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## Effect of *Momordica chorantia* (Bitter Melon) Fruit extract on Homocysteine Levels and Lipid Profile in experimentally induced Hyperlipidemia in Rabbits

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### Article Info

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Received: March 21, 2019

Accepted: April 5, 2019

Published: April 18, 2019

**Citation:** Sethi J, Dahiya K. Effect of *Momordica chorantia* (Bitter Melon) Fruit extract on Homocysteine Levels and Lipid Profile in experimentally induced Hyperlipidemia in Rabbits. *Madridge J Case Rep Stud.* 2019; 3(2): 136-139.  
doi: 10.18689/mjcrs-1000135

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Published by Madridge Publishers

### Abstract

**Background:** The major clinical sequelae of hyperlipidaemia are atherosclerosis, which is the leading cause of death worldwide. It has been estimated that up to one-third of the patients of cardiovascular disease with obesity use some form of complementary and alternative medicine.

**Objective:** The present study was planned to evaluate the effect of *Momordica charantia* on plasma homocysteine levels and lipid profile in experimental animals.

**Material and methods:** Albino rabbits (1.5-2.5 kg) of either sex were divided into three groups with six animals in each group. Group I received the standard chow diet; group II rabbits received HFD; and group III rabbits received HFD supplemented with aqueous MC fruit extract (100 mg/kg). After 14 weeks of the experimental period, animals were fasted overnight and blood was taken for estimation of total cholesterol (TC), triglyceride (TG), high density cholesterol (HDL-C) and homocysteine.

**Results:** MC significantly lowered the TC and TG levels in Group III rabbits as compared to Group II. In rabbits fed on HFD, Homocysteine and TC were significantly increased.

**Conclusion:** This study suggests that MC can prove to be a significant cardioprotective substance and an important adjuvant in the treatment of hyperhomocysteinemia and dyslipidemia.

**Keywords:** *Momordica charantia*; High-fat diet; Cardioprotective; Homocysteine; Atherogenic indices.

**Abbreviations:** MC: *Momordica chorantia*; HFD: High Fat Diet; TC: Total Cholesterol; TG: Triglycerides; HDL-C: High Density Lipoprotein; LDL: Low Density Lipoprotein; Hcy: Homocysteine; CHD: Coronary Heart Disorder.

### Background

Atherosclerosis has been found to be the most frequent cause of myocardial infarction, stroke and peripheral vascular disease. Hypercholesterolemia and hyperlipidemia were previously recognized as causative agents for it, extending the area to lipoproteins especially low-density lipoprotein (LDL) as the most potential causative agents [1]. Recent evidences indicate that LDL in its native form may not be so but when oxidised by the oxidants, produced *in vivo*, becomes atherogenic [2]. Hypolipidemic drugs have their limitation due to their side effects, non-compliance due to prolonged use and rebound effect after withdrawal. Therefore, the judicious use of certain medicinal plants and drugs has been found to be effective in numerous clinical and experimental trials [3].

*Momordica charantia* (MC) is a member of cucurbitaceae family (also known as bitter melon or karela), and is traditionally used as a food in South Asia. The roots, leaves, seeds and fruits of this plant have been used in traditional medicine for treating various diseases [4]. There are studies showing the hypoglycaemic [5], antipyretic, antibacterial [6], antihelminthic, antimalarial [7], antiulcerogenic [8] and immunomodulatory [9] properties of MC. The medicinal value of the *Momordica charantia* fruit extract has been attributed to its high antioxidant properties, due in part to the presence of phenols, flavonoids, isoflavones, terpenes, anthraquinones and glucosinolates, all of which confer a bitter taste. The fruit is also rich in minerals, including potassium, calcium, magnesium, phosphorous and iron, and is a good source of dietary fibre [10].

Homocysteine (Hcy) is a sulphur containing non-essential amino acid formed from demethylation of methionine. Homocysteine has been recognized as a risk factor as early as 1990s, for the development of atherosclerotic vascular disease and hypercoagulability states [11]. In our previous study, *Momordica charantia* was reported to reduce the levels of cholesterol and triglycerides (TG) and to increase the levels of high density lipoprotein cholesterol (HDL-C) in serum, but its effect on homocysteine has not been reported in the literature yet. Therefore, the present study was planned to study the effects of the aqueous extract of *Momordica charantia* on serum homocysteine levels and atherogenic index in experimentally induced hyperlipidemia in rabbits.

