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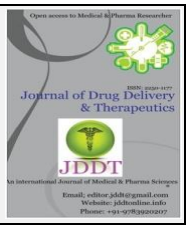

Open Access Research Article

Protective role of *Carica papaya* and *Ficus bengalensis* latex against CCl_4 induced liver toxicity in experimental rats

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ABSTRACT

Objective: To study the hepatoprotective activity of Carica Papaya Latex at the dose 400mg/kg/b.w. per oral and *Ficus Bengalensis* latex at dose 300mg/kg/b.w. per oral against CCl_4 induce Hepatotoxicity in albino rats.
Method: Animals were divided into 5 groups of 6 animals in each group.
Group I – Served as a normal control received saline 1ml /Kg for 21 days. The group -II, III, IV and V animals were received CCl_4 at dose 1ml/Kg b.w./day intra- peritoneally. Animals from group –III to V received Carica Papaya Latex (400mg/Kg.p.o.), Ficus Bengalensis Latex (300mg/Kg.p.o.) and standard drug Silymarin (30mg/Kg.p.o.) once daily for 21 days. All groups animals were sacrificed on 22 days under light ether anesthesia. Blood sample were collected and used for bio-chemical parameters like serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), Bilirubin (BRN), alkaline phosphate (ALP) and total protein.
Result: The results were observed that Carica Papaya latex at dose 400 mg/kg.b.w and CCl_4 treated group , *Ficus Bengalensis* latex at dose 300 mg/kg.B.w and CCl_4 treated groups were found the decreased levels of SGPT,SGOT,, ALP and Bilirubin and increased total protein level compare to CCl_4 treated group .So that this study indicated hepatoprotective effect .
Conclusion: Present investigation indicated that both latex of *Carica papaya* and *Ficus Bengalensis* showed significant protection against CCl_4 induced hepatotoxicity in Rats.
Keywords: *Carica Papaya*, *Ficus Bengalensis*, Hepatoprotective, Carbon Tetra Chloride, Silymarin.

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INTRODUCTION

Liver injury induced by various hepatotoxins has been recognized as major toxicological problem for year [1]. Hepatic injury is associated with alteration of these metabolic functions [2]. *Ficus Bengalensis* is commonly known as banyan tree belong to family Moraceae. This tree is considered to be sacred tree in India. The plant is a large evergreen tree distributed all over the India from sub Himalayan region and in the deciduous forest of Deccan and South India. It is a grown in gardens and roadsides for shades [3].

It is a very large tree up to 30m in height with widely spreading branches bearing many aerial roots functioning as a prop roots, bark greenish white, leaves simple , alternate , often in clusters at end of branches stipulated, 10-20cm long and 5-12.5cm broad. All parts of the plants are astringent anti-inflammatory, ophthalmic, diaphoretic, antidiarrheal and anti-emetic [4].

The leave contains crude protein, CaO, Phosphorus, crude fibres, taraxosterol [5]. Leaves also contain bengalenoside, Aglucoside[6]. The latex of *ficus Bengalensis* contains sugar, resin, albumin, malic acid and cerin [7, 8].

Ficus Bengalensis extracts reported anti-inflammatory activity [9]. Aqueous extract of bark of *Ficus Bengalensis* has been reported hypolipidemic effect [10].

Carica papaya belongs to family Caricaceae. It traditionally used to treat skin disorders [11]. *Carica papaya* is cultivated in tropical and subtropical regions all around the world as a

fruit due to its palatable test nutritive value and easy digestion [12].

Plant is a small, soft wood, fast growing, and soft live laticiferous tree upto 8m in height. Fruits are bitter, aphrodisiac, appetizer, digestive, carminative, anthelmintic, anti-inflammatory. The latex is used as a laxative digestive galactogogue[13]. Seed extract have been reported bactericidal activity [14]. Pulverized seeds also reported anti-parasitic and for anti-fertility activity [15].

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.

Carica Papaya Latex Collection

Latex was collected regionally in early morning 7:00 to 8:00 am, as the flow of latex is low during the day. Collection was done by making 1-2 mm deep vertical incisions on the skin of unripe fruit. The latex was then dried at the room temperature until it became breakable and non-sticky. The dried latex was triturated using a mortar and pestle. It was stored at 4-8 ºC until use [16].

