

ORAL HYPOGLYCAEMIC ACTIVITY OF DIFFERENT PREPARATIONS OF *MOMORDICA CHARANTIA*

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Abstract : Four different preparations of *Momordica charantia*, namely, fruit juice, seed extract, freeze dried fruit juice and commercially available capsules were evaluated for oral hypoglycaemic activity using normal healthy Sprague Dawley rats as the animal model. Fruit juice, freeze dried fruit juice and seed extract of *M. charantia* significantly ($P < 0.01 - 0.001$) improved the ability to tolerate an oral glucose load and the oral hypoglycaemic activity of these three preparations were comparable. However, the commercially available *M. charantia* capsules failed to improve significantly glucose tolerance at the dosage used in this study.

1. Introduction

Momordica charantia Linn (Family: Cucurbitaceae, Sinhala name: Karawila) has been used to control diabetes mellitus in the Ayurvedic system of medicine for a considerable time. Previous studies have shown that fruit juice of *M. charantia* exerts an oral hypoglycaemic activity in healthy laboratory animals^{4,7} and in maturity onset diabetics.¹⁰ Recently commercial preparation of *M. charantia* in the form of capsules has begun, thus providing an easily available source of *M. charantia* for self medication. However, the presently available data are inadequate for recommending continuous use of *M. charantia* by diabetics.

The present study was designed to investigate and compare the oral hypoglycaemic activity of four different preparations of *M. charantia* namely, fruit juice, freeze dried fruit juice, seed extract and the commercially available capsules using male Sprague Dawley rats as the animal model.

2. Materials and Methods

2.1 Experimental Animals

In all experiments normal healthy male Sprague-Dawley rats of body weight 200 ± 25 g maintained on a standard laboratory diet were used. The animals were fasted overnight (14-16 h) before the commencement of all experiments.

2.2 Preparation of *M.charantia* Extracts

2.2.1. Fruit juice of *M.charantia*

Ten Kg of mature unripe fresh fruits of *M. charantia* were washed and seeds and placentae removed. The weight of the fruit after removing seeds and placentae was 6 Kg and these were cut into thin slices, macerated in a mechanical grinder and squeezed through a muslin cloth. The juice (3000 ml) was aliquoted and stored at - 20 °C till the time of use.

2.2.2 Seed extract of *M. charantia*

The seeds with placentae (4 Kg) were cut into thin slices, macerated in a mechanical grinder and squeezed through a muslin cloth. The juice (600 ml) was aliquoted and stored at -20 °C till the time of use.

2.2.3 Freeze dried fruit juice of *M. charantia*

An aliquot (200 ml) of fresh fruit juice of *M.charantia* was freeze dried and the powder obtained (40 g) was reconstituted in distilled water to yield a solution of 200 ml.

2.2.4 Commercially available "Karawila" capsules

Commercially available "Karawila" capsules (Environmental Laboratories Ltd., Sri Lanka) were bought from a pharmacy. According to the manufacturer each capsule contains an equivalent of 10 g of karawila extract and the recommended dosage for the control of diabetes mellitus is 1 capsule twice a day after meals. The powder in the "Karawila" capsules was weighed and dissolved in distilled water. Average weight of the powder in one capsule was 25 mg. The ratio of distilled water to "Karawila" powder was calculated on the basis of the weight of freeze dried powder obtained by freeze drying a given volume of fresh fruit juice.

2.3 Dosage and Administration of Plant Extracts

All preparations including distilled water to the control group were administered via an oral feeding tube while the animal was under light ether anaesthesia. The dosage administered was 1 ml/100 g body wt. with all preparations. Animals (N = 50) were fasted overnight. After collecting blood samples (50 µl) for estimation of fasting blood glucose concentrations, animals were randomly divided into 5 groups of 10 each. Groups 1, 2, 3 and 4 were given fruit juice, freeze dried fruit juice, seed extract and the aqueous solution of "Karawila" capsules respectively while Group 5 which was the control group was given distilled water.

2.4 Oral Glucose Tolerance Test (OGTT)

Thirty minutes after administration of different preparations of *M. charantia* or distilled water, all animals received an oral dose of glucose (1 ml/100g body wt., 50% W/V). Blood samples (50 μ l) were then collected at hourly intervals for three hours. The blood glucose concentrations were then determined by the glucose oxidase method.³

2.5 Calculations and Statistical Analyses

The results are given as percentage (mean \pm SEM) increases of fasting blood glucose concentrations. Student's t test was used to compare the percentage increases in blood glucose concentrations between treatment groups and the control group.

