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EFFECT OF ORAL ADMINISTRATION OF AQUEOUS LEAF EXTRACT OF *MOMORDICA CHARANTIA* (BITTER MELON) ON SERUM GLUCOSE, AND LIPID PROFILE IN ALLOXAN-INDUCED DIABETIC RATS

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ABSTRACT
Momordica charantia (bitter melon) has been used extensively in herbal medicine as remedy for many disease conditions. The present study was undertaken to evaluate the effect of Momordica charantia (MC) aqueous leaf extract on serum fasting blood glucose (FBG) and lipid profile (total cholesterol TC, triglyceride TAG, high density lipoprotein HDL, low density lipoprotein LDL) in alloxan-induced diabetic rat. The extract was administered orally at the dose of 200mg/kg, 400mg/kg, and 600mg/kg body weight either for a period of 2 or 4 week. A significant ($p<0.05$) improvement in the biochemical parameters such as FBG, TC, TAG, HDL, and LDL levels was observed in MC treated rats as compared to diabetic control rats. The response to treatment was gradual and dose-dependent with maximum effect at higher dose of 600mg/kg body weight for 4 weeks.
Keywords: Momordica charantia, blood glucose, Lipid profile, Diabetes.

INTRODUCTION

Diabetes mellitus is considered as one of the five leading causes of death in the world (Joseph and Jini, 2011). Diabetes mellitus is a major global health concern with a projected rise in prevalence from 171 million in 2000 to 366 million 2030 (Shaw, *et al.,* 2010). It is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormal high blood sugar levels (hyperglycemia) (Patel *et al.,* 2012). Being a degenerative disease, diabetes is found in all parts of the world and it is becoming the third most lethal disease of mankind and increasing rapidly (Ogbonnia *et al.,* 2008). It is the most common endocrine disorder, affecting 16 million individuals in the United States and as many as 200 million individuals worldwide (Shaw, *et al.,* 2010). The prevalence rate of diabetes in Nigeria is estimated at 4.7% with rural areas having the lowest rates (Shaw, *et al*., 2010). The cure for diabetes is currently unknown, but could adequately be managed by the use of agents that exhibit hypoglycemic effect. The most popular and effective of such agents is insulin. A good number of oral hypoglycemic agents are also available, which include sulphonylureas, biguanides and alpha glucosidase inhibitors (Tunbrige and Home, 1991). However, majority of these hypoglycemic agents are either too expensive or their use is associated with some undesirable side effects and contraindications or both (Tunbrige and Home, 1991; Kameswara *et al.,* 1999; Jaouhari *et al.,* 2000). On the basis of these shortcomings and keeping in view the dangers associated with diabetic complications, some of which might result in premature death, the WHO study groups (WHO, 1985 & 1994), recommended among other things the need for the development and evaluation of better, safe and affordable pharmacological agents. The report further recommended the evaluation of the efficacy of traditional medicine and other nonpharmacological methods in use for the management of the disease. In lieu of these recommendations, interest in fostering research on plant products and screening for agents with hypoglycemic agents is being pursued in various laboratories across the globe (WHO, 1985; 1994; Mei *et al.,* 2005). Several medicinal plants have been used as dietary adjunct and in the treatment of numerous diseases without proper knowledge of their action. The multiple roles of wild traditional vegetables as both food and medicinal sources have widely been documented (Lee *et al.,* 2003; Ogle *et al.,* 2003; Adeboye and Opabode, 2004; Ayodele, 2005).

Mormodica charantia (*Linn Family:* Cucubaceae*),* also known as bitter melon, karela, pear, balsam pear, or bitter gourd, is a popular plant used for the treatment of many disease conditions amongst the indigenous population of Asia, South America, India, the Caribbean and East Africa (Cefalu *et. al,* 2008; Cousens 2008). Several studies have shown that bitter melon extract from the fruits, seeds, stem bark and leaves contain several bioactive compounds which could have pharmacological effects against many ailments such as hyperlipidemia, digestive disorder, microbial infections and menstrual problems in both animals and humans. (Wehash, *et. al.,* 2012; Fuangchana *et. al.,* 2011). Therefore, this present

study was conducted to assess the antidiabetic effect of the leaf extract in alloxan-induced diabetic rats.