## Materials and Methods

### Animals

Albino rabbits of either sex weighing 1.5-2.5 Kg were used as subjects for this study. Animals were procured from disease free animal house of CCS Haryana Agriculture University, Hisar (Haryana, India). They had free access to food and water and were maintained under 12:12 hour light and dark cycles. Institutional Animal Ethical Committee (IAEC) approved the experimental protocol (No. Phy/09/413 dated 13.5.09) and care of animals was taken as per guidelines of CPCSEA, Department of Animal Welfare, Government of India.

### Experimental design

Rabbits were divided into three groups of six each, depending on the diet received.

**Group I (n=6):** Rabbits received standard chow diet throughout the experiment for 14 weeks (Control group).

**Group II (n=6):** Rabbits received high fat diet [12] (HFD) daily throughout the experiment for 14 weeks (HFD group).

**Group III (n=6):** Rabbits received aqueous MC fruit extract (100 mg/Kg, p.o.) daily along with HFD for 14 weeks (HFD with MC group).

The composition of two diets [12] was as follows:

**Control diet:** Wheat flour 22.5%, roasted Bengal gram powder 60%, skimmed milk powder 5%, casein 4%, refined oil 4%, salt mixture with starch 4% and vitamins and choline mixture 0.5%.

**HFD:** Wheat flour 20.5%, roasted Bengal gram powder 52.6%, skimmed milk powder 5%, casein 4%, refined oil 4%, coconut oil 9%, salt mixture with starch 4%, vitamins and choline mixture 0.5% and cholesterol 0.4%.

Aqueous extract from powdered fruit of *Momordica charantia* was prepared by standard procedure. Oral dose of the extract was selected after a pilot study using three doses i.e. 50, 75 and 100 mg/Kg. All the drugs were administered orally (using an intragastric tube) as a single dose in the morning.

### Sample collection

After 14 weeks, blood samples were collected from the marginal vein of the pinna of overnight fasted rabbits in EDTA (ethylene diamine tetra acetic acid) vacutainers. The plasma was separated immediately and subjected to estimation of lipid profile. Total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were estimated on autoanalyser (Konelab 30i, Triviron) by enzymatic methods using kits by Randox [13]. Homocysteine was estimated by immunoassay using direct chemiluminometer [14] (Advia Centaur, Siemens). Atherogenic Index (AI), which is a measure of the atherogenic potential of an agent [15], and protection percentage were calculated using the following formulas and the results were tabulated.

$$\text{Atherogenic index} = \frac{(\text{Total cholesterol} - \text{HDL})}{\text{HDL}}$$

$$\text{Protection (\%)} = \frac{\text{Atherogenic index of control} - \text{Atherogenic index treated group}}{\text{Atherogenic index of control}} \times 100$$

### Statistical analysis

Results were expressed as mean  $\pm$  SEM of six rabbits in each group. Data was analyzed statistically using SPSS software version 14.0 in each group by applying students' *t*-test (unpaired).

## Results

The results reveal that feeding of atherogenic diet increased serum levels of total cholesterol, triglycerides, homocysteine and decreased serum HDL-C levels when compared to normal group over a period of 14 weeks. Administration of *Momordica charantia* fruit extract along with atherogenic diet (group III) led to statistically significant decrease in total cholesterol, triglycerides and homocysteine levels as compared to animals on atherogenic diet only (group II) (Table 1). At this time an increase of HDL-cholesterol level was also observed. *Momordica charantia* treated animals showed decrease in the atherogenic index and increased percentage of protection.

**Table 1.** Lipid profile, atherogenic index and homocysteine levels in rabbits in different experimental groups.

Group	TC (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	Atherogenic index	Homocysteine ( $\mu$ mol/L)
Group I (Control)	93.00 $\pm$ 0.01	67.33 $\pm$ 0.74	27.33 $\pm$ 0.49	2.40	17.08 $\pm$ 8.75
Group II (HFD)	130.16 $\pm$ 0.70***a	98.33 $\pm$ 0.49***a	21.33 $\pm$ 0.96**a	5.10***a	22.68 $\pm$ 9.25**a
Group III (HFD+MC)	121.33 $\pm$ 1.20***ab	53.11 $\pm$ 0.80***ab	22.14 $\pm$ 0.47* <sup>b</sup>	4.48***ab	19.98 $\pm$ 5.23***ab

level of significance: \*:  $p < 0.05$ ; \*\*:  $p < 0.01$ ; \*\*\*:  $p < 0.001$ .

a: significant difference from animals in control group.

b: significant difference from animals in HFD group.

