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A water extract of leaves and stems of *Psychotria sarmentosa* has analgesic and antihyperalgesic activity in rats

W.D. Ratnasooriya and M.G. Dharmasiri

Department of Zoology, University of Colombo, Colombo 3, Sri Lanka

Requests for reprints to Professor W.D. Ratnasooriya, Department of Zoology, University of Colombo, Colombo 03, Sri Lanka

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Abstract: An unboiled water extract (UBE) of stems and leaves of *Psychotria sarmentosa* Blume (Family: Rubiaceae) is drunk by some men in Sri Lanka after being physically assaulted, indicating that it may have potent analgesic and/or anti-inflammatory activity. However, these activities are not described in either the Sri Lankan Ayurveda Pharmacopoeia or the Deshiya Chikithsa system of medicine practised in Sri Lanka. The aim of this study was to investigate whether an UBE of these parts of *P. sarmentosa* has such activities. Different doses of the UBE (7.5, 15.0 and 22.5 ml/kg) or vehicle were administered orally to rats. 1 and 3 h later, the analgesic potential was determined using hot plate and tail flick tests. In another set of rats, the highest dose of UBE was orally administered, and paw oedema induced with 1% carrageenan. Anti-inflammatory activity (up to 4 h) and antihyperalgesic activity (at 1 h) were determined (by the hot plate technique). All the doses of UBE were well tolerated and the highest had potent analgesic activity (in both tests, in terms of reaction time and % maximum possible effect) and antihyperalgesic activity (measured 1 h post-treatment). The UBE had no anti-inflammatory activity. Its analgesic activity was comparable to that of indomethacin and was not blocked by naloxone, (opioid receptor blocker), metochlopramide (dopamine receptor blocker) or atropine (cholinergic receptor blocker). We conclude that the antinociceptive activity of the UBE was mediated both spinally and supraspinally, and the antihyperalgesic activity spinally. Both actions may have been mediated through a paracetamol type of action.

Keywords: analgesia, antihyperalgesia, *Psychotria sarmentosa*, Sri Lanka

Introduction: *Psychotria sarmentosa* Blume (Family: Rubiaceae, Gonica in Sinhala) is a twinning shrub with oblanceolate or elliptic leaves growing in low elevation forests (< 700 m) in southern and southwestern parts of Sri Lanka [1]. In the Deshiya Chikitsa system of medicine in Sri Lanka the leaves and stems of this plant are used to treat bone fractures [2], although their therapeutic potential is not indicated in the Sri Lankan Ayurvedic Pharmacopoeia [3].

However, some men in Sri Lanka drink an unboiled water extract of leaves and stems of this plant when they are physically assaulted. Further, aggressive captive elephants at musth, when physically assaulted by their keepers to calm them, are given *P. sarmentosa* to eat, possibly to relieve pain. These uses suggest that the plant may possess pain killing and anti-inflammatory activities. But this has not been scientifically evaluated.

The objective of this study was to evaluate the antinociceptive, antihyperalgesic and anti-inflammatory activities of an unboiled water extract (UBE) of leaves and stems of this plant in rats.

Materials and methods: Fresh *P. sarmentosa* stems with leaves were purchased from the main vegetable market in Colombo, Sri Lanka, and authenticated by Professor A.S. Seneviratna, Department of Botany, University of Colombo. These were cut into small pieces (5 – 10 mm) using a pen knife. 200 g was macerated with 200 ml of distilled water using a porcelain mortar and pestle. The resulting greenish extract was filtered using cotton wool and the filtrate was considered as the UBE. It was stored at 4 °C until use (usually within 2 days).

The pH of the extract was determined using an electronic pH meter. The presence (qualitatively) or absence of alkaloids, flavonoids, phenols steroids and triterpenoids, coumarins, saponins, amino acids and peptides determined using standard chemical tests as described by Farnsworth [4].

Healthy adult cross-bred male albino rats (weighing 175 – 225 g) from our colony were used. They were kept under standardized animal house conditions (temperature: 28–31 °C; photoperiod approximately 12 h natural light per day; relatively humidity: 50 – 55%) with free access to pelleted food (Master Feed Ltd., Colombo, Sri Lanka) and tap water.

71 male rats were randomly divided into eight groups. They were treated orally (between 10.00 and 11.00 h) either with the UBE or distilled water (DW) in the following manner. Group 1 ($n = 9$, 7.5 ml/kg UBE), 2 ($n = 9$, 15 ml/kg UBE), 3 ($n = 10$, 22.5 ml/kg UBE), 4 ($n = 9$, 7.5 ml/kg DW), 5 ($n = 9$, 15 ml/kg DW), 6 ($n = 10$, 22.5 ml/kg DW), 7 ($n = 9$, 4 mg/kg indomethacin in 1 ml of methyl cellulose), 8 $n = 6$, 1 ml 1% methyl cellulose). Following treatment, the rats were continuously observed for 3 – 5 h for overt clinical signs of toxicity, stress and gross behavioural abnormalities.

12 male rats were randomly selected and divided into two equal groups (six per group). Group 1 animals received 0.1 ml of 5 mg/kg of naloxone hydrochloride (Fluka Chemicals, Buchs, Switzerland) in normal saline (0.9% NaCl w/v) and Group 2 0.1 ml of normal saline, subcutaneously. 45 min later, these rats were orally treated with 22.5 ml/kg UWE.

15 male rats were randomly selected and divided into two groups. Group 1 animals ($n = 9$) were orally treated with 1 ml of 0.3 mg/kg metochlopramide (Ipca Laboratories Ltd., Mumbai, India) in 1% methyl cellulose (Griffin and George Ltd., Wembley, UK) and Group 2 animals with 1 ml 1% methyl cellulose. After 1 h, both groups received 22.5 ml/kg UBE.