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PROTECTIVE ABILITY OF *MOMORDICA CHARANTIA L* AGAINST CCL_4 INDUCED HEPATIC DAMAGE IN RATS

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ABSTRACT
The aim of this study is to evaluate the efficacy of *Momordica charantia* on the experimental hepatotoxicity induced by carbon tetrachloride (CCl_4). Carbon tetrachloride was administered once and simultaneously suspension of dry fruit powder was prepared in aqueous medium and was daily administered at a dose level of 1mg/kg body weight for 4 days. Silymarin was used as a standard drug for this study. Administration of carbon tetrachloride showed significant changes in the levels of serum aminotransferase, alkaline phosphatase, bilirubin and total proteins levels, however necrosis, collagen deposition and altered hepatic architecture were also observed. Markers of liver injury, altered aminotransferase, alkaline phosphatase, bilirubin etc. and morphological changes such as necrosis and collagen deposition were significantly decreased in the rats treated with *Momordica charantia* fruit powder. These results suggest that the *Momordica charantia* showed hepatoprotective effect on carbon tetrachloride induced hepatic damage and may be a potential clinical application for treatment of liver diseases.

KEYWORDS: *Momordica charantia,* hepatoprotective, AST, ALT, Silymarin

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INTRODUCTION

Momordica charantia L is used for treatment of gastrointestinal infection, against breast cancer, against diabetes and has no known side effects.[1] It stimulates digestion and is helpful in people with sluggish digestion, dyspepsia, and constipation, it can sometimes make heartburn, as demulcent, shows anti-malarial activity. It is effective for treating HIV infection.[2] It is used as an immunomodulator and increases insulin sensitivity. It lowers elevated blood sugar levels.[3]

Liver has an important place in toxicology by virtue of its function, both qualitatively and quantitatively. It plays a major role in detoxification and excretion of many endogenous and exogenous compounds, any injury to it or impairment of its functions may lead to many implications on ones health. Management of liver diseases is still a challenge to the modern system of medicine[4]. The modern medicines have little to offer for alleviation of hepatic ailments, whereas most important representatives are of phytoconstituents[5].

MATERIALS AND METHODS

Plant Material

The fruits of *Momordica charantia* L were collected from the fields around Rajgurunagar, Pune, Maharastra, India. After collection of the required quantity, they were washed, carefully segregated, cut down into small pieces and dried in shade to a constant weight. The plant material was kept in preset oven for a week at 40°C and powdered in high speed electronic mixer and sieved through a BSS Mesh No. 85 sieve and stored in an airtight container. This plant material was used for animal trials.

Animals

Albino rats of either sex (120-150g) were used for this study. The animals were maintained under standard laboratory conditions at temperature 23±2^{0}C with relative humidity 55±10 % and 12 h light and dark cycle throughout all the experiments. Animals had free access to food and water *ad libitum*.[5, 6] The dose selected for fruit powder of *Momordica charantia* in the form of aqueous slurry is 1g/Kg body weight against CCl_4 damaged liver in rats. Animals were grouped into five groups. Each group consists of 12 animals, 6 males and 6 females. Reversible liver damage was induced by 0.7ml/Kg of CCl_4 in 0.5 ml. Liquid Paraffin per animal i.p. The dose of plant powder in the form of aqueous slurry was given orally via gavages as per dose chart in **Table 1**.

Gr. I served as Normal Control; Gr. II served as CCl_4 Control, Gr. III served as CCl_4 Recovery, Gr. IV served as CCl_4 + fruit powder of *Momordica charantia* in the form of aqueous slurry and Gr. V served as CCl_4+ Silymarin (a known hepatoprotectant).

Assessment of Liver Function

The animals from all groups were sacrificed on IVth day and for of the study except the natural recovery group which was sacrificed on VIIth day after natural recovery of liver was initiated. The blood sample was collected by cardiac puncture, blood and biochemical investigations were carried out to assess liver function by using commercial diagnostic kits

A single dose dministration of CCl_4 resulted in a significant change in serum AST, ALT, Alkaline Phosphate, bilirubin, total proteins levels etc. The treatment with *Momordica charantia* L fruit powder exhibited an ability to counter act the CCl_4 induced hepatotoxicity by regaining the AST, ALT, Alkaline Phosphate and bilirubin levels like normal rats. Histopathology of liver of the normal control rats showed prominent central vein and normal arrangement of hepatic cell (**Fig. 1**). CCl_4 treated rats showed various degrees of pathological changes starting from centrilobular necrosis of hepatic cells to central lobular fatty degeneration (**Fig. 2**). The natural recovery group shows some initial signs of recovery indicating slight recovery (**Fig 3**). Liver section of rats treated with *Momordica charantia* L fruit powder in the form of aqueous slurry showed significant protection against CCl_4 induce liver damage(**Fig 4**). The sections of liver taken from the rats treated with standard drug Silymarin showed the hepatic architecture, which was similar to that of control (**Fig. 5**).

