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Research Article

Glucose-lowering effects of *Momordica charantia* (Karela) extract in diabetic rats

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Background: *Momordica charantia* (MC) is a plant commonly used for both its nutritional and glucose-lowering effects. It has however not been fully validated in diabetes management due to insufficient empirical evidence. The current study thus investigated its effects on blood glucose levels in diabetic rats.

Method: Fourteen six-month old, alloxan-induced diabetic *Sprague Dawley* rats weighing between 200 – 250 g were assigned to two equal groups (control and experimental). *Momordica charantia* juice extract was administered (10ml/kg) to the experimental group for 28 consecutive days. An equal dose of normal saline was administered to the controls. Fasting blood glucose (FBG) levels were assessed once weekly for 4 consecutive weeks. Thereafter, intraperitoneal glucose tolerance test (IPGTT) was performed.

Results: The experimental group achieved normal glucose levels within 14 days of MC administration. At day 28, FBG levels were significantly lower in the experimental group compared to the control (3.27±0.20 vs. 7.59±1.26 mmol/l, p=0.01). In IPGTT, FBG levels were significantly lower in the experimental group compared to the control through the 180 minute period of observation.

Conclusion: *Momordica charantia* has a glucose-lowering effect in diabetic rats within 14 days of administration. It also prevents fluctuations in FBG levels, and thus has potential therapeutic use in diabetes management.

Key words: *Momordica charantia*, diabetes mellitus, alloxan, intraperitoneal glucose tolerance test (IPGTT).

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1. Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by increased blood glucose levels (Hogan et al, 2003). It occurs due to either lack of insulin production (Type 1 DM) or deficient activity in the presence of normal or even elevated levels of insulin (Type 2 DM). Type 2 DM, which accounts for over 90% of the cases, leads to disordered metabolism of carbohydrate and fat. Chronically, DM causes micro-vascular and macro-vascular complications, where the micro-vascular effects include retinopathy, nephropathy and neuropathy. Macro-vascular complications, on the other hand, include hypertension, dyslipidemia, myocardial infarction and stroke (Lucy et al, 2002).

Diabetes is a great challenge to the world's healthcare system, with its worldwide prevalence estimated at 366 million people in 2011 (International Diabetes Federation, 2011). If no measures are taken, its prevalence is projected to reach 552 million people by 2030, representing around 10% of the global adult population (International Diabetes Federation, 2011). From the 366 million affected, 4.6 million people were projected to die in 2011 from the disease (International Diabetes Federation, 2011). This was an increase from the 3.9 million global diabetes deaths in 2010 (World Diabetes Foundation, 2010). Furthermore, global health care expenditure on DM is estimated to cost US$465 billion annually (International Diabetes Federation, 2011).

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In the management of type 2 DM, lifestyle modification (exercise, weight control and proper nutrition) is crucial. Oral glucose-lowering drugs and insulin injections are the conventional therapies. However, these medications are expensive and often associated with adverse effects, making the search for alternative treatment modalities crucial. The use of complementary and alternative medicine (CAM) has thus been on the rise in the treatment of DM (Su and Li, 2011). *Momordica charantia* (MC), also known as karela, bitter melon or balsam pear, is one of the plants commonly used for its glucose-lowering effects (Ahmed et al, 1998). The parts of the plant commonly used include the whole plant, its fruit or seeds, all of which are bitter due to the presence of the chemical momordicin (Beloin et al, 2005). Preparations that have been reported range from injectable extracts and fruit juice to fried melon bits (Welihinda et al, 1986; Shane-McWhorter, 2001; Beloin et al, 2005). It is also an established fact that many pharmaceutical drugs used for the treatment of different diseases have a plant origin (Bailey and Day, 1989). *Momordica charantia* has however not been validated in DM management due to inadequate empirical evidence. With the increasing use of MC among diabetics in Kenya and the uncertainty of its efficacy, it was imperative to investigate its glycemic effects.

2. Materials and Methods

2.1 Study animals

Fourteen (14) six month old, non-gravid alloxan-induced diabetic female *Sprague Dawley* rats weighing between 200 - 250 g were used (Shubhashish et al, 1996; Ahmed et al, 1998). The animals were housed in plastic cages in the animal house of the Department of Medical Physiology, University of Nairobi. A twelve hour light/dark cycle was maintained and the animals were fed on commercial pellets from a local supplier (Unga Feeds Ltd). Water was provided *ad libitum*. The rats were randomly assigned to control and experimental groups of 7 animals each and allowed a 15 day acclimatization period during which DM was induced using alloxan (Jennifer and Ransom, 2006).

