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ANTIHYPERGLYCEMIC EFFECT OF METHANOL EXTRACT OF *DRYNARIA QUERCIFOLIA* WHOLE PLANT IN GLUCOSE-CHALLENGED MICE

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ABSTRACT

Background: The objective of the present study was to determine the antihyperglycemic effects of methanol extract of *Drynaria quercifolia* whole plant in glucose-challenged mice. This is a part of our ongoing anti-diabetic project to identify local plant species and plant parts which can lower blood glucose levels, **Methods**: Antihyperglycemic activity was determined through oral glucose tolerance test (OGTT) in mice. **Results:** Administration of methanol extract of *Drynaria quercifolia* whole plant (MEDQ) at doses of 50, 100, 200, and 400 mg per kg body weight each to glucose-loaded mice reduced blood glucose levels by 14.6, 25.4, 31.4, and 39.4%, respectively compared to control (untreated) mice. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 40.8%. **Conclusion:** Methanolic extract of whole plants of *Drynaria quercifolia* is effective in lowering elevated blood glucose levels, which at the highest dose tested was nearly as effective as glibenclamide.

KEYWORDS: Antihyperglycemic, *Drynaria quercifolia*, glibenclamide, OGTT.

BACKGROUND

Drynaria quercifolia (L.) J. Sm., also known as oakleaf fern in English belongs to the Polypodiaceae family. In Bangladesh, it is known as Bandarmul in the Sylhet Division. The plant is considered to have medicinal properties. The Marakh sect of the Garo tribe living in Mymensingh district, Bangladesh, uses the plant to treat diabetes.[1] The roots of the plant are used to treat jaundice, cough, and rheumatic fever by the folk medicinal practitioners around the Rema-Kalenga Wildlife Sanctuary in Sylhet Division, Bangladesh.[2] The Tonchongya tribe of Cox's Bazar, Bangladesh use leaves of the plant to treat severe pain, diarrhea, and fever.[3] The Hajong tribe of Tangail district, Bangladesh uses the plant to treat bone injury, diabetes, and weakness.[4]

Diabetes is a progressively debilitating disease and is fast increasing throughout the world. In 2015, 30.3 million Americans or 9.4% of the population had diabetes. Bangladesh has also a high prevalence of diabetes with the added disadvantage of most diabetic patients being unable to bear treatment costs. Notably, the disease cannot be cured with allopathic medicines. Allopathic medicines like sulphonyl ureas and biguanides can lower elevated blood glucose levels but have side effects.[5,6] As such, we had been screening Bangladesh plants for a number of years for their blood glucose lowering effects in an effort to find affordable substitutes for allopathic drugs.[7-34] It was therefore the objective of the present study to determine the antihyperglycemic effect of methanolic extract of *Drynaria quercifolia* whole plants (MEDQ), since they have ethnomedicinal blood glucose lowering use, being used by several tribes in Bangladesh, as noted earlier. Antihyperglycemic ability was measured through oral glucose tolerance test (OGTT), which is a reliable test for impaired glucose tolerance as happens during pre-diabetic and diabetic conditions.[35]

METHODS

Plant material collection and extraction

Drynaria quercifolia whole plants were collected from Rema-Kalenga Wildlife Sanctuary in Habiganj district, Sylhet Division in December 2016. Plant specimen was taxonomically identified by the Bangladesh National Herbarium, who provided an Accession Number of 43768. The sliced air-dried whole plants were grounded into a fine powder and 66g of the powder was extracted with methanol (1:5, w/v) for 48 hours. The extract (MEDQ) was evaporated to dryness at 50^{o}C and stored at -20^{o}C till use. The final weight of MEDQ was 2.016g.

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)[36] 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 3-6 received MEDQ at doses of 50, 100, 200, and 400 mg per kg body weight, respectively. 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 = $(1 – W_e/W_c) X 100$,

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.[28]

RESULTS

Oral glucose tolerance test (OGTT) results

Administration of methanol extract of *Drynaria quercifolia* whole plants (MEDQ) at doses of 50, 100, 200, and 400 mg per kg body weight each to glucose-loaded mice reduced blood glucose levels by 14.6, 25.4, 31.4, and 39.4%, respectively, compared to control (untreated) mice. By comparison, a standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 40.8%. Thus at the highest dose tested, MEDQ demonstrated comparable ability to glibenclamide in its antihyperglycemic activity. The results are shown in Table 1. As this fern is commonly available in Bangladesh, it has the potential to be a replacement for costly anti-diabetic drugs.

Table 1: Effect of MEDQ 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	5.74 ± 0.07	-
Glibenclamide	10 mg	3.40 ± 0.07	40.8*
(MEDQ)	50 mg	4.90 ± 0.10	14.6*
(MEDQ)	100 mg	4.28 ± 0.09	25.4*
(MEDQ)	200 mg	3.94 ± 0.13	31.4*
(MEDQ)	400 mg	3.48 ± 0.13	39.4*

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

DISCUSSION

Ethanolic and chloroform extract of rhizomes of *Drynaria quercifolia* have previously been reported to demonstrate anti-diabetic and hypolipidemic activity.[37] The present observations suggest that the whole plant has anti-diabetic potential. It is thus important to investigate the phytochemical constituents of the plant and identify the active component(s) responsible for the observed antihyperglycemic activity.

CONCLUSION

The results suggest that methanolic extract of *Drynaria quercifolia* whole plants (MEDQ) possess antihyperglycemic effects as demonstrated through OGTT.

CONFLICTS OF INTEREST

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

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