METHODOLOGY

Experimental animals

A total of 40 rats weighing 100g to 140g were obtained from animal house of Zoology Department, Bayero University, Kano. The rats were placed under standard condition and fed with standard (vital feed) diet and water *ad libitum.* The experiment was performed according to the principles of laboratory animal care.

Collection and preparation of the plant extract

Fresh leaves of *Momordica charantia* was obtained from Botany Department, Faculty of Science Bayero University, Kano-State, Nigeria, in the month of march, 2014, following identification by Botanist. The Leaves were air dried under shade and grounded into powder. The powder was weighed (10g) and soaked in distilled water (100ml) for 48 hours. The mixture was filtered using whatman No.1 filter paper; the residue was dried and reweighed. The concentration of aqueous leaf extract (filtrate) was determined as the difference in weight/final volume of the solution using the relation,

$$\text{Conc. (g/ml)} = \frac{\text{(Initial weight of sample - final weight of residue)}}{\text{Final volume of the filtrate}}$$

The concentration of the aqueous leaf extract was found to be 135mg/ml.The volume of the extract to be administered was determined based on the weight of the rats and required dose, using the relation.

$$\text{Volume administered (ml)} = \frac{\text{Weight of rat (kg) x Dose (mg/kg)}}{\text{Concentration of the filtrate (mg/ml)}}$$

Induction of diabetes mellitus

Diabetes was induced using Alloxan monohydrate (Triverdi *et al.,*2004). Rats were allowed to fast for 24hrs after which they were administered with 100mg/kg body weight of alloxan mononhydrate (Sigma, U.S.A.) intraperitoneally as a single dose to induce diabetes (Trivedi *et al*. 2004). Two days after the administration of alloxan, the fasting blood glucose levels of the rats were measured and rats with blood glucose level above 200mg/dl were considered diabetic and were used for the experiments (Trivedi *et al*., 2004).

Experimental design

The experimental animals (40) were divided into eight groups of five rats each. Diabetes was induced in group II – VIII using alloxan as described above. Group I was the normal group neither induced with diabetic nor administered with the extract. Group II (Diabetic control) was induced with alloxn but not administered with the extract. Groups III, IV and V after induction with alloxan were administered with 200, 400 and 600mg/kg body weight of the extract respectively for 2 weeks, while groups VI, VII and VIII were also administered 200, 400 and 600mg/kg body weight of the extract, respectively for 4 weeks after alloxan treatment.

Experimental procedures

Fasting blood glucose was determined using Glucometre (BG-102, Hangzhou Sejoy Electronic &Co., Ltd, Zhejiang, China). Serum Total cholesterol (CHOL) was determined using the method of Lothar *et al.,* (1998). Triglycerides (TRIG), High density lipoprotein (HDL) and Low density lipoprotein (LDL) were determined by the method of Jacob *et al.,* (1990). All these methods have been adopted from commercially available Randox Lipid profile diagnostic kits (Randox Laboratories Ltd, Antrim, United Kingdom) and all determinations were conducted following manufacturer's instructions.

Statistical Analysis

The data obtained was statistically evaluated using SPSS v.20

RESULTS

Effect of *Momordica Charantia* aqueous leaf extract on fasting blood glucose (FBG)

The diabetic rats (Group II) showed significant increase in the FBG level ($P<0.05$) when compared to the normal rats (Table 1). The administration of the MC aqueous leaf extract in the diabetic rats reduced significantly ($p<0.05$) the levels of FBG in the 2nd and 4th weeks post-treatment compared to the untreated diabetic control and the decrease was found to be dose dependent (Table 1 and 2). Two weeks administration of MC aqueous leaf extract compared with four weeks administration showed significant reduction ($P<0.05$) in the mean serum levels of FBG (Table 3).

Effect of *Momordica Charantia* aqueous leaf extract on TC, TAG, HDL and LDL.

