ORIGINAL ARTICLE

Indonesian Jamu medicines – antinociceptive activity evaluation of two herbal preparations Anrat and Donrat

Budrun Nahar, Md. Tanvir Morshed, Alok Kumar Paul, Anjila Tabassum Zabir, Ishtiaq Ahmed, Mohammed Rahmatullah

Faculty of Life Sciences, University of Development Alternative, Dhanmondi, Dhaka-1209, Bangladesh.

ABSTRACT

The antinociceptive activities of two Indonesian Jamu herbal formulations, namely Anrat and Donrat were evaluated in acetic acid-induced gastric pain model in Swiss albino mice. At doses of 50, 100 and 200 mg per kg body weight, the herbal formulation Anrat dose-dependently and significantly reduced the number of abdominal constrictions induced by intraperitoneal injection of acetic acid in mice by 43.7, 46.9, and 53.1%, respectively, compared to control animals. Anrat, when administered at a dose of 25 mg per kg body weight to mice led to reductions in the number of abdominal constrictions, but the results were not statistically significant. The other herbal formulation, Donrat, when administered at a dose of 25 mg per kg body weight reduced the number of abdominal constrictions in mice, but the results were not statistically significant. When administered at doses of 50, 100, and 200 mg per kg body weight, Donrat dose-dependently and significantly reduced the number of abdominal concentrations in mice by 56.2, 59.4, and 65.6%, respectively. Thus, dose for dose, Donrat was more effective than Anrat in alleviation of pain. By comparison, a standard antinociceptive drug, aspirin, when administered at doses of 200 and 400 mg per kg body weight in mice, reduced the number of gastric constrictions in mice by 40.6 and 59.4%, respectively. The results suggest that Donrat is more effective than aspirin in alleviating pain, while Anrat can be said to have comparable effects to that of aspirin. Taken together, the results point out the effectiveness of these two Indonesian traditional (Jamu) herbal preparations in pain relief and validate the folk medicinal uses of these preparations for treatment of pain.

Key words: Antinociceptive, Indonesia, pain, Anrat, Donrat

Introduction

Pain has been defined by the International Association for the study of pain as ‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage’. Pain can arise from a variety of causes, resulting in discomfort and even restriction of movement for individuals suffering from the condition. Under certain conditions, pain can become chronic, as for example in individuals suffering from rheumatoid arthritis, gout, or certain forms of cancer. There are a number of ‘over the counter’ (OTC) drugs against pain, like aspirin or paracetamol, which can provide temporary relief. However, these drugs suffer from the problems of either causing gastric ulceration or causing hepatotoxicity from prolonged use or over-dosage. Other opioid drugs can be addictive and cause more harm than good in the long run. As a result, a better pain killing drug or drugs is essential, which can alleviate pain with less or no adverse side-effects.

Indonesian traditional medicine (Jamu) is used both inside and outside Indonesia for treatment of various ailments. These medicines mostly consist of herbal formulations and have been in use within Indonesia for centuries. It may be noted that Indonesia, possibly after Brazil, contains the most floral species in the world, many of which are used in Jamu medicine. This diversity of floral species have spurred interest among scientists towards discovery of newer drugs from these species. Over the years, many of these formulations have been claimed to be effective in their uses, although full scientific studies are yet to be carried out on a number of these herbal formulations.

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 potential. Anrat and Donrat are herbal products of Indonesia and are used, respectively, to obtain relief from stiff joints and arthritis, and to treat pain and to treat red and hot flashes due to excess uric acid, which mainly attacks the joints of the foot. As such, the treatment with either of these two Indonesian herbal products can result in relief from pain occurring during arthritis or gout. It was the objective of the present study to evaluate the antinociceptive potential of Anrat and Donrat in acetic acid-induced gastric pain model in Swiss albino mice. Scientific validation of these two herbal formulations as to their effectiveness in treatment of pain occurring due to arthritis or gout (both pains being chronic), can be beneficial to millions of people throughout the world affected by these two debilitating diseases.

Materials and Methods

Anrat and Donrat were obtained from an herbal shop in Kuala Lumpur, Malaysia in 2012. Anrat was sold in 7g sealed packets, the contents of which were to be used for two doses on a single day. The front side of the packet (Fig 1) bore the words Jamu Tradisional Jaya Asli, made from nutritious plants and Anrat. The address of the manufacturer was given on the reverse side as Kopja Aneka Sari Unit II Sembung Jaya, PJ. Jaya Asli, Pom Tr No. 053.248 511, Cilacap, Indonesia. The composition given on the reverse side of the packet (Fig 2) listed the following ingredients – Zingiberis Rhizoma, 1.05g; Andrographi dis Follium, 1.40g; Kaempferia Rhizoma, 1.40g; Curcuma domestica Rhizoma, 1.05g; Myristicae Semen, 1.40g; and Retrotractil fructus, 0.70g. Indications given on packet mentioned usability to help relieve stiff joints and arthritis. Directions given on the reverse side of the packet mentioned the packet contents to be brewed with hot water to approximately 100 ml and which is to be taken in two doses on a single day. The contents of each packet of Anrat were weighed and found to be 7g. Storage was recommended in a dry place.

