



# HEPATOPROTECTIVE ACTIVITY OF *MOMORDICA CYMBALARIA* HOOK. F AGAINST PARACETAMOL INDUCED HEPATIC INJURY IN RATS

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## ABSTRACT

Methanolic extract of *Momordica cymbalaria* Hook. F. (MEMC) was studied against paracetamol induced hepatitis in rats. Alteration in the levels of biochemical markers of hepatic damage like SGPT, SGOT, ALP, bilirubin, cholesterol, HDL, tissue GSH and lipid peroxidation were tested in both; treated and untreated groups. Pre-treatment with MEMC reduced biochemical markers of hepatic injury like SGPT, SGOT, ALP, bilirubin, cholesterol and lipid peroxide levels and increased HDL, GSH levels. Treatment with MEMC (200, 400, 600 mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner. A significant hepatoprotective activity of the methanol extract of *Momordica cymbalaria* has been reported.

**Key words:** MEMC, *Momordica cymbalaria*, Hepatoprotective, Paracetamol

## INTRODUCTION

The liver is a vital organ of paramount importance involved in the maintenance of metabolic functions and detoxification from the exogenous and endogenous challenges, like xenobiotics, drugs, viral infections and chronic alcoholism. If during all such exposures to the above mentioned challenges, the natural protective mechanisms of the liver are overpowered, the result is hepatic injury. Liver damage is always associated with cellular necrosis, increase in tissue lipid peroxidation and depletion in the tissue GSH levels. In addition, serum levels of many biochemical markers like SGOT, SGPT, triglycerides, cholesterol, bilirubin, alkaline phosphatase, are elevated. In spite of phenomenal growth of modern medicine, there are no synthetic drugs available for the

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treatment of hepatic disorders. However, there are several herbs/herbal formulations claimed to have possess beneficial activity in treating hepatic disorders.

*Momordica cymbalaria* Hook. F. belongs to the Cucurbitaceae family. The plant is a perennial herbaceous climber either allowed to trail on the ground or to climb on supports with the aid of tendrils. It is found in the south Indian states of Andhra Pradesh, Karnataka, Madhya Pradesh, Maharashtra and Tamil Nadu as a weed. Flowering occurs during October; fruits are harvested from November to January. The yield of each plant is 1.25 to 1.5 kg. The tender fruits closely resemble those of a small variety of bitter gourd *Athalakkai* and is used as a vegetable by the rural people of South Tamil Nadu and North Karnataka, India<sup>1</sup>. The phytochemicals reported in this plant are tannins, alkaloids, phenols, proteins, amino acids<sup>2</sup>, vitamin C, carbohydrate and  $\beta$ -carotene<sup>1</sup>. The fruits of this plant reported to have antidiabetic and antihyperlipidemic activities<sup>2</sup>. The tubers were reported as antiovolatory activity<sup>3</sup>.

Furthermore, literature survey of *M. cymbalaria* revealed that no researcher has yet reported hepatoprotective activity of this plant. However, there is no scientific basis or reports in the modern literature regarding its usefulness as hepatoprotective agent. Thus, the present study was conducted to evaluate the hepatoprotective activity of the methanolic extract of *Momordica cymbalaria* by using paracetamol-induced hepatic injury in rats.

## EXPERIMENTAL

### Plant material

The fruits of *Momordica cymbalaria* Hook F. were collected in November 2006 from the Bellary, Karnataka, India. The fruit material was taxonomically identified by the Regional Research Institute, Karnataka, India and kept as the voucher specimen RRI/BNG/DSRU/F53/2006-07. The fruits were dried under shade with occasional shifting and then powdered with a mechanical grinder and stored in an airtight container.

### Preparation of extract

The powder obtained was subjected to successive Soxhlet extraction with the solvents with increasing order of polarity i.e. pet. ether (60-80°), chloroform (59.5-61.5°), methanol (64.5-65.5°) and water. Yields were 3.29, 6.19, 11.70, and 15.71%, respectively.

### Phytochemical screening

A preliminary phytochemical screening of all extracts was carried out as described

by Khandelwal<sup>4</sup>.

