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Research Article

Effect of *Momordica charantia* Aqueous Leaf Extract on the Isolated Mammalian Heart

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Background: *Momordica charantia* is one of the most commonly used medicinal plants for both ritual and ethnomedical practices. Its use includes as an abortifacient, laxative and in the treatment of pneumonia. Despite the widespread use of its aqueous leaf extract, its pharmacological effects on the heart are not sufficiently investigated.

Objectives: The main objective was to determine the effect of *Momordica charantia* aqueous leaf extract on the isolated mammalian heart. A secondary objective was to investigate possible effects on β adrenergic receptors of the heart.

Methodology: Six healthy rabbits were included in the study. Each rabbit was sacrificed and the heart mounted on the Langerndorff apparatus. Baseline rate and force of contraction were taken, after which the aqueous leaf extract administered in increasing doses and changes in rate and force of contraction noted. The effects of the extract on the heart were similarly investigated in the presence of propranolol (a non-selective β adrenergic receptor antagonist) were also noted. Unpaired T-test and repeated measures ANOVA were used to test for statistical significance. P-values greater than < 0.05 indicated statistical significance.

Results: There was significant, dose dependent, increase in the force and rate of contraction after administering the extract ($P < 0.0001$). However, in the presence of propranolol, the increase noted was not statistically significant.

Discussion: The study shows that *Momordica charantia* aqueous leaf extract has dose dependent effect on both force and rate of cardiac muscle contraction.

Keywords*: Momordica charantia,* aqueous extract, rate and force of contraction, heart.

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1. Introduction

Momordica charantia, also known as bitter gourd, belongs to the family of Cucurbitaceae. It is a common plant found in the tropical and subtropical regions (Africa and Asia). The parts of the plant used are leaf, roots and fruits. Diverse medicinal properties have been exploited in various African and ayurvedic medicinal systems.

Herbal extracts have been shown to modulate amplitude and frequency of slow waves in the circular smooth muscle of small intestine (Ricardo et al, 2004). A postulated mechanism of amplitude and frequency modulation is blockage of calcium channels. It has also been demonstrated that herbal extracts have beneficial effects on the heart. *Crataegus oxyacantha* for example, has been shown to improve cellular metabolism and increasing strength of smooth muscle contraction. (Qi et al, 2013; Ringelsky et al, 2002).

The fruit of *Momordica charantia* has been universally used as a blood glucose lowering agent as it increases insulin sensitivity as well as insulin levels (Chaturvedi, 2011; Norbert et al, 2013). Tea prepared from *Momordica charantia* leaves is also used in the management of diabetes. (Bakare et al, 2010). Additionally, *Momordica charantia* possesses antiviral properties against chicken pox, measles (Nadine et al, 2005) and also Human Immunodeficiency Virus (HIV) (Nerurkar et al, 2006) although the latter has not been fully investigated. Other properties attributed to

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Momordica charantia include antimalarial (Singh, 2006), anthelminthic, especially against *Caenorhabditis elegans* (Nadine et al, 2005) and anticancer (Ray et al, 2010; Kohno et al, 2004; Ivan 2005; Kumar et al, 2010).

The traditional preparation of the aqueous leaf extract is by boiling in water and leaving the mixture on the table for use the following day. It is also stored in the fridge to be used after 24 hours. Despite its wide medicinal value, *Momordica charantia* aqueous leaf extract is contraindicated in certain physiological conditions such as pregnancy because it has been reported to stimulate uterine smooth muscle contraction leading to abortion (Nadine et al, 2005). Consequently, it is used as an abortifacient by some communities e.g. in the Philippines (Sabira et al, 1997).

