

Antihyperglycemic activity Evaluation of Rhizomes of *Curcuma zedoaria* (Christm.) Roscoe and Fruits of *Sonneratia caseolaris* (L.)Engl.

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Abstract: Diabetes is a debilitating disease affecting millions of people worldwide for which allopathic medicine has no known complete cure. Since the disease is projected to rise, significant scientific interest has focused on the plant kingdom towards discovery of newer anti-hyperglycemic drugs. The objective of the present research was to evaluate in oral glucose tolerance tests, the anti-hyperglycemic potential of methanol extract of *Curcuma zedoaria* rhizomes and fruits of *Sonneratia caseolaris*, both of which are used as anti-diabetics in the folk medicinal system of Bangladesh. Methanolic extract of rhizomes, when orally administered to glucose-loaded mice significantly and dose-dependently reduced concentrations of serum glucose. At extract doses of 50, 100, 200 and 400 mg per kg body weight serum glucose concentrations were reduced by, respectively, 36.9, 39.4, 41.1 and 55.1%. In comparison, a standard anti-hyperglycemic drug, glibenclamide reduced serum glucose concentration by 63.9% at a dose of 10 mg per kg body weight. Methanol extract of fruits also significantly and dose-dependently reduced serum glucose concentrations following administration, but the percent reductions were less than that obtained with rhizomes. At same doses of extract, serum glucose concentrations were reduced by 19.3, 27.6, 28.6 and 41.4%, respectively. The demonstrated anti-hyperglycemic activities by rhizomes of *C. zedoaria* and fruits of *S. caseolaris* validate their folk medicinal uses and warrants further studies towards elucidation of responsible phytochemical components, which can be potentially more efficacious drugs for treatment of diabetes.

Key words: *Curcuma zedoaria*, *Sonneratia caseolaris*, anti-hyperglycemic, oral glucose tolerance.

Introduction

Diabetes is a debilitating disease affecting millions of people worldwide for which allopathic medicine has no complete cure. Incidences of the disease are projected to rise because of changes in the food habits and lifestyle of the population in both developed and developing countries. Since the plant kingdom has provided modern medicine with many useful drugs, scientific interest has focused on the plant kingdom for discovery of newer and more efficacious drugs for treatment of diabetes and which drugs have lesser or no side-effects. Traditional medicines of various countries claim to have plants for complete treatment of diabetes, alternately, at least plants with blood sugar reducing effects when administered. The rhizomes of *Curcuma zedoaria* (Christm.) Roscoe (Zingiberaceae) and fruits of *Sonneratia caseolaris* (L.) Engl. (Sonneratiaceae) are two such plant parts used traditionally as anti-diabetics in the folk medicinal system of Bangladesh.

C. zedoaria (local name: shoti, English name: red leaf spice ginger) is a perennial herb native from India to Indonesia. Rhizomes of the plant reportedly exhibited analgesic property in acetic acid-induced abdominal constriction model in mice.¹ Anti-hyperglycemic and antinociceptive activities have been demonstrated with leaf extract of the plant.² In the folk medicinal system of Bangladesh, the rhizomes of the plant are used for treatment of leprosy, mental disorders, leucorrhea, diabetes, hepatitis, diarrhea and hemorrhoids. In traditional Eastern medicine, rhizomes of the plant are used to aid digestion, as relief for colic and as a blood purifier. It is also used to neutralize the venom of the Indian cobra.³

S. caseolaris (local name: choilani, English name: crabapple mangrove) is a mangrove species with a wide distributional range from Sri Lanka to Malay Peninsula as well as the Philippines, Timor, New Guinea, Solomon Islands and Indonesia. Steroids, flavonoids, triterpenoids and benzene carboxylic derivatives have been reported from the plant.⁴ Phytochemicals isolated from fruits of the plant include (-)-(R)-4-O-methylnyasol, (-)-(R)-nyasol, and maslinic acid.⁵ Two flavonoids – luteolin and luteolin 7-O- β -glucoside have been reported from leaves.⁶ Administration of dried leaf powder to diet of Wistar rats reportedly led to decreases in levels of serum glucose, total cholesterol, triglycerides, and low density lipoprotein cholesterol levels.⁷ The plant or plant parts is widely used in the traditional medicinal systems of various countries. For instance, in Myanmar, the fruit is used for poultices. In Malay, old fruit walls are used for helminthic infections, half-ripe fruit for coughs, and pounded leaves for hematuria and

small pox.⁸ In Bangladesh, the plant has folk medicinal uses as an anti-diabetic, astringent, antiseptic, and in arresting hemorrhage.

Considering that the rhizomes of *C. zedoaria* and fruits of *S. caseolaris* have folk medicinal uses in Bangladesh as anti-diabetics, the present study was conducted to evaluate the anti-hyperglycemic activities of methanol extract of the two plant parts in oral glucose tolerance tests conducted with glucose-loaded Swiss albino mice.

Materials and Methods

Plant material and extraction

Rhizomes of *C. zedoaria* and fruits of *S. caseolaris* were collected, respectively, from Bogra and Bagerhat districts, Bangladesh in November 2010. Rhizomes and fruits were separately sliced and air-dried in the shade for 120 hours, grounded into a fine powder, and were extracted with methanol at a ratio of 1:5 (w/v). The initial weight of dried powder used for extraction was 100g; the final weight of the extract was 15g for rhizomes and 6g for fruits. Plants were taxonomically identified at the Bangladesh National Herbarium, and voucher specimens were deposited both at the Bangladesh National Herbarium and the Medicinal Plant Collection Wing of the University of Development Alternative.