2.2 Induction of diabetes mellitus

The animals were fasted for 16 hours before inducing DM. All the rats were intraperitoneally injected with a single dose of alloxan (125 mg/kg), a known β-cell toxin (Lenzen et al, 1988) dissolved in 10% sodium chloride (Reyes et al, 2006). The FBG levels were assessed on days 0, 3, 6, 13, 20 and 27 following administration of alloxan (Matheka et al, 2012). Animals were considered diabetic if FBG level was above 7.1 mmol/l (Kwanghee et al, 2009).

2.3 Extract preparation

Fresh unripe MC fruits obtained from the local market were identified by the Herbarium of the University of Nairobi. The fruits were thoroughly washed, weighed and the seeds removed (Sridhar et al, 2008). Thereafter, the remaining part of the fruit was shredded into small pieces and squeezed using a domestic juice extractor. The resulting crude juice extract was administered to the animals using an oral gavage. Any leftover juice was stored at 4 °C for a maximum of two days (Matheka et al, 2011).

2.4 Animal treatment

Baseline blood glucose and body weight measurements were taken on the first day of the experiment immediately following the acclimatization period. MC fruit juice extract (10 ml/kg) (Sridhar et al, 2008) was administered orally to the experimental group once daily after DM induction, while an equal dose of normal saline was given to the controls, for a period of 28 days (Eichenbaum et al, 2011). All the animals were bled on days 0, 7, 14, 21 and 28 by sequential snipping of the tip of the tail as described by Fluttert et al. (2000). A glucometer (On Call® Plus, Acon Industries, Inc. 4108, San Diego, USA) was used to measure the FBG levels.

2.5 Intraperitoneal glucose tolerance test (IPGTT)

At the end of the 28-day experiment, all the rats were fasted overnight (12 hours) and IPGTT performed (Jae-Jeong et al, 2003). The experimental and control groups were fed orally with the extract and normal saline, respectively. The rats were then injected intraperitoneally with 2 g/kg glucose, 45 minutes after MC/normal saline administration (Jae-Jeong et al, 2003). Blood samples were collected at 30-min intervals for 3 hours for glucose measurement (Matheka et al, 2011).

2.6 Statistical analysis

Data were expressed as mean ± standard error of mean (SEM). Student's t-test was used to test statistical significance using SPSS version 16.0. Significance levels were set at $p < 0.05$.

2.7 Ethical considerations

The study protocol was approved by the Postgraduate Research Committee, Department of Medical Physiology, University of Nairobi. Animals were handled in accordance to the guidelines of the US National Research Council for the care and use of laboratory animals (National Academy Press, 1996).

3. Results

3.1 Effect of *Momordica charantia* on glucose levels

Baseline FBG levels were 18.19 ± 2.20 and 19.26 ± 2.58 mmol/l in the experimental and control groups, respectively. However, after oral administration of MC juice extract to the rats for 28 consecutive days, the FBG levels decreased significantly in the experimental group (3.27 ± 0.20 vs. 7.59 ± 1.26 mmol/l, $p = 0.01$), with normal glucose levels being achieved within 14 days of extract administration (**Figure 1**). Inter-individual rat differences were observed with even some rats achieving normal glucose levels within 7 days. The FBG levels among the control rats also reduced gradually and by a small margin (**Figure 1**). This reduction was not statistically significant.

