

Group 4- Received Paracetamol (3g/kg.) and ficus bengalensis latex (300mg/kg) P.O..

Group 5- Received Paracetamol(3g/kg) and Silymarin (100mg/kg) P.O.

Animals were divided into 5 groups of six animals in each. Group I – Served as a normal control received saline 1ml /Kg for 10 days. Group -II were administered with Paracetamol (3g/Kg)b.w. orally for 10 days. Animals of test group III, IV, and V std group were given pretreatment of Caraca Papaya Latex dose 400mg/Kg. b.w. orally, Ficus Latex dose 300mg.Kg b.w. per oral and Silymarin 100mg/Kg b.w. per day once daily for 10 days in succession followed by single administration of Paracetamol 3mg/Kg b.w. per oral 1hour after Caraca Papaya Latex , Ficus Bengalasis Latex and Silymarin standard drug administration for 10 days.

All the animals were sacrificed on 10 days under ether anaesthesia blood sample were collected and centrifuged. Separated serum sample were used for estimation

Of SGOT, SGPT ,Bilirubin,total protein and ALP through the auto analyzer for the study of the Toxic effect of paracetamol and also therapeutic effect of plants Latex.

A. Histological studies.

The Liver were isolated from the animals and washed with normal Saline. The liver were fixed in Formalin diluted to 10% with normal Saline then processed further for histological studies. The results were analyzed by student t-test.

B. Estimation of liver functional markers

Estimation of SGPT on blood serum was carried out using AGD Clinipak from AGD Biomedicals Pvt. Ltd. Mumbai.

Estimation of Alkaline Phosphate, Total Protein, SGOT on blood serum was carried out using Diagnostic test kit from Beacon Diagnostic Pvt. Ltd., NAVSARI.

Estimation of Bilirubin on blood serum was carried out using diagnostic kit from SIEMENS Ltd., Vadodara, Gujrat.

C. Statistical analysis

All the values are expressed as mean ±S.D. result were analyzed statistically by analysis of variance (ANOVA) followed by student T-Test was used for determining significance.

III. RESULT

Preliminary phytochemical screening like Flavonoids,

triterpenouds, Saponins and alkaloids are known to posses hepatoprotective activity. Phytochemical investigation of Carica papaya and Ficus Bengelenesis latex revealed the presence of alkaloids, Phenols ,Saponins, Glycosides ,Flavonoids, Triterpenoids, Sterols and tannins.

TABLE I

HEPATOPROTECTIVE ACTIVITY OF CARICA PAPAYA LATEX & FICUS BENGALENSIS LATEX IN PARACETAMOL INDUCE HEPATOTOXICITY IN ALBINO RAT

S.No.	Groups	SGPT(1u/L)	SGOT(1u/L)	Bilirubin(myp/L)	ALP	Total Protein
1.	Control	48.28±1.42	73.26±2.86	0.82±0.02	98.6±6.80	8.12±0.046
2.	Paracetamol treated(3g/Kg) P.O.	192.42±36.2	210± 18.9	3.62±0.12	242.17±5.67	5.24±0.028
3.	Paracetamol (3g/Kg) + Carica Papaya Latex (400mg/Kg) P.O.	106.3±12.50*	145±14.2*	1.98±0.28*	156.14±3.21	6.84±0.14
4.	Paracetamol (3g/Kg) + Ficus Bengalensis Latex(300mg/Kg) P.O.	116.3±14.50*	160±17.5*	2.67±0.32	186.54±2.46	6.18±0.08
5.	Paracetamol (3g/Kg) + Sylimarin(100mg/Kg) P.O.	52.12±2.32*	84.35±3.14*	0.98±0.25*	108.4±4.31*	7.18±0.2