A wide range of active components principally momordicin I , momordicin II, and cucurbitacin B are responsible for the biological activity of *Momordica charantia* (Majekodunmi et al, 1990). Mormodicin I, mormodicin II and cucurbitacin B possess purgative and cytotoxic properties. Charantin, a steroid saponin with insulin like effect, is the main anti diabetic agent in *Momordica charantia* plant. (Ernest et al, 2011). *Momordica charantia* leaf also contains bioactive glycosides including momordin, charantosides, glycosides, momordicosides, goyaglycosides and other terpenoid compounds that include momordicin-28, momordicinin, momordicilin, momordenol, and momordol (Sabira et al, 1997; Kimura et al, 2005). The terpenoids are also responsible for the anti-diabetic, anti-cancer, anti-obesity and anti-HIV properties that are attributed to *Momordica charantia.* (Sook et al, 2009). Momorcharin and momordicin (cytotoxic proteins) are also present.

Momordica charantia leaves are consumed by many despite the paucity of knowledge on its effects on the cardiac muscle. Regardless of the numerous uses of *Momordica charantia* aqueous leaf extract, few studies have been carried out to investigate its effects on the heart muscle rate and force of contraction. Additionally, effects pertaining to utilization of the extract on cardiac rate and force of contraction are poorly documented.

Therefore, current study set out to demonstrate the effects of *Momordica charantia* aqueous leaf extract on isolated mammalian heart. The primary objective of the study was to investigate the effect of *Momordica charantia* aqueous leaf extract on rate and force of contraction of isolated mammalian heart. A secondary objective was to investigate possible effects on β adrenergic receptors of the heart.

2. Methods

2.1 Preparation of *Momordica charantia* aqueous leaf extract

Fresh leaves of *Momordica charantia* were procured from the local market and authenticated by the Department of Botany, University Of Nairobi. The leaves were assigned voucher number: **JA2012/01**. A voucher specimen was deposited in the herbarium.

The leaves were air dried under the shade for three days. The dried leaves were wrapped in water proof paper bags and stored for 2 weeks until the time of extraction (Bakare et al, 2011). Extraction of the dried leaves was done by hot infusion using 20 ml of hot water for every 1 g of leaf powder. The extract was allowed to cool before filtering.

2.2 Preparation of the physiological salt solution

Ringer-Locke solution was prepared using standard procedures. The composition of Ringer's solution was (g/L): Sodium chloride (9.0); Sodium bicarbonate (0.2); Glucose (1); Potassium chloride (0.42); and Calcium chloride (0.24). During mixing, calcium chloride was dissolved separately in distilled water and added last to avoid precipitation. The salts were manufactured by Muby Chemicals (India).

2.3 Animal Husbandry

New Zealand White rabbits were procured locally from Tony Rabbits and Guinea Pigs Farm (Kenya). They were housed in a clean environment in the animal house, Department of Medical Physiology. Standard laboratory conditions of humidity 50 ±15% and temperature of 25 ±2 ^{0}C, 12h/12h light-dark cycle was maintained. They had free access to food and water. The procedures and experiments were performed according to the guidelines stated by the Federation of European Laboratory Animal Science Associations (FELASA).

2.4 Investigating effects of aqueous leaf extract on isolated heart

The rabbit was sacrifice by cervical dislocation. The heart was removed and mounted on a Langendorff apparatus. Baseline myocardial rate and force of contraction was then recorded.

The extract's effects on the heart were determined before and after administration of propranolol (a non-selective β adrenergic receptor antagonist).

Starting with the least volume, 0.2 ml (1 mg equivalent of dried leaf powder) of the fresh extract was administered by infusion into the aorta and the effects recorded. The volume of the extract was successfully increased in 0.2 ml increments to a maximum of 1.0 ml. thereafter, propranolol 0.6 ml (0.2 mM) and then the fresh extract (0.6 ml) were administered and the response recorded. This was repeated 6 times.

Adrenaline (0.01 IU) was used as the positive control. Before administration of each concentration, perfusate was allowed to wash the heart for 10 seconds and baseline recordings taken.

2.5 Data and statistical analysis

Rate and strength of contraction was determined using the Langendorff apparatus.

Data generated from the study was analyzed in terms of frequency and force of contraction. Frequency referred to the number of contractions per unit time while force referred to height of amplitude (in mm).