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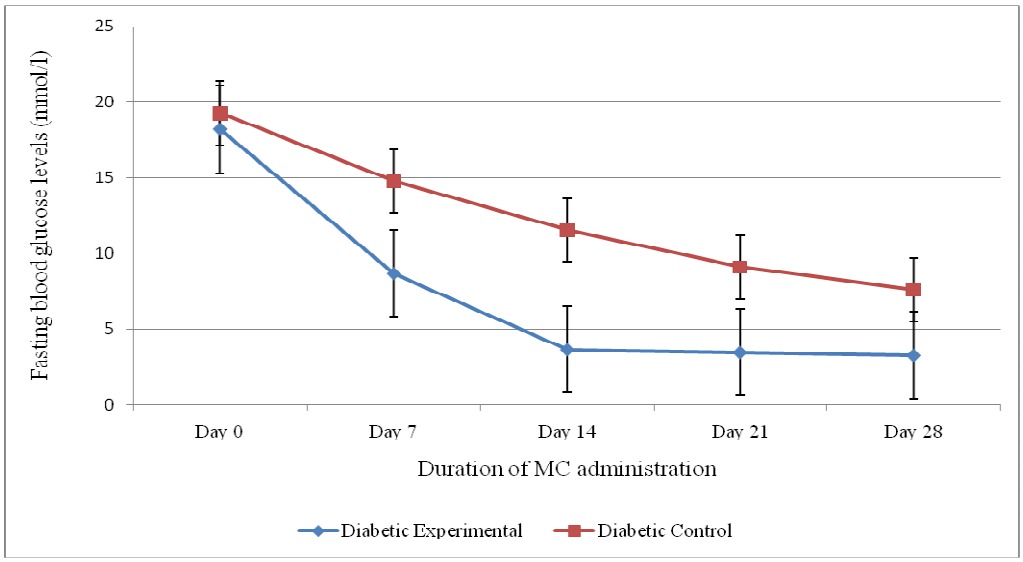
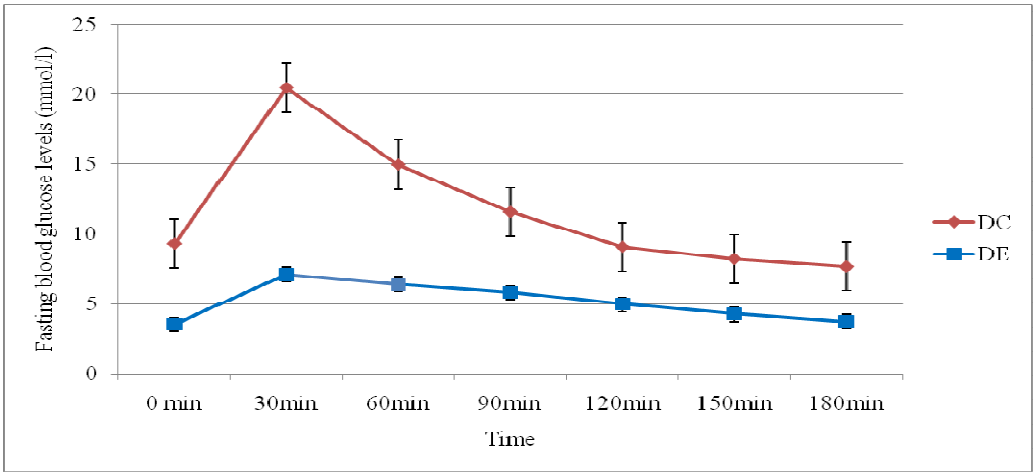
3.2 Effect of IPGTT on blood glucose levels

Before IPGTT, there were significant differences in the baseline glucose levels between the two groups (7.68 ± 1.05 in control *vs*. 3.75 ± 0.12 mmol/l in experimental, $p = 0.01$). At a dose of 10 ml/kg of MC followed by 2 g/kg intraperitoneal glucose injection, the blood glucose level increased by 100% to 7.10 ± 0.25 mmol/l at 30 min. Thereafter, it decreased by 10% at 60 min, 10% at 90 min and 14% at 120 min (**Figure 2**). On the other hand, the control group (on 10 ml/kg normal saline) had an initial sharp increase of 120% in glucose level at 30 min to 20.48 ± 1.31 mmol/l, which progressively decreased by 27% at 60 min, 23% at 90 min and 22% at 120 min. In the experimental group, the initial glucose level at 30 min increased gradually and by a smaller margin compared to the control. The decline in blood glucose thereafter was also more gradual in the experiment group compared to the control (**Figure 2**).



Error bars represent ± SEM

Figure 1: Comparison of fasting blood glucose level in experimental and control groups after administration of *Momordica charantia*



Error bars represent ± SEM
DC, Diabetic Control; DE, Diabetic Experimental

Figure 2: Effect of *Momordica charantia* on intraperitoneal glucose tolerance test in diabetic rats

4. Discussion

Diabetes mellitus is associated with significant morbidity and mortality (Shaw et al, 2010). Its management through pharmacotherapeutic interventions is associated with high cost and adverse effects, hence the rising use of alternative interventions (Chang et al, 2007). Despite insufficient empirical evidence on the efficacy of MC, it is commonly used in DM management. The present study investigated the glucose profiles of MC treated alloxan-induced diabetic rats.

