Med. Sci. Res., 1994; **22**, 307–308

Analgesic activity of *Mormodica dioica* fruit extract in rats

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Keywords: *Mormodica dioica* fruits, analgesia, tail flick technique.

Introduction: The fruits of *Mormodica dioica* Roxb. (Family: cucurbitaceae and referred to as Thumba Karawila in Sinhalese and Thumbai in Tamil) have been used in traditional medicine in Sri Lanka as a stomachic, laxative and antipyretic, and also to treat jaundice, leprosy, tuberculosis, hypersalivation and certain heart conditions [1]. One of the reasons for the use of *M. dioica* fruits as a stomachic could be their analgesic activity. As yet, this possibility has not been tested.

This study was initiated to investigate the analgesic potential of *M. dioica* fruits using an aqueous crude extract and rats as the test animals.

Materials and methods: Fresh fruits of *M. dioica* were purchased from local vegetable markets in the district of Monaragala in the months of December and January (when it is seasonal). The identity of these fruits were authenticated by Professor R.N. de Fonseka of the Department of Botany, University of Colombo, Sri Lanka.

The fruits were washed in tap water, deseeded and cut into thin slices. These were immediately minced in a domestic mincer (National, Model: MX-T 110PN, Matsushita Electric Co. Ltd, Taiwan) and the pulp obtained was squeezed through four layers of medical gauze. The filtrate was stored at −20°C until use. The extract had a greenish appearance.

Healthy adult cross bred male albino rats (weight: 200–250 g) from the Zoology Department colony were used. They were housed in groups (6 per cage) under standardised animal house conditions, with free access to pelleted food (Oils and Fats Co. Ltd, Seeduwa, Sri Lanka) and tap water up to 12 h before the commencement of the experiment.

The analgesic potential of the extract was evaluated in rats (in five groups each consisting of six animals) using a tail flick analgesic meter (Model MK 330A, Muromachi Kikai Co. Ltd, Tokyo, Japan) at a beam level of 55, using a single acute gastric intubation. Two doses of extract were tested: 1 mL/100 g ($n = 6$) and 2 mL/100 g ($n = 6$). The vehicle control was 1 mL 100/g ($n = 6$) and 2 mL/100 g ($n = 6$) distilled water (the results of the vehicle controls were pooled). One reference analgesic drug was also used: morphine (P&D Pharmaceuticals, Poole, UK) 1 mg/100 g ($n = 6$). All experiments were initiated between 8.30 and 9.30 h.

30 min prior to the oral administration of the extract, vehicle or reference drug, the animals were placed on the tail flick analgesia meter and their reaction times were measured (time taken to flick the tail following the application of the light beam). The procedure was then repeated 1, 2, 3, 4 and 6 h post administration. The development of any overt physical and behavioural signs, if any, were also noted.

The results are represented as means ± SEM. Statistical comparisons were made using a Chi-squared test. Threshold significance value was set at $p < 0.05$.

Results: As shown in Table 1, as compared with pre-treatment, the administration of the vehicle (distilled water) had no significant ($p > 0.05$) effect on the reaction time during the study period (6 h). Likewise, the lower dose of the extract (1 mL/100 g) had no significant effect ($p > 0.05$) on the reaction time as compared with its own pre-treatment value.

On the other hand, a higher dose of 2 mL/100 g evoked a significant ($p < 0.05$) prolongation (by 31%) of the reaction time at 1 h. Morphine, the reference drug used, caused significant ($p < 0.05$) increases in the reaction time at all the time points tested: 1 h (by 141%), 2 h (by 90%) and 3 h (by 58%). Furthermore, the analgesic activity of morphine was associated with the characteristic Straub reaction (erection of tail across the back of the animal in an S-shaped curve due to contraction of the sacro-cocygeus dorsalis muscle). Such a phenomenon was not evident in the rats treated with the *M. dioica* extract. Furthermore, no overt signs of clinical toxicity were evident in any of the extract-treated rats.

Discussion: In this study two doses (1 mL/100 g and 2 mL/100 g) of *M. dioica* fruit extract were evaluated for analgesic activity in rats using the tail flick reflex test. The results demonstrate that the higher dose exhibited significant analgesic activity, which was short-lived (only up to 1 h). Furthermore, this analgesic activity was approximately 4.5 times less potent than that of morphine. A lower dose, on the other hand, had no significant effect on the reaction time.

The extract mechanisms responsible for the analgesic

Table 1: Effect of Mormodica dioica *fruit extract on the reaction time of rats in the tail flick reflex test (means ± SEM; ranges in brackets).*

Treatment	*n*	Reaction time (s) Pre-treatment	Pos-treatment 1 h	2 h	3 h	4 h	6 h
Control	12	6.35 ± 1.07 (4.30–11.50)	6.73 ± 1.68 (1.50–12.20)	4.27 ± 0.88 (1.20–7.00)	5.1[illegible] ± 0.59 (3.40–7.60)	6.28 ± 1.04 (4.60–12.40)	7.78 ± 1.63 (4.60–14.40)
Mormodica dioica 1 mL/100 g	6	7.27 ± 0.05 (4.50–10.40)	7.17 ± 1.09 (4.50–11.60)	6.38 ± 0.62 (4.30–8.10)	6.72 ± 1.61 (0.80–10.50)	6.00 ± 0.75 (4.30–9.50)	6.97 ± 1.17 (3.80–12.00)
Mormodica dioica 2 mL/100 g	6	5.77 ± 0.93 (2.70–8.60)	7.55 ± 0.69* (6.00–14.50)	7.63 ± 0.59 (5.00–8.80)	6.7[illegible] ± 0.91 (5.[illegible]–10.80)	5.70 ± 0.79 (2.70–8.20)	6.42 ± 0.63 (5.30–9.40)
Morphine 1 mg/100 g	6	3.95 ± 1.35 (1.00–10.40)	9.53 ± 2.85* (3.40–20.00)	6.48 ± 2.78* (1.90–20.00)	6.2[illegible] ± 2.87 (1.0[illegible]–20.00)	NI	NI