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 1-2 mm deep vertical incisions on the skin [16]. Latex was extracted by maceration method (48h) in methyl alcohol once defatted with Petroleum ether at (72h) at room temperature. The extracted was dried by rotatory evaporator under reduced pressure [17]. The dried latex was triturated using a mortar and pestle. It was stored at 4-8^{0}C until use.

Chemicals and Drugs

Silymarin (gift sample from Ranbaxy Laboratories, Delhi), Carbon Tetra Chloride (Tomar Biological Centre, Agra), Alkaline Phosphate, Total Protein, SGOT (Diagnostic test kit from Beacon Diagnostic Pvt. Ltd., NAVSARI), SGPT kit (AGD Clinipak from AGD Biomedicals Pvt. Ltd. Mumbai), Bilirubin (Diagnostic kit from SIEMENS Ltd., Vadodara, Gujrat), other chemicals were obtained from commercial supplier.

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.

Phytochemical Screening

The chemical compounds that occur naturally in plants are known as Phytochemicals. The term is generally used to refer to those chemicals that may affect health, but are not established as essential nutrients. The presence of, alkaloids, general test for glycosides (reducing sugars), tannins, anthraquinones, sterols and saponins, flavonoids, were tested by simple qualitative methods (Trease and Evans, 1989)[18].

Experimental Animals

Albino rats of either sex (Wister strain) weighing 150-200g and female albino mice weighing 20-25g were used in this study.

The animals were acclimatized for 10 days beneath laboratory conditions. They were housed in polypropene cages and maintained at twenty seven 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.

Determination of acute toxicity LD_{50}

The acute toxicity for *Carica Papaya* Latex and *Ficus bengalensis* latex were determined in female albino mice. The animals were fasted nightlong before 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 [19].

CARBON TETRA CHLORIDE HEPATOTOXICITY:

Animals were divided into five groups of 6 animals in each (n=6)

Group I- Serve as control

Group II- Received Carbon tetrachloride (1 ml /kg. i.p.)

Group III- Received Carbon tetrachloride (1 ml /kg. i.p.) and *Carica papaya* latex (400mg/k.g p.o.).

Group IV- Received Carbon tetrachloride (1 ml /kg. i.p.) and *Ficus Bengalensis* Latex(300mg/k.g p.o.)

Group V- Received Carbon tetrachloride (1 ml /kg. i.p.) and Silymarin(30mg/kg p.o.)

Group I – Served as a normal control received saline 1ml /Kg for 21 days. The group -II, III, IV and V were received 1ml/Kg b.w./day dose of CCl_4 intra- peritoneally . Animals from group –III to V received *Carica Papaya* Latex (400mg/ Kg.p.o.), *Ficus Bengalensis* Latex (300mg/Kg.p.o.) and standard drug Silymarin (30mg/Kg.p.o.) once daily for 21 days [20, 21].

All groups animals were sacrificed on 22 days under light ether anesthesia. Blood sample were collected.

Blood sample were centrifuged at 2500 rpm for 10 min.[22] and separated serum sample used for estimation of SGOT, SGPT , Bilirubin, ALP and total protein through the auto analyzer for the study of the toxic effect of CCl4 .

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

Biochemical Analysis

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

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

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

Histological studies

The Liver were isolated from the animals and washed with normal Saline. The liver was fixed in Formalin diluted to

10% with normal Saline then processed further for histological studies. The results were analyzed by student t-test.

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.

RESULTS

Table 1: Hepatoprotective activity of *Carica papaya* Latex & *Ficus Bengalensis* Latex in CCl_4 induced albino rats