ues are mean ± SD; n=6 compare to Control vs P<0.05

A. Histology of Paracetamol Induced Hepatotoxicity

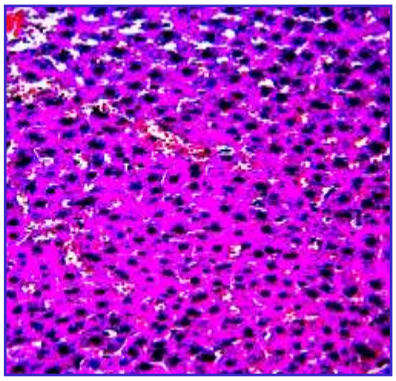

Figure 1: Control group

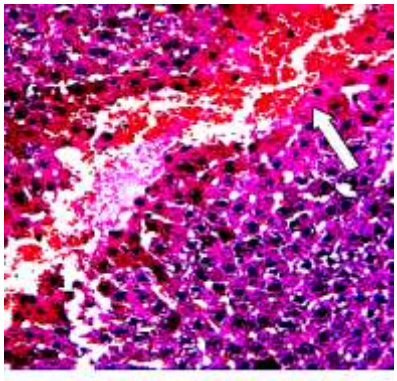

Figure 2: Paracetamol Treated Group

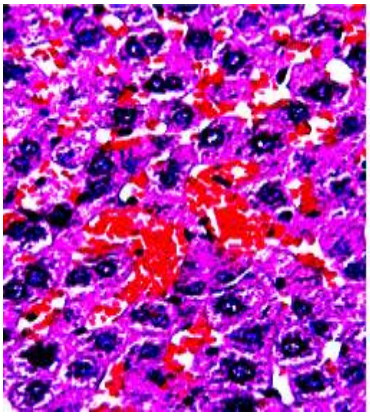

Figure 3: Paracetamol + Carica Papaya Latex Treated Group

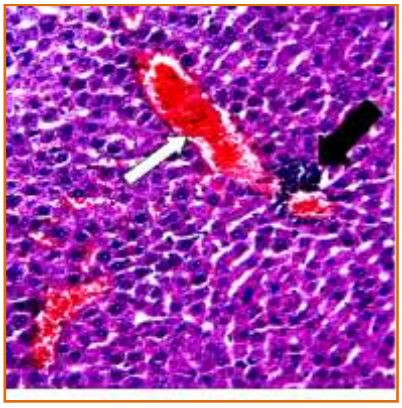

Figure 4: Paracetamol + Ficus Bengalensis Treated Group

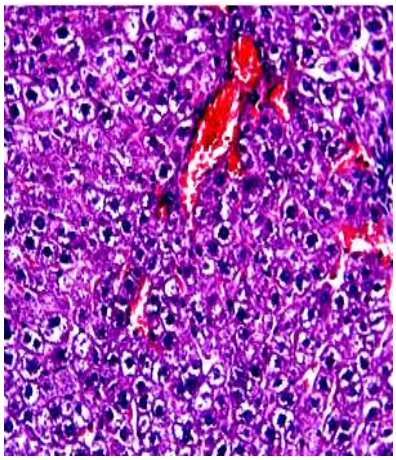

Figure 5: Silymarin treated group

The result of present study reveals that Group treated with Paracetamol shown in table no I to increase the serum level of SGPT (192.42±36.2), SGOT(210.00±18.9), Bilirubin (3.62±0.12) and ALP (242.17±5.67) and decreased in total proteins(5.24±0.028).

Whereas group treated Paracetamol+Carica Papaya Latex at the dose of 400mg/kg b.w. were found to decrease in the serum level SGPT (106.3±12.50), SGOT(145.00±14.2), Bilirubin(1.98±0.28) and ALP(156.14±3.21) and increased total protein(6.84±0.14) compare to Paracetamol treated group.

We found that group treated with Paracetamol + Ficus Bengalensis Latex at the dose of 300mg/kg b.w. were found to decrease in the serum level SGPT (116.3±14.50), SGOT(160.00±17.5), Bilirubin(2.67±0.32) , and ALP(186.54±2.46) and increased in total proteins (6.18±0.08) compare to Paracetamol treated group.