The changes in rate and force of contraction were analyzed and expressed as Mean and Standard Error of

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Mean. Statistical analysis to find out whether there was significant change in rate and force of contraction after administration of the various dosages was done using Analysis of Variance (ANOVA) and unpaired t test. Data analysis was done using Statistical Package for Social Sciences (SPSS version 17.0). Changes in rate and force of contraction after administration of the various extracts was compared with baseline readings using a unpaired sample t test with the p value set at $p<0.05$.

2.6 Ethical considerations

The animals that were used in the study were handled with care as the welfare of the laboratory animals is important in influencing results. Moreover, the standard operating procedures (SOP) of the Department of Medical Physiology animal laboratory was adhered to. In addition to FELASA guidelines, the 3R principles (reduction, refinement and replacement) were adhered to.

3. Results

The rate and force of contraction of the heart after administration of the various doses of the extract are shown in **Table 1**. There was a significant increase in both the force and rate with each increase in dosage. However, there was a larger increase in force as compared to rate of contraction. The increase in rate and force of contraction was directly proportional to the increase in the extract's dose. This increase was statistically significant ($P < 0.0001$) for both force and rate.

The effects of the extract was however irreversible after wash out.

Table 1: Rate and force of contraction of the heart after administration of various concentrations of aqueous extract of *Momordica charantia* (N=6)

Concentration of extract (mg/ml)	Force of contraction (mm) (mean±SEM)		Frequency of contraction (per min) (mean±SEM)	
	Baseline	After extract administration	Baseline	After extract administration
0.2	18.36±0.37	20.58 ± 1.40	1.04±0.16	3.68 ± 0.22
0.4	18.21±0.41	31.83 ± 0.50	1.27±0.19	7.31 ± 0.23
0.6	19.37±0.43	42.67 ± 0.84	1.33±0.23	10.67 ± 0.55
0.8	18.74±1.01	52.43 ± 1.74	1.94±0.27	16.21 ± 0.60
1.0	17.83±1.04	60.84 ± 2.07	1.01±0.32	21.96 ± 0.42

Table 2: Effect of fresh *Momordica charantia* aqueous leaf extract on heart rate before and after administration of β-receptor blocker. Adrenaline is used as the positive control.

	Contractions (per min)				
	Baseline	*Momordica charantia*		Control (Adrenaline)	
		Unblocked β receptor	Blocked β receptor	Unblocked β receptor	Blocked β receptor
Rabbit 1	11.94	52.37	12.23	93.23	17.62
Rabbit 2	9.71	49.33	10.15	87.62	18.47
Rabbit 3	11.39	51	12.64	91.77	17.71
Rabbit 4	9.04	50.33	9.56	93.21	19.38
Rabbit 5	12.27	49.67	12.65	90.02	18.65
Rabbit 6	10.92	51.67	11.2	91.13	17.93
Mean ± SEM	10.88 ± 0.519	50.73 ± 0.479	11.41 ± 0.541	91.16 ± 0.870	18.29 ± 0.275

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Table 2 illustrates the effect of *Momordica charantia* aqueous leaf extract on rate of contraction of isolated rabbit heart before and after administration of propranolol. There was increase in rate of contraction with administration of propranolol followed by the extract. However, this increase was not statistically significant. The mean rate of contraction without administration of the receptor blocker was 50.73±0.479 which was higher than 11.41±0.5409 with blocked receptors. The p-value (<0.0001) computed from this difference was significant at 5%.

A Tukey's post hoc test was performed to find out the probability that the difference noted in rate of contraction after administration of *Momordica charantia* and or adrenaline was due to chance. The level of significance was set at $p < 0.05$. The test demonstrated that this probability was less than < 0.0001

4. Discussion

The current study was objectively set out to determine the effect of fresh *Momordica charantia* aqueous leaf extract on rate and force of contraction of isolated mammalian heart. The two parameters assessed, magnitude and frequency of contraction, were surrogate markers for force and rate, respectively.

