ORIGINAL ARTICLE

Antihyperglycemic and antinociceptive activity of Fabaceae family plants – an evaluation of *Mimosa pigra* L. stems


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**ABSTRACT**

*Mimosa pigra* is widely used in folk medicinal systems of Bangladesh to lower blood sugar in diabetic patients and for treatment of pain. The present study was conducted to evaluate the antihyperglycemic and antinociceptive potential of methanolic extract of *Mimosa pigra* stems, respectively, through oral glucose tolerance tests in glucose-loaded Swiss albino mice and intraperitoneally acetic acid injected gastric pain mouse model. Oral administration of the extract at doses of 50, 100, 200 and 400 mg per kg body weight led to dose-dependent significant reductions in the levels of blood glucose in glucose-loaded mice. At these four doses, the extract reduced the concentrations of glucose in blood by, respectively, 37.84, 39.83, 42.39 and 50.50%. A standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 56.33%, thus demonstrating that the extract at least at the highest dose of 400 mg, possessed comparable antihyperglycemic activity to glibenclamide. In antinociceptive activity tests, the extract also dose-dependently and significantly, caused reductions in the number of gastric writhings arising from gastric pain in mice as a result of intraperitoneal administration of acetic acid. The percent reductions in the number of writhings at extract doses of 50, 100, 200 and 400 mg per kg body weight were, respectively, 70.01, 74.96, 77.51 and 85.01. The antinociceptive activity of the extract was more potent than that of a standard antinociceptive drug aspirin, which when administered at doses of 200 and 400 mg per kg body weight, reduced the number of writhings by 37.48 and 59.97%, respectively. The almost complete alleviation of gastric pain by the extract at the highest dose of 400 mg per kg body weight strongly suggests that the extract may be further investigated for isolation of possibly novel pain-killing components. At the same time, the results obtained in the present study, validates the use of this plant by folk medicinal practitioners of Bangladesh for treatment of high blood sugar levels in diabetic patients as well as pain. The results highlight the importance of close observation of traditional medicinal practices along with pharmacological activity studies on the materials used in such practices towards discovery of what can be more efficacious drugs.

**Key words:** *Mimosa pigra*, antihyperglycemic, antinociceptive, Fabaceae

**Introduction**

Diabetes is reaching endemic proportions throughout the world, possibly because of a change in lifestyle and dietary habits of human beings in general. The disease is characterized by the primary symptom of high blood sugar levels due to inability of the body to utilize sugar as a result of insulin deficiency or resistance to insulin. Progression of the disease leads to increased risks of cardiovascular complications as well as development of diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy. Increasing incidences of this disease is being reported in Bangladesh, which includes both rural and the urban population. Antidiabetic drugs can lead to lowering of blood sugar levels but such drugs are costly and more or less unavailable to the rural population either because of non-affordability or because of non-availability. As a result, the mainly rural population of Bangladesh relies on folk medicinal practitioners, who use various medicinal plants for lowering of blood sugar in diabetic patients or treatment of diabetes.

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Pain arising from various internal or external factors, afflicts millions of people throughout the world on a daily basis. A number of pain-killing drugs are available including over-the-counter drugs like aspirin or paracetamol. However, excessive use or over-dosage of these two medications can lead to gastric ulceration and hepatotoxicity. The rural people of Bangladesh also rely on folk medicinal practitioners for treatment of pain, who in turn utilize various plants for treatment.

