AENSI Journals

Advances in Natural and Applied Sciences

ISSN:1995-0772 EISSN: 1998-1090

Journal home page: www.aensiweb.com/ANAS

Antihyperglycemic and Antinociceptive Activity Evaluation of Methanolic Extract of *Trichosanthes Anguina* Fruits in Swiss Albino Mice

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ARTICLE INFO

Article history:
Received 2 April 2014
Received in revised form
13 May 2014
Accepted 28 May 2014
Available online 27 June 2014

Keywords:
Trichosanthes anguina, antihyperglycemic, antinociceptive, Cucurbitaceae

ABSTRACT

The methanolic extract of *Trichosanthes anguina* fruits was evaluated for its antihyperglycemic and antinociceptive potentials in Swiss albino mice. Antihyperglycemic activity was evaluated through oral glucose tolerance tests in glucose-loaded mice, while antinociceptive potential was evaluated in pain model mice, where pain was induced through intraperitoneal administration of acetic acid, resulting in pain and concomitant abdominal constrictions (writhings). In antihyperglycemic activity tests conducted with glucose-loaded Swiss albino mice, methanolic extract of fruits significantly and dose-dependently reduced blood glucose concentrations. At extract doses of 50, 100, 200 and 400 mg per kg body weight mice, the percent lowering of blood sugar by the extract was, respectively, 18.9, 27.6, 35.0, and 51.4. The results were both dose-dependent and statistically significant. A standard antihyperglycemic drug, glibenclamide, when administered to glucose-loaded mice at a dose of 10 mg per kg body weight, reduced blood sugar levels by 55.2%. The results demonstrate that the methanolic extract possesses antihyperglycemic potential. In antinociceptive activity tests conducted with intraperitoneally administered acetic acid-induced pain model in mice, the extract at the afore-mentioned four doses dose-dependently and significantly reduced the number of abdominal constrictions in mice caused by pain, respectively, by 35.3, 38.2, 41.2, and 44.1%. A standard antinociceptive drug, aspirin, when administered at doses of 200 and 400 mg per kg body weight, reduced the number of writhings by 47.1 and 61.8%, respectively. The results thus demonstrate also significant antinociceptive potential of fruits of the plant. The results suggest that phytochemicals present in fruits deserve further scientific attention towards possible discovery of antihyperglycemic and pain-alleviating drugs.

To Cite This Article: Mahfuza Akter, Israt Zebin Mitu, Jajiratul Jannat Proma, Sk. Mizanur Rahman, Md. Rashedul Islam, Shahnaz Rahman, Mohammed Rahmatullah., Antihyperglycemic and Antinociceptive Activity Evaluation of Methanolic Extract of Trichosanthes Anguina Fruits in Swiss Albino Mice. **Adv. in Nat. Appl. Sci.,** *8(8): 70-74, 2014*

INTRODUCTION

Trichosanthes anguina L. (Cucurbitaceae) is a climbing plant cultivated in Bangladesh for its fruits, which are cooked and eaten as vegetable. In English, the plant is known as snake gourd, and in Bengali, the plant is known as chichinga. The fruits of the plant have ethnomedicinal uses in Bangladesh as a laxative and as a tonic. The roots and seeds are considered anthelmintic and antidiarrheal, and also used for biliousness and in syphilis (Rahman, 2013).

Various extracts of the leaves of the plant have reported antibacterial activity (Reddy *et al*., 2010). In rats with streptozotocin-induced severe diabetes mellitus, aqueous extract of the fruit of a related plant, *Trichosanthes dioica*, at dose of 1g per kg body weight daily one for 28 days have been found to reduce levels of fasting blood glucose, postprandial glucose and urine sugar (Rai *et al*., 2008).

We have been conducting extensive pharmacological studies on Bangladeshi medicinal plants towards identifying plants with antihyperglycemic, antinociceptive, and cytotoxic activities (Anwar *et al*., 2010; Jahan *et al*., 2010; Rahman *et al*., 2010; Rahmatullah *et al*., 2010; Shoha *et al*., 2010; Ali *et al*., 2011; Barman *et al*., 2011; Hossan *et al*., 2011; Jahan *et al*., 2011; Rahman *et al*., 2011; Sutradhar *et al*., 2011; Ahmed *et al*., 2012; Arefin *et al*., 2012; Haque *et al*., 2012; Sathi *et al*., 2012). The objective of this study was to evaluate the antihyperglycemic and antinociceptive potential of methanol extract of fruits of *Trichosanthes anguina*.

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Advances in Natural and Applied Sciences, 8(8) July 2014, Pages: 70-74

Antihyperglycemic activity of methanolic fruit extract was evaluated through oral glucose tolerance test (OGTT) in glucose-loaded mice, while antinociceptive activity was evaluated in intraperitoneally administered acetic acid mice. Intraperitoneal administration of acetic acid causes pain, which is manifested by abdominal constrictions (writhings). Any decrease in the number of writhings was taken as an indicator of pain alleviation.

MATERIALS AND METHODS

Fruits of *Trichosanthes anguina* were collected from Dhaka district, Bangladesh during May 2013. The plant was taxonomically identified at the Bangladesh National Herbarium at Dhaka (Accession Number 38,362). The sliced and air-dried fruits of *Trichosanthes anguina* were grounded into a fine powder and 66g of the powder was extracted with 350 ml methanol for 48 hours. The extract was evaporated to dryness at 40^{o}C. The final weight of the extract was 8.54g.

Chemicals:

Glacial acetic acid was obtained from Sigma Chemicals, USA; aspirin, glibenclamide and glucose were obtained from Square Pharmaceuticals Ltd., Bangladesh.

