Analgesic Effect of the Alcoholic Extract from the Fruits of *Morinda citrifolia*

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**Abstract**

The alcoholic extract from the fruits of *Morinda citrifolia* (noni) was evaluated for analgesic effect in mice using the acetic acid-induced writhing test. The extract was administered by i.p. injection in doses of 1, 2, 3 and 4 g of dried plant material kg\(^{-1}\) of animal body weight, 15 min before i.p. injection of acetic acid (0.75%). Morphine sulfate (1.5 mg kg\(^{-1}\), i.p.) was used as the reference drug. Control animals received i.p. injections of 0.9% NaCl solution, instead of the extract. In control mice, the number of writhes during the 20 min test period was 43.0 ± 1.4 (mean ± S.E.M., n=6). The extracts produced a significant dose-dependent inhibition of acetic acid-induced abdominal constriction. The percentage inhibition was 4.4 ± 4.5, 21.2 ± 11.2, 71.4 ± 5.0, 93.1 ± 1.7 (mean ± S.E.M., n=6) at the doses of 1, 2, 3 and 4 g kg\(^{-1}\) respectively, compared to control animals. The inhibitory effect of the 4 g kg\(^{-1}\) dose of extract was similar to that produced by morphine in a dose of 1.5 mg kg\(^{-1}\). The antinociceptive effect in writhing test was statistically significant (p<0.001) for 15 min until 5 hr of administration. The data obtained suggest that the alcoholic extraction from the fruits of *Morinda citrifolia* appears to have analgesic effect. Further studies are necessary for the identification of the active principles and more detailed elucidation of its mechanism of action is required.

**INTRODUCTION**

*Morinda citrifolia* (Rubiaceae) commonly known as “noni”, has been used for more than 1,000 years in traditional healing practices of native Hawaiians and other Pacific islanders and Asian populations. The stem, bark, root, leaf, and fruit of the plant have been used traditionally as a folk remedy of many diseases, including diabetes, hypertension, and cancer (Abbott and Shimazu, 1985). In the earlier pharmacological studies, the juice of noni fruits was found to prolong the life of mice implanted Lewis lung carcinoma (Hirazumi et al., 1994). The chemioimmunotherapy of the fruit juice of noni containing a polysaccharide-rich substance with conventional chemotherapeutic agents has been reported to increase the life span as well as cure rates in tumor-bearing animals (Hirazumi and Furusawa, 1999, 1996). Two novel glycosides extracted from the juice of noni fruits were found to inhibit AP-1 transactivation and cell transformation in the mouse epidermal JB6 cell line (Liu et al., 2001). The extracts of noni roots have been found to posses a significant, dose-dependent, central analgesic activity in the treated mice (Younos et al., 1990). In Thai traditional medicine, the fruits of *Morinda citrifolia* have been used as analgesic agent for the alleviation of pain in rheumatoid arthritis patients. However, there are no known scientific information or data to validate the claim by the traditional medicine practitioners about the effectiveness of this plant. This study, therefore, intends to screen the analgesic activity of *Morinda citrifolia* by studying the effect of the alcoholic extract from fruits of this plant on nociception induced by acetic acid.
MATERIALS AND METHODS

Preparation of Plant Extract

Yellowish-white noni fruits used in the present study were collected from Saraburi province, in April 2002. Fresh fruits were dried and pulverized yielding 14.51% w/w. For the alcoholic extract preparation, 50 g of dried powdered fruits were macerated with 500 ml of 95% methanol for 2 days. The alcoholic extract was filtered and evaporated to dryness in an oven set at 40°C. The yield was 8.42% (w/w). The dried extract was dissolved and made up to the appropriate volume with distilled water before intraperitoneal (i.p.) administration. The extract solution was injected in a volume of 10 ml kg⁻¹ of animal. All doses were expressed in term of dried powdered fruit (mg kg⁻¹ body weight).

Drugs and Reagents

The drug used was morphine sulphate obtained from Merck, AG, Darmstadt, Germany. Sodium chloride, acetic acid and methanol (Sigma, St. Louis, USA) used were analytical grade and purchased locally.

Animals

Male Swiss mice weighting 30-35 g were used for the analgesic test. They were obtained from National Laboratory Animal Centre, Mahidol University, Thailand. The animals were housed at 22 ± 2°C temperature under 12-h light/12-h dark cycle and with access to food and water ad libitum. Before experiments began, the animals were deprived of food for 24 h and allowed to adapt to the laboratory for at least 2 h before testing. Each animal was used for one experiment only. The experimental protocol was approved by the Institutional Animal Ethics Committee.