Donrat was sold in 7g sealed packets, the contents of which were to be used for two doses on a single day for treatment and one dose a day for prevention, the contents to be taken after meals. The front side of the packet (Fig 3) bore the words Jamu Tradisional Donrat (Asam Urat). The address of the manufacturer was given on the front side as PJ. Cipta Rasa, Cilacap, Indonesia. The composition given on the reverse side of the packet (Fig 4) listed the following ingredients – Curcumae Rhizoma, 15%; Zingiberis Rhizoma, 25%; Carryophylli Flos, 15%; Gandarusae Follium, 25%; and Andrographidis Follium, 20%. Indications given on packet mentioned usability to treat pain, swollen, red and hot flashes due to excess uric acid which mainly attacks the joints of the foot. It was also suggested on the packet to avoid all types of uric acid foods such as organ meats and drinks that contain alcohol. The contents of each packet of Donrat were weighed and found to be 7g.

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 aforementioned calculation as 25, 50, 100 and 200 mg per kg body weight of mice. Stock solutions of Anrat and Donrat were 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 Anrat and Donrat was examined using previously described procedures (Shanmugasundaram and Venkataraman, 2005). Briefly, mice were divided into eleven 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 Anrat at doses of 25, 50, 100 and 200 mg per kg body weight, respectively. Groups 8-11 were administered Donrat 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 bioavailability 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**

At doses of 50, 100 and 200 mg per kg body weight, the herbal formulation Anrat dose-dependently and significantly reduced the number of abdominal constrictions induced by intraperitoneal injection of acetic acid in mice by 43.7, 46.9, and 53.1%, respectively, compared to control animals. Anrat, when administered at a dose of 25 mg per kg body weight to mice led to reductions in the number of abdominal constrictions, but the results were not statistically significant. The other herbal formulation, Donrat, when administered at a dose of 25 mg per kg body weight reduced the number of abdominal constrictions in mice, but the results were not statistically significant. When administered at doses of 50, 100, and 200 mg per kg body weight, Donrat dose-dependently and significantly reduced the number of abdominal concentrations in mice by 56.2, 59.4, and 65.6%, respectively. Thus, dose for dose, Donrat was more effective than Anrat in alleviation of pain. By comparison, a standard antinociceptive drug, aspirin, when administered at doses of 200 and 400 mg per kg body weight in mice, reduced the number of gastric constrictions in mice by 40.6 and 59.4%, respectively. The results are shown in Table 1. The results suggest that Donrat is more effective than aspirin in alleviating pain, while Anrat can be said to have comparable effects to that of aspirin.

The use of several plant parts used in this herbal formulation as analgesic agents 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). The anti-inflammatory and analgesic properties of *Zingiber officinale* rhizome extract has also been shown (Raji et al., 2002). Notably, both plants are used in both Anrat and Donrat herbal preparations. Andrographolide and 14-deoxy-11,12-didehydroandrographolide are two major constituents in *Andrographis paniculata*, a component of Anrat. Both constituents reportedly demonstrated analgesic and anti-inflammatory effects in experimental animals (Suebsasana et al., 2009), thus showing the scientific validation of use of this herbal preparation to help relieve stiff joints and arthritis. Another constituent plant of Anrat, namely, *Kaempferia rotunda*, has also been shown to give antinociceptive activity in gastric pain model mice (Sultana et al., 2012). Thus of the individual constituent plants of both Anrat and Donrat, if not all, then at least several have been shown to have analgesic activities, and so synergistically can produce a strong pain-relieving effect.

**Table 1:** Antinociceptive effect of Anrat and Donrat 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 abdominal constrictions</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Group 1)</td>
<td>10 ml</td>
<td>6.4 ± 0.75</td>
<td>-</td>
</tr>
<tr>
<td>Aspirin (Group 2)</td>
<td>200 mg</td>
<td>3.8 ± 0.66</td>
<td>40.6*</td>
</tr>
<tr>
<td>Aspirin (Group 3)</td>
<td>400 mg</td>
<td>2.6 ± 1.08</td>
<td>59.4*</td>
</tr>
<tr>
<td>Anrat (Group 4)</td>
<td>25 mg</td>
<td>4.4 ± 0.93</td>
<td>31.2</td>
</tr>
<tr>
<td>Anrat (Group 5)</td>
<td>50 mg</td>
<td>3.6 ± 0.40</td>
<td>43.3*</td>
</tr>
<tr>
<td>Anrat (Group 6)</td>
<td>100 mg</td>
<td>3.4 ± 0.81</td>
<td>46.9*</td>
</tr>
<tr>
<td>Anrat (Group 7)</td>
<td>200 mg</td>
<td>3.0 ± 0.58</td>
<td>53.1*</td>
</tr>
<tr>
<td>Donrat (Group 8)</td>
<td>25 mg</td>
<td>4.2 ± 1.02</td>
<td>34.4</td>
</tr>
<tr>
<td>Donrat (Group 9)</td>
<td>50 mg</td>
<td>2.8 ± 1.16</td>
<td>56.2*</td>
</tr>
<tr>
<td>Donrat (Group 10)</td>
<td>100 mg</td>
<td>2.6 ± 0.51</td>
<td>59.4*</td>
</tr>
<tr>
<td>Donrat (Group 11)</td>
<td>200 mg</td>
<td>2.2 ± 0.49</td>
<td>65.6*</td>
</tr>
</tbody>
</table>

All administrations (aspirin, Anrat and Donrat) were made orally. Values represented as mean ± SEM, (n=5); *P* < 0.05; significant compared to control.
Fig. 1: Front side of Anrat packet.

Fig. 2: Reverse side of Anrat packet.

Fig. 3: Front side of Donrat packet.
The results obtained in the present study validate the traditional medicinal use of Anrat and Donrat in relieving pain. Herbal medicines can prove extremely useful for they are cheaper and more readily available than many allopathic drugs. If toxicological studies can prove them safe for using, they may prove a good alternate source of pain-killing medicines versus existing allopathic drugs.

Financial disclosure:

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

References


