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Research Article

Oral Glucose Tolerance Tests (OGTT) with *Alpinia malaccensis* Aerial Parts and Rhizome Extracts

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Abstract

Diabetes is a metabolic disorder affecting glucose metabolism and homeostasis within the body. In recent years, diabetes has been affecting both young and old, and the number of diabetic and pre-diabetic people have risen to alarming proportions throughout the world. The disease, characterized by high blood glucose levels, rapidly leads to other serious disorders affecting the eyes, kidneys, heart, and brain. Allopathic and traditional medicines can treat only the symptoms but cannot totally cure the disease. Scientists have focused their attention on the plant kingdom in efforts to discover better and more affordable allopathic drugs. Oral glucose tolerance test (OGTT) is one of the ways in which the anti-hyperglycemic efficacy of a drug or formulation can be tested rapidly. We report here that in OGTT, methanol extract of both aerial parts and rhizomes of a Zingiberaceae family plant, *Alpinia malaccensis* showed promising anti-hyperglycemic efficacy comparable to that of a standard drug, glibenclamide.

Keywords: *Diabetes Mellitus; Alpinia malaccensis; Zingiberaceae; OGTT*

Abbreviations

DM: Diabetes Mellitus; FMP: Folk Medicinal Practitioners; TM: Traditional Medicine; TMP: Tribal Medicinal Practitioners; WHO: World Health Organization

Introduction

Diabetes mellitus (DM) is a metabolic disorder affecting glucose metabolism and homeostasis within the body. There are two major types of diabetes, Type 1 and Type 2. The disease is rising at an alarming rate throughout the world and is affecting both the young and the old. If left untreated, high blood glucose levels can lead to disorders of the heart, kidneys, eyes, and the brain and also increase the level of reactive oxygen species within the body.

As per the World Health Organization (WHO) statistics, there were 171 million people in the world with diabetes in the year 2000 and the figure was estimated to more than double by year 2030. The reasons for this sharp increase are unknown; experts believe that the causes may lie in more sedentary lifestyle of human beings currently as compared to our ancestors (who were nomadic hunter-gatherers) and change in food habits like consuming more refined sugar and refined sugar containing products. Treatment of even uncomplicated diabetes can be costly; according to WHO, the national costs for treatment of diabetes in USA alone in year 2002 was US$ 132 billion [1].

In 2017, the treatment costs for diabetes in USA amounted to US$ 327 billion with a per person cost of around US$ 16,750 [2]. Quite obviously, treatment of diabetes along with diabetes-induced complications like cardiovascular disorders, diabetic nephropathy, diabetic neuropathy, and diabetic retinopathy are much higher.

In many developing countries, lack of enough diagnostic centers and doctors particularly in remote or less accessible rural areas as well as the general illiteracy of the rural folks combined with the lack of availability and affordability of modern anti-diabetic medications is a serious problem in treatment of diabetes. Such people usually depend on traditional medicine (TM) administered by folk medicinal practitioners (FMPs) and tribal medicinal practitioners (TMPs) for treatment. Traditional medicine treatment, in turn, is highly reliant on plants.

Medicinal plants have pre-historically been used against diabetes and still used in many traditional medicinal systems and in many regions of the world [3]. Available ethnobotanical reports in the scientific literature suggest that at least 800 plants are used against diabetes throughout the world [4]. Anti-diabetic or rather blood glucose lowering medicinal plants and their dispensers (FMPs and TMPs) offer the advantages of low cost and easy affordability. For the scientist and the researcher, the plants used in traditional medicine offer a tremendous potential for discovery of new drugs.

Alpinia malaccensis (Burm.f.) Roscoe is an herbaceous plant belonging to the Zingiberaceae family and found throughout Bangladesh. The plant has not been studied in details. In rhizome oil, the major component was reported as β-sesquiphellandrene [5]. A new pyrone derivative, malakavalactone, has been reportedly isolated from the plant along with kavalactone [6]. Rhizome extract of the plant reportedly showed anti-microbial activity [7].

A number of Zingiberaceae family plants have been previously reported to improve oral glucose tolerance and reduce blood glucose in diabetic models. Juice of *Zingiber officinale* rhizomes reportedly reduced blood glucose levels in streptozotocin-induced Type 1 diabetic rats [8]. 6-Paradol and 6-Shogaol seemed to be the active principles of *Zingiber officinale* responsible for stimulating glucose utilization and so lowering blood glucose [9]. Ingestion of *Curcuma longa* rhizomes appeared to increase insulin secretion in human volunteers [10]. *Alpinia oxyphylla* extract reportedly reduced blood glucose levels and significantly reduced damage of renal pathology in Type 2 DM mice by modulating gut microbiota composition [11]. Considering that no anti-diabetic studies have been conducted with *Alpinia malaccensis* and that the plant is available in Bangladesh and belongs to the Zingiberaceae family.

Objective of the Study

The objective of this study was to evaluate the efficacy of aerial parts and rhizomes of this plant in OGTT to lower blood glucose.

Materials and Methods

Plant material collection

Whole plants of *Alpinia malaccensis* including both aerial parts and rhizomes were collected from Khulna city, Bangladesh and identified by a competent botanist at the University of Development Alternative. Voucher specimen was deposited with the Medicinal Plant Collection Wing of the University of Development Alternative.

Preparation of methanolic extracts

Aerial parts and rhizomes were separately cut into small pieces and separately dried in the shade. 150g of dried aerial parts and rhizomes were then separately pulverized and mixed with 750 ml of methanol each and extracted for 48 hours at room temperature (30°C) with frequent stirring. Methanol was evaporated at 60°C and the extract stored at -20°C and used within 96 hours. The amounts of extract obtained from 150g aerial parts and 150g rhizomes were 14.36g and 9.49g, respectively. Prior to experiment, extract was dissolved in 10% Tween 20.