## Discussion

Dyslipidemia is an important risk factor in the initiation and progression of atherosclerotic lesions [6] and has promoted widespread search for plant based compounds which effectively control the lipid profile in the blood and tissues with least or no toxic effect. High fat diet feeding in laboratory animals leads to an elevation of plasma lipids such as cholesterol, fatty acids, and TG [17]. In accordance with studies by Park et al. [18], in the present study also, high fat diet feeding in laboratory animals for 14 weeks resulted in obesity and hyperlipidemia as evidenced by the enhanced levels of TC, TG and decreased HDL-C level in group II animals. One of the reason for increase in coronary heart disorder (CHD), being observed in the developing countries since past few decades is an increase in intake of fast foods, which are rich in saturated fats [19]. Atherogenic lipid profile (increased TC and TG and decreased HDL-C) is often associated with increased propensity for developing CHD [20].

Lowering of plasma lipid levels through diet or drug therapy is associated with a decrease in the risk of CHD [21]. In the present study, the levels of total serum cholesterol, triglyceride and homocysteine which were increased in group II, were lowered significantly with MC fruit extract supplementation group III (HFD+MC). He et al. have reported the hypolipidemic and antioxidant potential of bitter gourd leaf extract in HFD fed mice [22].

Atherogenic indices are powerful indicators of the risk of heart disease, a higher value indicating a higher risk of developing cardiovascular disease [23]. In the present study, atherogenic index was significantly decreased in the *Momordica charantia* fruit extract group; probably by an increase in plasma HDL-cholesterol with a concomitant percentage decrease of atherogenic lipids. The percentage of protection against the hyperlipidemia in the plant extract treated group was 12.15%, which further confirms the significant protective effect of the *Momordica charantia* fruit extract against hyperlipidemia. A 1% decrease in HDL-cholesterol is associated with a 3-4% increase in the risk of heart disease. For male and female, concentration of HDL-cholesterol below 1.0 and 1.2 mmol/L (39, 46 mg/dL) and especially below 0.8 and 1.0 and 1.2 mmol/L (31, 39 mg/dL) confer an increased risk of CHD, whereas concentration exceeding 1.5 and 1.7 mmol/L (58, 66 mg/dL) diminishes the influence of other risk factors [24].

Rohajati et al. [25] reported improvement of lipid profile in diabetic animals treated with bitter melon and attributed it to inhibition of cholesterol absorption by diosgenin (a steroidal saponin), dietary fibre, and phytosterol content of bitter melon fruit. In a randomized controlled trial conducted by Kumari et al. [26], type-2 diabetes mellitus patients were supplemented with *Momordica charantia* tablets along with oral antidiabetic agents. They reported favourable effect of *Momordica charantia* on fat metabolism and concluded that *Momordica charantia* could prevent cardiovascular risk in type 2 diabetes mellitus by improving dyslipidemia. The *Momordica charantia* fruit

consists of glycosides, saponins, alkaloids, reducing sugars, resins, phenolic constituents, fixed oils and free acids. Effects are likely induced by more than one bioactive ingredients present in the *Momordica charantia* [27].

Evidence is emerging that the risk for cardiovascular disease from hyperhomocysteinemia may be additive to abnormalities in lipid metabolism. High homocysteine levels in the blood causes oxidation of low density lipoprotein which damages the arteries by creation of a plaque inside artery walls [28].

## Conclusion

Synthetic hypocholesteromic drugs such as statins, fibrates, resins and nicotinic acid though efficiently reduce plasma TC levels, but LDL does not undergo any significant alteration. Moreover, synthetic hypolipidemic agents usually have one or more side effects and are unable to increase HDL levels [29]. It is well known that the oxidative modification of LDL plays a pivotal role in the progression of atherosclerosis and plaque formation [20] and fruit extract of *Momordica charantia* with its potential to reduce plasma cholesterol, TG and homocysteine levels can provide protection against hypercholesterolemia and also enhance the safety profile by elevating HDL levels. Thus, *Momordica charantia* may be utilized for providing dietary management in the prevention of atherosclerosis in hyperlipidemic patients.

## Declarations

### Ethics approval and consent to participate

All animal experimentation protocols were approved by Institutional Animal Ethical Committee (IAEC), and in agreement with the Ethical Principles for Animal Research established by CPCSEA, Department of Animal Welfare, Government of India.

### Consent for publication

Not applicable

### Availability of data and materials

The datasets generated and analyzed during the current study is available from the corresponding author on reasonable request.

### Competing interests

The author declares no competing interests.

### Funding

The research reported is funded by personal means.

### Authors' contributions

Dr Jyoti Sethi contributed in planning, execution of methodology and compilation and analysis of data in writing of the paper.

Dr Kiran Dahiya contributed in planning, execution of the biochemical samples, analysis of data and writing of the biochemical aspect in the paper.

**Acknowledgements**

We acknowledge the contribution of technical staff of Physiology and Biochemistry.

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