## **Animals**

Albino rats (Wistar) weighing 150-200 g and albino mice weighing 20-25 g of either sex were used in this study. They were procured from Sri Venkateshwara Enterprises, Bangalore. The animals were acclimatized for one week under laboratory conditions. They were housed in polypropylene cages and maintained at  $27^{\circ}\text{C} \pm 2^{\circ}\text{C}$  under 12 hrs dark / light cycle. They were fed with standard rat feed (Gold Mohr Lipton India Ltd.) and water *ad libitum* was provided. The litter in the cages was renewed thrice a week to ensure hygeinicity and maximum comfort for animals. Ethical clearance for handling the animals was obtained from the Institutional Animals Ethical Committee (RCP/IAEC/07/2006) prior to the beginning of the project work. (129/1999/CPCSEA).

## **Acute oral toxicity studies**

The acute oral toxicity was performed according to OPPTS following up and down procedure. Colony bred female albino rats Wistar strain (150-200 g) were maintained under controlled animal house condition with access to food and water *ad libitum*. The limit test was carried out first at 5000 mg/kg. b.w. All animals were observed for toxic symptoms and mortality for 72 h.<sup>5</sup>.

## **Hepatoprotective activity**

The method of Chattopadhyay<sup>6</sup> was used in the study. Animals were divided into six groups of 6 animals each. The first group received saline 1 mL/kg for one week (control). The group II received saline 1 mL/kg for one week (positive control). The groups III, IV, V and VI received silymarin (100 mg/kg p.o.) and 200, 400 and 600 mg/kg of MEMC, respectively once a day for seven days. On the fifth day, after the administration of the respective treatments, all the animals of groups II, III, IV, V and VI were administered with paracetamol 2 g/kg orally. On the seventh day after 2 h of respective treatments, the blood samples were collected for the estimation of biochemical marker enzymes. Then animals under ether anesthesia were sacrificed. The livers from all the animals were collected, washed and used for the estimation of tissue GSH and lipid peroxide levels.

## **Biochemical analysis**

The collected blood samples were used for the analysis of biochemical markers SGPT<sup>7</sup>, SGOT<sup>8</sup>, ALP<sup>9</sup>, bilirubin<sup>10</sup>, cholesterol<sup>11</sup> and HDL<sup>12</sup> levels.

Liver slices were collected from the above groups of animals and these were subjected to the determination of tissue glutathione (GSH) level and lipid peroxidation. Tissue GSH levels were estimated by using Ellanm method<sup>13</sup> as modified by Aykae et. al<sup>14</sup>. Similarly, inhibition of CCl<sub>4</sub> induced tissue lipid peroxidation was done using the method of Buege and Steven<sup>15</sup>.

### **Statistical analysis**

The results are expressed as mean  $\pm$  SEM, (N = 6). Statistical significance was determined by one-way analysis of variance with  $p < 0.05$  considered significant. The analysis was performed by prism software.

## **RESULTS AND DISCUSSION**

Preliminary phytochemical studies of MEMC revealed that presence of tannins, alkaloids, phenols, proteins, amino acids, flavanoids, triterpenoids,  $\beta$ -sitosterol, vitamins and glycosides. The MEMC was found to be non-toxic up to 5000 mg/kg.

Paracetamol has enhanced the levels of SGPT, SGOT, bilirubin (both total and direct bilirubin levels), alkaline phosphatase level (ALP), total cholesterol, whereas HDL and tissue GSH levels are decreased significantly. Treatment with silymarin and 200, 400 and 600 mg/kg of MEMC has significantly brought down the elevated levels of SGPT, SGOT, ALP, bilirubin, cholesterol and also significantly enhanced the decreased levels of tissue GSH and HDL. Results are reported in Tables 1 and 2.

Paracetamol is normally eliminated mainly as sulfate and glucuronide. Only 5% of the paracetamol is converted into N-acetyl-p-benzoquinoneimine. However, upon administration of toxic doses of paracetamol, the sulfation and glucuronidation routes become saturated and hence, higher percentage of paracetamol molecules are oxidized to highly reactive N-acetyl-p-benzoquinoneimine (NAPQI) by cytochrome-450 enzymes. Semiquinone radicals obtained by one electron reduction of NAPQI, can covalently binds to macromolecules of cellular membrane and increase the lipid peroxidation resulting in the tissue damage.

