ORIGINAL ARTICLE

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


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ABSTRACT

The objective of the present study was to evaluate the antihyperglycemic and antinociceptive activity of methanolic extract of leaves of *Mimosa pigra*, a plant used by folk medicinal practitioners of Bangladesh for lowering of blood sugar in diabetic patients and for the treatment of pain. Antihyperglycemic activity tests were conducted in glucose-loaded Swiss albino mice. The extract at doses of 50, 100, 200 and 400 mg per kg body weight was observed to significantly and dose-dependently reduce the concentration of blood glucose levels in glucose-loaded mice. At the above four doses, the extract, respectively, lowered blood glucose levels by 32.75, 35.16, 47.59 and 56.82%. A standard antihyperglycemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight in mice, lowered blood glucose levels by 56.82% thus showing that the highest dose of the extract had equivalent potency to that of glibenclamide in reducing blood glucose levels, and so merits further potential for isolation and identification of responsible phytochemical constituents, which can possibly be used as novel antihyperglycemic drugs. Antinociceptive activity tests were done in gastric pain model mice where gastric pain was induced by intraperitoneal administration of acetic acid, and subsequently the number of gastric pain-induced writhings was counted. The extract was also observed to significantly and dose-dependently reduce the number of gastric writhings. At doses of 50, 100, 200 and 400 mg per kg body weight, the extract reduced the number of writhings, respectively, by 27.27, 33.27, 51.45 and 54.55%. In comparison, a standard antinociceptive drug, aspirin, reduced the number of writhings, respectively, by 27.27 and 36.36% when administered to mice. Thus dose for dose, the extract was more potent than aspirin in reducing pain. The results not only validates the folk medicinal use of this plant in reducing blood sugar and for alleviation of pain, but also suggests that the plant can be further explored for discovery of possible antihyperglycemic and pain-killing drugs.

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

Introduction

A number of Fabaceae family plants have been reported in the scientific literature for their antihyperglycemic and antinociceptive activities. To cite a few reports on antihyperglycemic activity, the total saponins from the plant *Entada phaseoloides* (L.) Merr. have been reported to exhibit antidiabetic activity in type 2 diabetic rats (Zheng et al., 2012). Antihyperglycemic effect has been reported of hydroethanolic extract of *Butea monosperma* (Lam.) Taub. bark in diabetic mice (Sharma and Garg, 2012). The hypoglycemic effects of an aqueous extract of *Bauhinia forficata* Link on the salivary glands of diabetic mice has been shown (Curcio et al., 2012). The hypoglycemic effect of *Lupinus mutabilis* Sweet has been demonstrated in healthy volunteers and subjects with dysglycemia (Fornasini et al., 2012).

Similarly, regarding antinociceptive activity, anti-inflammatory and analgesic effects of 6alpha, 7beta-dihydroxy-vouacapan-17beta-oic acid isolated from *Pterodon emarginatus* Vog. Fruits (Galcera et al., 2011). The analgesic and anti-inflammatory activity of ethanol extract of *Desmodium caudatum* (Thunb.) DC. has also been reported (Ma et al., 2011). Antinociceptive activity of the chloroform fraction of *Dioclea virgata* (Rich.) Amshoff has been observed in mice (Mota et al., 2011). Cassana furanoterpenes, isolated from *Caesalpinia*

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volkensii. H. root bark has been shown to possess antinociceptive and antiplasmodial activities (Ochieng’ et al., 2012). A preliminary study has also confirmed antinociceptive activity of Sesbania sesban L. wood extracts (Nirmal et al., 2012).

Mimosa pigra L. (Fabaceae, English: Giant Sensitive Tree, Bengali: Lojjaboti) is commonly found in Bangladesh. It is a leguminous shrub, which can reach up to 6 meters in height. Leaves and stems of this plant are commonly prescribed by the folk medicinal practitioners (Kavirajes) of Bangladesh for lowering of blood sugar in diabetic patients and for alleviation of pain. We had been conducting ethnomedicinal surveys within Bangladesh for the last few years to document the various plant species used for treatment of a variety of ailments (Rahmatullah et al., 2009a-c; Rahmatullah et al., 2010a-g; Rahmatullah et al., 2011a,b; Rahmatullah et al., 2012a-d). A number of these plant species, particularly those that are used in the folk medicinal system for treatment of diabetes and pain, have been further screened in our laboratory for evaluation of their antihyperglycemic, antinociceptive and cytotoxic potentials (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; Hossan et al., 2011; Jahan et al., 2011; Rahman et al., 2011; Sutradhar et al., 2011). The objective of the present study was to determine whether methanolic extract of leaves of Mimosa pigra possess antihyperglycemic and antinociceptive activities, and thus validate their folk medicinal uses. In a parallel paper, we will also be describing antihyperglycemic and antinociceptive activity studies with methanolic extract of Mimosa pigra stems. This plant was selected more so because it is a Fabaceae family plant, and a number of plants belonging to this family has been shown to demonstrate antihyperglycemic and antinociceptive potential, as described above.

