

**HEPATOPROTECTIVE EFFECT OF *JATROPHA CURCAS* FRUIT EXTRACTS
AGAINST CARBON TETRACHLORIDE INDUCED LIVER FIBROSIS IN RATS**

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ABSTRACT

The present study was undertaken to explore the hepatoprotective potential of *Jatropha curcas* fruit extracts against carbon tetrachloride (CCl₄) induced liver fibrosis in wistar rats. Liver fibrosis was induced by carbon tetrachloride (3ml/kg body weight) in animals. Blood biochemical, urine analysis and histological studies were carried to assess the hepatoprotective effect. Carbon tetrachloride administration induced severe liver fibrosis in rats, which was evident from enhanced levels of albumin, total bilirubin, direct bilirubin, indirect bilirubin, serum glutamate-O-methyl transferase, serum glutamate pyruvate transferase and alkaline phosphate. Pretreatment with silymarin (50mg/kg dose orally) significantly reversed carbon tetrachloride induced liver fibrosis. *Jatropha curcas* methanolic extract (250mg/kg body weight) showed significant effect than *Jatropha curcas* aqueous extract (250mg/kg body weight). From the obtained results it may be concluded that *Jatropha curcas* methanolic extract exerted a significant effect against CCl₄ induced hepatotoxicity in rats than *Jatropha curcas* aqueous extract (p<0.001) for most of the blood biochemical, urine analysis as well in attenuation of liver fibrosis.

KEYWORDS: Hepatoprotective, carbon tetrachloride, silymarin, *Jatropha curcas*, liver fibrosis.**INTRODUCTION**

Liver is one of the major organs for biotransformation of drugs or chemicals. It not only helps in eliminating the therapeutically useful agents but also helps in the treatment of poisoning by enhancing the elimination of drugs or toxins. Certain drugs in excess dose or toxins through their reactive metabolites may cause liver injury because of the covalent or non covalent interactions with the liver cells. Therapeutically useful drugs like paracetamol, isoniazid, iproniazid, halothane, methotrexate, chlorpromazine, androgens, antimicrobials, certain toxins such as aflatoxins, carbon tetrachloride as well as alcohol can cause liver injury.^[1]

MATERIALS AND METHODS**Animals**

Wistar rats of either sex, weighing around 200- 250 g were employed in the present study. They were obtained from animal house of Chalapathi Institute of Pharmaceutical Sciences, Guntur. The rats are provided with standard conditions (12 hr cycle; 25⁰ C room temperature, laboratory rat feed, e.g., Amrut[®] and water. The animals were acclimatized to the laboratory conditions for at least 5 days before the study. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Chalapathi Institute of Pharmaceutical Sciences, Guntur, Andhra Pradesh (Approval No: 09/IAEC/CIPS/2016-17; dt 05/04/2016) and care of the animals was taken as per standard

operating procedures of the Committee for the Purpose of Control and Supervision of Experiments on Animals, Ministry of Forests, Environment and Climate Change, Government of India.

Plant material

The plant material consists of dried powdered fruit of *Jatropha curcas* Linn. belonging to the family Euphorbiaceae.

Preparation of plant extract

Fresh fruits of *Jatropha curcas* linn. Were collected from Ongole, Prakasam(Dt). India. The fruits were dried for one month and latter powdered. This powder was packed into the thimble then by using a soxhlet apparatus, it was run until the color turns to white by using methanol and aqueous extracts. Then it was evaporated by using a rotator evaporator until it gets dried.

Experimental groups

The efficacy of *Jatropha curcas* aqueous extract was compared with *Jatropha curcas* methanolic extract by evaluating in vivo hepatoprotective activity in rats against liver fibrosis.^[13,18]

Five groups, each comprising of five wistar rats, were employed in the present study.

➤ Group I (Control group): Rats received only normal saline orally for 14 days.

- Group II (CCl₄ - treated control group): Rats were administered CCl₄ (3ml/kg, i.p.) on the day 14.
- Group III (Silymarin + CCl₄ - treated group): Rats were treated with silymarin (50 mg/kg, orally) for 14 days. On the 14th day Silymarin was administered 60 min prior the administration of CCl₄.
- Group IV (JCAE + CCl₄ -treated group): Rats were treated with JCAE (250mg/kg body weight) for 14 days. On 14th day JCAE was administered 60 min before the administration of CCl₄.
- Group V (JCME + CCl₄ -treated group): Rats were treated with JCME (250mg/kg body weight) for 14 days. On 14th day JCME was administered 60 min before the administration of CCl₄.

