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Analgesia and sedation induced by *Mucuna prurita* seeds in rats

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Abstract: In Sri Lankan folk medicine, seeds of *Mucuna prurita* (Hook) (Family: Leguminosae) are recommended to be consumed as a curry ingredient to relieve aches and pains. The seeds contain large quantities of dopa and nicotine. Thus it is possible that they have antinociceptive and perhaps also sedative activities. The aim of this study was to investigate these possibilities. A powdered seed suspension (PSS) of the seeds was made in 1% methyl cellulose. Different doses (750, 1,500 or 3,000 mg/kg) or vehicle were administered orally to male rats and the mid dose to female rats. 3 h later, analgesic potential (using hot plate and tail flick tests) and sedative potential (only with mid dose, and male rats, using the rat hole-board technique) were determined. All three doses were well tolerated and significantly ($P < 0.05$) increased both the reaction time and % maximum possible effect in hot plate test, indicating potent antinociception mediated supraspinally. In contrast, no analgesic activity was evident in the tail flick test. These effects were dose-related and not blocked by naloxone, an opioid receptor blocker. The mid dose caused only mild sedation. Further, in the females, the mid dose exhibited potent analgesia, as in males. This was not affected by the stage of the oestrous cycle. In addition, the treatment did not alter intestinal transit, muscle strength (as judged by a bar holding test) or muscle co-ordination (evaluated by bridge test). We conclude that antinociception of *M. prurita* seeds is not mediated by the opioid mechanism but possibly via dopamine and nicotine.

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Keywords: analgesia, antinociception, hypoalgesia, *Mucuna prurita*, nicotine, sedative

Introduction: In the Sri Lankan Ayurveda Pharmacopoeia, the seed of *Mucuna prurita* (Hook) (Family: Leguminosae) in the form of a powder are recommended as an astringent, spermatogenic and powerful aphrodisiac [1]. There are two varieties: seeds with fully black coats and those with brown stripes and spots. The former type is generally used as a therapeutic and the latter as a curry taken with rice.

Mucuna seeds contain dopa (the precursor of neurotransmitters, dopamine and noradrenaline) and a variety of alkaloids such as mucunine, mucunodine, pruriendine and nicotine [2]. Dopamine, noradrenaline and drugs inhibiting spinal noradrenaline uptake show analgesic activity (see [3] and refs therein). Nicotine is also an analgesic and causes the release of dopamine and acetylcholine, both of which are analgesics by themselves [4]. Potent analgesics such as morphine, cocaine and epibatidine are alkaloids [5].

Further, in Sri Lankan folk medicine, *M. prurita* seeds are recommended to be applied as a paste on scorpion stings and to be consumed as a curry to relieve body aches and pains. Overall, these experimental observations and claims indicate that *Mucuna* seeds may have analgesic activity. But this has not been scientifically documented.

The aim of this study was to ascertain whether *Mucuna* seeds possess analgesic activity. This was tested with powdered seeds in rats using two widely used, reliable, sensitive and valid algesimetric techniques [6].

Materials and methods: Dried *M. prurita* seeds having dark brown stripes and spots were purchased from an Ayurvedic drug store in Colombo, Sri Lanka. They were decoated using a sharp nut cracker and the kernel exposed. The kernel was finely powdered by an electrical grinder. Appropriate weights of this powder was then suspended in 1% methyl cellulose (Griffin and George Ltd., London, UK) (vehicle) to obtain three different concentrations of the powdered seed suspension (PSS) in 1 ml (750, 1,500 or 3,000 mg/kg). The PSS was freshly made daily for oral administration.

We used healthy adult cross bred albino rats (males weighing 200–250 g and females weighing 200–225 g) from our own colony. The animals were kept in plastic cages (six/cage) under standardized animal house conditions (temperature: 28–31°C; photoperiod: approximately 12 h natural light per day; relative humidity: 50–55%) with free access to pelleted food (Master Feed Ltd, Colombo, Sri Lanka) and tap water. Except at the time of experimental procedures the animals were handled only during cage cleaning.

Male rats ($n = 48$) were randomly divided into four equal groups. Those in the first group were orally treated with 1 ml of 1% methyl cellulose (vehicle) (between 12.00 and 13.00 h) and those in groups 2, 3 and 4 respectively with 750, 1,500 and 3,000 mg/kg of PSS in 1 ml of vehicle.

Pro-oestrus ($n = 12$), oestrus ($n = 12$) and dioestrus ($n = 12$) females were selected by vaginal smearing using normal saline (0.9% NaCl; w/v). These rats in each stage of oestrous cycle were randomly divided into two groups. One group was given 1 ml of vehicle and the other 1 ml of 1,500 mg/kg of PSS orally.

Ten adult male rats were randomly selected and divided into two groups. Those in first group ($n = 5$) received 0.1 ml of 5 mg/kg of naloxone hydrochloride (Sigma Chemical Company, St. Louis, MO, USA) in normal saline and those in the other ($n = 5$) 0.1 ml normal saline, subcutaneously. 45 min following these treatments, all the rats were orally treated with 1 ml of 1,500 mg/kg of PSS. The rats were continuously observed for 3 h for overt clinical signs of toxicity, stress and changes in behavior.