DISCUSSION

Liver has an important place in toxicology by virtue of its function, both qualitatively and quantitatively. The single dose of CCl_4 has been used as a tool to induce hepatotoxicity in experimental animals. CCl_4 induce hepatic damage is due to its cytochrome P-450 enzyme system catalyzed hepatic conversion into highly reactive trichloromethyl radical (CCl_3), which upon reaction with oxygen radical gives trichloromethyl peroxide radical ($OOCCl_3$). The radical form a covalent bond with sulfhydryl group of several membrane molecules like glutathione, considered as the initial step in the chain of events leading to lipid peroxidation and hepatic tissue destruction. Normal liver functions are characterized by the balanced activities of serum marker enzymes AST, ALT and Alkaline Phosphate, bilirubin as well as total protein. Hepatocellular necrosis leads to very high level of AST and ALT released from liver in the blood. Among the two, ALT is a better index of liver injury, as liver ALT activity represents 90% of total enzyme present in the body. Alkaline phosphate activities on the other hand are related to the functioning of the hepatocytes, increase in its activity is due to increased synthesis in presence of increased biliary pressure.

The *Momordica charantia* L fruit powder decreases the elevated enzyme levels of AST and ALT, which suggest the protection of structural integrity of hepatocyte cell membrane or regeneration of damaged liver cells by the extract caused by carbon tetrachloride. This effect is an agreement with the view that serum levels of amino transferases return to normal with healing of hepatic parenchyma and regeneration of hepatocytes.

The observations of blood and tissue Biochemical Parameters for all Groups were given in **table 2** and **table 3**. However considerable increase in total proteins supports the normal function of the liver. *Momordica charantia* L fruit powder exerts a clear-cut protective action against carbon tetrachloride induced hepatic damage in rats.

CONCLUSION

The present work was carried out to investigate the hepatoprotective action of *Momordica charantia* L fruit powder on CCl_4 (Carbon tetra Chloride) induced liver damage in rats. Blood biochemical assays like GPT(ALT), GOT(AST), Cholesterol, Bilirubin, Triglecerides and √GT and tissue biochemical assays like Glycogen, T. Protein, Cholesterol, DNA, and RNA have been studied for evaluation of hepatoprotection. From the results of these parameters it is clear that *Momordica charantia* L fruit powder gave best recovery for hepatoprotection. The observations of "Group I" were matching with "Group IV" than all other groups. The combined synergistic effect of its constituents and micronutrients rather than to any single factor through free radicals scavenging activity play important role in regeneration of liver cells.

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Table 1: Daily Doses Regime

DAYS	Group I Normal control	Group II CCl_4. control	Group III CCl_4 treated natural recovery	Group lV CCl_4 + plant material treated	GroupV Silymarin treated
1	0.5cc liq. Paraffin & 2 cc d/w oral	0.7cc/kg CCl_4 in 0.5cc liq. Paraffin i.p.& 2cc d/w oral	0.7cc/kg CCl_4 in 0.5cc liq. Paraffin i.p. & 2cc d/w oral	0.7cc/kg CCl_4 in 0.5cc liq. Paraffin i.p. & 1gm/kg plant material in 2cc d/w oral	0.7cc/kg CCl_4 in 0.5cc liq. Paraffin i.p., 0.007gm/kg Silymarin in 2cc d/w oral
2	2cc d/w oral	2cc d/w oral	2cc d/w oral	1gm/kg plant material in 2cc d/w oral	0.007gm/kg Silymarin in 2cc d/w oral
3	2cc d/w oral	2cc d/w oral	2cc d/w oral	1 gm/kg plant material in 2cc d/w oral	0.007gm/kg Silymarin in 2cc d/w oral
4	Sacrifice	Sacrifice	2cc d/w oral	Sacrifice	Sacrifice
5	-	-	2cc d/w oral	-	-
6	-	-	2cc d/w oral	-	-
7	-	-	Sacrifice	-	-

All dosages are for each individual animal in the group.
The number of animals in each group 12 (6 males + 6 females)
i.p. : intraperitoneal.
d/w : Distilled Water.