Parameters evaluated

- a) Blood biochemical parameters: albumin (g/dl), total bilirubin (mg/dl), direct bilirubin (mg/dl), indirect bilirubin (mg/dl), SGOT (U/lit), SGPT (U/lit), ALP (U/lit).
- b) Urine analysis: acetone / ketone bodies, bile salts, bile pigments, urobilinogen.
- c) Histological studies of liver tissues.

Effect on blood biochemical and urine analysis parameters

Administration of CCl₄ (3ml/kg, i.p.) showed significantly increased levels of all blood biochemical parameters except decreased direct bilirubin levels, when compared to normal control group. JCAE and JCME treatment groups showed significant hepatoprotective effect ($p < 0.001$) against CCl₄ group as described in Table 1.

Silymarin (50 mg/kg, orally) pre-treated animals showed significant difference in SGOT, SGPT and in ALP which is evident from Table 1.

JCAE (250mg/kg body weight) pre-treated animals showed significant increased levels of all blood biochemical parameters except ALP.

JCME (250mg/kg body weight) to pre-treated animals showed significant increased levels of all blood biochemical parameters except ALP.

The urine analysis parameters of various treatment groups were found to be negative Table 2.

RESULTS

Various pharmacological interventions employed in the present study did not show any significant mortality.

Table 1: Blood biochemical parameters of various treatment groups.

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
1	Albumin(g/dl)	4.74±0.15	5.4±0.57	5.29±0.07	4.08±0.26	4.5±0.24
2	Total Bilirubin(mg/dl)	0.64±0.09	0.79±0.01	0.66±0.08	0.52±0.05	0.72±0.05
3	Direct Bilirubin(mg/dl)	0.32±0.07	0.3±0.04	0.22±0.07	0.2±0.03	0.27±0.01
4	Indirect Bilirubin(mg/dl)	0.3±0.05	0.46±0.099	0.36±0.024	0.32±0.04	0.43±0.05
5	SGOT(IU/L)	294.8±21.73	785.6±19.94	170.4±20.06	307±41.14	459±14.17
6	SGPT (IU/L)	181.6±10.94	573.4±10.14	162±17.31	191±32.40	182.6±16.56
7	ALP(IU/L)	64.8±1.93	89±3.16	79.6±2.29	194±14.39	123±2.16

Table 1(a): Effect of various treatments on albumin.

Sl. No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
1	Albumin(g/dl)	4.74±0.15	5.4±0.57	5.29±0.07	4.08±0.26	4.5±0.24

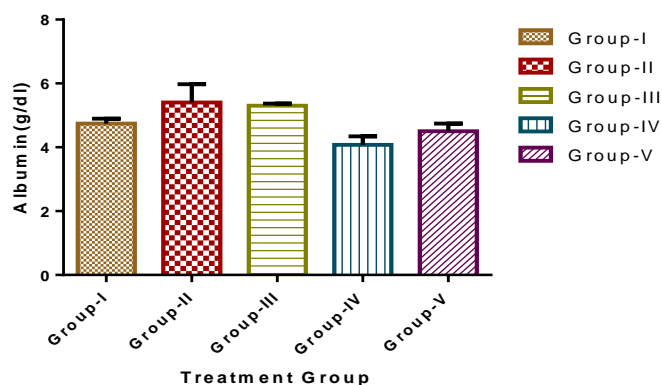
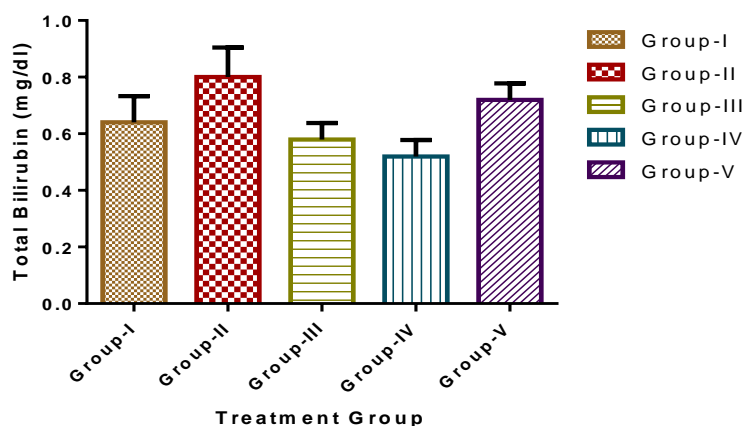