Chemicals and Drugs

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

Animals

In the present study, Swiss albino mice (male), which weighed between 16-20 g were used. The animals were obtained from International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B). All animals were kept under ambient temperature with 12h light followed by a 12h dark cycle. The animals were acclimatized for three days prior to actual experiments. The study was conducted following approval by the Institutional Animal Ethical Committee of the University of Development Alternative, Dhaka, Bangladesh.

Antihyperglycemic activity

Glucose tolerance property of methanol extract of either rhizomes or fruits was determined as per the procedure previously described by Joy and Kuttan⁹ with minor modifications. In brief, fasted mice were grouped into ten groups. Groups 1-6 had six mice per group, while Groups 7-10 had eight mice per group. The various groups received different treatments like

Group 1 received vehicle (1% Tween 80 in water, 10 ml/kg body weight) and served as control; group 2 received standard drug (glibenclamide, 10 mg/kg body weight). Groups 3-6 received methanol extract of *C. zedoaria* rhizomes at doses of 50, 100, 200 and 400 mg per kg body weight. Groups 7-10 received methanol extract of *S. caseolaris* fruits at doses of 50, 100, 200 and 400 mg per kg body weight. Each mouse was weighed and doses adjusted accordingly prior to administration of vehicle, standard drug, and test samples. All substances were orally administered. Following a period of one hour, all mice were orally administered 2 g glucose per kg of body weight. Blood samples were collected 120 minutes after the glucose administration through puncturing heart. Serum glucose levels were measured by glucose oxidase method.¹⁰

Statistical analysis

Experimental values are expressed as mean \pm SEM (standard error of mean). 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.

Results

The methanol extract of *C. zedoaria* rhizomes demonstrated dose-dependent and significant anti-

hyperglycemic activity when evaluated in oral glucose tolerance (OGT) tests with glucose-loaded mice. When administered at doses of 50, 100, 200 and 400 mg per kg body weight, the reductions in serum glucose levels were, respectively, 36.9, 39.4, 41.1 and 55.1%. In comparison, a standard anti-hyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced serum glucose levels by 63.9%. The extract, because of its ability to significantly reduce serum glucose levels, merit further studies towards isolation of phytochemical components responsible for the glucose lowering effect.

The methanol extract of fruits of *S. caseolaris* also demonstrated a dose-dependent and significant ability to lower serum glucose levels in glucose-loaded mice. However, the percentage lowering of serum glucose levels was lesser than observed with *C. zedoaria* rhizomes, when compared dose per dose. At *S. caseolaris* fruit extract doses of 50, 100, 200 and 400 mg per kg body weight, the observed reductions in serum glucose levels were, respectively 19.3, 27.6, 28.6 and 41.4%. Although not so effective as *C. zedoaria* rhizomes, the fruits of *S. caseolaris* also warrants further studies for isolation of effective anti-hyperglycemic components, which may be present in the extract. The results are shown in Table 1.

Table 1: Effect of methanol extract of the two plant parts on serum glucose level in hyperglycemic mice following 120 minutes of glucose loading.

Treatment	Plant part used	Dose (mg/kg body weight)	Serum glucose level (mmol/liter)	% lowering of serum glucose level
Control (Group 1)	-	10 ml	13.20 \pm 1.40	-
Glibenclamide (Group 2)	-	10 mg	4.77 \pm 0.51	63.9*
<i>C. zedoaria</i> (Group 3)	Rhizome	50 mg	8.33 \pm 0.54	36.9*
<i>C. zedoaria</i> (Group 4)	Rhizome	100 mg	8.00 \pm 0.62	39.4*
<i>C. zedoaria</i> (Group 5)	Rhizome	200 mg	7.78 \pm 0.61	41.1*
<i>C. zedoaria</i> (Group 6)	Rhizome	400 mg	5.93 \pm 0.87	55.1*
<i>S. caseolaris</i> (Group 7)	Fruit	50 mg	10.65 \pm 0.26	19.3*
<i>S. caseolaris</i> (Group 8)	Fruit	100 mg	9.56 \pm 0.59	27.6*
<i>S. caseolaris</i> (Group 9)	Fruit	200 mg	9.42 \pm 0.83	28.6*
<i>S. caseolaris</i> (Group 10)	Fruit	400 mg	7.73 \pm 0.81	41.4*

All administrations were made orally. Values represented as mean \pm SEM, (n=6 for Groups 1-6, and n = 8 for Groups 7-10); *P < 0.05 ; significant compared to hyperglycemic control animals.

Discussion

In our previous study, we have observed anti-hyperglycemic activities in methanol extract of leaves of both *C. zedoaria* as well as *S. caseolaris*.^{2,7} Results obtained in the present study shows that methanol extract of rhizomes of *C. zedoaria* and fruits of *S. caseolaris* are also effective as anti-hyperglycemic agents. Rhizomes of *C. zedoaria* are known to contain antidiabetic compounds like α -pinene and curcumin, which can account for the observed antihyperglycemic activity.¹¹⁻¹³ Maslinic acid, reported from fruits of *S. caseolaris*⁵ have been shown to have moderate α -glucosidase inhibitory effect.¹⁴ Taken together, the various phytochemicals reported from, respectively,

rhizomes and fruits of the two plant species can account for their observed anti-hyperglycemic effects.

The observed lowering of blood sugar by the extracts of the two plant parts may have been achieved through various mechanisms. The extracts may have potentiated pancreatic secretion of insulin, increased glucose uptake from serum, or decreased glucose absorption from gut.¹⁵⁻¹⁷ The anti-hyperglycemic activities exhibited by the extracts merit further studies for isolation of responsible phytochemical components and elucidation of the mechanisms involved and such studies are now being actively pursued in our laboratory.

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