Table 2: Tissue Biochemical Parameters of All Groups

Parameter	Gr.I	Gr.II	Gr.III	Gr.IV	Gr.V
Gycogen	20.5±1.2	20.40±1.3	22.30±1.2	19.20±1.4	17.5±1.4
T. Protein	4.4±1.0	20.2±1.1	10.5±1.3	5.1±1.1	9.1±1.3
Cholesterol	1.6±0.4	2.30±0.5	1.90±0.5	2.1±0.4	2.8±0.7
DNA	0.5±0.01	0.45±0.12	0.90±0.14	0.44±0.22	0.7±0.13
RNA	2.4±0.1	4.9±0.1	3.75±0.2	2.2±0.2	6.5±0.3

Table 3: Blood Biochemical Parameters of All Groups

Parameter	Gr.I	Gr.II	Gr.III	Gr.IV	Gr.V
GPT(ALT)	55.60±1.1	50.08±1.1	41.20±1.2	56.30±1.2	66.50±1.1
GOT(AST)	44.00±1.0	46.20±1.4	48.30±1.3	46.10±1.3	56.84±1.2
Cholesterol	75.60±1.3	82.40±1.2	75.40±1.2	74.40±1.0	69.50±1.4
Bilirubin	0.58±0.2	0.68±0.3	0.64±0.3	0.57±0.1	0.65±0.2
Triglecerides	124.50±1.2	130.00±2.1	94.80±2.1	122.10±2.2	124.50±2.3
√GT	18.30±1.0	41.20±1.5	33.40±1.3	20.30±1.4	24.80±1.2

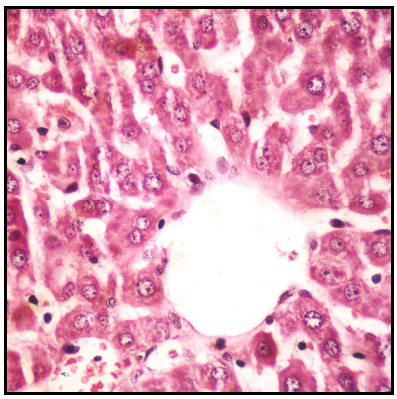

Fig. 1: Light micrograph of Normal rat Liver

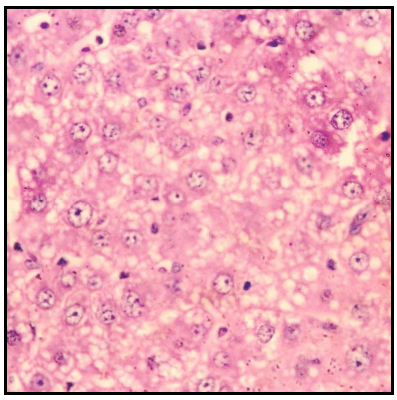

Fig. 2: Light micrograph of rat liver after CCl_4 Treatment

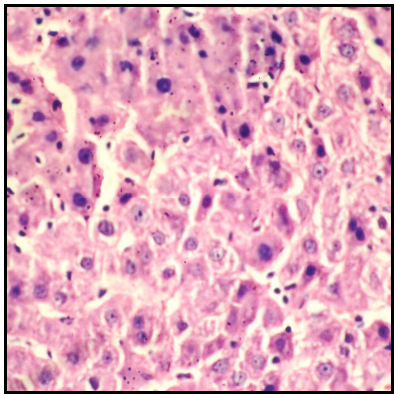

Fig. 3 : Light micrograph of rat liver after Natural Recovery

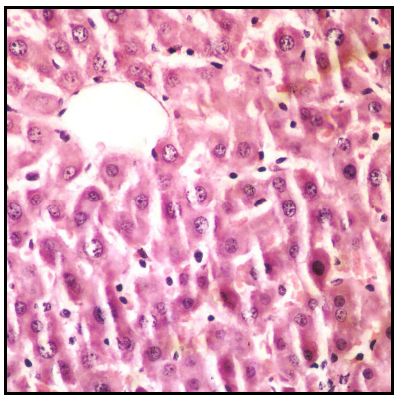

Fig. 4: Light micrograph of rat liver treated with CCl_4 and Plant material

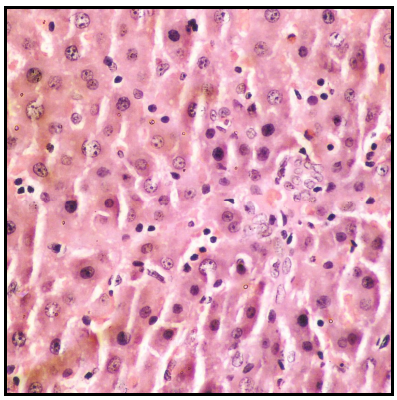

Fig. 5: Light micrograph of rat liver treated with CCl_4 and Silymarin

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