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ORIGINAL ARTICLE

Antihyperglycemic and Antinociceptive Effects of *Curcuma Zedoaria* (Christm.) Roscoe Leaf Extract in Swiss Albino Mice

[1]Joynab Shoha, [2]Hosne Jahan, [3]Abdullah Al Mamun, [4]Md. Tozammal Hossain, [5]Salman Ahmed, [6]Md. Mobasser Hosain, [7]Shahnaz Rahman, [8]Rownak Jahan, [9]Mohammed Rahmatullah

[1-9]*Faculty of Life Sciences, University of Development Alternative, House No. 78, Road No. 11A, Dhanmondi R/A, Dhaka-1205, Bangladesh*

Joynab Shoha, Hosne Jahan, Abdullah Al Mamun, Md. Tozammal Hossain, Salman Ahmed, Md. Mobasser Hosain, Shahnaz Rahman, Rownak Jahan, Mohammed Rahmatullah: Antihyperglycemic and Antinociceptive Effects of Curcuma Zedoaria (Christm.) Roscoe Leaf Extract in Swiss Albino Mice

ABSTRACT

The methanol extract of leaves of *Curcuma zedoaria* showed dose-dependent and statistically significant antihyperglycemic activity following glucose loading in mice. The extract also significantly attenuated the abdominal constrictions induced by intraperitoneal injection of acetic acid in mice. Our studies indicate that the leaves of this plant possess significant antihyperglycemic and antinociceptive potential.

Key words: Curcuma zedoaria, antihyperglycemic, antinociceptive, Bangladesh, mice.

Introduction

Curcuma zedoaria (Christm.) Roscoe (Family: Zingiberaceae, English name: red leaf spice ginger, local name: shoti) is a small herbaceous plant found in the wild throughout Bangladesh. Folk medicinal practitioners of Bangladesh use the plant for treatment of diabetes, pain, and diarrhea. Since scientific studies are yet to be carried out on the plant, it was the objective of the present study to evaluate methanol extract of leaves of the plant for potential antihyperglycemic activity in oral glucose tolerance tests conducted with glucose-challenged Swiss albino mice, as well as antinociceptive activity of the extract in acetic acid-induced abdominal constriction in the same mouse model. The rhizomes of the plant have previously been reported to exhibit analgesic property using the acetic acid-induced abdominal constriction model in mice (Pamplona *et al*. 2006).

Materials and methods

The leaves of *C. zedoaria* were collected from Konabari in Gazipur district, Bangladesh during December, 2009. The plant was taxonomically identified at the Bangladesh National Herbarium at Dhaka (Voucher specimen No. 35,353). The air-dried leaves of *C. zedoaria* were grounded into a fine powder and 100g of the powder was extracted twice with methanol (1:3 and 1:2, w/v) for 24 hrs each. The extracts were combined and evaporated to dryness using rotary evaporator and freeze dryer. The final weight of the extract was 3.7g.

Glacial acetic acid was obtained from Sigma Chemicals, USA; aspirin, glibenclamide and glucose were obtained from Square Pharmaceuticals Ltd., Bangladesh. In the present study, Swiss albino male mice, which weighed between 20-25g were used. The animals were obtained from International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). Prior to experiments, all the animals were acclimatized for one week. The study was conducted following approval by the Institutional Animal Ethical Committee of University of Development Alternatives, Dhaka, Bangladesh.

Corresponding Author: Mohammed Rahmatullah, Faculty of Life Sciences, University of Development Alternative, House No. 78, Road No. 11A, Dhanmondi R/A, Dhaka-1205, Bangladesh.
Phone: 88-02-9136285 Fax: 88-02-8157339.
E-mail: rahamatm@hotmail.com

Antihyperglycemic effect of *C. zedoaria* leaves was determined following the procedure previously described by Joy and Kuttan (1999). Blood samples were collected two hours after the glucose administration through puncturing heart. Serum glucose levels were measured by glucose oxidase method (Venkatesh et al. 2004).

Antinociceptive activity of methanol extract of *C. zedoaria* leaves was examined using previously described procedures (Shanmugasundaram and Venkataraman, 2005).

Acute toxicity test was carried out as previously described (Ganapaty *et al.* 2002). Student's *t*-test was used to analyze any significant differences between control and experimental groups. $P < 0.05$, was considered significant as compared to control.