Materials and Methods

Leaves of Mimosa pigra were collected from Dhaka district, Bangladesh during March, 2011. The plant was taxonomically identified at the Bangladesh National Herbarium at Dhaka. The sliced and air-dried leaves of Mimosa pigra were grounded into a fine powder and 100g of the powder was extracted with methanol (1:5, w/v) for 48 hours. The extract was evaporated to dryness. The final weight of the extract was 5.80g.

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 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 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 leaves 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 leaves 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,
Groups 4-7 were administered methanolic leaf 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 methanolic extract of *Mimosa pigra* leaves prior to glucose loading was found to significantly and dose-dependently reduce blood sugar levels in glucose-loaded mice in oral glucose tolerance tests. At extract doses of 50, 100, 200 and 400 mg per kg body weight, the respective percentage lowering of blood sugar levels were 32.75, 35.16, 47.59 and 56.82, as compared to control vehicle only administered animals. A standard antihyperglycemic drug, glibenclamide, when administered to mice at a dose of 10 mg per kg body weight reduced blood sugar level by 56.82%. Thus the highest dose of the extract was comparable to that of glibenclamide and the results indicate that the extract possess significant antihyperglycemic activity. The results are shown in Table 1. The severe or irreversible adverse effects of glibenclamide, which may give rise to further complications, include thrombocytopenia, cholestatic jaundice, aplastic anemia, hemolytic anemia, leukopenia, agranulocytosis, and pancytopenia. Thus newer antihyperglycemic drugs need to be discovered, which may minimize or will not have any adverse effects on the body as currently observed with many available anti-diabetic drugs. As such, the leaves of *Mimosa pigra* can be potentially useful in the discovery of newer and more efficacious antidiabetic drugs from phytochemical constituents present in the leaves of this plant. The observed results suggest more intensive studies on leaf extract of this plant because of its strong antidiabetic potential.

The observed reduction of blood sugar by the extract in glucose-loaded mice 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 *Artemesia* extract and extract of *Ageratum conyzoides* L. (Asteraceae), respectively (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.

In intraperitoneally-administered acetic acid-induced gastric pain model in mice, the number of writhings as a result of the gastric pain was also observed to be significantly and dose-dependently reduced when the extract was orally administered prior to acetic acid injection. At extract doses of 50, 100, 200 and 400 mg per kg body weight, the percent reductions in the number of writhings were, respectively, 27.27, 33.27, 51.45, and 54.55. The results are shown in Table 2. The results compare favorably with that of a standard antinociceptive drug, aspirin, which when orally administered at doses of 200 and 400 mg per kg body weight, reduced the number of writhings by 27.27 and 36.36%, respectively. Thus dose for dose, the extract possessed greater antinociceptive activity than aspirin. The results from this study also not only validates the folk medicinal use of the plant for treatment of pain, but also strongly suggests that the extract needs to be further studied towards possible discovery of novel pain-killing drugs. It may be noted that any reports on the total phytochemical constituents of this plant are lacking in the scientific literature, and this gap needs to be addressed.

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 prostaglandins- (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 leaves 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. However, further studies are needed to validate this hypothesis.

To summarize, we have observed strong antihyperglycemic and antinociceptive activities in both leaves (present paper) and stems (accompanying paper) of *Mimosa pigra*. Although this plant is usually considered a serious invasive weed species, it is very much possible that novel antidiabetic and antinociceptive compounds may be isolated from the plant and it may be necessary to cultivate this plant instead of destroying it as an invasive weed species. Furthermore, more efficacious antihyperglycemic and antinociceptive compounds are necessary and the plant may well form a good source of such compounds.

**Table 1:** Effect of methanol extract of *Mimosa pigra* leaves 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>7.48 ± 0.69</td>
<td>-</td>
</tr>
<tr>
<td>Glibenclamide (Group 2)</td>
<td>10 mg</td>
<td>3.23 ± 0.41</td>
<td>56.82*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 3)</td>
<td>50 mg</td>
<td>5.03 ± 1.07</td>
<td>32.75*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 4)</td>
<td>100 mg</td>
<td>4.85 ± 0.40</td>
<td>35.16*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 5)</td>
<td>200 mg</td>
<td>3.92 ± 0.14</td>
<td>47.59*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 6)</td>
<td>400 mg</td>
<td>3.23 ± 0.18</td>
<td>56.82*</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* leaves 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>5.50 ± 0.34</td>
<td>-</td>
</tr>
<tr>
<td>Aspirin (Group 2)</td>
<td>200 mg</td>
<td>4.00 ± 0.63</td>
<td>27.27*</td>
</tr>
<tr>
<td>Aspirin (Group 3)</td>
<td>400 mg</td>
<td>3.50 ± 0.76</td>
<td>36.36*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 4)</td>
<td>50 mg</td>
<td>4.00 ± 0.63</td>
<td>27.27*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 5)</td>
<td>100 mg</td>
<td>3.67 ± 0.67</td>
<td>33.27*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 6)</td>
<td>200 mg</td>
<td>2.67 ± 0.56</td>
<td>51.45*</td>
</tr>
<tr>
<td><em>Mimosa pigra</em> (Group 7)</td>
<td>400 mg</td>
<td>2.50 ± 0.88</td>
<td>54.55*</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**


