Original article:

Cardio-protective properties of Momordica charantia in Albino Rats

Sheriff OL[1], Yusuf FA[2]

Abstract:
Momordica charantia, commonly known as bitter gourd, is used as a vegetable by the Asian community in Africa. It is frequently used as an anti-diabetic herb for the management of disease in the Ayurvedic system of Medicine. This present study was aimed at evaluating possible cardio-protective properties of *M. charantia* by determining its effect on blood cholesterol levels in albino rats. The study involved 25 rats and they were divided into 5 groups each comprising of 5 rats. The aqueous extract of *M. Charantia* was administered orally with syringes and cannula to 4 groups at different doses (80mg/kg, 100mg/kg, 120mg/kg and 140mg/kg body weights per day, respectively) and the last group served as the control and were given drug vehicle (normal saline) only. After two weeks of administration, the 25 rats were sacrificed and blood samples were collected and assayed for total blood cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein levels. Results indicated that *M. charantia* plant extract increased significantly ($P < 0.05$) the low density lipoprotein levels in the experimental group B (100mg/kg), and significantly reduced low density lipoprotein levels ($P < 0.05$) in the experimental group A (80mg/kg), when compared to the control group. This study showed that *M. charantia* plant extract has cardio-protective properties by its dose-dependent effects on blood cholesterol.

Key Words: *momordica charantia*, cardio-protective, orally, dose-dependent, cholesterol

Introduction

Finding healing powers in plants is an ancient idea. People on all continents have long applied poultices and imbibed infusions of hundreds, if not thousands, of indigenous plants, dating back to prehistory[1].

It is estimated that there are 250,000 to 500,000 species of plants on Earth[2]. Relatively small percentages (1 to 10%) of these are used as foods by both humans and other animal species. It is possible that even more are used for medicinal purposes[3]. Momordica charantia (MC), a member of the Cucurbitaceae family, is known as bitter melon, bitter gourd, balsam pear, karela, and pare. It grows in tropical areas of the Amazon, East Africa, Asia, India, South America, and the Caribbean and is used traditionally as both food and medicine.

Several studies revealed that this plant has anti-ulcer, anti-diabetic, antifungal, anti-leukemic, anti-protozoan, antibacterial, anti-fertility, antiviral, and hypoglycemic effects[3, 4, 5].

Cholesterol is a waxy steroid metabolite found in the cell membrane and transported in the blood plasma of animals[6]. It is an essential structural component of mammalian cell membranes and also an important component for the manufacture of bile acids, steroid hormones and fat soluble vitamins[7]. Cholesterol, being amphipathic, is transported in the surface monolayer of the lipoprotein particle.

There are several lipoproteins within the blood; these include chylomicrons, very-low density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL). The lipoprotein particles are molecular addresses that determine the start- and endpoint for cholesterol transport. The more cholesterol and less protein a lipoprotein has, the less dense it is. The LDL molecules are the major carriers of cholesterol in the blood[8]. Studies have shown that having large numbers of HDL particles correlates with better health outcomes; in contrast to having small numbers which has been associated with atheromatous disease progression within the arteries[2]. Low HDL cholesterol is an independent cardiovascular risk factor.

1. Ojulari Lekan Sheriff, Department of Physiology, University of Ilorin.
2. Yusuf FA, Department of Physiology, University of Ilorin.

Corresponds to: Ojulari Lekan Sheriff, Department of Physiology, University of Ilorin, Nigeria. ***e-mail:*** Ojulari@unilorin.edu.ng

Clinical evidence also indicates that a low level of HDL is a major risk factor of atherosclerosis. Raising HDL significantly reduces this risk, making HDL levels an important target of treatment, particularly in patients with pre-existing atherosclerosis.

Both LDL and HDL cholesterol levels are important factors to determining the risk for coronary artery disease. An increase in coronary artery disease is associated with increased LDL and decreased HDL cholesterol levels[10].