The diabetic rats (Group II) showed dose significant increase in the serum levels of total cholesterol TC, triglycerides TAG, low density lipoprotein LDL ($P<0.05$), while serum level of high density lipoprotein HDL, reduced significantly ($P<0.05$) as shown in Table 1. Administration of the MC aqueous extract for 2 and 4 weeks produced a significant ($p<0.05$) dose-related reduction in TC, TAG, LDL and elevation in HDL levels (Table 1 & 2). Two weeks administration of MC aqueous leaf extract compared with four weeks adminstration (Table 3) shows significant decrease ($P<0.05$) in the mean serum levels of TC, TAG, LDL. At daily dose of 400mg/kg and 600mg/kg, mean serum level of HDL increases significantly ($P<0.05$) when 2 weeks treatment was compared with four weeks treatment.

Table 1: Serum levels of FBG and lipid Profile (mg/dl) two weeks after administration of different concentrations of MC aqueous leaf extract.

Group	FBS (mg/dl)	TC(mg/dl)	TG(mg/dl)	HDL(mg/dl)	LDL(mg/dl)
I (NC)	88.40±2.88^{abcd}	58.60±3.91^{abcd}	45.20±4.40^{abcd}	41.20±3.40^{abcd}	8.36±2.17^{abcd}
II (PC)	251.40±30.42^{aghi}	144.80±14.48^{aghi}	96.60±6.27^{aghi}	25.80±4.21^{afgh}	99.68±16.43^{aghi}
III	202.60±5.03^{bgmn}	94.60±6.44^{bgmn}	79.00±8.34^{bgn}	31.00±2.74^{bf}	47.20±7.90^{bg}
IV	187.80±3.56^{chs}	83.20±4.44^{chm}	67.60±6.07^{chms}	31.00±2.54^{cg}	38.68±6.80^{ch}
V	157.00±10.37^{dns}	82.00±7.07^{din}	58.80±2.86^{dins}	33.20±5.40^{dh}	37.04±7.92^{di}

Key: NC: Negative control; PC: Positive control; MC: *Mormodica charantia*; FBS: Fasting blood sugar; TC: Total cholesterol; TG: Triglycerides; HDL: High density lipoprotein and LDL: Low density lipoprotein. Groups 1, II and III were administered 200, 400 and 600mg/kg body weight of the MC aqueous extract respectively. Values are presented as mean ± SD, n= 5. Figures bearing similar superscript in the same column are significantly different (P<0.05).

Table 2: Serum level of FBG (mg/dl), lipid Profile in (mg/dl) four weeks after treatment with different concentration MC aqueous leaves extract.

Group	FBS (mg/dl)	TC(mg/dl)	TG(mg/dl)	HDL(mg/dl)	LDL(mg/dl)
I (NC)	88.40±2.88^{ef}	58.60±3.91^{ef}	45.20±4.40^{ef}	41.20±3.40^{ef}	8.36±2.17^{ef}
II (PC)	251.40±30.42^{jkl}	144.80±14.48^{jkl}	96.60±6.27^{jkl}	25.80±4.21^{jkl}	99.68±16.43^{jkl}
VI	172.00±10.66^{ejzå}	81.20±5.61^{eju}	63.60±6.99^{ejv}	34.00±6.63^{ei}	34.48±9.74^{ejxy}
VII	136.00±6.63^{fkzß}	71.20±6.80^{fkv}	63.60±4.85^{fkw}	39.40±2.70^{j}	25.20±5.70^{fkxz}
VIII	92.00±12.19^{laß}	58.80±4.15^{luv}	58.80±7.35^{lvw}	33.20±4.39^{k}	37.04±1.60^{lyz}

Key: NC: Negative control; PC: Positive control; MC: *Mormodica charantia*; FBS: Fasting blood sugar; TC: Total cholesterol; TG: Triglycerides; HDL: High density lipoprotein and LDL: Low density lipoprotein. Groups VI,VII and VIII were administered 200, 400 and 600mg/kg body weight of the MC aqueous extract respectively. Values are presented as mean ± SD, n= 5. Figures bearing similar superscript in the same column are significantly different (P<0.05).