3. Results and Discussion

The effect of oral administration of fruit juice, freeze dried fruit juice and seed extract of *M. charantia* and aqueous solution of "Karawila" capsules, 30 min prior to an external glucose load on oral glucose tolerance of normal healthy Sprague-Dawley rats is shown in Figure 1. The results are given as percentage increases of fasting blood glucose concentrations. With all experimental groups the peak percentage increase in blood glucose concentration was observed 1 h after the administration of the glucose load.

The peak percentage (mean \pm SEM) increases in blood glucose concentration at 1 h after the glucose load following treatment with fruit juice (70.35 ± 9.63 , $P < 0.001$), freeze dried fruit juice (71.68 ± 7.4 , $P < 0.001$) and the seed extract (76.31 ± 9.90 , $P < 0.01$) were significantly lower when compared with the control group (134.02 ± 10.2). The peak percentage increase in blood glucose concentration 1 h after the glucose load in the group treated with the aqueous solution of "Karawila" capsules (100.88 ± 12.93) was not significantly different from that of the control group.

The percentage (mean \pm SEM) increases in blood glucose concentration at 2 h after the glucose load in the groups treated with fruit juice (58.42 ± 11.47 , $P < 0.01$), freeze dried fruit juice (45.24 ± 4.89 , $P < 0.001$) and the seed extract (65.83 ± 6.21 , $P < 0.01$) were also significantly lower when compared with the control group (106.4 ± 10.2). The percentage increase (mean \pm SEM) in blood glucose concentration 2 h after the glucose load in the group treated with the aqueous solution of "Karawila" capsules (78.22 ± 13.44) was again not significantly different from that of the control group.

Similarly the percentage (mean \pm SEM) increases in blood glucose concentration at 3 h after the glucose load in the groups treated with fruit juice (43.71 ± 8.84 , $P < 0.01$), freeze dried fruit juice (37.96 ± 3.62 , $P < 0.001$) and the seed extract (40.20 ± 5.53 , $P < 0.001$) were also significantly lower when compared with the control group (88.73 ± 9.78). The percentage increase (mean \pm

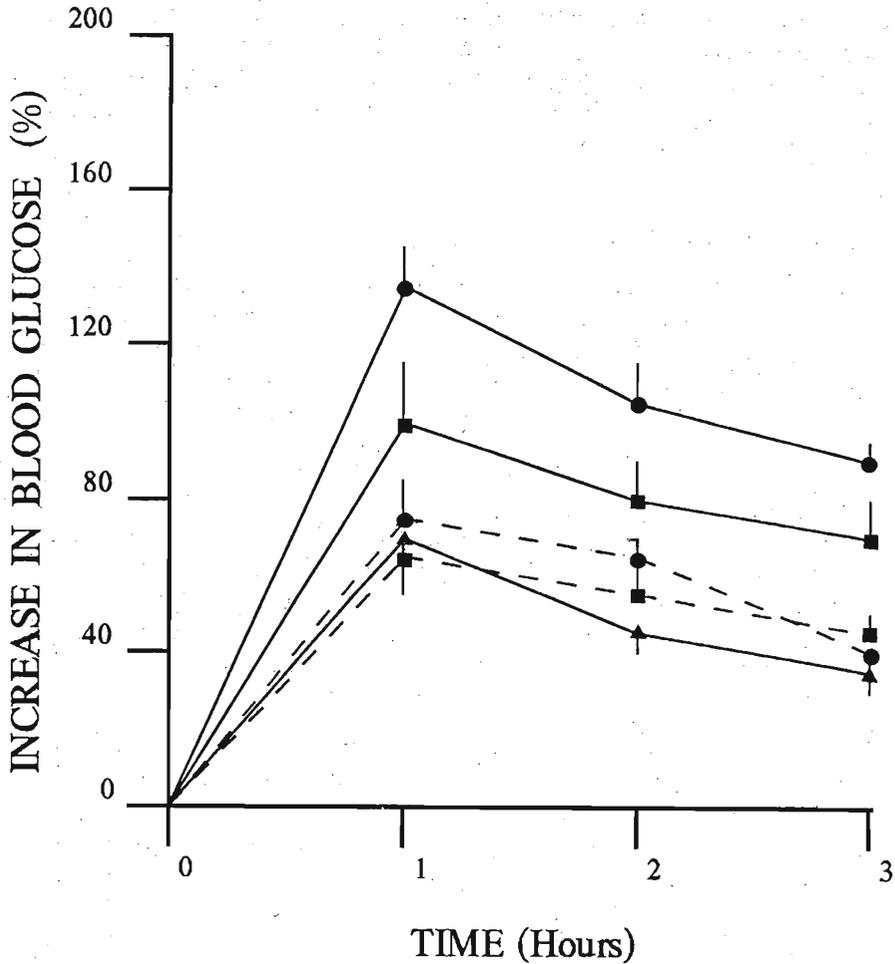


Figure 1 : Effect of oral administration of fruit juice ■ - - - ■ freeze dried fruit juice ▲ — ▲ seed extract ● - - - ● and an aqueous extract of commercially available capsules ■ — ■ of *Momordica charantia* and distilled water (control group) ● — ● 30 min prior to an oral glucose tolerance test on the blood glucose concentrations in normal healthy male Sprague-Dawley rats (n = 10 in each group). Blood glucose concentrations are expressed as percentage increases of fasting blood glucose concentrations.