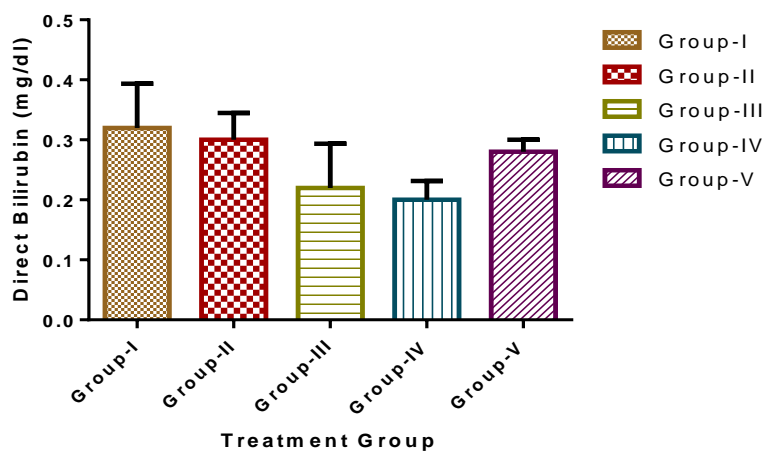
Figure 1: Effect of various treatments on albumin.

Table 1(b): Effect of various treatments on total bilirubin.

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
2	Total bilirubin(mg/dl)	0.64±0.09	0.79±0.01	0.66±0.08	0.52±0.05	0.72±0.05

**Figure 2: Effect of various treatments on total bilirubin.****Table 1(c): Effect of various treatments on direct bilirubin.**

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
3	Direct bilirubin(mg/dl)	0.32±0.07	0.3±0.04	0.22±0.07	0.2±0.03	0.27±0.01

**Figure 3: Effect of various treatments on direct bilirubin.****Table 1(d): Effect of various treatments on indirect bilirubin.**

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
4	Indirect bilirubin (mg/dl)	0.3±0.05	0.46±0.099	0.36±0.024	0.32±0.04	0.43±0.05

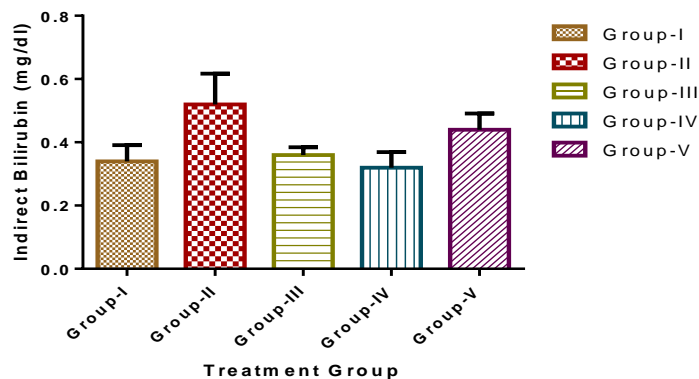


Figure 4: Effect of various treatments on indirect bilirubin.

Table 1(e): Effect of various treatments on SGOT.

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
5	SGOT(IU/L)	294.8±21.73	785.6±19.94	170.4±20.06	307±41.14	459±14.17

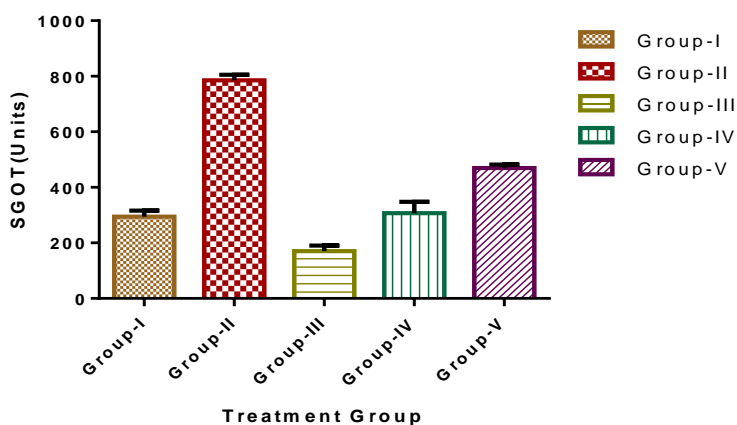


Figure 5: Effect of various treatments on SGOT.

Table 1(f): Effect of various treatments on SGPT.

