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ORIGINAL ARTICLE

An Evaluation of Antihyperglycemic and Antinociceptive Effects of Crude Methanol Extract of Coccinia Grandis (L.) J. Voigt. (Cucurbitaceae) Leaves in Swiss Albino Mice

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Biplob Kumar Sutradhar, Md. Jahidul Islam, Md. Abu Shoyeb, Himel Nahreen Khaleque, Mariz Sintaha, Farzana Akther Noor, Walid Newaz, Mohammed Rahmatullah: An Evaluation of Antihyperglycemic and Antinociceptive Effects of Crude Methanol Extract of Coccinia Grandis (L.) J. Voigt. (Cucurbitaceae) Leaves in Swiss Albino Mice

ABSTRACT

Coccinia grandis (L.) Voigt. (Family: Cucurbitaceae, English name: ivy gourd, local name: telakucha) is a vinous plant found in the wild and in fallow lands of Bangladesh. The leaves of the plant are believed to have medicinal properties by the folk medicinal practitioners (Kavirajes) of the country, and are often used for treatment of diabetes as well as pain. Since scientific studies are lacking on the plant about these two pharmacological properties, it was the objective of the present study to evaluate the antihyperglycemic and antinociceptive effects of crude methanol extract of leaves in Swiss albino mice. Antihyperglycemic activity study was done through oral glucose tolerance tests in glucose-loaded mice. The methanol extract of the leaf demonstrated significant dose-dependent antihyperglycemic activity, when administered to mice at doses of 50, 100, 200 and 400 mg extract per kg body weight. The highest level of serum glucose reduction was observed with an extract dose of 400 mg per kg body weight, when serum glucose level was found to be reduced by 56.3%. In comparison, the standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight reduced serum glucose level in mice by 55.5%, suggesting that the leaf extract has considerable antihyperglycemic properties. Antinociceptive activity tests were conducted in acetic acid-induced gastric pain writhing in the same mouse model. The methanolic extract of leaf also demonstrated significant and dose-dependent antinociceptive activity. The number of writhings induced by intraperitoneal administration of acetic acid in mice was reduced by 36.4% with the lowest dose of extract tested (100 mg per kg body weight). At a dose of 400 mg per kg body weight, the extract reduced the number of writhings by 47.5%, which was significantly higher than that observed with a standard antinociceptive drug, aspirin. Taken together, the results demonstrate that the leaf extract possess significant antihyperglycemic and antinociceptive activities and validate the folk medicinal use of the plant for treatment of diabetes and pain.

Key words: *Coccinia grandis*, antihyperglycemic, antinociceptive, mice.

Introduction

Coccinia grandis (L.) Voigt. (Family: Cucubitaceae, English name: ivy gourd) is a tropical vine whose native range includes Africa, Asia, and the Northern Territories of Australia. It can be found growing in the wild and on fallow lands throughout Bangladesh. The plant is considered to be a significant medicinal plant by the folk medicinal practitioners of Bangladesh, being used for treatment of diabetes, pain, hypertension, fever, jaundice, and gastrointestinal problems. Locally, the plant is known as telakucha or telakochu.

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A polyprenol has been isolated from the plant, which showed significant triglyceride and cholesterol-lowering effects in dyslipidemic hamster model (Singh *et al*., 2007). Antioxidant activity has been shown for hydromethanolic extract of leaves from the plant (Umamaheswari and Chatterjee, 2007). The methanolic extract of the plant reportedly exhibited xanthine oxidase inhibitory activity, thus validating its traditional use for treatment of gout and related symptoms by the indigenous people of India (Umamaheswari *et al*., 2007).
For the last few years, we have been documenting the folk medicinal uses of various medicinal plants in Bangladesh for treatment of various ailments (Rahmatullah *et al*., 2009 a-e). In parallel with our ethnomedicinal surveys, we also had been studying, for scientific validation purposes, the pharmacological activities of various medicinal plant extracts (Morshed *et al*., 2010; Ahmed *et al*., 2010; Moushumi *et al*., 2010). In continuation of our previous studies, the objective of the present study was to evaluate the antihyperglycemic and antinociceptive potential of the crude methanol extract of leaves of *Coccinia grandis*, respectively, in glucose-challenged and acetic acid-induced gastric pain models in Swiss albino mice.