As high LDL and low HDL are both independent risk factors for heart disease, the ratio of the two numbers is a useful tool to evaluate cardiovascular risk. Numerous natural substances have been shown to positively affect the HDL/LDL ratio.
Triglycerides are esters composed of a glycerol bound to three fatty acids. They are major components of VLDL and chylomicrons and play an important role in metabolism as energy sources and transporters of dietary fat. High levels in the bloodstream have been linked to some cardiovascular diseases[11].

Despite the widespread usage of this plant in folk medicine in the management of many health conditions, only a few, nonrandomized clinical studies have investigated the effects of MC in humans[12, 13, 16, 15]. It is therefore crucial to conduct more studies which will shed more light on its other physiological effects. This study therefore seeks to assess possible cardio-protective properties of MC by determining its effect on the blood cholesterol level in rats.

Materials and methods:

Experimental protocol: Twenty-five albino rats (mean weight 150-180g) were maintained under standard laboratory conditions and were allowed free access to food and water ad libitum. Animals were divided randomly into five groups. Control (distilled water): group A, MC (80mg/kg for 14 days); group B, MC (100mg/kg for 14 days), group C, MC (120mg/kg for 14 days); and group D, MC (140mg/kg for 14 days).

Extract, route and blood collection: The leaves of MC were aired and dried and milled into powder. 1.5 kg of the sample was percolated in 13 liters of water for about 48 hours, after which it was filtered and evaporated using water bath to give about 220g of a dark solid extract which was stored at 4^0C temperature before physiological studies were made before oral administration. After two weeks of administration, the 25 rats were sacrificed by cervical dislocation after being anaesthetized with chloroform. Blood samples were obtained through cardiac puncture.

Statistical analysis: All results were expressed as mean$\pm$SEM. Data was analysed by one-way analysis of variance (ANOVA) and Duncan New Multiple Range Test (DMRT). Differences in means were considered significant at $P < 0.05$. All analysis was performed using SPSS Version 17.

Results

Effect of *Momordica charantia* (MC) on total cholesterol: Administration of MC caused insignificant changes in the total cholesterol levels in experimental groups after 14 days of treatment when compared to the control group (fig1).

Effect of *Momordica charantia* on Triglyceride: The effect of MC on triglyceride is shown in fig 2. Triglyceride levels for the treated groups A, B, C and D (1.4, 1.6, 1.2,1.6 mmol/L) were not significantly different from the compared controls after 14 days of treatment.

Effect of *Momordica charantia* on HDL-C: The effect of MC on HDL-C was depicted in fig 3. Administration of MC had no significant impact on HDL as evidenced by measured values of 0.5, 1.0, 0.5, 1.0 mmol/L for groups A, B, C, and D respectively.

Effect of *Momordica charantia* on LDL-C: The measured levels of LDL-C showed significant changes in the groups A (80mg/kg) and B (100mg/kg). It was significantly lowered in group A (1.1 mmol/L) and signicantly raised in group B, when compared with the control. The other experimental groups showed no significant changes when compared to the control (fig 4).

Discussion

The study revealed insignificant changes in total cholesterol level in MC administered rats as com-

pared with controls. The blood triglyceride levels and HDL-C levels exhibited insignificant increases and decreases while the LDL-C levels showed significant changes at different doses of administration. These results suggest that MC, when administered orally and at doses employed, has a significant dose/duration modulating effect on blood cholesterol levels.

Table 1: Total Cholesterol level in Control and Experimental rats

Groups	Mean (mg/ml)	S.E.M.	P-value
Control	2.4	2.4 ± 0.2	
A (80mg/kg)	3.2	3.2 ± 0.3	P > 0.05
B (100mg/kg)	2.5	2.5 ± 0.3	P > 0.05
C (120mg/kg)	2.6	2.6 ± 0.2	P > 0.05
D (140mg/kg)	2.1	2.1 ± 0.2	P > 0.05