Chemicals and drugs

Glibenclamide and glucose were obtained from Square Pharmaceuticals Ltd., Bangladesh. Methanol and Tween 20 were from E. Merck, Germany and Sigma Chemical Co., USA, respectively. Glucometer and strips were from Lazz Pharma, Bangladesh.

Animals

Swiss albino mice comprising of both sexes and weighing between 15 - 18g were obtained from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). The animals were housed in cages (5 mice per cage) and acclimatized for 72 hours prior to experiment under conditions of 12h light and 12h darkness. During this time, the mice were fed with mice chow obtained from ICDDR,B and water *ad libitum*. Permission to carry out the experiment with mice was obtained from the Institutional Animal Ethical Committee of the University of Development Alternative. Care was taken that the animals did not suffer from unnecessary pain prior to or during the experiment.

Oral glucose tolerance test (OGTT)

OGTT was carried out as described previously by Joy and Kuttan [12] with only minor modifications. Mice, fasted for 12h, were divided into ten groups of 5 mice each. All mice were weighed carefully prior to start of experiment and various doses of glucose, glibenclamide and extract calculated according to body weight. Group 1 (Control) received vehicle only, that is Tween 20 and water. Group 2 (Standard) was administered a standard anti-hyperglycemic drug glibenclamide at a dose of 10 mg per kg body weight mice. Groups 3 - 6 were administered methanol extract of aerial parts of *Alpinia malaccensis* (MEAMA) at doses of 50, 100, 200 and 400 mg extract per kg body weight, respectively. Groups 7-10 were administered methanol extract of rhizomes of *Alpinia malaccensis* (MEAMR) at doses of 50, 100, 200 and 400 mg extract per kg body weight, respectively. Following a period of 1 hour as described previously after administration of vehicle, glibenclamide or extract [13,14], all mice were given by oral administration 2g glucose per kg body weight. All administrations were done orally by gavaging, taking care that pain was not inflicted on mice. Blood samples were collected 2h following glucose administration as described previously [13,14]. A glucometer was used to measure blood glucose levels. The percent lowering of blood glucose levels were calculated as 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 MEAMA and MEAMR, administered mice (Groups 2 - 10) 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 [15].

Results and Discussion

Administration of a standard drug, glibenclamide, at a dose of 10 mg per kg body weight led to blood glucose reduction by 39.1% in Group 2 mice compared to Group 1 (Control) mice. By comparison, administration of MEAMA at doses of 50, 100, 200 and 400 mg per kg led to blood glucose reductions, respectively, by 28.3, 32.0, 32.0, and 34.3%. Administration of MEAMR at the above four doses of 50, 100, 200 and 400 mg per kg led to blood glucose reductions, respectively, by 22.6, 30.0, 39.1 and 42.1%. The results are shown in table 1 and indicates that MEAMR at the highest dose of 400 mg per kg was better than MEAMA in demonstrating improved oral glucose tolerance, signifying MEAMR was more anti-hyperglycemic, and at the highest dose, the reduction in blood glucose by MEAMR was comparable to that of glibenclamide.

Treatment	Dose (mg/kg body weight)	Blood glucose level (mmol/l)	% lowering of blood glucose level
Control	10 ml	5.94 ± 0.13	-
Glibenclamide	10 mg	3.62 ± 0.14	39.1*
MEAMA	50 mg	4.26 ± 0.16	28.3*
MEAMA	100 mg	4.04 ± 0.11	32.0*
MEAMA	200 mg	4.04 ± 0.09	32.0*
MEAMA	400 mg	3.90 ± 0.08	34.3*
MEAMR	50 mg	4.60 ± 0.13	22.6*
MEAMR	100 mg	4.16± 0.05	30.0*
MEAMR	200 mg	3.62 ± 0.15	39.1*
MEAMR	400 mg	3.44 ± 0.14	42.1*

Table 1: *Lowering action of MEAMA and MEAMR on blood glucose level in hyperglycemic mice following 120 minutes of glucose loading. All administrations were made orally. Values represented as mean ± SEM, (n = 5); *P < 0.05; significant compared to hyperglycemic control animals.*

The rhizomes of the plant (Figure 1) are occasionally used as spice in Bangladesh and India and consumed as a vegetable in India. The plant is readily available in Bangladesh (locally known as deotara) and can be found growing in the wild and fallow lands. As such, it is both available and affordable and the rhizome can possibly act as a substitute for costly allopathic anti-hyperglycemic drugs. Consumption of the rhizome as spice and vegetable would suggest that the rhizomes are non-toxic. If the present study is further confirmed through trials in diabetic persons, it can be an affordable means to control high blood glucose.

Figure 1: *Alpinia malaccensis aerial part without (left) and with rhizome (right).*

In the present study, we did not isolate and identify the phytochemical constituent(s) responsible for the observed anti-hyperglycemic activity. However, crude phytochemical analysis of the plant by us showed presence of alkaloids, flavonoids, steroids and saponins in both aerial parts and rhizomes. These groups of compounds have previously been implicated in anti-hyperglycemic activity [16,17] and might as well play a part in the anti-hyperglycemic effects observed in the present study with MEAMA and MEAMR. However, more work is necessary to identify the bio-active principles, and current work in our laboratory is focusing on isolating and identifying the active principles.

Conclusion

We report for the first time (to our knowledge) that methanol extract of both aerial parts and rhizomes of *Alpinia malaccensis* demonstrate improved oral glucose tolerance and reduce blood glucose levels in glucose-loaded mice.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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