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
6	SGPT (IU/L)	181.6±10.94	573.4±10.14	162±17.31	191±32.40	182.6±16.56

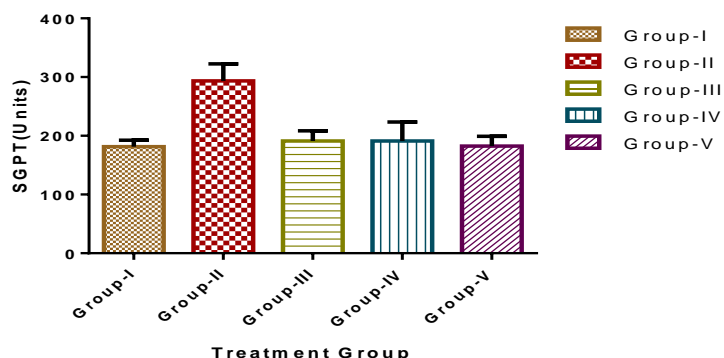


Figure 6: Effect of various treatments on SGPT.

Table 1(g): Effect of various treatments on ALP.

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
7	ALP(IU/L)	64.8±1.93	89±3.16	79.6±2.29	194±14.39	123±2.16

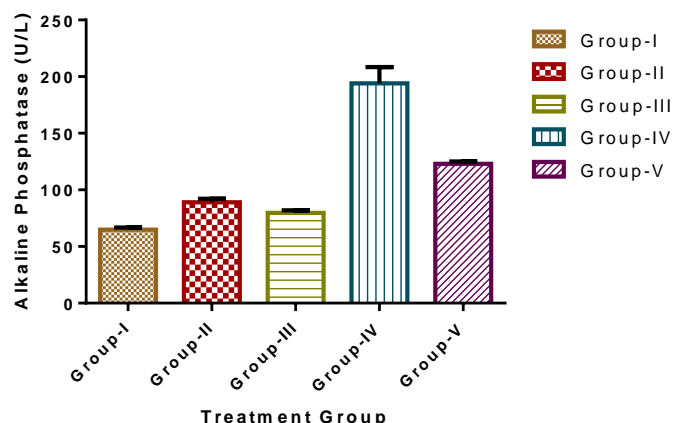


Figure 7: Effect of various treatments on ALP.

Table 2: Urine analysis parameters of various treatment groups.

Sl.No.	Parameters	Group-I	Group-II	Group-III	Group-IV	Group-V
1	Bile pigments	Negative	Negative	Negative	Negative	Negative
2	Bile salts	Negative	Negative	Negative	Negative	Negative
3	Ketone/ acetone bodies	Negative	Negative	Negative	Negative	Negative
4	Urobilinogen	Nil	Nil	Nil	Nil	Nil

Histopathological studies

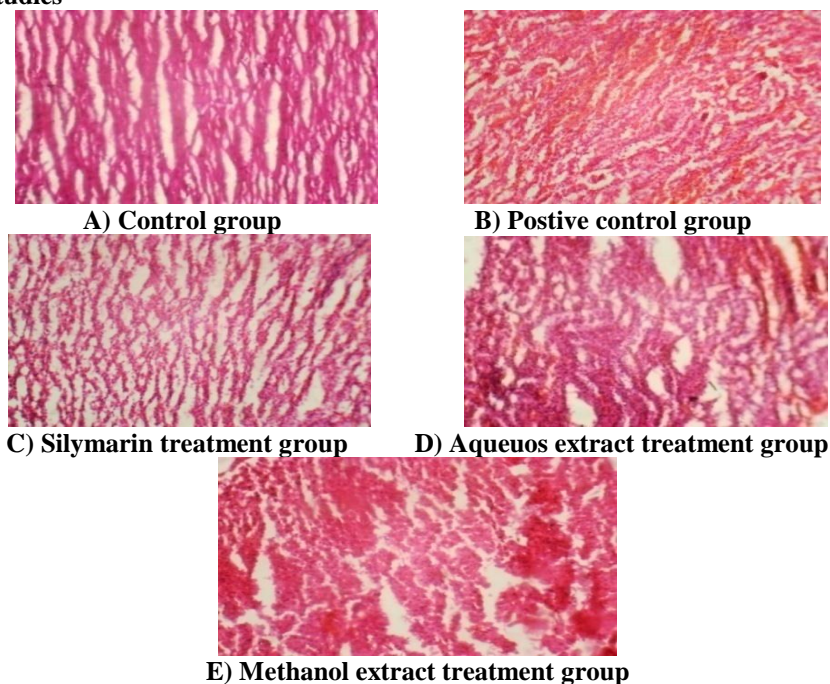


Figure 8: Histology slides of the isolated liver of various treatment groups showing haematoxylin and eosin stained cells.

CONCLUSION

From the obtained results it may be concluded that *Jatropha curcas* methanolic extract exerted a significant effect against CCl₄ induced hepatotoxicity in rats than *Jatropha curcas* aqueous extract ($p < 0.001$) for most of the blood biochemical parameters, urine analysis as well in attenuation of liver fibrosis.

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