S.No.	Groups	SGPT(1u/L)	SGOT(1u/L)	Bilirubin(mg/dL)	ALP	Total Protein
1.	Control	58.28±0.62	46.32±0.52	0.72±0.04	68±1.62	9.02±0.036
2.	CCl_4 (1ml/Kg,i.p)	126.42±3.42	108.46± 1.48	0.99±0.17	242±4.18	5.44±0.023
3.	CCl_4 (1ml/Kg,i.p)+ *Carica Papaya* Latex(400mg/kg)	94.24±2.10*	76.48±1.28	0.85±0.22*	205±6.07	6.94±0.34
4.	CCl_4 (1ml/Kg,i.p)+ *Ficus Bengalensis* Latex(300mg/kg,P.O)	98.84±4.05	84.62±2.34*	0.92±0.32	214±8.02	7.08±0.12*
5.	CCl_4 (1ml/Kg,i.p) + Silymarin(30mg/Kg/P.O)	66.18±1.24**	48.56±0.65**	0.88±0.08	74±2.76	8.27±0.06**

All values are expressed in mean ± SE; n=6 significance vs Control *P <0.01

Effect of *Carica Papaya* and *Ficus Bengalensis* Latex on Carbon Tetra Chloride induced liver damage in rats with reference to biological changes in serum is shown in Table1. The Carbon Tetra Chloride treated control group showed a significant increase in total SGPT (126.42±3.42), SGOT (108.46± 1.48), Bilirubin (0.99±0.17), ALP (242 ± 4.18) and a decrease in total protein (5.44±0.023) indicating the liver injury caused by Carbon Tetra Chloride. Whereas animal treated with *Carica Papaya* and *Ficus Bengalensis* Latex exhibited a decrease in SGPT (94.24±2.10, 98.84±4.05), SGOT(76.48± 1.28, 84.62±2.34), Bilirubin(0.85±0.22, 0.92±0.32), ALP (205 ± 6.07, 214± 8.02) along with a significant increase in total protein (6.94±0.34, 7.08±0.12).

Histology :-

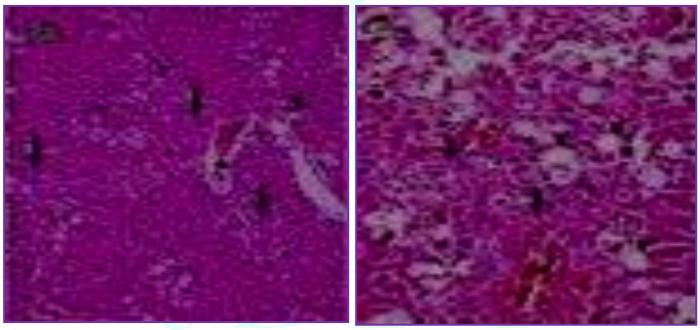

Figure A: Control Group Figure B: CCl4 Treated group

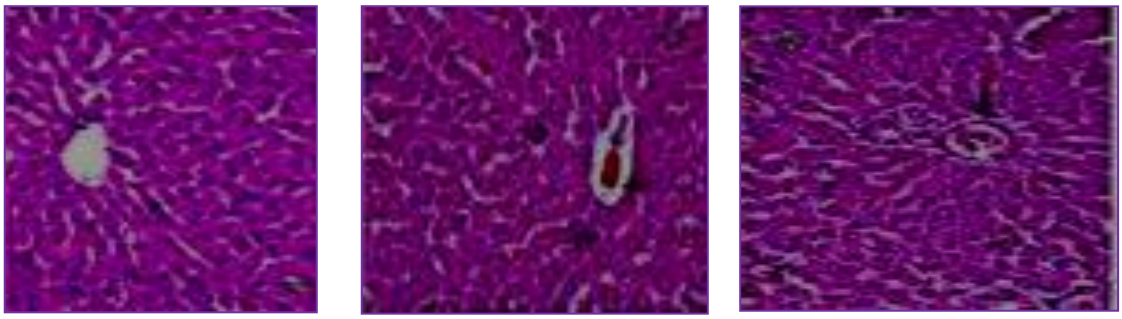

Fig. C: *Carica Papaya* & CCl4 **Fig. D: *Ficus Bengalensis* & CCl4** **Fig. E: Silymarin & CCl4**