Momordica charantia treatment for 28 days showed a significant decrease in FBG levels in the diabetic rats. This demonstrated the blood glucose-lowering effect of MC. On the other hand, a slight decrease in blood glucose was spontaneously observed in the control

group. This was probably due to the recovery of partially destroyed β-cells that could occur over time. The glucose levels eventually stabilized two weeks following treatment with alloxan, probably due to the full recovery of the β-cells. Furthermore, hormones that counter hyperglycemia may have contributed to the FBG level decline in the control group (Gelfand et al, 1984; Matheka et al, 2012).

There was a significant decrease in the blood glucose level of the MC treated diabetic animals as early as within two weeks of administration. This corroborates previous similar evidence (Akhtar et al, 1981; Welihinda et al, 1986; Srivastava et al, 1993; Chaturvedi et al, 2004; Sridhar et al, 2008). Inter-individual differences were also observed within the experimental group, with some rats achieving normal glucose levels within 7 days following MC administration. This may partly be explained by the inherent physiological variation in the amount of β-cells reserve, thus the varied response in the development and management of DM among the general population under similar environmental conditions.

During IPGTT, the increase in blood glucose was smaller in the experimental group compared to the control group. In addition, both the rise to the peak and the decline back to baseline were more gradual in the experimental group than in the controls. Accordingly, these findings emphasize the potential role of MC in modulating glucose levels in diabetes. Thus, it is evident that MC has important glucose-lowering properties. Its mode of action is however unclear (Chaturvedi et al, 2004), with several hypotheses having been postulated in an earlier study (Matheka et al, 2011). These include the facilitation of glycogen storage, glucose uptake by peripheral tissues, insulin secretion by isolated β-cells of the islets of Langerhans and recovery of partially destroyed β-cells (Sridhar et al, 2008).

Although some similar studies have been conducted in the past (Srivastava et al, 1993; Chaturvedi et al, 2004; Sridhar et al, 2008), very few had IPGTT done to demonstrate the short-term effects of MC. Moreover, the present study is unique in that it employs the use of crude juice extracts. This is the preparation that is commonly used among the population, and which is likely to contain all the active compounds. This study therefore investigates more accurately the benefit of MC consumption for diabetes management - a practice that is becoming more popular by the day. Human trials and comparison of efficacy of MC relative to known hypoglycemic drugs are recommended.

5. Conclusion

Momordica charantia crude juice extract has a marked glucose-lowering effect in diabetic rats within 14 days of oral administration. It furthermore prevents fluctuations in blood glucose levels thus its potential therapeutic use in the management of type 2 DM.

Conflict of Interest declaration

The authors declare no conflict of interest

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References

Ahmed I, Adeghate E, Sharma AK, Pallot DJ, Singh J (1998). Effects of *Momordica charantia* fruit juice on islet morphology in the pancreas of the streptozotocin-diabetic rat. *Diab. Res. Clin. Pract.* **40**: 145-51.

Akhtar MS, Athar MA, Yaqub M (1981). Effect of *Momordica charantia* on blood glucose level of normal and alloxan-diabetic rabbits. *Planta Med.* **42**: 205-12.

Bailey CJ, Day C (1989). Traditional plant medicines as treatments for diabetes. *Diabetes Care* **12**: 553-64.

Beloin N, Gbeassor M, Akpagana K, Hudson J, de Soussa K, Koumaglo K, Arnason J (2005). Ethnomedicinal uses of *Momordica charantia* (Cucurbitaceae) in Togo and relation to its phytochemistry and biological activity. *J. Ethnopharmacol.* **496**: 49-55.

Chang H, Wallis M, Tiralongo E (2007). Use of complementary and alternative medicine among people living with diabetes: literature review**.** *J. Adv. Nurs.* **58**: 307-19.

Chaturvedi P, George S, Milinganyo M, Tripathi YB (2004). Effect of *Momordica charantia* on the lipid profile and oral glucose tolerance in Diabetic rats. *Phytother. Res.* **18**: 954-56.

Eichenbaum G, Damsch S, Looszova A, Vandenberghe J, Van den Bulck K, Roels K, Megens A, Knight E, Hillsamer V, Feyen B, Kelley MF, Tonelli A, Lammens L (2011). Impact of gavage dosing procedure and gastric content on adverse respiratory effects and mortality in rat toxicity studies. *J. Appl. Toxic.* **31**: 342-54.

Gelfand RA, Mathews DE, Bier DM, Sherwin RS (1984). Role of counter-regulatory hormones in the catabolic response to stress. *J. Clin. Invest.* **74**: 2238-40.