Since the above two ailments are suffered by millions of people worldwide on a daily basis, it is important that drugs be discovered which can cure the ailment totally (like diabetes) or have less or no undesirable side-effects (like treatment of pain). Many modern medicines have been discovered from close observations of traditional medicinal practices or medicinal practices of indigenous peoples (Balick and Cox, 1996; Cotton, 1996; Gilani and Rahman, 2005). Close observations of traditional medicinal practices necessitate proper ethnomedicinal surveys among traditional medicinal practitioners and careful documentation of the results. We have been doing such surveys among mainstream traditional medicinal practitioners as well as tribal medicinal practitioners for the last few years and have documented a number of the survey reports (Rahmatullah et al., 2009a-c; Rahmatullah et al., 2010a-g; Rahmatullah et al., 2011a,b; Rahmatullah et al., 2012a-d). Additionally, we have been screening appropriate medicinal plants as obtained from our ethnomedicinal surveys for their antidiabetic and antinociceptive activities towards further isolation and characterization of effective drugs against these two ailments from these plants (Anwar et al., 2010; Jahan et al., 2010; Khan et al., 2010; Mannan et al., 2010; Rahman et al., 2010; Rahmatullah et al., 2010h; Shoha et al., 2010; Ali et al., 2011; Barman et al., 2011; Hossain et al., 2011; Jahan et al., 2011; Rahman et al., 2011; Sutradhar et al., 2011). Since Mimosa pigra was found to be quite widely used by the folk medicinal practitioners of Bangladesh for treatment of diabetes and pain, the objective of the present study was to evaluate a methanolic extract of stems of this plant for its antihyperglycemic and antinociceptive potential.

Materials and Methods

Stems of Mimosa pigra were collected from Dhaka district, Bangladesh during June, 2011. The plant was taxonomically identified at the Bangladesh National Herbarium at Dhaka. The sliced and air-dried whole stems of Mimosa pigra were grounded into a fine powder and 100g of the powder was extracted with methanol (1:10, w/v) for 48 hours. The extract was evaporated to dryness. The final weight of the extract was 2.73g.

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 15-22 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 University of Development Alternative, Dhaka, Bangladesh.

Antihyperglycemic activity:

Glucose tolerance property of methanol extract of Mimosa pigra stems 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 six 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 Mimosa pigra stems 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 *Mimosa pigra* stems was examined using previously described procedures (Shanmugasundaram and Venkataraman, 2005). Briefly, mice were divided into seven groups of six 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 stem extract of *Mimosa pigra* 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 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

Oral administration of the extract at doses of 50, 100, 200 and 400 mg per kg body weight led to dose-dependent significant reductions in the levels of blood glucose in glucose-loaded mice. At these four doses, the extract reduced the concentrations of glucose in blood of mice by, respectively, 37.84, 39.83, 42.39 and 50.50%. A standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, reduced blood glucose level by 56.33%, thus demonstrating that the extract at least at the highest dose of 400 mg, possessed comparable antihyperglycemic activity to glibenclamide. The results are shown in Table 1. The results further validate the folk medicinal use of the stems for lowering of blood sugar in diabetic patients.

In antinociceptive activity tests, the extract also dose-dependently and significantly, caused reductions in the number of gastric writhings arising from gastric pain in mice as a result of intraperitoneal administration of acetic acid. The percent reductions in the number of writhings at extract doses of 50, 100, 200 and 400 mg per kg body weight were, respectively, 70.01, 74.96, 77.51 and 85.01. The antinociceptive activity of the extract was much more potent than that of a standard antinociceptive drug aspirin, which when administered at doses of 200 and 400 mg per kg body weight, reduced the number of writhings by 37.48 and 59.97%, respectively. The antinociceptive activity of the extract was much more potent than that of a standard antinociceptive drug aspirin, which when administered at doses of 200 and 400 mg per kg body weight, reduced the number of writhings by 37.48 and 59.97%, respectively. The results are shown in Table 2. Similar to antihyperglycemic activity, the results of antinociceptive activity tests also validate the use of the stem in folk medicine of Bangladesh for treatment of pain.

The observed reduction of blood sugar by the extract can be attributed to any of several possible mechanisms or a combination of the mechanisms. Any bio-active compound or compounds present in the extract may lower blood sugar either by potentiating the pancreatic secretion of insulin or increasing the glucose uptake, as has been observed in studies with *Artemisia* extract or extract of *Ageratum conyzoides* L. (Asteraceae) (Farjou et al., 1987; Nyunai et al., 2009). Alternately, a compound or compounds may inhibit glucose absorption in gut, as observed with *Mangifera indica* L. (Anacardiaceae) stem-barks (Bhowmik et al., 2009). A further mechanism can possibly be increase of peripheral glucose consumption induced by the extract, as has been seen with ethanolic extract of *Sapindus trifoliatus* L. (Sapindaceae) (Sahoo et al., 2010). In either of these mechanisms or a combination of these mechanisms, the resultant effect will be reduction of sugar levels in the blood. Further experiments are necessary to elucidate the glucose lowering mechanism of the present extract.

