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Antinociceptive activity evaluation of an Indonesian herbal product Ulu Hati in Swiss albino mice

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ABSTRACT

The antinociceptive activity of an Indonesian herbal product named Ulu Hati was evaluated in Swiss albino mice in acetic acid-induced abdominal pain model. The product, when administered to mice at doses of 25, 50, 100 and 200 mg per kg body weight, reduced the number of acetic acid-induced gastric constrictions by 10.0, 23.4, 46.6, and 50.0%, respectively. The results were statistically significant at the two higher doses of the product when compared to control animals. In comparison, a standard antinociceptive drug, aspirin, when administered at doses of 200 and 400 mg per kg body weight, reduced the number of gastric constrictions in mice, respectively, by 33.4 and 66.6%. The results suggest that the herbal product is comparable to aspirin in alleviation of pain and validates the use of this product for colic pain occurring during gastritis.

Key words: Antinociceptive, Indonesia, herbal, pain, Ulu Hati

Introduction

Gastritis is frequently accompanied by colic (abdominal pain) in the vast majority of patients. Although allopathic drugs are available for treatment of gastritis, it is desirable for the poorer segments of the population to get cheaper herbal drugs, which may be not only more affordable but also more available particularly in rural areas of developing countries, which lack modern doctors and clinics. Moreover, an herbal drug that proves useful in the alleviation of colic may also prove useful in the alleviation of other types of chronic or acute pain and can be used as such for other types of pain relief.

We had been conducting ethnomedicinal surveys among the folk and tribal medicinal practitioners of Bangladesh for the last several years (Rahmatullah et al., 2009a-c; Rahmatullah et al., 2010a-g; Rahmatullah et al., 2011a,b; Rahmatullah et al., 2012a-d). From the information obtained from the traditional healers, further studies are conducted on selected floral species towards evaluation of their antinociceptive, antihyperglycemic, and cytotoxic potential (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; Ahmed et al., 2012; Arefin et al., 2012; Haque et al., 2012; Sathi et al., 2012). Towards an extension of this research, we have recently also started conducting studies on herbal products of other countries, particularly to evaluate their claimed antinociceptive and antihyperglycemic potential. Ulu Hati is an herbal product of Indonesia and is used to obtain relief from gastritis with the symptoms of nausea, upset, puffed-up stomach and colic. It was the objective of the present study to evaluate the antinociceptive potential of Ulu Hati in acetic acid-induced gastric pain model in Swiss albino mice.

Materials and Methods

Ulu Hati was obtained from an herbal shop in Kuala Lumpur, Malaysia in 2012. The product was sold in 7g sealed packets, the contents of which were to be used for a single dosage. The front side of the packet (Fig 1) bore the words Jamu Obat Alami, Jamu Obat Alami, ULU HATI, Halal – 52AP. The address of the manufacturer was given as Pabrik Jamu, AIR MANCUR®, Wonogiri-SOLO-Indonesia. The reverse side of the product package bore the word “Halal”. The product was yellow in color and consisted of several small pieces of dried herbs and plant material. The herb under study was used in the concentration of 25, 50, 100 and 200 mg per kg body weight and aspirin as standard was used at the concentration of 200 and 400 mg per kg body weight to evaluate the antinociceptive activity of the herb.

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Terminal ileum method

The antinociceptive activity of Ulu Hati was evaluated in the acetic acid-induced gastric pain model in Swiss albino mice. This method is widely accepted and is known to produce reproducible results. In the study, male Swiss albino mice (35-45 g body weight) were used. The animals were obtained from the animal house of the National Institute of Health, Bangladesh. Each mouse was randomly allocated to one of five experimental groups of 10 mice each. The control group received normal saline intraperitoneally (i.p.) while the other experimental groups received Ulu Hati at doses of 25, 50, 100 and 200 mg per kg body weight. A separate group of animals received aspirin at doses of 200 and 400 mg per kg body weight. All treatments were given orally to the experimental groups. The animals were fasted for 18 hours but were allowed free access to water. The animals were divided into five groups of 10 animals each and treated with the following:

1. Control group: Saline
2. Group 1: Saline + Ulu Hati 25 mg/kg
3. Group 2: Saline + Ulu Hati 50 mg/kg
4. Group 3: Saline + Ulu Hati 100 mg/kg
5. Group 4: Saline + Ulu Hati 200 mg/kg
6. Group 5: Saline + Aspirin 200 mg/kg
7. Group 6: Saline + Aspirin 400 mg/kg