Animals:

In the present study, Swiss albino mice (male), which weighed between 12-18g 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 *Trichosanthes anguina* fruits was determined as per the procedure previously described by Joy and Kuttan (1999) with minor modifications. In brief, fasted mice were grouped into six groups of five mice each. 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 *Trichosanthes anguina* fruits (TAME) 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/kg of body weight. Blood samples were collected 120 minutes after the glucose administration through puncturing heart. Blood glucose levels were measured by glucose oxidase method (Venkatesh *et al*., 2004).

Antinociceptive activity:

Antinociceptive activity of the methanol extract of *Trichosanthes anguina* fruits was examined using previously described procedures (Shanmugasundaram and Venkataraman, 2005). Briefly, mice were divided into seven groups of five mice each. Group 1 served as control and was administered vehicle only. Groups 2 and 3 were orally administered the standard antinociceptive drug aspirin at a dose of 200 and 400 mg per kg body weight, respectively. Groups 4-7 were administered methanolic fruit extract of *Trichosanthes anguina* (TAME) at doses of 50, 100, 200 and 400 mg per kg body weight, respectively. Following a period of 60 minutes after oral administration of standard drug or extract, all mice were intraperitoneally injected with 1% acetic acid at a dose of 10 ml per kg body weight. A period of 15 minutes was given to each animal to ensure bio-availability of acetic acid, following which period the number of abdominal constrictions (writhings) was counted for 10 min.

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.

RESULTS AND DISCUSSION

Preliminary phytochemical analysis showed the presence of saponins, alkaloids, tannins, and flavonoids in the extract (TAME).

In antihyperglycemic activity tests conducted with glucose-loaded Swiss albino mice, methanolic extract of fruits significantly and dose-dependently reduced blood glucose concentrations. At extract doses of 50, 100, 200 and 400 mg per kg body weight mice, the percent lowering of blood sugar by the extract was, respectively, 18.9, 27.6, 35.0, and 51.4. The results were both dose-dependent and statistically significant. A standard antihyperglycemic drug, glibenclamide, when administered to glucose-loaded mice at a dose of 10 mg per kg

body weight, reduced blood sugar levels by 55.2%. The results are shown in Table 1 and demonstrate that the methanolic extract possesses antihyperglycemic potential.

In antinociceptive activity tests conducted with intraperitoneally administered acetic acid-induced pain model in mice, the extract at the afore-mentioned four doses dose-dependently and significantly reduced the number of abdominal constrictions in mice caused by pain, respectively, by 35.3, 38.2, 41.2, and 44.1%. A standard antinociceptive drug, aspirin, when administered at doses of 200 and 400 mg per kg body weight, reduced the number of writhings by 47.1 and 61.8%, respectively. The results are shown in Table 2. The results thus demonstrate also significant antinociceptive potential of fruits of the plant. At the highest dose of the

Table 1: Effect of methanol extract of *Trichosanthes anguina* fruits 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 (Group 1)	10 ml	5.72 ± 0.31	-
Glibenclamide (Group 2)	10 mg	2.56 ± 0.20	55.2*
TAME (Group 3)	50 mg	4.64 ± 0.21	18.9*
TAME (Group 4)	100 mg	4.14 ± 0.22	27.6*
TAME (Group 5)	200 mg	3.72 ± 0.27	35.0*
TAME (Group 6)	400 mg	2.78 ± 0.24	51.4*

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

Table 2: Antinociceptive effect of crude methanol extract of *Trichosanthes anguina* fruits in the acetic acid-induced gastric pain model mice.

Treatment	Dose (mg/kg body weight)	Mean number of writhings	% inhibition
Control (Group 1)	10 ml	6.80 ± 0.37	-
Aspirin (Group 2)	200 mg	3.60 ± 0.40	47.1*
Aspirin (Group 3)	400 mg	2.60 ± 0.51	61.8*
TAME (Group 4)	50 mg	4.40 ± 0.40	35.3*
TAME (Group 5)	100 mg	4.20 ± 0.37	38.2*
TAME (Group 6)	200 mg	4.00 ± 0.45	41.2*
TAME (Group 7)	400 mg	3.80 ± 0.58	44.1*

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

extract (400 mg), the obtained antinociceptive results were comparable with aspirin, administered at a dose of 200 mg per kg body weight.

To our knowledge, this is the first report of antihyperglycemic and antinociceptive activities of methanolic extract of *Trichosanthes anguina* fruits. However, the plant has been reported to improve glucose tolerance and tissue glycogen in non-insulin dependent diabetes mellitus induced rats (Kirana and Srinivasan, 2008). Although antihyperglycemic effects of *Trichosanthes anguina* whole plant or plant part(s) are not known, the antihyperglycemic activity of several other plants belonging to the same genera have been reported. Glycans with hypoglycemic activity, named Trichosans A-E, have been isolated from *Trichosanthes kirilowii* roots (Hikino *et al*., 1989). Hypoglycemic activity of a lectin isolated from *Trichosanthes kirilowii* has been reported (Li *et al*., 2012). The hypoglycemic effect of aqueous extract of *Trichosanthes dioica* has been reported in normal and diabetic rats (Adiga *et al*., 2010). The plant extract has also been shown to reduce oxidative stress in experimentally induced diabetic rats (Kumar Rai *et al*., 2011). Finally, both antihyperglycemic and antihyperlipidemic activities have been attributed to *Trichosanthes dioica* (Rai *et al*., 2013).

Any antinociceptive activity of *Trichosanthes anguina* plant or plant part(s) is yet to be reported. However, a protective role of a triterpenoid-enriched extract of *Trichosanthes dioica* root has been reported against experimentally induced pain and inflammation in rodents (Bhattacharya and Haldar, 2012). Taken together, the fruits of the plant merit further scientific studies for possible new antihyperglycemic and antinociceptive constituents, which may prove to be useful drugs in diabetes and pain.

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