Group treated with Paracetamol + Silymarin 100mg/kg b.w. was found more significant decrease in above said parameters. It shown in Table No.I.

The findings from the present study of result of Carica Papaya Latex, were found that significantly decrease in Serum level of above said parameters of Carica Papaya Latex group treated rat shows better significant activity compare to Ficus Bengalensis Latex.

B. Histopathology

The normal architecture of liver (figure1) was completely lost in rats Paracetamol treated group (figure 2) with a:earance of vacuolated Hepatocytes and degenerated nuclie, fatty changes and necrosis of Hepatocytes were severe in the centrilobular region and these changes were also observed in area other than centrilobular region.

The liver of rats treated group with Carica Papaya Latex , Ficus Bengalensis latex and Silymarin were showed in significant recovery compared to Paracetamol treated group. It was shown in figure no 3, 4 and 5.

IV. Discussion

The present study reveals the Hepatoprotective activity of Carica Papaya Latex and Ficus Bengalensis against well known Hepatotoxin like Paracetamol.

Paracetamol is a common antipyretic agent, which is safe therapeutic dose but can produce fatal hepatic necrosis in man, rat and mice with high dose/toxic doses. The Paracetamol is normally eliminated mainly as Sulfate and Glocoronide. Only 5% of Paracetamol is converted into N-acetyl-P-benzoquineimine. However administration of toxic doses of Paracetamol the Sulfation and Glucoronidation routes become satured and hence, higher percentage of Paracetamol molecules are oxidized to highly reactive N-acetyl-P-benzoquineimine (NAPQI) by Cytochrome 450 enzymes.

Higher dose of Paracetamol and NAPQI can alkylate and oxidized intracellular GSH & Proteins Thiol Group[18].

Which results in the depletion of liver GSH pool subsequently to increase Lipid Peroxidation and liver damage. This is further evident from the fact that there is elevation in the Level of various Bio-Chemical markers of Hepatic damage like SGPT, SGOT, Bilirubin, and ALP and decreased total protein.[16].

Treatment with Silymarin, Ficus-Bengalensis Carica Papaya Latex was increased tissue GSH Level and elevated levels of above mentioned Bio-Chemical markers to near healthy levels. The treatment was also demonstrated the reduced hepatic damage.

Paracetamol at the dose of 3g/kg,b.w and Carica Papaya Latex treated group at the dose of 400mg/kg b.w. were found to decrease in the serum level SGPT (106.3±12.50), SGOT (145.00±14.2), Bilirubin (1.98±0.28), ALP (156.14±3.21) and increased total protein(6.84±0.14) compare to Paracetamol treated group. The Group treated with Paracetamol + Ficus Bengalensis Latex at the dose of 300mg/kg b.w. were found to decrease in the serum level SGPT (116.3±14.50), SGOT (160.00±17.5), Bilirubin(2.67±0.32), and ALP(186.54±2.46) and increased in total proteins (6.18±0.08) compare to Paracetamol treated group. Phytochemical investigations of Carica Papaya and Ficus Bengalensis latex revealed the presence of flavonoid,Carbohydrate,Tannins, Saponins and Alkaloid.

This study was found Hepatoprotective effect of Carica Papaya and Ficus Bengalensis latex against Paracetamol induced Hepatotoxicity in experimental model.

V. Conclusions

The present study reveals that Carica Papaya Latex and Ficus Bengalensis Latex posses hepatoprotective activity. Both plant latex have demonstrated significant hepatoprotective activity against paracetamol induced hepatotoxicity in rats as evidence by reduction in serum parameters such as SGPT,

SGOT, Bilirubin, ALT, and total proteins. Both plant latex significantly reduce the elevated serum parameters induce by hepatotoxin in rats whereas Carica Papaya Latex more significant compare to Ficus Bengalensis Latex.

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REFERENCES

[1]. Vijay kumar R., Venkat Raji Reddy. G. and Bikshapathi. T. (2014), Hepatoprotective activity of extract of *Erythroxylum monogynum* in Albino rats, International Journal of pure and a:lied bioscience, 2(3) :58-62.