The experiment was started by an intraperitoneal injection of 0.6% acetic acid solution (0.1 ml per 100 g body weight) into the peritoneal cavity. After 15 minutes, the number of gastric constrictions was counted. The number of constrictions was recorded as a measure of nociception.
Jamu Ulu Hati 52AP (Lambung/Maag), Antacids, For Men and Women” (Fig 2). The composition given on the reverse side of the packet listed the following ingredients – Curcumae domesticae Rhizoma 30%, Kaempferiae Rhizome 20%, Zingiberis Rhizoma 25%, and Corrigents 25%. Indications given on the reverse side of the packet mentioned “Prevent and cure gastritis with the symptoms of nausea, upset, puffed-up stomach and colic”. Directions given on the reverse side of the packet mentioned “Mix the contents of 1 packet with half a glass (100 ml) of boiling water. Take 1 packet twice daily”. The contents of each packet were weighed and found to be 7g. Further recommendations made on the reverse side of the packet said “Avoid highly seasoned, sourish, body-healing food (sheep flesh), ice, coffee and alcoholic drinks”. Storage was recommended in a dry place.

Experimental dosages for mice experiments were determined on the basis of the packet content of 7g per human being, the average weight of a human being taken as 70 kg, i.e. 1g per 10 kg body weight, or 100 mg per kg body weight. The various doses for experimental purposes were fixed based on this afore-mentioned calculation as 25, 50, 100 and 200 mg per kg body weight of mice. Stock solution of Ulu Hati was made by suspending 1g of packet contents in 10 ml distilled water.

Chemicals:

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

Animals:

In the present study, Swiss albino mice (male), which weighed between 22-25g 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.

Antinociceptive activity:

Antinociceptive activity of Ulu Hati 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 Ulu Hati at doses of 25, 50, 100 and 200 mg per kg body weight, respectively. All mice were individually weighed and dose determined on the basis of individual weight. 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 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

The herbal product Ulu Hati, when administered at doses of 25, 50, 100 and 200 mg per kg body weight demonstrated dose-dependent reductions in the number of abdominal constrictions in mice induced by intraperitoneal administration of acetic acid. The results were statistically significant at the two higher doses of 100 and 200 mg per kg body weight. At the lower doses of 25 and 50 mg per kg body weight, the number of abdominal constrictions (writhings) was less than control animals, but the results were not statistically significant. At the afore-mentioned four doses, the percent reductions in the number of constrictions were, respectively, 10.0, 23.4, 46.6, and 50.0. A standard antinociceptive drug, aspirin, by comparison, when administered at doses of 200 and 400 mg per kg body weight, reduced the number of abdominal constrictions in mice, respectively, by 33.4 and 66.6%. The results demonstrate that Ulu Hati, at least at the higher two doses is better than aspirin (200 mg per kg body weight) in terms of alleviation of gastric pain induced by acetic acid injection. The results are shown in Table 1.
Table 1: Antinociceptive effect of Ulu Hati 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>5.00 ± 0.26</td>
<td>-</td>
</tr>
<tr>
<td>Aspirin (Group 2)</td>
<td>200 mg</td>
<td>3.33 ± 0.56</td>
<td>33.4*</td>
</tr>
<tr>
<td>Aspirin (Group 3)</td>
<td>400 mg</td>
<td>1.67 ± 0.76</td>
<td>66.6*</td>
</tr>
<tr>
<td>Ulu Hati (Group 4)</td>
<td>25 mg</td>
<td>4.50 ± 0.56</td>
<td>10.0</td>
</tr>
<tr>
<td>Ulu Hati (Group 5)</td>
<td>50 mg</td>
<td>3.83 ± 0.79</td>
<td>23.4</td>
</tr>
<tr>
<td>Ulu Hati (Group 6)</td>
<td>100 mg</td>
<td>2.67 ± 0.33</td>
<td>46.6*</td>
</tr>
<tr>
<td>Ulu Hati (Group 7)</td>
<td>200 mg</td>
<td>2.50 ± 0.56</td>
<td>50.0*</td>
</tr>
</tbody>
</table>

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

Fig. 1: Front side of Ulu Hati Packet

Fig. 2: Reverse side of Ulu Hati Packet
The use of at least three of the plant parts used in this herbal formulation has been scientifically validated. The analgesic and anti-pyretic activities of *Curcuma longa* (synonym: *Curcuma domestica*) rhizome extracts has been shown in rats (Neha et al., 2009). Methanolic extract of *Kaempferia rotunda* rhizomes reportedly demonstrated antinociceptive activity in rodent model (Sultana et al., 2012). The anti-inflammatory and analgesic properties of *Zingiber officinale* rhizome extract has also been shown (Raji et al., 2002). Rhizomes of *Zingiber officinale* are also in use in folk medicines of Bangladesh to alleviate stomach discomforts. Thus the plants, used in combination, can prove effective in relief of colic, which is also borne out by scientific studies on their analgesic properties.

Financial disclosure:

Authors of this study have no financial interest in any of the product(s) or manufacturer(s) mentioned in this article.

References