Materials and methods

Plant Material and Extraction:

The leaves of *Coccinia grandis* were collected from Dhaka district, Bangladesh. The plant was taxonomically identified by Mr. Manjur-ul-Kadir Mia, ex-Curator and Principal Scientific officer of Bangladesh National Herbarium at Dhaka. The leaves of *Coccinia grandis* were air-dried in the shade for 120 hours, grounded into a fine powder, and were extracted with methanol at a ratio of 1:4 (w/v). After 24 hrs, the mixture was filtered; filtrate was collected and the residue was again extracted with methanol at a ratio of 1:3 (w/v) for 24 hrs. Filtrates were combined and evaporated to dryness. The initial weight of dried leaf powder used for extraction was 100g; the final weight of the extract was 7.2g.

Chemicals and Drugs:

Glacial acetic acid was obtained from Sigma Chemicals, USA; aspirin, 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 15-19g 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 one week prior to actual experiments. The study was conducted following approval by the Institutional Animal Ethical Committee of University of Development Alternative, Dhaka, Bangladesh.

Anti-hyperglycemic Activity:

Glucose tolerance property of methanol extract of *Coccinia grandis* leaves 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 eight mice each. The various groups received different treatments like Group-I received vehicle (1% Tween 80 in water, 10 ml/kg body weight) and served as control, group-II received standard drug (glibenclamide, 10 mg/kg body weight) and the other four groups (III-VI) received the methanol extract of *Coccinia grandis* leaves at four different doses of 50, 100, 200 and 400 mg/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 two hours after the glucose administration through puncturing heart. Serum glucose levels were measured by glucose oxidase method (Venkatesh *et al*., 2004).

Acetic Acid-induced Writhing Method:

Antinociceptive activity of methanol extract of *Coccinia grandis* leaves was examined using previously described procedures of Shanmugasundaram and Venkataraman (2005) with minor modifications. Pain was induced in mice in the writhing test through intraperitoneal administration of 1% acetic acid at a dose of 10 ml/kg body weight. Mice were separated into five groups of five mice each.

Group-I served as control and was administered vehicle (1% Tween 80 in water, 10 ml/kg body weight). The standard drug, aspirin was administered to Group-II mice at a dose of 250 mg/kg body weight. Groups-III to V received extract, respectively at 100, 200, and 400 mg extract/kg body weight orally 30 min before acetic acid injection. A period of 5 minutes was given to each animal to ensure bio-availability of acetic acid, following which period, the number of 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

Antihyperglycemic Effect:

The methanolic extract of *Coccinia grandis* leaves demonstrated dose-dependent and significant antihyperglycemic effects when administered to glucose-loaded mice in oral glucose tolerance tests. The results are summarized in Table 1. Even at the lowest dose tested of 50 mg extract per kg body weight, the extract caused a 38.8% reduction in serum glucose levels. Serum glucose levels were reduced by 56.3% at the highest dose of 400 mg extract per kg body weight. In comparison, the standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced serum glucose level by 55.5%. The result obtained with methanolic extract of *Coccinia grandis* leaves clearly is indicative of its antihyperglycemic potential and validates its folk medicinal use for treatment of diabetes. Flavonoids and glycosides have been reported to have antidiabetic effects (Chakravarthy *et al*., 1980; Sheeja and Augusti, 1993), and the results obtained in the present study suggest that the leaves may contain phytochemical constituents in the form of flavonoids or glycosides or both.

Table 1: Effect of crude methanol extract of *Coccinia grandis* leaves on serum glucose levels in hyperglycemic mice.

Treatment	Dose (mg/kg body weight)	Serum glucose level (mg/dl)	% lowering of serum glucose level
Control	10 ml	192.50 ± 6.53	-
Glibenclamide	10 mg	85.63 ± 6.26	55.5*
Coccinia grandis	50 mg	117.81 ± 6.26	38.8*
Coccinia grandis	100 mg	102.50 ± 7.06	46.8*
Coccinia grandis	200 mg	92.50 ± 9.03	51.9*
Coccinia grandis	400 mg	84.06 ± 2.83	56.3*

All administrations were made orally. Values represented as mean ± SEM, (n=8);*P<0.05; significant compared to hyperglycemic control animals.