[2]. Joydeep Paul, Mohammad Nasiruddin, rahat Ali Khan (2016), protective role of Nigella sativa Oil in Isonizid induced hepatotoxicity in rats, European Journal of Pharmaceutical and Medical Research, 3(10), :. 307-312.

[3]. Lalit Singh Ranavat, Jagruti Patel (2013), Antioxidant and Hepatoprotective activity of Ethanolic Extract of Bark of Zanthoxylum armatum DC in Paracetamol induced hepatotoxicity, International Journal of Pharmaceutical science and drug research, 5(3), : 120-124.

[4]. Md. Zafor Sadeque and Zinnat Ara Begum (2010), Protective effect of dried fruits of Carica Papaya on Hepatotoxicity in rats, A Journal of Bangladesh Pharmacological Society,(5) : 48-50.

[5]. Venkateshwarlu E, Dileep P, rakesh Kumar Reddy P, (2013), Evaluation of anti diabetic activity of Carica papaya seeds on Streptozotocin induced type- II diabetic rat, Journal of Advanced Scientific research, 4(2) : 38-41.

[6]. Ghani A. (2003), Medicinal Plants of Bagladesh 2nd Edition Dhaka, Asiatic society of Bangladesh : 1-149.

[7]. Emeruwa AC 1982, journal of Natural Products, 45(2) : 123-127.

[8]. Chinoy NJ, patel KG, Suneeta Singh (1997), Journal of Medicinal Aromatic Plant Science 19(2) :. 422-426.

[9]. A A Adeneye, JA Olagunju (2009), Preliminary hypoglycemic and hypolipidamic activities of the aqueous seed extract of carica Papaya Linn in Wistar rats, Biology and Medicine, vol 1 (1), : 1-10.

[10]. Emeruva AC (1982), Antibacterial substance from Carica papya fruit extract , journal of Natural Products45(2): 123-127.

[11]. Shandavi C, Bhangale, Vikas V. Patil, Vijay R. Patil, (2010), Antibacterial activity of Ficus Bengalensis Linn. Bark on Actinomyces Viscosus, International Journal of Pharmaceutical Science, Vol 2(1), 39-43.

[12]. Mousa O, Vuorela P, Kiviranta J, Wahab SA, Hiltohen R.(1994), Bioactivity of certain Egiptiyan Ficus species, J, Ethnopharmacol, 41: 71-6.

[13]. Mukharjee PK , Saha K, MurugesanT, Mandal SC, Pal M, Saha BP, (1998), Screening of anti-diarrhoeal profile of some plant extracts of a specific region of West Bengal India, Journal of Ethnopharmacol, 60: 85-9.

[14]. Husain A, Virmani OP, Popli SP, Mishra LN, Gupta MM, Shrivastava GN, (1992), Dictionary of Indian Medicinal Plants, Lucknow, India, CIMAP, p.546.

[15]. Geetha BS, Mathew BC, Augusti KT, (1994), Hypoglycimic effects Leucodelphinidin derivative isolated from Ficus Bengalensis, Indian Journal Physiol Pharmacol, 38: 220-2.

[16]. Augusti KT(1975), Hypoglycimic action of Bengalenoside : A glucoside isolated from Ficus Bengalensis Linn in normal and Alloxandiabetic rabbits, Indian Journal Physiol Pharmacol,19: 218-20.

[17]. Patil VV, Pimprikar R. B., Patil VR, (2009), Pharmacognostical studies and evaluation of Anti- Inflammatory Activity of Ficus Bengalensis Linn. , JYP Vol 1 Issue 1, Jan-March, 49-53.

[18]. Chanchal K Roy, Jagadish V Kamath and Mohammed Asad, (2005), Hepatoprotective activity of Psidium guajava leaf extract, Indian Journal of Experimental Biology, vol. 44, 305-311.