Table 2: Triglyceride level in Control and Experimental rats

Groups	Mean (mg/ml)	S.E.M.	P-value
Control	1.4	1.4 ± 0.1	
A (80mg/kg)	1.4	1.4 ± 0.2	P > 0.05
B (100mg/kg)	1.6	1.6 ± 0.1	P > 0.05
C (120mg/kg)	1.2	1.2 ± 0.2	P > 0.05
D (140mg/kg)	1.6	1.6 ± 0.2	P > 0.05

Table 3: High-density lipoprotein cholesterol (HDL-C) in Control and Experimental rats

Groups	Mean (mg/ml)	S.E.M.	P-value
Control	0.8	0.8 ± 0.1	
A (80mg/kg)	0.5	0.5 ± 0.2	P > 0.05
B (100mg/kg)	1.0	1.0 ± 0.1	P > 0.05
C (120mg/kg)	0.5	0.5 ± 0.1	P > 0.05
D (140mg/kg)	1.0	1.0 ± 0.2	P > 0.05

Table 4: Low-density lipoprotein cholesterol (LDL-C) in Control and Experimental rats

Groups	Mean (mg/ml)	S.E.M.	P-value
Control	1.3	1.3 ± 0.1	
A (80mg/kg)	1.1	1.1 ± 0.4	P ? 0.05
B (100mg/kg)	1.4	1.4 ± 0.2	P ? 0.05
C (120mg/kg)	1.0	1.0 ± 0.2	P > 0.05
D (140mg/kg)	1.2	1.2 ± 0.1	P > 0.05

The normal total cholesterol levels seen in our study indicates that MC possibly has no effect on total cholesterol levels. This is contrary to findings of Chaturvedi et al; 2004[16], who reported that rats exposed to MC for 30 days had significantly lowered total blood cholesterol levels. This differing result is probably due to the difference in duration and dose of administration. It therefore appears that the effect of MC on total cholesterol levels in rats is both dose and duration dependent, with the duration factor being more pronounced.

The triglyceride level usually provides a useful index for cardiovascular risk assessment in experimental studies. The observed levels in control and experimental rats suggest that the administration of MC at doses and duration used had no effect on blood levels. This is contrary to results by Chatuvedi and Ahmed et al in which triglyceride levels showed a dose-dependent response to the MC extract[16,17]. It may therefore be plausible to note that the levels of blood triglyceride may be associated with the insensitivity of triglyceride to MC in-vivo, which is likely due to the short duration of treatment.

The LDL-C level in this study showed significant increase and decrease at differing doses. Experimental rats in group B showed significantly lowered LDL-C levels. This corresponds to results observed in studies carried out by Chaturvedi (2005) in which LDL-C levels where found to be low, even in the groups on 80mg/kg dose[18]. This is probably due to the lowering effect of MC on apolipoprotein B (Apo B) secretion by the liver, with a consequent reduction in LDL-C levels[19].

Experimental rats in group B showed significantly increased LDL-C blood levels. This also corresponds to results in studies by Chaturvedi in which LDL-C levels increased significantly after administration of higher doses of MC[18].

Serum lipids are important markers for overall cardiovascular risk. According to the Centres for Disease Control and Prevention (CDC), an estimated 106.9 million American adults have elevated total blood cholesterol levels; approximately 47.9 percent of men and 49.7 percent of women[20]. The World health Organization states that 18 percent of stroke events and about 56 percent of heart disease is attributable to total cholesterol levels above 3.2 mmol/l, which amounts to about 4.4 million deaths[21].