Results and discussion

The result of extract administration on serum glucose levels is shown in Table 1. There was a progressive reduction in serum glucose levels, when the extract was administered at doses of 50, 100, 200 and 400 mg per kg body weight. Although the level of serum glucose did not show any significant changes at a dose of 50 mg extract/kg body weight, as compared to control animals, the extract caused significant falls in serum glucose levels at all the other doses tested. At the highest dose tested (400 mg), the extract lowered serum glucose levels by 43.2% versus the reduction of serum glucose levels by 65.5%, obtained with the standard drug glibenclamide, administered at a dose of 10 mg per kg body weight.

In acetic acid-induced abdominal constriction tests, the extract caused dose-dependent and significant reductions in the number of abdominal constrictions induced by acetic acid. At a dose of 100 mg/kg body weight, administration of extract reduced the number of constrictions (writhings) by 53.9%, which compared favorably with the 42.3% and 57.7% reductions in constrictions obtained with the administration of a standard drug, aspirin, respectively, at doses of 200 and 400 mg/kg body weight. At the dose of 400 mg/kg body weight, the extract reduced the number of constrictions by 75%, which was considerably higher than that of aspirin, even with a dose of 400 mg/kg body weight. The results are shown in Table 2.

Table 1: Effect of administration of methanol extract of *Curcuma zedoaria* leaf on serum glucose levels in hyperglycemic mice.

Treatment	Dose (mg/kg body weight)	Serum glucose level (mg/dl)	% decrease in serum glucose levels
Control	-	79.9 ± 5.5	-
Glibenclamide	10 mg	27.6 ± 4.4	65.5*
C. zedoaria	50 mg	75.9 ± 8.2	5.0
C. zedoaria	100 mg	52.9 ± 8.9	33.8*
C. zedoaria	200 mg	50.6 ± 7.7	36.7*
C. zedoaria	400 mg	45.4 ± 5.9	43.2*

All administrations were made orally. Values represented as mean ± SEM, (n=6); $^{*}P < 0.05$; significant compared to hyperglycemic control animals.

Table 2: Antinociceptive effect of crude methanol extract of *Curcuma zedoaria* leaves in the acetic acid-induced gastric pain model mice.

Groups	Dose (mg/kg body weight)	Mean number of abdominal constrictions	Inhibition (%)
Control (vehicle)	-	8.67 ± 1.36	-
Aspirin	200 mg	5.00 ± 1.32	42.3*
Aspirin	400 mg	3.67 ± 1.12	57.7*
C. zedoaria	50 mg	5.67 ± 0.92	34.6*
C. zedoaria	100 mg	4.00 ± 1.00	53.9*
C. zedoaria	200 mg	3.17 ± 0.75	63.4*
C. zedoaria	400 mg	2.17 ± 0.48	75.0*

All administrations were made orally. Values represented as mean ± SEM, (n = 6); *P < 0.05.

In acute toxicity tests, mortality was not observed with any of the extract doses till the end of the observation period of 14 days. The observation of antihyperglycemic activity suggests that the extract may be acting through potentiating the pancreatic secretion of insulin or increasing the glucose uptake (Nyunai et al. 2009; Farjou *et al*. 1987). Alternately, the extract may be acting through inhibition of glucose absorption in the gut (Bhowmik *et al*. 2009).

Both central and peripheral analgesia can be suitably detected with the acetic acid-induced writhing test (Shanmugasundaram and Venkataraman 2005). Intraperitoneal administration of acetic acid (1%) leads to pain and inflammation mediated through production of prostaglandins [mainly prostacyclines (PGI_2) and prostaglandin-E (PG-E)], which are reported to be responsible for excitation of the Ad-nerve fibers, leading to sensation of pain (Reynolds 1982). Therefore any agent that lowers the number of abdominal constrictions will demonstrate analgesia by inhibition of prostaglandin synthesis.

The major conclusion is that methanol extract of leaves of *C. zedoaria* demonstrated both antihyperglycemic and antinociceptive activities in mice, as demonstrated through oral glucose tolerance and abdominal constriction tests.

The exact mechanisms through which the extract exerted its antihyperglycemic as well as antinociceptive actions are currently under investigation in our laboratory, along with identification of phytochemical(s) present in leaves responsible for both actions. The results validate the folk medicinal uses of the plant in Bangladesh for diabetes and pain.

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