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ORAL GLUCOSE TOLERANCE TESTS WITH A COMBINATION OF *MOMORDICA CHARANTIA* FRUITS AND *TRIGONELLA FOENUM-GRAECUM* SEEDS

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ABSTRACT

Background: The fruits of *Momordica charantia* L. and seeds of *Trigonella foenum-graecum* L. are considered traditionally in Bangladesh to lower elevated blood glucose levels in glucose-impaired persons. The fruits and seeds are also consumed in the cooked form as a vegetable and spice, respectively. It was of interest to evaluate the antihyperglycemic activity of a combination of methanolic extract of both fruits and seeds. **Methods**: Antihyperglycemic activity was determined through oral glucose tolerance test (OGTT) in mice. **Results:** Administration of methanol extract of *Momordica charantia* fruits (MEMC) and methanol extract of *Trigonella foenum-graecum* seeds (METF), separately at a dose of 400 mg per kg body weight each to glucose-loaded mice reduced blood glucose levels by 26.2 and 21.3%, respectively compared to control (untreated) mice. A combination of (MEMC + METF) at doses of 50, 100, 200 and 400 mg each extract reduced blood glucose levels, respectively by 24.9, 30.2, 34.9, and 40.5%. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 41.9%. **Conclusion:** A combination of MEMC and METF (at 400 mg per kg each) can be effective in reducing blood glucose (that is improve oral glucose tolerance) nearly as efficiently as glibenclamide, and so can reduce dependency on this antidiabetic drug.

KEYWORDS: Antihyperglycemic, *Momordica charantia*, *Trigonella foenum-graecum*, glibenclamide, OGTT.

BACKGROUND

The fruits of *Momordica charantia* L. (Cucurbitaceae family, bitter gourd in English, korolla in Bengali) are prized in Bangladesh and are cooked and eaten as a vegetable. The plant is widely grown throughout the country and fruits can be found year around. Tia F1 (large fruits) is the most cultivated variety of the plant in Bangladesh. *Trigonella foenum-graecum* L. (Fabaceae family, fenugreek in English, methi in Bengali) is also cultivated in Bangladesh for culinary use of the seeds as a spice. BARI – Methi 1 and BARI – Methi 2 are two of the varieties cultivated among others. The fruits of *Momordica charantia* and seeds of *Trigonella foenum-graecum* are also considered medicinal in the various traditional medicinal systems of the country.

Apart from being consumed in the cooked form, the fruits (and sometimes leaves) of *Momordica charantia* are eaten raw in Bangladesh as a traditional medicine to lower blood glucose in diabetic patients.[1-3] The fruits are also reportedly consumed for the same purpose in other Asian, African and South American countries.[4] The seeds of *Trigonella foenum-graecum* have also been reported to be used to lower blood glucose in traditional medicinal systems of various countries.[5-7] The blood glucose lowering properties of fruits of *Momordica charantia* and seeds of *Trigonella foenum-graecum* have been scientifically validated.[8-10]

Diabetes has been known from ancient times, being mentioned in both Egyptian and Indian texts of old.[11] However, in recent times, the disease (a metabolic disorder, primarily characterized by elevated blood glucose levels) has been increasing dramatically with 422 million adults having diabetes reported in 2014.[12] The disease cannot be cured with any known medications, modern or traditional. However, allopathic drugs and various plants may be used to lower elevated blood glucose levels[which can be elevated also during impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)]. IGT is also known as pre-diabetes.

IGT is diagnosed by oral glucose tolerance test (OGTT) when blood glucose level remains at higher than normal range two hours following oral administration of glucose. As such, OGTT[13] can be used to diagnose pre-diabetes and diabetes. A given medication can be

checked for its blood glucose lowering or improving oral glucose tolerance efficacy through OGTT by administering the medication before administration of glucose.