Table 1. Effect of MEMC on biochemical parameters of CCl4 induced hepatic injury

Treatment	SGPT(U/l)	SGOT(U/l)	ALP(U/l)	Total bilirubin (mg/dL)	Direct bilirubin (mg/dL)	Cholesterol (mg/dL)	HDL (mg/dL)
Control (Saline 0.5 mL)	47.51 ± 1.82	101.01 ± 1.12	132.14 ± 1.44	0.91 ± 0.01	0.17 ± 0.01	104.76 ± 2.31	49.41 ± 1.41
Paracetamol (PCM, 2g/kg s.c)	289.31 ± 1.71	474.01 ± 1.82	257.55 ± 1.65	4.05 ± 0.06	1.31 ± 0.04	161.61 ± 3.29	28.29 ± 1.82
Silymarin (100 mg/kg + PCM)	58.32 ± 0.39*	137.73 ± 1.86*	92.09 ± 1.87*	1.22 ± 0.04*	0.33 ± 0.02*	129.16 ± 4.93*	45.81 ± 1.14*
MEMC (200 mg/kg + PCM)	137.71 ± 0.013*	248.42 ± 1.43*	156.11 ± 1.57*	2.09 ± 0.03*	0.79 ± 0.01*	142.12 ± 4.33*	44.38 ± 1.67*
MEMC (400 mg/kg + PCM)	109.34 ± 0.019*	187.81 ± 2.22*	121.01 ± 2.31*	1.72 ± 0.01*	0.63 ± 0.04*	131.31 ± 3.71*	46.71 ± 1.83*
MEMC (600 mg/kg + PCM)	77.42 ± 0.11*	154.67 ± 0.91*	89.71 ± 1.161*	1.41 ± 0.01*	0.41 ± 0.01*	119.32 ± 3.92*	43.32 ± 1.70*

\* p , 0.01 v/s PCM group, PCM: paracetamol, values are mean ± SE from 6 animals in each treatment

Higher dose of paracetamol and NAPQI can alkylate and oxidize intracellular GSH and protein thiol group, which results in the depletion of liver GSH pool subsequently, leading to increased lipid peroxidation and liver damage<sup>16</sup>. In our experiments, it was observed that tissue GSH levels in the paracetamol group decreased to the extent of around 65%. This clearly indicates that there is a significant hepatic damage due to paracetamol.

**Table 2. Effect of MEMC on the liver tissue levels of GSH and lipid peroxidation in the CCl<sub>4</sub> treated rats**

Group	Tissue levels of GSH	Tissue lipid peroxidation
Control saline (0.5 mL)	0.912 ± 0.04	0.251 ± 0.02
PCM (2 g/kg)	0.417 ± 0.06	0.363 ± 0.04
Silymarin (100 mg/kg + PCM)	0.813 ± 0.04 (+94.96) *	0.131 ± 0.04 (- 63.91) *
MEMC (200 mg/kg+ PCM)	0.566 ± 0.07 (+35.73) *	0.181 ± 0.05 (- 50.14) *
MEMC (400 mg/kg + PCM)	0.637 ± 0.05 (+52.75) *	0.167 ± 0.05 (- 53.99) *
MEMC (600 mg/kg + PCM)	0.749 ± 0.04 (+79.62) *	0.137 ± 0.04 (-62.26) *

\*p < 0.01 Vs PCM group, PCM: Paracetamol; Values are mean ± SE from 6 animals. Figures are % increase (+) and decrease (-) in absorbance

This is further evident from the fact that there is elevation in the levels of various biochemical markers of hepatic damage like SGPT, SGOT, bilirubin, and cholesterol. Treatment with silymarin and MEMC has increased tissue GSH level and reduced levels of lipid peroxide. The elevated levels of above mentioned biochemical markers reach near to the healthy levels.

It may be concluded that the hepatoprotective effect of *M. cymbalaria* is due to the prevention of the depletion in the tissue GSH levels. Upon literature review it is found that the *M. cymbalaria* contains tannins, alkaloids, phenols, proteins, amino acids, Vitamin C, carbohydrate and β-carotene<sup>1,2</sup>, which may be involved in the hepatoprotective property of this plant.

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