According to the lipid hypothesis, abnormal cho-

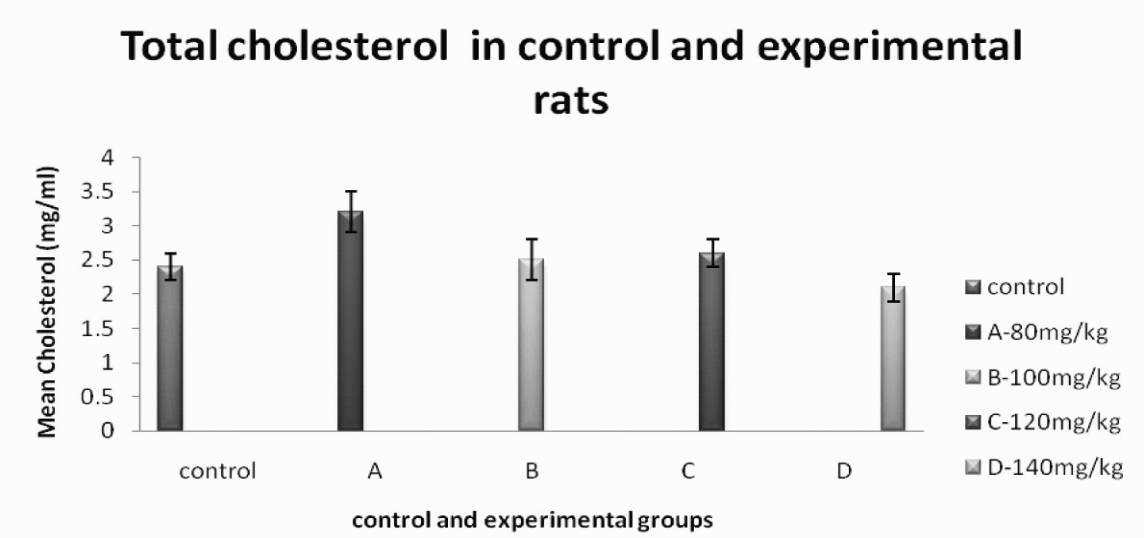

fig 1: P>0.05 in all experimental groups

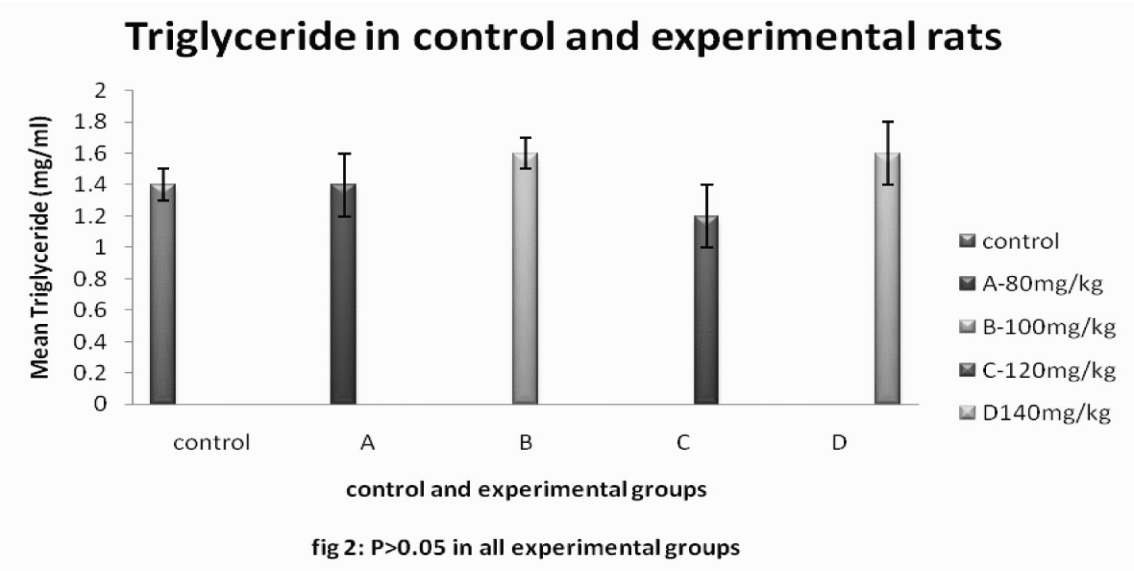

fig 2: P>0.05 in all experimental groups

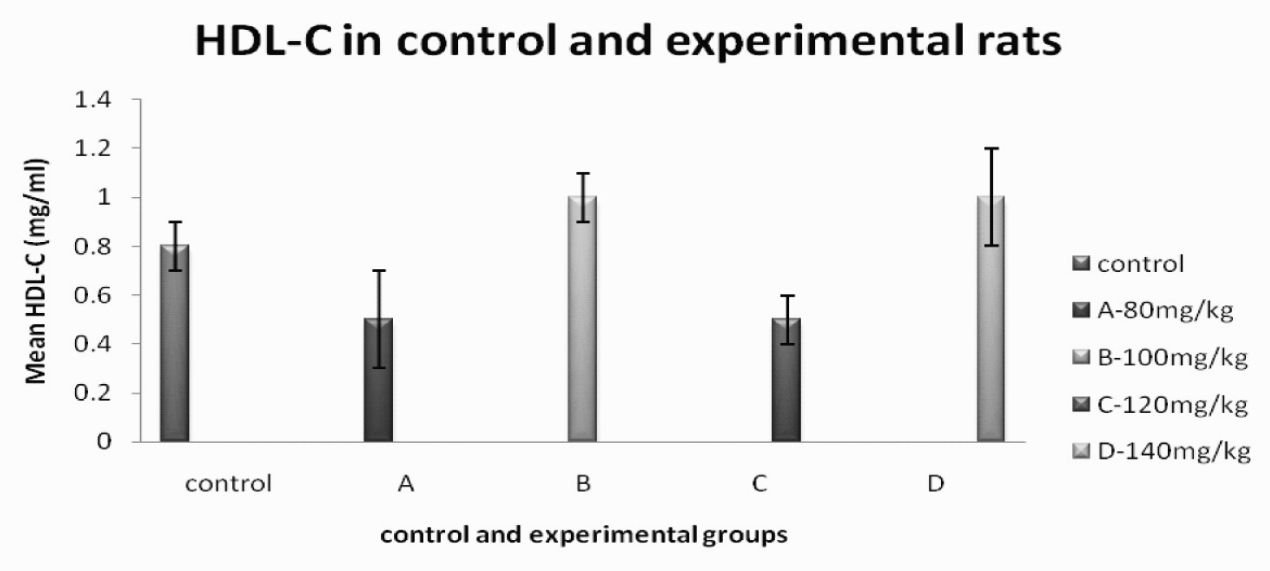

fig 3: P>0.05 in all experimental groups

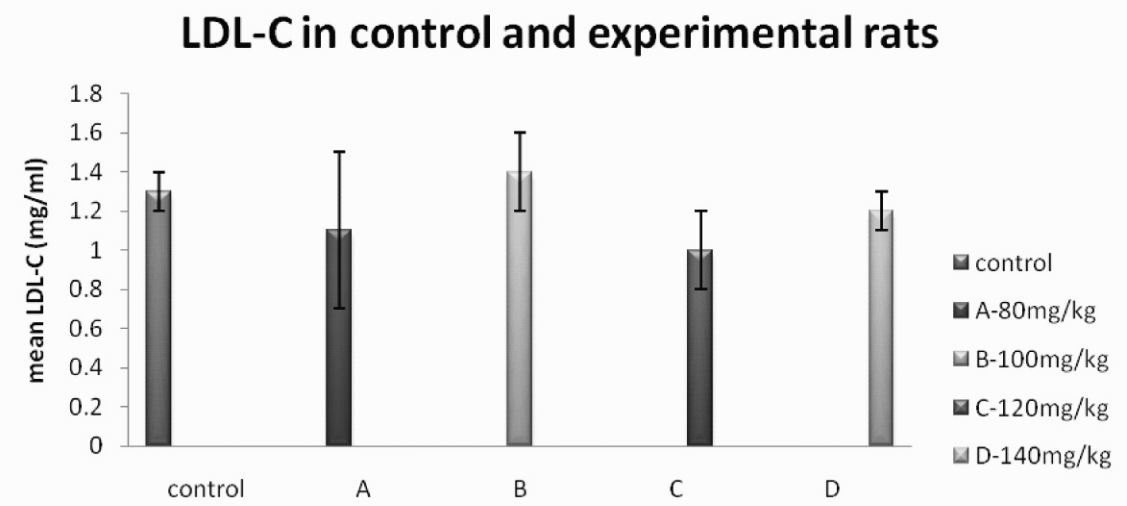

fig 4: P>0.05 in groups C & D
P<0.05 in groups A&B

lesterol levels (hypercholesterolemia)—that is, higher concentrations of LDL and lower concentrations of functional HDL, are strongly associated with cardiovascular disease[22]. High levels of cholesterol in blood, depending on how it is transported within lipoproteins, are strongly associated with progression of atherosclerosis. LDL molecules are the major carriers of cholesterol in blood. When there is high level of cholesterol, the molecules are oxidized and taken up by macrophages, which become engorged and form foam cells. These cells often become entrapped in the walls of blood vessels and contribute to atherosclerotic plaque formation. These plaques are the main causes of heart attacks, strokes and other serious medical problems[19].

