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ENHANCED ANTIHYPERGLYCEMIC ACTIVITY WITH A COMBINATION OF GLIBENCLAMIDE AND FRUITS OF *MOMORDICA CHARANTIA* L.

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ABSTRACT

Background. *Momordica charantia* L. is a Cucurbitaceae family plant whose fruits are both consumed as vegetable and to lower elevated blood glucose levels in diabetic patients in Bangladesh. As such, it was of interest to examine whether an extract of the fruit can be of value in enhanced lowering of elevated blood glucose levels when administered with a standard antihyperglycemic drug, glibenclamide. **Methods**. Antihyperglycemic activity was determined through oral glucose tolerance test (OGTT) in mice. **Results.** Administration of methanol extract of *Momordica charantia* fruits (MEMC) at doses of 200 and 400 mg per kg to glucose-loaded mice reduced blood glucose levels by 35.6 and 38.8%, respectively. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 46.1%. MEMC, when administered at doses of 200 and 400 mg per kg along with glibenclamide at 10 mg per kg, respectively reduced blood glucose levels by 49.2 and 53.0%. **Conclusion**. Methanolic extract of fruits of *Momordica charantia* (MEMC) can be antihyperglycemic alone, as well as enhance the effect of antihyperglycemic drugs like glibenclamide, and so can reduce glibenclamide dependence.

KEYWORDS: Antihyperglycemic, *Momordica charantia*, glibenclamide, OGTT, mice.

BACKGROUND

Momordica charantia L. is a vinous plant belonging to the Cucurbitaceae family. It is known in English as 'bitter gourd' and in Bengali as 'korolla'. The plant is widely cultivated in Bangladesh because of its fruits, which are cooked and consumed as a popular vegetable in their unripe state. The fruits are also eaten in Bangladesh by diabetic patients in the raw form to lower elevated blood glucose levels and such oral consumption of fruit is also recommended by folk and tribal medicinal practitioners of the country for treatment of diabetes.[1-3]

The antidiabetic property of fruits of *Momordica charantia* has been quite well-studied. Perumal et al[4] reported antidiabetic effect of fruits in streptozotocin diabetic rats. Fruits of the plant have been reported to have potential for improved glycemic control in patients with insulin resistance and pre-diabetes.[5] Diabetes is a complicated disorder with no known total cure. Moreover, it is a disorder, which can quickly lead to other problems with potentially fatal complications like cardiovascular diseases, kidney failure and blindness.[6] On top of it many antidiabetic drugs belonging to sulfonylureas, meglitinides and biguanides among others can give adverse effects including hypoglycemic, metallic after-taste, diarrhea, nausea, and water retention.[7]

The rural population of Bangladesh lacks adequate access to modern doctors and clinics. They also lack sufficient literacy to measure blood glucose with a glucometer or take insulin injections by themselves. There is also the question of affordability; a glucometer alone can cost BDT 5000 (1 USD = 81 BDT), glucometer strips will cost extra. Such costs are difficult to bear by both the rural and the urban poor.[8] Towards mitigation of both diabetes and high diabetic health-care costs, we had been screening medicinal plants of Bangladesh for their blood glucose lowering properties towards finding an easily available and affordable solution to the incidental medicinal costs of the people suffering from diabetes.[9-34] Lately, our studies have also included evaluation of synergistic blood glucose lowering effects with combination of allopathic antidiabetic drugs and local antidiabetic plants or plant parts.[35, 36] The objective of the present study was to determine through oral glucose tolerance test (OGTT) any possible synergistic antihyperglycemic action with a combination of a standard antihyperglycemic drug glibenclamide and methanolic extract of *Momordica charantia* (MEMC) fruits.

METHODS

Plant material collection and extraction

Fruits (unripe) of *Momordica charantia* were collected from a local market in Dhaka city, Bangladesh during December, 2016. Plant specimen was taxonomically identified by a trained botanist at the University of Development Alternative. The sliced air-dried fruits were grounded into a fine powder and 100g of the powder was extracted with methanol (1:5, w/v) for 48 hours. The extract was evaporated to dryness and stored at -20^{o}C till use.