There was a pattern of increase in rate and force of contraction after the administration of the various doses of the extract. This increase was directly proportional to the dose of the extract administered. The maximum increase was seen with 1 ml (1 mg equivalent of dried leaves powder). The effects of the extract were however irreversible after wash out, suggesting that the extract irreversibly binds to receptors involved.

The rate of contraction observed for *Momordica charantia* aqueous leaf extract was lowered by approximately 40% ($p < 0.05$) in the presence of propranolol. This could be explained by propranolol blocking the agonist's receptors i.e. the β receptors; hence the effects of the extract could not be fully manifested. This suggested that the effect of the extract on the heart was via the sympathetic system, most probably through the β receptors. A similar decrease in rate of contraction was noted with the positive control used i.e. adrenaline. The partial decrease in rate of contraction after the administration of propranolol was postulated to be due to incomplete receptor blockade, hence leaving some receptors free to bind the agonist molecules.

The current study shows that even low doses of *Momordica Charantia* aqueous leaf extract have effect on the mammalian heart. The limitation in carrying out the current study however was an old Langerndof apparatus.

5. Conclusion

The present study demonstrated that *Momordica charantia* aqueous leaf extract has effects on myocardial rate and force of contraction. Specifically, the extract has a dose dependent increase in myocardial rate and force of contraction.

The current study postulated a probable mechanism of action of *Momordica charantia* to be via the β receptors. However, further studies to investigate other possible mechanisms of action of *Momordica Charantia* aqueous leaf extract on the heart are recommended.

Conflict of Interest declaration

The authors declare no conflict of interest

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References

Bakare RI, Magbagbeola OA, Akinwande AI, Okunowo OW and Green M (2011). Anti-diarrhoreal activity of aqueous leaf extract of *Momordica charantia* in rats. *J. Pharmacogn. Phytother.* **3:**1-7.

Bakare RI, Magbagbeola OA, Akinwande AI, and Okunowo OW (2010). Nutritional and chemical evaluation of *Momordica charantia. J. Med. Plants Res.* **4:** 2189-2193.

Chaturvedi P (2012). Anti-diabetic potentials of *Momordica charantia*: multiple mechanisms behind the effects. *J. Med. Food* **15:** 101-107.

Clinton WR (2003). Smooth muscle contraction and relaxation. *Adv. Physiol. Ed.* **27:** 201-206.

Duke JA (1985). CRC Handbook of Medicinal Herbs. CRC Press, Boca Raton FL, pp 315–316.

Ernest A, Jaipaul S, Emmanuel C, Gunasekar M and Huba K (2011). Medicinal Chemistry of the Anti-Diabetic Effects of Momordica Charantia: Active Constituents and Modes of Actions. *Open Med. Chem. J.* **5:** 70-77.

Faraj OA, Duncan M, Fatma KA, Anne M (2012). Inhibitory effect of *Mangifera indica* on gastrointestinal motility. *Med. Chem. Drug Discov.* **2:** 9-16.

Francesca B, Francesco C, Raffaele C, Valeria A, Gabriella A, Rocco Land Angelo AI (2006). Effect of *Boswellia serrata* on intestinal motility in rodents: inhibition of diarrhoea without constipation. *Br. J. Pharmacol.* **148:** 553–560.

Grover JK and Yadav SP (2004). Pharmacological actions and potential uses of *Momordica charantia. J. Ethnopharmacol.* **93:** 123-132.

Kohno Hi, Yumiko Y, Rikako S, Masashi H, Kazuo M and Takuji T (2004).Dietary seed oil rich in conjugated linolenic acid from bitter melon inhibits azoxymethane-induced rat colon carcinogenesis through elevation of colonic PPAR γ expression and alteration of lipid composition. *Int. J. Cancer* **110:** 896–901.

Julius EO, Sheila, AE, Gabriel AA, and David FM. (2006). Effect of *Eremomastax speciosa* on experimental diarrhea. *Afr. J. Trad. Complement. Alt. Med.* **1:** 95-100.