Table 3: Comparison between two and four weeks of serum level of FBG and lipid profile after treatment with different concentration of MC aqueous leaves extract.

Group	FBS (mg/dl)	TC(mg/dl)	TG(mg/dl)	HDL(mg/dl)	LDL(mg/dl)
III	202.60±5.03^{mnpgr}	94.60±6.44^{mnpgr}	79.00±8.34^{mnpgr}	31.00±2.7^{m}	47.20±7.90^{mnp}
IV	187.80±3.56^{mstuv}	83.20±4.44^{ms}	67.60±6.07^{mst}	31.00±2.54^{np}	38.68±6.80^{qr}
V	157.00±10.37^{nswy}	82.00±7.07^{nt}	58.80±2.86^{nsu}	33.20±5.40^{qr}	37.04±7.92st
VI	172.00±10.66^{ptwzå}	81.20±5.61^{pu}	63.60±6.99^{pv}	34.00±6.63	34.48±9.74^{mu}
VII	136.00±6.63^{quxzß}	71.20±6.80^{qv}	63.60±4.85^{qw}	39.40±2.70^{nq}	25.20±5.70^{nqsv}
VIII	92.00±12.19^{rvyaß}	58.80±4.15^{rstuv}	58.80±7.35^{lrtuvw}	33.20±4.39^{mpr}	37.04±1.60^{prtv}

Figures bearing similar superscript in the same column are significantly different (P<0.05).

DISCUSSION

Oral administration of MC leaf extract on daily basis for 2 to 4 weeks produced a dose-dependent significant decrease (P<0.05) in fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), while high density lipoprotein (HDL) increased significantly (P<0.05) compared to group II (Table 1,and 2). These changes were significant different (P<0.05) with 200, 400 and 600mg/kg body weight of the extract. Group VIII which recieved daily dose of 600mg/kg body weight for 4 weeks did not show any significant difference (P<0.05) in serum levels of FBG, TC, TAG, HDL and LDL compared to group I (Table 2). Therefore MC aqueous leaf extract administration for 2 to 4 weeks produced a dose dependent changes (P<0.05).

The hypoglycemic effect of MC leaf extract recorded in this study is consistent with results of various previous studies (Virdi *et al*., 2003; Lotlikar and Rajarama 1966; Sathishsekar and Rajasekaran 2007; Miura *et al.,* 2001) where with treatment with different parts of bitter melon plant lower glucose levels in animal and human experiments. The increase in cholesterol levels observed in diabetes mellitus is a consequence of accelerated fatty acid oxidation to acetylcoA which is involved in cholesterol synthesis (Adeneye and Olagunju, 2009). Since insulin/glucagon ratio is low in diabetes mellitus, the function of lipoprotein lipase in clearing VLDL-cholesterol from blood is compromised (Harris and Crabbs, 1982) and this leads to hypercholesterolemia. This certainly contributes to the development of cardiovascular disease. The serum level of fasting blood glucose, total cholesterol, triglycerides and LDL were significantly increased, and significant decreased in HDL (P<0.05) with Alloxan induced diabetes in this study. These changes were significantly (p<0.05) reversed by oral administration of MC aqueous leaf extract towards normal, with highest effect at a daily dose of 600mg/Kg four weeks after treatment (Tables 1 and 2). This observations is also in consonant with various previous studies (Chaturvedi *et al.,* 2004; Chaturvedi 2005; Chen and Li 2005; Senanayake *et al.,* 2004) where extracts from the different parts of *Mormodica charantia* such as root

and stem bark were shown to significantly decrease levels of lipid profile in diabetic animals. alloxan induced diabetic rats. Oral administration of MC aqueous leaves extract at a dose of 600mg/kg for four weeks produce significant hypoglycaemic and hypolipidemic effect as seen in this study.

Conclusion

From the results of this study, it is clear that *Momordica charantia* aqueous leaves extract has dose dependent anti-diabetic, hypolipidemic effects on

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