Recent years are witnessing a paradigm shift, where interest has been switching from allopathic to plant-based medicines for lowering blood glucose and consequent treatment of diabetes.[14] For countries like Bangladesh, plant-based blood glucose lowering medications may offer a safer and viable alternative to the vast majority of rural people, who lack availability and affordability to allopathic drugs. As such, we had screening possible antidiabetic plants through OGTT in mice for a number of years.[15-42] The objective of the present study was to evaluate the antihyperglycemic potential through oral glucose tolerance test (OGTT) of a combination of methanol extract of fruits of *Momordica charantia* (MEMC) and seeds of *Trigonella foenum-graecum* (METF).

METHODS

Plant material collection and extraction

Fruits (unripe) of *Momordica charantia* (Tia F1) and seeds of *Trigonella foenum-graecum* (variety unknown) were collected from a local market in Dhaka city, Bangladesh during May, 2017. The sliced air-dried fruits and seeds were separately grounded into a fine powder and 100g of the powder was extracted with methanol (1:5, w/v) for 48 hours. The extract of the fruits (MEMC) and the seeds (METF) was separately evaporated to dryness and stored at -20^{o}C till use. The final weight of MEMC was 5.56g and that of METF was 3.098g. Each extract was stored in small aliquots and not subjected to repeat freeze-thaw cycle.

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 14-16g 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)[43] with minor modifications. Briefly, fasted mice were grouped into eight 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 and METF at doses of 400 mg each per kg body weight, respectively. Groups 5-8 received, respectively, 50, 100, 200 and 400 mg each of (MEMC + METF) per kg body weight. All substances were orally administered. Following a period of one hour, all mice were orally administered 2g 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 2-8), 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.[39]

RESULTS

Oral glucose tolerance test (OGTT) results

Administration of MEMC and METF separately at a dose of 400 mg per kg to glucose-loaded mice reduced blood glucose level significantly by 26.2 and 21.3%, respectively as compared to control mice (Group 1). A standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 41.9%. Administration of (MEMC + METF) at doses of 50, 100, 200 and 400 mg each (that is for instance 50 mg MEMC + 50 mg METF combined for the 50 mg dose) to glucose-loaded mice reduced blood glucose level significantly by 24.9, 30.2, 34.9, and 40.5%, respectively. The results are shown in Table 1 and suggest that the combination of MEMC + METF, dose for dose, improved oral glucose tolerance in glucose-challenged mice, when administered in combination than when administered by itself (for instance Groups 3 and 4 versus Group 7).

In fact, at the highest dose of combined (400 mg each of MEMC + METF), the extracts lowered blood glucose levels nearly as efficiently as glibenclamide.

Table 1: Effect of MEMC and METF 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	6.02 ± 0.17	-
Glibenclamide	10 mg	3.50 ± 0.05	41.9*
(MEMC)	400 mg	4.44 ± 0.14	26.2*
(METF)	400 mg	4.74 ± 0.09	21.3*
(MEMC + METF)	50 mg each	4.52 ± 0.18	24.9*
(MEMC + METF)	100 mg each	4.20 ± 0.11	30.2*
(MEMC + METF)	200 mg each	3.92 ± 0.10	34.9*
(MEMC + METF)	400 mg each	3.58 ± 0.11	40.5*

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

DISCUSSION

Herbal or plant-based formulations may have some advantages over allopathic drugs. For instance, the multifunctionality of *Momordica charantia* fruits have been described[44] besides being antidiabetic, the fruits can promote angiogenesis in diabetic wounds, and also reportedly are beneficial in cancer prevention and therapy.[45, 46] *Trigonella foenum-graecum* is beneficial in diabetes, hypercholesterolemia, and inflammation and probably in several kinds of cancers.[47] Thus this combination of two plant products, namely fruits of *Momordica charantia* and seeds of *Trigonella foenum-graecum* can benefit diabetic patients through giving preventive or therapeutic effect against other diseases.

CONCLUSION

The results suggest that methanolic extract of fruits of *Momordica charantia* combined with methanolic extract of seeds of *Trigonella foenum-graecum* demonstrate better antihyperglycemic activity than the extracts administered alone and can be beneficial for glucose-impaired persons.

Conflicts of interest

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

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