**Momordica charantia** Extracts Inhibit Uptake of Monosaccharide and Amino Acid across Rat Everted Gut Sacs in-Vitro

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The inhibitory effects of *Momordica charantia* extracts were studied on the uptake of glucose and tyrosine across rat everted gut sacs in vitro. The aqueous extract of the plant was found to inhibit primarily the uptake of glucose in a dose-dependent manner. Uptake of tyrosine was affected at high substrate concentrations only. The extract was also found to decrease the absorptive capacity of fluid across the small intestine and sodium ions. It is hypothesized that the effects of *Momordica* could involve a washout of glucose from the blood stream.

Key words *Momordica charantia*; glucose; tyrosine; transport; diabetes

During the past decade, traditional systems of medicine have become a topic of global importance. Current estimates suggest that, in many developing countries just like Mauritius, a large proportion of the population relies heavily on traditional practitioners and medicinal plants to meet primary health care needs. 1—4 Although modern medicine may be available in these countries, herbal medicines (phyto-medicines) have often maintained popularity for historical and cultural reasons. Concurrently, many people in developed countries have begun to turn to alternative or complementary therapies, including medicinal herbs.

The Mauritian population has a long-standing tradition in the use of ethnomedicine and the practice is still strong especially in the treatment of minor ailments. 1—4 Such interests stems from an existing culture and many “tisanes” are still prepared from plant materials and sold in several markets on the island. Reports have been published regarding the medicinal properties of local plants and an estimated number of 460 plant species are already known to exhibit some therapeutic value. 1—4 However only some of these data have been validated. 5

*Momordica charantia* is an alternative therapy that has primarily been used for lowering blood glucose level in patients with diabetes mellitus. 6 Components of bitter melon extract appear to have structural similarities to animal insulin. 7 Welinhinda et al. 8 have reported a method for the isolation of an active fraction called p (plant)-insulin from fruits, seeds and tissue culture of the *Momordica* plant. 8 Available report in the literature also show that *Momordica charantia* is used against diabetes mellitus, as a carminative for colic, topical for sores, wounds and infections. It has been reported that *Momordica charantia* is also used internally and externally for worms and parasites. 7 In Mauritius, *Momordica charantia* is grown mainly by the local residents for food purposes. However some people use the decoction of the plant against diabetes amongst other diseases. 1—4

This study was therefore undertaken to assess the possible biological properties of *Momordica charantia* extracts on glucose, tyrosine and electrolyte transport across rat everted gut sacs in vitro.

MATERIALS AND METHODS

**Preparation of the Extracts from Momordica charantia**

Fruits A powdered mixture (10 g) of *Momordica charantia* dry fruit was extracted with a Soxhlet apparatus at 90 °C for 5 h with 50-ml solvent (water). The solvent was evaporated under vacuum at 50 °C, and the precipitate was collected in 10 ml water. Percentage yield was calculated and the water suspension was diluted for further experiments.

**Preparation of Everted Gut Sac** Adult male Swiss albino rats weighing 200—250 g maintained on commercial feed were used for this study. After overnight fasting, rats were killed by a severe blow on the head against a hard surface. The abdomen was opened by a midline incision. The whole of the small intestine was removed by cutting across the upper end of the duodenum and the lower end of the ileum and manually stripping the mesentery. The small intestine was washed out with normal saline solution (0.9% w/v NaCl) using a syringe equipped with blunt end.

Intestinal segments (10±2 cm) were then everted according to the method described by Wilson and Wiseman. 9 After weighing, the empty sac was filled with 1 ml of Krebs–Henseleit bicarbonate buffer (KHB). The composition of the buffer was (mm/l): NaHCO3 25; NaCl 118; KCl 4.7; MgSO4 1.2; NaH2PO4 1.2; CaCl2 1.2; and Na2EDTA 9.7 mg/l. Glucose (2 g/l) was added to the medium just before the start of the appropriate experiments. The pH was maintained at 7.4. The sac was filled with a blunted-ended syringe and then slipped off the needle carefully and the loose ligature on the proximal end was tightened. After weighing, the distended sac was placed inside an organ bath containing 50 ml of the same incubation medium. The organ bath was surrounded by a water jacket maintained at 37—40 °C and placed in metabolic shaker at a frequency of 100—110 shakes/min. The incubation medium was continuously being bubbled with a mixture of 95% O2 and 5% CO2. At the end of the incubation period (30 min), the sacs were removed from the organ bath, blotted by a standardized procedure and weighted again. The serosal fluid was drained through a small incision into a test tube. The emptied sac was shaken gently to remove the adhered fluid and the tissue was weighted again. The weight of the empty sac before and after the incubation did not differ significantly. The initial serosal volume was determined as the difference between the weights of the empty and filled everted sac prior to incubation. The final serosal volume was calculated by subtracting (after incubation) the weight of the empty sac from that of the filled sac. The mucosal fluid
transfer was expressed in terms of the diminution in the volume of fluid of the mucosal side during the course of the experiments. The serosal fluid transfer was reflected in the increase in the volume inside the sac and the gut fluid uptake was determined by measuring the increase in the volume of fluid in the gut wall.

