



SYNERGISTIC ANTIHYPERGLYCEMIC ACTIVITY OF METHANOLIC EXTRACT OF AERIAL PARTS OF *SENNA* *OBTUSIFOLIA* AND GLIBENCLAMIDE

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ABSTRACT

Background: *Senna obtusifolia* is a Fabaceae family plant found in Bangladesh and which is used in traditional medicines of the country. Antidiabetic effect has been reported for seeds of the plant. It was therefore of interest to evaluate the antihyperglycemic activity of aerial parts of this plant and synergistic effect, if any, with an antihyperglycemic drug, glibenclamide. **Methods:** Antihyperglycemic activity was determined through oral glucose tolerance tests (OGTT) in mice. **Results:** Administration of methanol extract of *Senna obtusifolia* aerial parts (MESO) at a dose of 400 mg per kg to glucose-loaded mice reduced blood glucose level by 22.3%. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of

10mg per kg body weight, reduced blood glucose level by 38.3%. MESO, when administered at doses of 100, 200 and 400mg per kg along with glibenclamide at 10 mg per kg, respectively reduced blood glucose levels by 39.0, 42.3, and 44.0%. **Conclusion:** Methanolic extract of aerial parts of *Senna obtusifolia* (MESO) can be a potential source of antihyperglycemic compound(s) and also can act synergistically with antihyperglycemic drugs like glibenclamide.

KEYWORDS: Antihyperglycemic, *Senna obtusifolia*, glibenclamide, OGTT, mice.

BACKGROUND

Senna obtusifolia (L.) Irwin & Barneby (Fabaceae) is known in English as 'Java bean' and in Bengali as 'chakunda'. The plant is not so common in Bangladesh but occasionally observed to be growing in the wild. It is an annual plant growing up to 30 inches tall.

Various ethnomedicinal uses have been reported for the plant. Decoction of whole plant is used to treat male infertility by the Badagry people of Lagos State, Nigeria.^[1] Roots are boiled and taken for swollen penis, stomach problems, or dysmenorrhea in Lwamondo area, Limpopo province, South Africa.^[2] Seeds of the plant are used in skin diseases, ringworm, and eczema, while leaves are used to treat constipation by tribal people of Dantewada, Chhattisgarh, India.^[3] Leaves of the plant are used to treat itches in Bangladesh.^[4] The Takkad people of Kaduna State, Nigeria, use the plant against ailments of the digestive system.^[5] Leaves, bark and roots of the plant are used to treat diabetes in Kano Metropolis, Northern Nigeria.^[6]

Diabetes is a serious metabolic disorder characterized by elevated blood glucose levels, which is reaching endemic proportions throughout the world.^[7] Available allopathic medicines cannot cure the disease itself but are useful in lowering blood glucose levels. However, these medicines have adverse effects and are either not available or not affordable to the poorer sections of both the urban and rural people of Bangladesh. Diabetes progressively leads to more serious complications like rise in oxidative stress, and eye, kidney or cardiovascular disorders. We had been screening medicinal plants of Bangladesh for their blood glucose lowering properties towards finding an easily available and affordable solution to the diabetes and incidental medicinal costs of the people.^[8-33] The objective of the present study was to evaluate the antihyperglycemic potential of methanolic extract of *Senna obtusifolia* aerial parts (MESO) through oral glucose tolerance tests (OGTT) in mice.

METHODS

Plant material collection and extraction

Aerial parts of *Senna obtusifolia* were collected from Dhaka district, Bangladesh during December, 2016. Plant specimen was taxonomically identified by a trained botanist at the University of Development Alternative. The sliced air-dried aerial parts (leaves and stems) of *Senna obtusifolia* were grounded into a fine powder and 83g of the powder was extracted with methanol (1:5, w/v) for 48 hours. The extract was evaporated to dryness. The final weight of the extract (MESO) was 2.6g. The extract was stored at -20°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 15-20g 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°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)^[34] 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, 10mg/kg body weight). Group 3 received MESO at a dose of 400mg per kg body weight. Groups 4-6 received, respectively, 10mg/kg glibenclamide plus 100, 200 and 400mg per kg MESO. 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.

$$\text{Percent lowering of blood glucose level} = (1 - W_e/W_c) \times 100,$$

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 \pm 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.^[21]

RESULTS

Antihyperglycemic activity evaluation results

Administration of MESO at a dose of 400mg per kg to glucose-loaded mice reduced blood glucose level significantly by 22.3%. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10mg per kg body weight, reduced blood glucose level by 38.3%. A combination of 10mg/kg glibenclamide plus 100, 200 and 400mg MESO lowered blood glucose levels, respectively, by 39.0, 42.3, and 44.0%. The results are shown in Table 1 and suggest that MESO can give a synergistic antihyperglycemic effect when administered with glibenclamide. The results further suggest that administration of MESO can lower dependency on glibenclamide for lowering blood glucose.

Table 1: Effect of MESO 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	6.00 ± 0.07	-
Glibenclamide	10 mg	3.70 ± 0.08	38.3*
(MESO)	400 mg	4.66 ± 0.12	22.3*
(MESO + glibenclamide)	(100 + 10) mg	3.66 ± 0.07	39.0*
(MESO + glibenclamide)	(200 + 10) mg	3.46 ± 0.13	42.3*
(MESO + glibenclamide)	(400 + 10) mg	3.36 ± 0.08	44.0*

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

DISCUSSION

Glibenclamide is a sulfonylurea group of blood glucose lowering medicine and acts through increasing production of insulin from the pancreas. Some of the common glibenclamide adverse effects include nausea, vomiting, constipation, and diarrhea. It has been suggested that glibenclamide may cause fatal hypoglycemic coma in the elderly patients.^[35] As such, concomitant MESO administration can lead to lesser intake of glibenclamide and may reduce the adverse side-effects noted with the compound.

The exact mechanism of action of *Senna obtusifolia* aerial parts or the phytochemical constituents responsible for the antihyperglycemic effect remains to be elucidated. It is to be noted that other *Senna* genus plants have been shown to give beneficial effects in diabetic models. Antidiabetic components have been shown in *Senna alata* leaves.^[36] Alpha-

glucosidase and alpha-amylase inhibitory activities have been shown in *Senna surattensis* leaves.^[37] Antidiabetic effects have been observed with acetone fraction of *Senna singueana* stem bark.^[38] Thus it is highly possible that *Senna obtusifolia* may prove beneficial in more efficacious treatment of diabetes.

CONCLUSION

The results suggest that methanolic extract of aerial parts of *Senna obtusifolia* 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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