Guide for the Care and Use of Laboratory Animals (1996). Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council. National Academy Press, Washington DC.

Hogan P, Dall T, Nikolov P (2003). Economic costs of diabetes in the U.S. in 2002. *Diabetes Care* **26**: 917–32.

International Diabetes Federation (IDF) Diabetes Atlas, 5th Ed (2011). http://www.idf.org/diabetesatlas/news/fifth-edition-release. Accessed 24th May 2012.

Jae-Jeong L, Ho-Young Y, Jae-Won Y, Jun-Seop S, Jai-Hyun K, Chan-Wha K (2003). Characterization of Streptozotocin-induced Diabetic Rats and Pharmacodynamics of Insulin Formulations. *Biosci. Biotechnol. Biochem.* **67**: 2396-401.

 ISSN 2303-9841

Jennifer AO, Ransom LB (2006). Establishing an Appropriate Period of Acclimatization Following Transportation of Laboratory Animals. *ILAR J.* **47**: 364-69.

Kwanghee K, Hyunyul K, Jeunghak K, Sungwon L,Hyunseok K, Sun-A I, Young-Hee L, Young-Ran L, Sun-Tack O, Tae Hyung J, Young I, Chong-Kil L, Kyungjae K (2009). Hypoglycemic and hypolipidemic effects of processed *Aloe vera* gel in a mouse model of non-insulin-dependent diabetes mellitus. *Phytomedicine* **16**: 856-63.

Lenzen S, Brand F, Panten U (1988). Structural requirements of alloxan and ninhydrin for glucokinase inhibition and of glucose for protection against inhibition. *Br. J. Pharmacol.* **95**: 851-59.

Lucy D, Anoja SA, Chu-Su Y (2002). Alternative therapies for Type 2 diabetes. *Alternative Med. Rev.* **7**: 45-58.

Fluttert M, Dalm S, Oitzl MS (2000). A refined method for sequential blood sampling by tail incision in rats. *Lab. Animals* **34**: 372-378.

Matheka DM, Kitua M, Alkizim FO (2012). Peculiar glycemic patterns in alloxan-induced diabetes animal model. *Afr. J. Pharmacol. Ther.* **1**: 30-34.

Matheka DM, Kiama TN, Alkizim FO, Bukachi F (2011). Glucose-lowering effects of *Momordica charantia* in healthy rats. *Afr. J. Diab. Med.* **19**: 15-9.

Reyes BAS, Bautista ND, Tanquilut NC, Anunciado RV, Leung AB, Sanchez GC, Magtoto RL, Castronuevo P, Tsukamura H, Maeda KI (2006). Anti-diabetic potentials of *Momordica charantia* and *Andrographis paniculata* and their effects on estrous cyclicity of alloxan-induced diabetic rats. *J. Ethnopharmacol.* **105**: 196-200.

Shane-McWhorter L (2001). Biological complementary therapies: a focus on botanical products in diabetes. *Diabetes Spectrum* **14**: 199-208.

Shaw JE, Sicree RA, Zimmet PZ (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diab. Res. Clin. Pract.* **87**: 4-14.

Shubhashish S, Pranava M, Rosalind MA (1996). Demonstration of the hypoglycemic action of *Momordica charantia* in a validated animal model of diabetes. *Pharmacol. Res.* **33**: 1-4.

Sridhar MG, Vinayagamoorthi R, Suyambunathan VA, Bobby Z, Selvaraj N (2008). Bitter gourd (*Momordica charantia*) improves insulin sensitivity by increasing skeletal muscle insulin-stimulated IRS-1 tyrosine phosphorylation in high-fat-fed rats. *Brit. J. Nutr.* **99**: 806-12.

Srivastava Y, Venkatakrishna-Bhatt H, Verma Y, Venkaiah K (1993). Antidiabetic and adaptogenic properties of *Momordica charantia* extract. An experimental and clinical evaluation. *Phytother. Res.* **7**: 285-9.

Su D, Li L (2011). Trends in the use of complementary and alternative medicine in the United States: 2002-2007. *J. Health Care Poor Underserved* **22**: 296-310.

Welihinda J, Karunanayake EH, Sheriff MH, Jayasinghe KS (1986). Effect of *Momordica charantia* on the glucose tolerance in maturity onset diabetes. *J. Ethnopharmacol.* **17**: 277-82.

World Diabetes Foundation Report (2010). http://www.worlddiabetesfoundation.org/media(9358,1033)/Roglic, Gojka.pdf. Accessed 8th March 2012.

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