Chemicals and Drugs

Glibenclamide and glucose were obtained from Square Pharmaceuticals Ltd., Bangladesh. All other chemicals were of analytical grade.

Animals

Swiss albino mice, which weighed between 12-15g were used in the present study. The animals were obtained from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B). The animals were acclimatized for three days prior to actual experiments. During this period, they were kept in a temperature controlled room (25^{o}C) and given standard mice chow and water *ad libitum*. The study was conducted following approval by the Institutional Animal Ethical Committee of University of Development Alternative, Dhaka, Bangladesh.

Oral glucose tolerance tests (OGTT) for evaluation of antihyperglycemic activity

Oral glucose tolerance tests were carried out as per the procedure previously described by Joy and Kuttan (1999)[37] with minor modifications. Briefly, fasted mice were grouped into six groups of five mice each. The various groups received different treatments like Group 1 received vehicle and served as control, Group 2 received standard drug (glibenclamide, 10 mg/kg body weight). Groups 3 and 4 received MEMC at doses of 200 and 400 mg per kg body weight, respectively. Groups 5 and 6 received, respectively, 10 mg/kg glibenclamide plus 200 and 400 mg per kg MEMC. All substances were orally administered. Following a period of one hour, all mice were orally administered 8g glucose/kg of body weight. Blood samples were collected 120 minutes after the glucose administration through puncturing heart. Blood glucose levels were measured with a glucometer. The percent lowering of blood glucose levels were calculated according to the formula described below.

Percent lowering of blood glucose level = $(1 - W_e/W_c) \times 100$, where W_e and W_c represents the blood glucose concentration in glibenclamide or various extracts administered mice (Groups 2-6), and control mice (Group 1), respectively.

Statistical analysis

Experimental values are expressed as mean ± SEM. Independent Sample t-test was carried out for statistical comparison. Statistical significance was considered to be indicated by a p value < 0.05 in all cases.[22]

RESULTS

Oral glucose tolerance test (OGTT) results

Administration of MEMC at doses of 200 and 400 mg per kg to glucose-loaded mice reduced blood glucose level significantly by 35.6 and 38.8%, respectively. A standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 46.1%. A combination of 10 mg/kg glibenclamide plus 200 and 400 mg MEMC lowered blood glucose levels, respectively, by 49.2 and 53.0%. The results are shown in Table 1 and suggest that MEMC can give a synergistic antihyperglycemic effect (that is improve oral glucose tolerance) when administered with glibenclamide. Thus the results indicate that MEMC may be an effective agent to lower dependency on glibenclamide for lowering blood glucose.

Table 1: Effect of MEMC and glibenclamide on blood glucose level in hyperglycemic mice following 120 minutes of glucose loading.

Treatment	Dose (mg/kg body weight)	Blood glucose level (mmol/l)	% lowering of blood glucose level
Control	10 ml	6.34 ± 0.15	-
Glibenclamide	10 mg	3.42 ± 0.15	46.1*
(MEMC)	200 mg	4.08 ± 0.18	35.6*
(MEMC)	400 mg	3.88 ± 0.13	38.8*
(MEMC + glibenclamide)	(200 + 10) mg	3.22 ± 0.13	49.2*
(MEMC + glibenclamide)	(400 + 10) mg	2.98 ± 0.19	53.0*

All administrations were made orally. Values represented as mean ± SEM, (n=5); $^{*}P < 0.05$; significant compared to hyperglycemic control animals.

DISCUSSION

The present results suggest that a combination of MEMC and glibenclamide is more significant in lowering elevated blood glucose levels than either substance alone. As such, concomitant MEMC administration with glibenclamide can necessitate lesser intake of glibenclamide and may reduce the adverse side-effects noted with the compound. It would be of interest to conduct further studies to determine whether MEMC by itself can totally replace glibenclamide and whether that particular replacement dose is non-toxic. The latter is of importance because side-effects like mild diarrhea and abdominal pain has been reported for bitter melon.[38]

CONCLUSION

The results suggest that methanolic extract of fruits of *Momordica charantia* can act synergistically with glibenclamide for lowering blood glucose in glucose-loaded mice.

Conflicts of interest

The author(s) declare that they have no competing interests.

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