The Protective Role of Momordica charantia Fruit Extract on Diet-Induced Hypercholesterolemia in Rabbits

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Abstract

Background: Dyslipidemia is a prominent and modifiable risk factor for the development of atherosclerosis. This study was carried out to investigate the anti-atherogenic antioxidant potential of Momordica charantia (MC) Fruit Extract in hypercholesterolemic rabbits. Albino rabbits (1.5-2.5 kg) of either sex were divided into four groups of six each, depending on the diet. Group I received the standard chow diet; group II received aqueous MC fruit extract (100 mg/kg, p.o.); group III rabbits received high fat diet (HFD) supplemented with aqueous MC fruit extract (100 mg/kg). Blood samples were collected from the marginal vein of pinna of overnight fasted rabbits at the end of experimental period for estimation of total cholesterol (TC), triglyceride (TG) and high density lipoprotein cholesterol (HDL-C), Malondialdehyde (MDA), reduced glutathione (GSH) and Vitamin C. Result: Administration of aqueous MC fruit extract significantly lowered the serum levels of TC and TG in group II as well as group IV rabbits. Administration of aqueous MC fruit extract significantly increased antioxidant capacity and decreased MDA and Atherogenic index of plasma (AIP) (AIP = log TG/HDL) in plasma. Conclusion: The results of the present study indicate that the potent therapeutic phytocomponents present in MC i.e. phytosterols, saponins, polyphenols, flavonoids and ascorbic acid, could be responsible for augmenting endogenous antioxidant system and decreasing lipid peroxidation in hypercholesteremic conditions.

Key words: momordica charantia; high-fat diet; thiobarbituric acid-reactive substance; atherogenic index; coronary heart diseases

Introduction:

It is estimated that by 2020, coronary heart disease (CHD) will be the largest cause of disability and death in India. Reddy et al have reported that prevalence of coronary heart disease in adult surveys has risen four-fold in 40 years and even in rural areas the prevalence has doubled over the past 30 years (1). Oxidative modification of low density lipoproteins (LDL) in the arterial wall by reactive oxygen species (ROS) plays a major role in hypercholesterolaemia initiated atherosclerosis (2). Reduction in the endogenous antioxidant enzyme and Increased lipid peroxidation due to increased ROS generation have also been implicated in the pathogenesis of CHD with resultant vascular membrane damage (3). Pharmacological therapies to reduce lipid level, though effective, have limited patient compliance (4). Recent research indicates that foods rich in omega3 fatty acids, antioxidant vitamins and fibres may be beneficial for cardio-vascular health and thus the researchers have shifted their focus to food products containing functional ingredients having antioxidant potential along with hypolipidemic activity (5). Momordica charantia (MC) is a member of cucurbiteae family (also known as bitter gourd or karela), and is traditionally used as food in South Asia. The roots, leaves, seeds and fruits of this plant have been used in traditional medicine for treating various diseases(6). There are studies documenting the hypoglycaemic (7), antiyretic, antibacterial(8), antihelminthic, antimarialar (9), antilulcerogenic (10) and immunomodulatory (11) properties of MC. The fruit is also rich in minerals, including potassium, calcium, magnesium, phosphorous and iron, and is a good source of dietary fibre (12).

Shih et al demonstrated that bitter melon was effective in ameliorating the HF diet-induced hyperglycemia, hyperleptinemia, and decreased the levels of blood glycated hemoglobin (HbA1c) and free fatty acid (FFA) and concluded that bitter melon, is a food factor, but not a medicine, itself could influence dual PPAR alpha / PPAR gamma expression and the mediated gene expression, is effective in ameliorating insulin resistance and visceral obesity(13). Chan et al. have reported slower weight gain and reduced adiposity in rats fed on high-fat diet (HFD) supplemented with MC. They suggested that reduced adiposity was a consequence of increased lipid oxidation and mitochondrial uncoupling (14). Since dyslipidemia along with lipid peroxidation is known to play a role in the development of atherosclerosis ,so the present study was planned to evaluate the effect of aqueous extract of MC on atherogenic index, lipid peroxidation and antioxidant status in diet-Induced hypercholesterolemia in rabbits.

Material 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 the disease-free animal house of the 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. The Institutional Animal Ethical Committee (IAEC) approved the experimental protocol and the animals were cared for as per the guidelines of CPCSEA, Department of Animal Welfare, Government of India.

**Experimental Design**

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

**Group I Control group.** The rabbits received standard chow diet throughout the experiment for 14 weeks.

**Group II (MC group).** The rabbits received aqueous MC fruit extract (100 mg/kg, p.o.) daily throughout the experiment for 14 weeks.