Acetic Acid-Induced Abdominal Constriction (Writhing) Test in Mice

The test was carried out by using the classical method described previously (Jain and Kulkarni, 1999; Koster et al., 1959). Prior to testing each animal received the alcoholic extract of *Morinda citrifolia* at dose of 1, 2, 3 and 4 g kg⁻¹, i.p. Control animals received normal saline (10 ml kg⁻¹, i.p.) instead of the extract. Morphine (as sulphate, 1.5 mg kg⁻¹, i.p.) was used as a reference analgesic substance. Fifteen minutes after treatment, the mice were injected with 0.75% (v/v) acetic acid in normal saline (10 ml kg⁻¹, i.p.) and the incidences of writhes (arching of back, development of tension in abdominal muscles, elongation of the body in hind limb) were recorded for a period of 20 min. For evaluation of time-course analgesic effect, the alcoholic extract of *Morinda citrifolia* (4 g kg⁻¹, i.p.) was injected 15, 60, 120, 180, 300 and 480 min before experimentation.

Statistical Analysis

Number of writhes were expressed as mean ± S.E.M. and % protection (i.e., compound producing 100% protection prevents acetic acid-induced abdominal constriction) which was calculated using the formula

\[
\text{% Protection} = 100 - \left( \frac{\text{number of writhes in drug treated}}{\text{number of writhes in control}} \right) \times 100
\]

Statistical analysis of the data was done using Student’s t-test and the results were considered significant when p<0.05.

RESULTS AND DISCUSSION

In accordance with the medical uses of *Morinda citrifolia* fruits, the present study was carried out to evaluate the analgesic activity of the alcoholic extract of the fruits of this plant. The major finding of the current study was the demonstration, for the first time to our knowledge, that the alcoholic extract from the fruits of *Morinda citrifolia,*
administered systemically to mice, produced pronounced and dose-related antinociception when assessed in chemical model of nociception, namely acetic acid-induced writhing response (Table 1). This method has been used as model of chemonociception and validated for screening of virtually all classes of analgesics activity regardless of the central or peripheral causes by irritation of the tissue and stimulation of the sensory receptors (Jain and Kulkarni, 1999; Koster et al., 1959). In control mice, the number of writh during the 20 min test period was 43.0 ± 1.4 (n=6). Treatment of animals with *Morinda citrifolia* alcoholic extract (1-4 g kg\(^{-1}\), i.p.) decreased the number of contortions and stretchings of mice induced by acetic acid compared to the control group and produced a dose dependent inhibition. The extract at doses of 3 and 4 mg kg\(^{-1}\), i.p. produced a significant (p<0.001) decrease in the number of writhing response. Morphine sulfate induced a significant reduction of the noted parameter. The analgesic effect of the 4 g kg\(^{-1}\) dose of extract was similar to that produced by morphine in a dose of 1.5 mg kg\(^{-1}\) (93.1 ± 1.7% and 96.7 ± 1.6%, respectively) and it was statistically significant (p<0.001) for 15 min until 5 hr of pretreatment time (Fig. 1). Administration of the alcoholic extract of *Morinda citrifolia* fruits at doses of 1, 2, 3 and 4 g kg\(^{-1}\) did not produce mortality in mice.

**CONCLUSION**

The present results indicate that the alcoholic extract of the fruits and the aqueous extract of roots (Younos et al., 1990) of *Morinda citrifolia* appear to have analgesic effects, since this significantly reduced the contortions induced by acetic acid in the writhing test. This finding validated the traditional analgesic properties of this plant. The extract will, therefore, be of potential benefit in the management of pain, although further studies are necessary for the identification of the active principles and the elucidation of its mechanism of action.

**ACKNOWLEDGEMENTS**

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**Literature Cited**


Tables

Table 1. Effect of the alcoholic extract of *Morinda citrifolia* on acetic acid-induced writhing in mice.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg kg⁻¹, i.p.)</th>
<th>No. of writhes²</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (NSS, 10 ml kg⁻¹)</td>
<td>-</td>
<td>43.0 ± 1.4</td>
<td>-</td>
</tr>
<tr>
<td>Morphine sulphate</td>
<td>1.5</td>
<td>1.3 ± 0.6*</td>
<td>96.7 ± 1.6</td>
</tr>
<tr>
<td><em>Morinda citrifolia</em> extract</td>
<td>1,000</td>
<td>41.0 ± 1.9</td>
<td>4.4 ± 4.5</td>
</tr>
<tr>
<td></td>
<td>2,000</td>
<td>33.5 ± 4.6</td>
<td>21.2 ± 11.2</td>
</tr>
<tr>
<td></td>
<td>3,000</td>
<td>12.3 ± 2.2*</td>
<td>71.4 ± 5.0</td>
</tr>
<tr>
<td></td>
<td>4,000</td>
<td>3.0 ± 0.7*</td>
<td>93.1 ± 1.7</td>
</tr>
</tbody>
</table>

¹ Fifteen minutes after treatment, mice were injected i.p. with 0.75% (v/v) acetic acid (10 ml kg⁻¹); the number of induced writhings was counted for 20 min.
² Values are mean ± S.E.M. (n=6)
³ p<0.001 significantly different from control, Student’s t-test

Figures

Fig. 1. Time-course analgesic effect of *Morinda citrifolia* (4 mg kg⁻¹, i.p.) in acetic acid-induced abdominal constrictions (writhes) in mice. Vertical lines show S.E.M. (n=6). *p<0.001 as compared to 0 min.