Pain (analgesia) can be central or peripheral, and both central and peripheral analgesia can be detected with the test of acetic acid-induced gastric pain, followed by measurement of the number of writhings (Shanmugasundaram and Venkataraman, 2005), as has been done in the present study. Increased expression of prostaglandins [mainly prostacyclines (PGI2) and prostaglandin- (PG-E)] has been shown to be responsible for excitation of Adelta-nerve fibers, leading to the sensation of pain (Reynolds, 1982; Rang and Dale, 2003). As such, the antinociceptive activity exhibited by crude methanolic extract of the stems may be due to the extract’s ability to block any further expression of prostaglandins, which may be mediated through inhibition of cyclooxygenase and/or lipoxygenase activities. It is to be noted that a similar mechanism has been proposed for antinociceptive activity of *Ficus deltoidea* Jack (Moraceae) aqueous extract in acetic acid-induced gastric pain model (Sulaiman et al., 2008), and this may also be the mechanism operating in the present study.

Not much is known about the phytochemical constituents or pharmacological activities of *Mimosa pigra*. Triterpenoid saponins have been reported from the plant (Englert et al., 1995). Inhibition of growth of the microorganism, *Pseudomonas aeruginosa*, has also been reported for methanol and water extracts of the plant (Rosado-Vallado et al., 2000). As such, the results reported in the present study add more to the scientific literature on pharmacological activity studies of this plant or plant parts. The present study strongly suggests that...
more importance be given to folk medicinal uses on any given plant species, since the results obtained validate the folk medicinal practices.

Table 1: Effect of methanol extract of *Mimosa pigra* stems on blood glucose level in hyperglycemic mice following 120 minutes of glucose loading.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg body weight)</th>
<th>Blood glucose level (mmol/l)</th>
<th>% lowering of blood glucose level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Group 1)</td>
<td>10 ml</td>
<td>7.03 ± 0.77</td>
<td></td>
</tr>
<tr>
<td><em>Glibenclamide</em> (Group 2)</td>
<td>10 mg</td>
<td>3.07 ± 0.21</td>
<td>56.33*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 3)</td>
<td>50 mg</td>
<td>4.37 ± 0.34</td>
<td>37.84*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 4)</td>
<td>100 mg</td>
<td>4.23 ± 0.36</td>
<td>39.83*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 5)</td>
<td>200 mg</td>
<td>4.05 ± 0.31</td>
<td>42.39*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 6)</td>
<td>400 mg</td>
<td>3.48 ± 0.31</td>
<td>50.50*</td>
</tr>
</tbody>
</table>

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 *Mimosa pigra* stems in the acetic acid-induced gastric pain model mice.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg body weight)</th>
<th>Mean number of writhings</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Group 1)</td>
<td>10 ml</td>
<td>6.67 ± 0.56</td>
<td></td>
</tr>
<tr>
<td><em>Aspirin</em> (Group 2)</td>
<td>200 mg</td>
<td>4.17 ± 0.65</td>
<td>37.48*</td>
</tr>
<tr>
<td><em>Aspirin</em> (Group 3)</td>
<td>400 mg</td>
<td>2.67 ± 0.88</td>
<td>59.97*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 4)</td>
<td>50 mg</td>
<td>2.00 ± 0.63</td>
<td>70.01*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 5)</td>
<td>100 mg</td>
<td>1.67 ± 0.56</td>
<td>74.96*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 6)</td>
<td>200 mg</td>
<td>1.50 ± 0.43</td>
<td>77.51*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 7)</td>
<td>400 mg</td>
<td>1.10 ± 0.45</td>
<td>85.01*</td>
</tr>
</tbody>
</table>

All administrations (aspirin and extract) were made orally. Values represented as mean ± SEM, (n=6); *P < 0.05; significant compared to control.

References