Antinociceptive Activity:

The methanol extract of leaves of *Coccinia grandis* also demonstrated a dose-dependent and significant reduction in acetic acid-induced writhings in mice. The results are shown in Table 2. At doses, respectively, of 100, 200 and 400 mg extract/kg body weight, percent inhibitions of writhings were 36.4, 36.4, and 47.5. In comparison, the standard antinociceptive drug, aspirin, caused a 34.3% inhibition in writhings. As such, the leaf extract of *Coccinia grandis* demonstrated more potent antinociceptive activity than the standard drug, aspirin. Both central and peripheral analgesia can be detected with the acetic acid-induced writhing test (Shanmugasundaram and Venkataraman, 2005). Production of prostaglandins [mainly prostacyclines (PGI_2) and prostaglandin- (PG-E)] has been shown to be responsible for excitation of Ad-nerve fibers, leading to the sensation of pain (Reynolds, 1982; Rang and Dale, 1993). The mechanism behind intraperitoneal administration of acetic acid and subsequent evolvement of pain leading to gastric writhings, probably then involve a mechanism of increased production of prostaglandins. The mechanism behind the inhibition of gastric writhings by the extract may then be mediated through inhibition of prostaglandin synthesis. The obtained results are suggestive that the extract may contain phytochemical components, which following administration has lead to inhibition of lipooxygenase and/or cyclooxygenase. The inhibition of these enzymes will lead in turn to reduction of prostaglandin E2 synthesis, thereby causing amelioration of pain caused by intraperitoneal administration of acetic acid. A similar mechanism has been proposed for antinociceptive activity of *Ficus deltoidea* aqueous extract in acetic acid-induced gastric pain model (Sulaiman *et al*., 2008). Studies are being conducted in our laboratory to identify the constituents of the methanol extract of *Coccinia grandis* responsible for the antinociceptive effect observed in acetic acid-injected mice.

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

Groups	Dose (mg/kg body weight)	Mean no. of writhing	Inhibition (%)
Control (vehicle)	10 ml	19.8 ± 1.3	-
Aspirin	250 mg	13.0 ± 0.9	34.3*
Coccinia grandis	100 mg	12.6 ± 1.1	36.4*
Coccinia grandis	200 mg	12.6 ± 1.2	36.4*
Coccinia grandis	400 mg	10.4 ± 1.2	47.5*

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

The present study clearly validates the use of *Coccinia grandis* for treatment of diabetes and pain by the folk medicinal practitioners of Bangladesh. Many modern drugs have been obtained through observations of indigenous medical practices involving medicinal plants. Further studies are being conducted in our laboratory to identify the chemicals in *Coccinia grandis* responsible for the antihyperglycemic as well as antinociceptive effects. It is expected that identification of such chemicals can pave the way for obtaining novel compounds, which can prove efficacious for treatment of two debilitating diseases, namely diabetes and pain.

References

Ahmed, R., S.J. Moushumi, H. Ahmed, M. Ali, W.M. Haq, R. Jahan and M. Rahmatullah, 2010. Serum glucose and lipid profiles in rats following administration of *Sonneratia caseolaris* (L.) Engl. (Sonneratiaceae) leaf powder in diet. Advances in Natural and Applied Sciences, 4(2): 171-173.

Chakravarthy, B.K., S. Gupta, S.S. Gambir and K. Gode, 1980. Pancreatic b-cell regeneration – a novel antidiabetic mechanism of *Pterocarpus marsupium* Roxb. Indian Journal of Pharmacology, 12: 123-127.

Joy, K.L. and R.J. Kuttan, 1999. Anti-diabetic activity of *Picrorrhiza kurroa* extract. Journal of Ethnopharmacology, 67: 143-148.

Morshed, A., M.H. Hossain, S. Shakil, K. Nahar, S. Rahman, D. Ferdausi, T. Hossain, I. Ahmad, M.H. Chowdhury and M. Rahmatullah, 2010. Evaluation of Antinociceptive Activity of two Bangladeshi Medicinal Plants, Kalanchoe pinnata (Lam.) Pers. and Lagerstroemia speciosa (L.) Pers. Advances in Natural and Applied Sciences, 4: 193-197.