SEM) in blood glucose concentration 3 h after the glucose load in the group treated with the aqueous solution of "Karawila" capsules (71.86 ± 9.02) was again not significantly different from that of the control group.

There was no significant difference in the percentage increases in blood glucose concentration following treatment with fruit juice, freeze dried fruit juice or the seed extract when these were compared with each other at 1 h, 2 h and 3 h after the glucose load. The percentage increases (mean \pm SEM) in blood glucose concentrations 3 h after the glucose load were significantly lower in the groups treated with fruit juice ($P < 0.05$), freeze dried fruit juice ($P < 0.01$) and the seed extract ($P < 0.05$) when compared with the group treated with "Karawila" capsules, while at 2 h after the glucose load the percentage increase (mean \pm SEM) in blood glucose concentrations was significantly low ($P < 0.05$) only in the group treated with the freeze dried fruit juice when compared with the group treated with "Karawila" capsules.

The overall results of the present studies confirm the highly potent hypoglycaemic activity of *Momordica charantia*. Of the four preparations investigated all preparations from the plant showed a most profound effect on the ability of the experimental animals to tolerate an external glucose load. Although the prior treatment with commercially available "Karawila" capsules reduced the blood glucose concentration at 1 h, 2 h and 3 h after the glucose load, the effect was not significantly different when compared with the control group. The ability of the fruit juice, freeze dried fruit juice and seed extract to improve the utilization of glucose following an external glucose load was comparable. The degree of oral hypoglycaemic activity shown by fruit juice and the freeze dried fruit juice indicates that the biological activity of the fruit juice is preserved during freeze drying. In contrast the inability of the "Karawila" capsules to improve utilization of glucose following an external glucose load, in spite of being administered at a dosage comparable to the other preparations may perhaps be due to a significant loss of biological activity during preparation of this capsule. However we have not attempted to see whether oral hypoglycaemic activity similar to other preparations will be exerted by "Karawila" capsules if the dosage is increased. There has been no previous published reports on the evaluation of the oral hypoglycaemic activity of "Karawila" capsules in Sprague-Dawley rats.

The comparable oral hypoglycaemic activity shown by the fruit juice and the seed extract of *M. charantia* strongly suggest that the pulp as well as the seeds together with their placentae contain the same active principle(s). Previous investigators¹ have shown a significant hypoglycaemic activity following subcutaneous administration of an active principle called plant insulin (p-insulin) or vegetable insulin (v-insulin) isolated from fruits, seeds and tissue cultures of *M. charantia* to diabetic patients. If p-insulin or v-insulin is the only active principle with hypoglycaemic activity present in *M. charantia* then oral administration of *M. charantia* is unlikely to exert any hypoglycaemic activity as the insulin like peptides⁵ will be subjected to proteolysis by the digestive enzymes. Thus the present data as well as previous data from our laboratory^{4,9}

suggest that *M. charantia* contains a non-peptide hypoglycaemic agent.

The pronounced ability of the fruit juice, freeze dried fruit juice and the seed extract of *M. charantia* to improve utilization of glucose following an external glucose load may be due to direct stimulation of beta cells of the islets of Langerhans and/or facilitation of peripheral utilization of glucose either by direct stimulation of glucose uptake or due to enhanced insulin secretion. The possibility of the oral hypoglycaemic agents present in *M. charantia* acting directly on beta cells of the islets of Langerhans is further supported by in vitro studies in which freeze dried fruit juice of *M. charantia* was shown to stimulate insulin secretion by beta cells of the obese hyperglycaemic mice.⁸ On the contrary Leatherdale and co-workers⁶ had failed to observe a rise in insulin concentrations following administration of *M. charantia*. Karunanayake and Welihinda⁹ have demonstrated an improvement in the peripheral utilization of glucose following oral administration of fruit juice of *M. charantia* while earlier studies by Gupta and Seth² showed that the improvement of glucose tolerance following administration of *M. charantia* is not due to reduced intestinal absorption of glucose.

Thus further studies are mandatory to characterise the oral hypoglycaemic agent(s) in *M. charantia* as well as to ascertain the mode of their action.

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