As high LDL and low HDL are both independent risk factors for heart disease, the ratio of the two numbers is a useful tool to evaluate cardiovascular risk[11]. In fact, one study showed that a 1 percent greater LDL value is associated with slightly more than a 2 percent increase in coronary artery disease over 6 years, and a 1 percent lower HDL value is associated with a 3 to 4 percent increase in coronary artery disease, even at total cholesterol levels less than 200 mg/dl. Additionally, low HDL levels are associated with increased heart attacks and death from coronary artery disease[10]. Numerous natural substances have also been shown to positively affect the HDL/LDL ratio[23-24].

The HDL/LDL ratio which is a biomarker for cardiovascular disease was increased in rats given MC at longer duration of treatment. This was evidenced by the significant decrease in LDL levels at lower doses of administration of the extract. This development was shown to be mostly duration dependent and it appears that longer duration of treatment may play an important role in the development of higher HDL/LDL ratios.

In conclusion, administration of MC, at doses and duration employed in this study, had dose-dependent cardio-protective properties via its effect on the blood cholesterol levels. However, there is an indication that higher doses should be discouraged.

References:

1) Stockwell, C: Nature's pharmacy. Century Hutchinson Ltd., London, United Kingdom. 1988

2) Borris RP. Natural products research: perspectives from a major pharmaceutical company. *J Ethnopharmacol*. 1996; **51**:29–38. http://dx.doi.org/10.1016/0378-8741(95)01347-4

3) Moerman DE. An Analysis of the Food Plants and Drug Plants of Native North America. *Journal of Ethnopharmacology*1996; **52**: 1-22. http://dx.doi.org/10.1016/0378-8741(96)01393-1

4) Yesilada E, Gurbuz I and Shibata H. Screening of Turkish antiulserogenic folk remedies for anti Helicobacter pylori activity. *J Ethnopharmacol* 1999; **66**: 289-93. http://dx.doi.org/10.1016/S0378-8741(98)00219-0

5) Girini MM. Effect of graded doses of Momordica charantia seed extract on rat sperm: scanning electron microscope study. *J. Basic Clin. Physiol. Pharmacol* 2005; **16**(1):53-66. http://dx.doi.org/10.1515/JBCPP.2005.16.1.53PMid:16187486

6) Emma Leah : "Cholesterol". Lipidomics Gateway.doi:10.1038/lipidmaps.2009.3. http://www.lipidmaps.org/update/2009/090501/full/lipidmaps.2009.3.html. http://dx.doi.org/10.1038/lipidmaps.2009.3

7) Olson RE. Discovery of the lipoprotein, their role in fat transport and their significance as risk factors. J. Nutri. 1998; **128**(2): 4395-4435.

8) Tymoczko JL, Stryer B and Berg JM. Biochemistry. San Francisco: W.H. Freeman. 2002; 726–727.