Moushumi, S.J., R. Ahmed, H. Ahmed, M. Ali, W.M. Haq, R. Jahan and W.M. Rahmatullah, M. 2010. Hypoglycemic, hypocholesterolemic and hypotriglyceridemic activity of tuber roots of Ipomoea mauritiana Jacq. (Convolvulaceae) when administered to rats. Advances in Natural and Applied Sciences 4(2): 174-176.

Rahmatullah, M., I.J. Mukti, A.K.M.F. Haque, M.A.H. Mollik, K. Parvin, R. Jahan, M.H. Chowdhury and T. Rahman, 2009a. An Ethnobotanical Survey and Pharmacological Evaluation of Medicinal Plants used by the Garo Tribal Community living in Netrakona district, Bangladesh. Advances in Natural and Applied Sciences, 3(3): 402-418.

Rahmatullah, M., M.A.H. Mollik, A.T.M.A. Azam, M.R. Islam, M.A.M. Chowdhury, R. Jahan, M.H. Chowdhury, and T. Rahman, 2009b. Ethnobotanical Survey of the Santal tribe residing in Thakurgaon District, Bangladesh. American Eurasian Journal of Sustainable Agriculture, 3(4): 889-898.

Rahmatullah, M., A.K. Das, M.A.H. Mollik, R. Jahan, M. Khan, T. Rahman and M.H. Chowdhury, 2009c. An Ethnomedicinal Survey of Dhamrai Sub-district in Dhaka District, Bangladesh. American Eurasian Journal of Sustainable Agriculture, 3(4): 881-888.

Rahmatullah, M., A. Noman, M.S. Hossan, M.H. Rashid, T. Rahman, M.H. Chowdhury, and R. Jahan, 2009d. A survey of medicinal plants in two areas of Dinajpur district, Bangladesh including plants which can be used as functional foods. American Eurasian Journal of Sustainable Agriculture, 3(4): 862-876.

Rahmatullah, M., D. Ferdausi, M.A.H. Mollik, M.N.K. Azam, M.T. Rahman and R. Jahan, 2009e. Ethnomedicinal Survey of Bheramara Area in Kushtia District, Bangladesh. American Eurasian Journal of Sustainable Agriculture, 3(3): 534-541.

Rang, H.P. and M.M. Dale, 1993. "Pharmacology", 2nd edition. Churchill Livingstone Publishers, UK.

Reynolds, J.E.F., 1982. "Martindale: The Extra Pharmacopoeia", The Pharmaceutical Press, 28th edition; pp: 245.

Shanmugasundaram, P. and S. Venkataraman, 2005. Anti-nociceptive activity of Hygrophilous auriculata (Schum) Heine. African Journal of Traditional Complementary and Alternative Medicines, 2: 62- 69.

Sheeja, C. and K.T. Augusti, 1993. Antidiabetic effect of a glycoside of leucopelargon idin isolated from Ficus bengalensis. Indian Journal of Experimental Biology, 31: 26-29.

Singh, G., P. Gupta, P. Rawat, A. Puri, G. Bhatia and R. Maurya, 2007. Antidyslipidemic activity of polyprenol from Coccinia grandis in high-fat diet-fed hamster model. Phytomedicine, 14: 792-798.

Sulaiman, M.R., M.K. Hussain, Z.A. Zakaria, M.N. Somchit, S. Moin, A.S. Mohamad and D.A. Israf, 2008. Evaluation of the antinociceptive activity of Ficus deltoidea aqueous extract. Fitoterapia, 79: 557-561.

Umamaheswari, M. and T.K. Chatterjee, 2007. In vitro antioxidant activities of the fractions of Coccinia grandis L. leaf extract. African Journal of Traditional Complementary and Alternative Medicines, 5: 61-73.

Umamaheswari, M., K. AsokKumar, A. Somasundaram, T. Sivashanmugam, V. Subhadradevi and T.K. Ravi, 2007. Xanthine oxidase inhibitory activity of some Indian medicinal plants. Journal of Ethnopharmacology, 109: 547-551.

Venkatesh, S., G.D. Reddy, Y.S.R. Reddy, D. Sathyavathy and B.M. Reddy, 2004. Effect of Helicteres isora root extracts on glucose tolerance in glucose-induced hyperglycemic rats. Fitoterapia, 75: 364-367.