The plant extracts together with varying concentration of glucose and tyrosine (2.5 to 10 mM) were incubated in the mucosal solution in the organ bath. Tyrosine in the serosal solution was determined by a spectrophotometric method. Glucose was measured using a commercially available glucose oxidase kit (Boehringer Mannheim, GmbH, Mannheim, FRG). The amount of tyrosine and glucose transported from the mucosal compartment was characterized as ‘uptake’ while the serosal gain of the substances is treated as ‘release’. Uptake and release of glucose and tyrosine are expressed as μmol/g tissue wet weight/h. Na⁺ and K⁺ concentration in the serosal solution were determined by atomic absorption (Unicam 929). The quantity of Na⁺ and K⁺ taken in the serosal solution was calculated from the respective change in the volume of fluids and expressed in terms of amount per gm-wet wt of the tissue. All chemicals were procured from Sigma (U.K.).

Data Analysis The difference between the mean±S.E.M. between the controls and experimental groups were examined using the one way analysis of variance (ANOVA) test. p values less than 0.05 were considered as significant. All data were analyzed using Excel.

RESULTS

Incubation of the rat everted intestinal sacs with Momordica charantia extracts resulted in the inhibition of transport of tyrosine and glucose. However, the uptake of tyrosine was less inhibited compared to that of glucose except at higher concentration of the substrate (tyrosine) (Table 1).

With varying concentrations of substrate (glucose 2—10 mM), it was found that Momordica charantia significantly inhibited the uptake of glucose (p<0.05) while for tyrosine were not significantly different (p>0.05) at concentrations of 0.5 and 1.0 mM.

Table 2 shows the effects of aqueous extract of Momordica charantia on rat intestinal Na⁺ and K⁺ transport. Incubation of the everted intestinal sacs with 3.62 mg/ml of M. charantia caused a significant (p<0.05) inhibition in Na⁺ transport into the serosal solution. However, the uptake of K⁺ was not significantly affected.

Table 3 depicts the effects of 3.62 mg/ml M. charantia extract on fluid transport with respect to various concentrations of glucose (4—10 mM). The extract inhibited the net water movement across the intestine.

DISCUSSION

The present findings show that aqueous extract of Momordica inhibits glucose absorption, sodium ion and fluid transport significantly. Tyrosine uptake, on the other hand, was only inhibited at high concentration of the substrate whereas K⁺ uptake was not significantly affected in the presence of the plant extract.

This study has also shown that high doses of the aqueous extract of Momordica fruit decreased the absorptive capacity of fluid across the everted rat intestine. It is generally accepted that the net transport of fluid from the mucosal to serosal side of the intestine depends on the active transport of sodium from the intestinal epithelial cell to the serosal side. Therefore, the decrease in fluid transport across the intestine induced by Momordica charantia was probably related to the reduction in sodium transport. This hypothesis is in line with the diminished sodium ion transport observed in the present experiments. Interestingly, one of the documented
properties of *Momordica charantia* is its laxative property upon the consumption of large quantity of *Momordica* fruits.\(^{10}\)

Leatherdale *et al.*\(^{11}\) have shown that subcutaneous administration of a water extract of *M. charantia* fruits significantly lowered blood sugar in diabetic patients. Therefore, it is possible that the active components of *M. charantia* extract decrease blood glucose level by inhibiting the absorption of glucose from the alimentary tract.

Our results are consistent with the hypothesis that *M. charantia* extracts inhibit absorption of glucose at the brush border of the alimentary canal as well as the reabsorption of glucose in the urinary excretion system, thus leading to a wash out of glucose from the body. The lowered glucose uptake in the everted intestinal sac model by *Momordica* extract, in the present study, appears to be concentration gradient dependent. Therefore, the possible mechanism of inhibition of glucose by the everted sacs of rats by *Momordica charantia* could possibly involve the Na\(^+\)–K\(^+\) pump. However further kinetic studies are needed to establish the exact nature of these inhibitory effects.

In conclusion, as far as we know, the present study is the first to demonstrate the inhibitory properties of *Momordica* on glucose and amino acid transport and furthermore also provides evidence for possible laxative properties of *Momordica charantia*.

REFERENCES