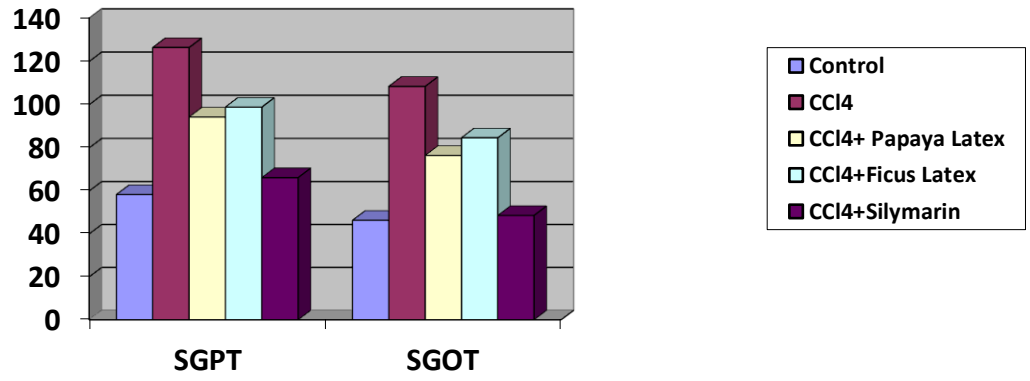

Fig. F: SGPT and SGOT Level of CCl4 Induced Hepatotoxicity

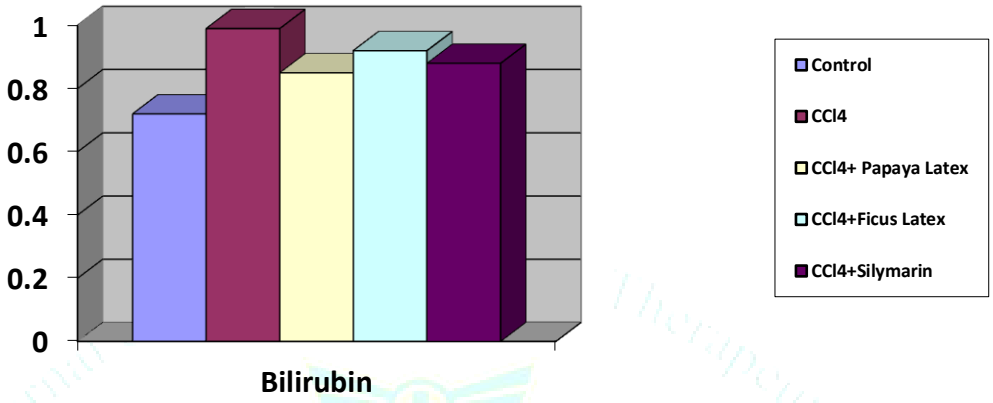

Fig. G: Bilirubin Level of CCl4 Induced Hepatotoxicity

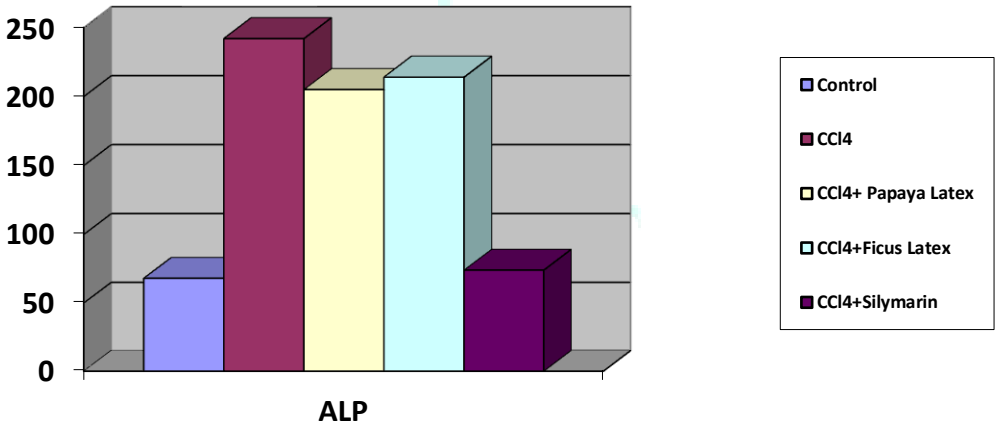

Fig. H: ALP Level of CCl4 Induced Hepatotoxicity

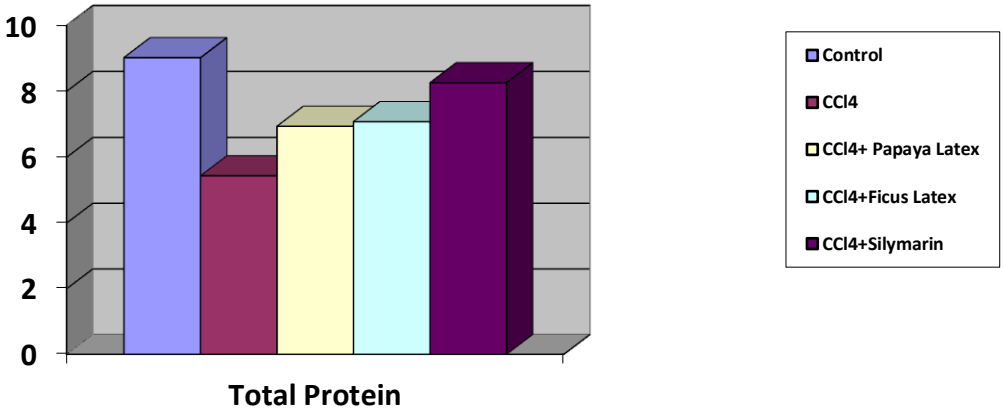

Fig. I: Total Protein Level of CCl4 Induced Hepatotoxicity

DISCUSSION

Preliminary Phytochemical investigation of *Carica papaya* and *Ficus Bengalensis* latex revealed the presence of alkaloids, Phenols, Saponins, Glycosides, Flavonoids, Triterpenoids, Sterols and tannins.

Present investigation indicated that both latex of *Carica papaya* and *Ficus Bengalenesis* showed significant protection against CCl_4 induced hepatotoxicity in Rats. CCl_4 is metabolized in liver by cytochrome P_{450} dependent electron transport chain system yielding trichloromethyl radical that in aerobic condition rapidly gets converted to its peroxyl radical .These radicals bind directly to lipids and proteins through covalent bonds and also interact with cell membrane phospholipids, leading to promotion of lipid peroxidation, disturb Ca2+ homeostasis and finally results in cell death [23].

Increased levels of serum enzymes are indication of cellular leakage and loss of functional integrity of cell membrane in liver. Damage to the liver cells cause leakage of cellular enzymes into serum [24]. A significant rise in SGOT, SGPT and reduction in the level of total protein could be taken as a index of liver damage [25]. The reversal of increase serum transaminases and reduction in the total proteins level return to normal by administration of Carica Papaya and *Ficus Bengalensis* Latex with healing of hepatic parenchyma and regeneration of hepatocytes.