Kimura Y, Akihisa T, Yuasa N, Ukiya M, Suzuki T, Toriyama M, Motohashi S, and Tokuda H (2005). Cucurbitane-type triterpenoids from the fruit of Momordica charantia. *J. Nat. Prod.* **68:** 807–809.

Majekodunmi OF, Yoshio T, Hiroyasu Y, Hikaru O, Tatsuo Y (1990). New cucurbitane triterpenoids from *Momordica charantia. J. Nat. Prod.* **53:**1491-1497.

Ivan AR (2005). Medicinal plants of the world. Vol 1. Humana Press, New Jersy, pp 337-341.

Nadine B, Gbeassor M and Akpagana K (2005). Ethnomedicinal uses of *Momordica charantia (Cucurbitaceae)* in Togo and relation to its phytochemistry and biological activity. *J. Ethnopharmacol.* **96:** 49-55.

Norbert A, Nkambo W and Onegi B (2013). *In vivo* hypoglycemic effect of methanolic fruit extract of *Momordica charantia* L. *African Health Sciences*. **13:** 933–939.

Nerurkar PV, Yun KL, Ellen HL, Steven L, Laurel P, Jennifer F, Vivek RN (2009). Lipid lowering effects of *Momordica charantia* (Bitter Melon) in HIV-1-protease inhibitor-treated human hepatoma cells, HepG2. *Br. J. Pharmacol.* **148:**1156–1164.

Pulok K, Mukherjee, Kuntal M, Kakali M and Peter JH (2006). Leads from Indian medicinal plants with hypoglycemic potentials. *J. Ethnopharmacol.* **106**, 1-28.

The side effects of *Momordica ccharantia*. http://www.livestrong.com/article/392687-the-side-effects-of-momordica-charantia/. (Accessed 21May 2012).

Ratna B. Ray, Amit R, Robert S and Pratibha N (2010). Bitter Melon (*Momordica charantia*) extract inhibits breast cancer cell proliferation by modulating cell cycle regulatory genes and promotes apoptosis. *Cancer Res.* **70:** 1925-1931.

Ricardo CH , and Fong WP (2004). Multiple trypsin inhibitors from *Momordica cochinchinensis* seeds, the Chinese drug mubiezhi. *Peptides* **25:** 163-169

Rigelsky JM and Sweet BV (2002). Hawthorn: pharmacology and therapeutic uses. *Am. J. Health Syst. Pharm.* **59:** 417-422.

Rojas A, Hernandez L, Pereda RM (1992). Screening for antimicrobial activity of crude drug extracts and pure natural products from Mexican medicinal plants. *J. Ethnopharmacol.* **35:** 275 –283.

Sabira B, Mansoor A, Bina S. Siddiqui, Abdullah K, Zafar SS and Mohammed A (1997). Triterpenes, a sterol, and a monocyclic alcohol from *Momordica charantia. J. Phytochem.* **44:** 1313-1320.

Sampath, Kumar KPand Debjit B (2004). Traditional medicinal uses and therapeutic benefits of *Momordica charantia* linn. *Int. J. Pharmaceut. Sci. Review and Research* **4:** 23-28.

Sook YL, Seok HE, Yong KK, Nam P and Sang UP (2009). Cucurbitane-type triterpenoids in *Momordica charantia* Linn. *J. Med. Plants Res.* **3:** 1264-1269.

Spencer NJ, Smith CB and Smith TK (2001). Role of muscle tone in peristalsis in guinea-pig small intestine. *J. Physiol.* **530:** 295-306.

Subbroto KS, Ezazul H, Dipa I, Matiar R, Rezuanul I, Anzana P, Shahedur R (2012). Comparative study between the effect of *Momordica charantia* (wild and hybrid variety) on hypoglycemic and hypolipidemic activity of alloxan induced type 2 diabetic long-Evans rats. *Int. J. Diabetes Mellit.* **2:** 131-137.

Qi C , Zhong Z, Francisco H, and Moses SS (2013). Hawthorn. *J. Clinical Pharmacol.* **42**: 605–612.

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