**Group III (HFD group).** The rabbits received HFD [15] daily throughout the experiment for 14 weeks.

**Group IV (HFD with MC group).** The rabbits received aqueous MC fruit extract (100 mg/kg, p.o.) daily along with HFD for 14 weeks. The composition of the two diets [15] 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%).

The aqueous extract from the powdered fruit of MC was prepared using the standard procedure. Oral dose of the extract was selected after a pilot study using thrice doses, i.e., 50, 75, and 100 mg/kg. All the drugs were administered orally (using an intragastric tube) in a single dose in the morning.

**Sample collection:**

| Group          | Log (TG/HDL) | MDA (nmol/ml) | GSH U mol/ml | Vit C mg/dl |
|----------------|--------------|---------------|--------------|-------------|
| Group I (control) | 0.390        | 3.20 ± 0.75   | 0.60 ± 0.82  | 1.021 ± 0.50 |
| Group II (MC)    | 0.322        | 2.40 ± 0.72   | 0.88 ± 0.060 | 1.980 ± 0.46 |
| Group III (HFD)  | 0.662        | 6.50 ± 0.78   | 0.391 ± 0.15 | 0.72 ± 0.42  |
| Group IV (HFD +MC)| 0.378*      | 4.32 ± 0.70   | 0.491 ± 0.28 | 0.86 ± 0.48* |

* #: p<0.01 as compared to group-I
# #: p<0.05 as compared to group-III

**Results:**

Administration of dietary cholesterol in group III animals significantly increased (P < 0.05) triglycerides, cholesterol, and lipid peroxidation (LPO) products as compared to control animals (group I) (Table 3). However, treatment with Momordica charantia (group IV) ameliorated dietary cholesterol-induced increase in MDA and atherogenic index. Hyperlipemic oxidative stress led to depletion of endogenous antioxidant system (GSH, Vit C) in group III animals as compared to control group animals. Supplementation of Momordica charantia (100 mg/kg) in HFD diet reversed the adverse effect of high dietary cholesterol by normalizing these enzymatic antioxidant indices.

**Discussion:**

The atherogenic index of plasma (AIP), is the logarithm of molar ratio of triglyceridemia to high-density lipoprotein cholesterol (Log 10TG/HDL-cholesterol), is said to reflect the true relationship between protective and atherogenic lipoprotein and is thus considered as a reliable predictor of coronary heart disease [21]. Lowering of AIP as observed by Momordica charantia supplementation in group IV rabbits could be achieved only by lowering of plasma concentrations of atherogenic lipoproteins, particularly non-esterified plasma lipids such as triglycerides and total cholesterol, with corresponding elevation of plasma concentration of HDL-C as observed in the study. Chen and Li [22] have reported lower visceral fat and hepatic triglyceride content in the bitter melon fed rats and attributed it to enhanced sympathetic activity and lipolysis. A comprehensive array of antioxidant defence exists in mammalian cells comprising of both enzymatic and non-enzymatic molecules, which effectively neutralize reactive oxygen species (ROS) . Gluthathione (GSH), a cysteine-containing tripeptide, is the most abundant non-protein thiol in mammalian cells and acts as primary line of defence to cope with deleterious effects of ROS [23]. Decreased levels of glutathione in hypercholesterolemic animals (group II) indicates increased susceptibility to oxidative stress. Ascorbic acid (or vitamin C) is considered an important plasma antioxidant because of its fast reaction with many ROS and the poor reactivity of the resultant semidehydroascorbic radical [24]. Diets rich in fruits and vegetables, and hence high in vitamin C, have been found to be associated with lower risk of cardiovascular diseases [25].
Superoxide anion, hydrogen peroxides and lipid hydroperoxides are produced in vivo in metabolic oxidation and trigger the function of membrane proteins, genetic material and lipids modifying their structure that may be exhibited in various forms of diseases including coronary artery disease (26). Hypercholesterolemia and lipid peroxidation are believed to be critically involved in development of Atherosclerosis (27). In our study a significant (p<0.05) increase in MDA levels was observed in HFD group (group III) as compared to the control group. Momordica charantia supplementation ameliorated oxidative stress as evidenced by decrease in the level of MDA to near normal and positive modulation of anti oxidant parameters. 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, anthroquinones and glucosinolates, all of which confer a bitter taste (12). Thus it can be concluded that Momordica charantia by virtue of its ability to suppress free radical generation and augment endogenous antioxidant system can be used therapeutically to provide cardiac protection. The International Life Sciences Institute of North America (ILSI) has defined functional foods as, ‘foods that by virtue of physiologically active food components provide health benefits beyond basic nutrition’ (28). Thus Momordica charantia can be considered as functional food with atheroprotective potential and may be a useful adjunct to cardio protective dietary pattern.

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