The effect of *Carica Papaya* and *Ficus Bengalensis* Latex on serum marker enzymes was presented in Table No.1. the level of serum parameter SGPT, SGOT, Bilirubin, ALP were markedly elevated and that of protein was decreased in CCl4 treated animals indicated liver damage. The administration of *Carica Papaya* (400mg/kg.p.o.) and *Ficus Bengalensis* Latex (300mg/kg.p.o.) remarkably prevented CCl4 induced hepatotoxicity. The effect of *Carica Papaya* and *Ficus Bengalensis* Latex was comparable to that of standard drug Silymarin (Table no.1).

Control group animals showed normal hepatic architecture (Figure A). The group-II animals exhibited intense centrilobular necrosis, vacuolization and macrovesicular fatty changes (Figure B). Silymarin treated animals showed a normal hepatic architecture (Figure E). Moderate accumulation of fatty lobules and cellular necrosis (Figure C,D) were observed in the animals treated with *Carica Papaya* and *Ficus Bengalensis* Latex. However *Carica Papaya* Latex treated animals exhibited significant liver protection against CCl4 induced liver damage (Figure C).

CONCLUSION

The present investigation concluded that both plant *Carica Papaya* Latex and Ficus *Bengalensis* Latex were observed significant protection against CCl_4 induced hepatotoxicity in rats.

We found that the treatment with both latex prevented elevation of serum parameter like SGPT, SGOT, Bilirubin, ALP and increase the decreased level of total proteins due to CCl_4, challenge models. Whereas *Carica papaya* latex was possess better hepatoprotective activity compare to *Ficus Bengalensis* latex.

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