9) Gordon DJ, Probsfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR, Bangdiwala S, and Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation* 1989; **79** (1): 8-15. http://dx.doi.org/10.1161/01.CIR.79.1.8 PMid:2642759

10) Wilson PW. High-density lipoprotein, low-density lipoprotein and coronary artery disease. *Am J Cardiol* 1990; **66**(6):7A-10A. http://dx.doi.org/10.1016/0002-9149(90)90562-F

11) American Heart Association. Cholesterol Statistics from National Health and Nutrition Examination Survey (NHANES), 1999-2004, National Center for Health Statistics and the NHLBI. Available at: http://www.american-heart.org/presenter.

12) Basch E, Gabardi S and Ulbricht C. Bitter melon (Momordica charantia): a review of efficacy and safety. A*m J Health Syst Pharm* 2003; **60**: 356-359.PMid:12625217

13) Leatherdale BA, Panesar RK, Singh G, Atkins TW, Bailey CJ and Bignell AH. Improvement in glucose tolerance due to Momordica charantia (karela). *Br Med J (Clin Res Ed)* 1981; **282**:1823. http://dx.doi.org/10.1136/bmj.282.6279.1823

14) Stivastava Y, Venkatakishna- Bhatt H and Verma Y. Antidiabetic and adaptogenic properties of Momordica charantia extract. An experimental and clinical evaluation. *Phytother Res* 1993; **7**:285-289.http://dx.doi.org/10.1002/ptr.2650070405

15) Welihinda J, Karunanayake EH, Sheriff MHH, and Jayasinghe KSA. Effect of Momordica charantia on the glucose tolerance in maturity onset diabetes. *Journal of Ethnopharmacology* 1986; **17**(3): 277-282.http://dx.doi.org/10.1016/0378-8741(86)90116-9

16) Chaturvedi P, George S, Miliganyo M and Trpathi Y. Effect of M. Charantia on lipid profile and oral glucose tolerance in diabetic rats. *Phytother res* 2004; **18**:954-9.http://dx.doi.org/10.1002/ptr.1589PMid:15597317

17) Ahmed I, Lakhani MS, Gillett M, John A and Raza H. Hypotriglyceridemic and hypocholesterolemic effects of anti-diabetic Momordica charantia (karela) fruit extract in streptozo-

tocin-induced diabetic rats. *Diabetes Res Clin Pract* 2001; **51**(3):155-61.http://dx.doi.org/10.1016/S0168-8227(00)00224-2

18) Chaturvedi P. Role of Momordica charantia in maintaining the normal levels of lipids and glucose in diabetic rats fed a high-fat and low-carbohydrate diet. *British Journal of Biomedical Science*. 2005PMid:16196458

19) Umesh CS, Yadav K and Najma Z. Combined treatment of sodium orthovanadate and Momordica charantia fruit extract prevents alterations in lipid profile and lipogenic enzymes in alloxan diabetic rats. *Baquer Molecular and Cellular Biochemistry* 2005; **268**(1-2): 111-120. http://dx.doi.org/10.1007/s11010-005-3703-y

20) Center for Disease Control and Prevention. Division for Heart Disease and Stroke Prevention Cholesterol Fact Sheet. Available at:http://www.cdc.gov/DHDSP/library/fs_cholesterol.htm.

21) World Health Organization. Chronic disease risk factors. Available at: http://www.who.int/dietphysicalactivity/publications/facts/riskfactors/en/index.html.

22) Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH and Witztum JL. Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes Care* 2008; **31** (4): 811–22. http://dx.doi.org/10.2337/dc08-9018PMid:18375431

23. K Matira, ZF Dewan, TC Rehnuma, A Farhana, UN Zeba, S Shahin. Pre treatment by the crude and the n-hexane extract of *Nigella sativa* Linn. (Kalajira) alleviates diabetes mellitus. *Bangladesh Journal of Medical Science* 2009; 8 (1-2): 5-9. doi: 10.3329/bjms.v8i1.3182

24. *DC Nanjunda*. Ethno-medico-botanical Investigation of *Jenu Kuruba* Ethnic Group of Karnataka State, India. *Bangladesh Journal of Medical Science* 2010: 09 (3): 161-169. DOI: 10.3329/bjms.v9i3.6479