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Aqueous root extracts from *Mimosa albida* Humb. & Bonpl. ex Willd display antinociceptive activity in mice

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ABSTRACT

Ethnopharmacological relevance: In this work, we study whether aqueous extracts from the roots of *Mimosa albida* Humb. & Bonpl. ex Willd, a plant known in the Highlands of Chiapas, Mexico as "Lotóm chíx" are endowed with both antinociceptive and anxiolytic effects.
Materials and methods: ICR mice were systemically treated with aqueous extracts from *Mimosa albida* and the reference compounds (diazepam, dipyrone and/or fentanyl) and their behavior was evaluated in several behavioral tests.
Results: Administration of aqueous extracts from the roots of *Mimosa albida* resulted in a reduction of the nociception elicited in mice by both the hot plate (12.5, 25 and 50 mg/kg; i.p.) and the acetic acid-induced writhing (25 and 50 mg/kg; i.p.) tests. No effects were however observed both in the elevated plus-maze and hole board test (3.2, 12.5 and 25 mg/kg; i.p.). In contrast, both locomotion (open field test) and motor coordination (rotarod test) were affected at doses (50, 100 y 200 mg/kg; i.p.) higher than those having antinociceptive effects.
Conclusion: These data suggest that in mice the systemic administration of low doses of aqueous extracts from the roots of *Mimosa albida* results in antinociceptive effects in several models of pain through mechanisms that do not involve the opioid system pathway. These results support the ethnopharmacological use of *Mimosa albida* in popular medicine.

1. Introduction

Mimosa albida Humb. & Bonpl. ex Willd is a species of a plant belonging to the Fabacea family which is commonly found in rain forests. Extracts of *Mimosa albida* are widely used in the traditional medicine of Mexico and other countries to treat several human disorders. In Chiapas, Mexico, aqueous extracts from the dried root of *Mimosa albida* are used to treat pain and anxiety (OMIECH, 2006). In Honduras, extracts from this plant are used in combination with other plants for miscarriage (Ticktin and Dalle, 2005). In addition, several other *Mimosa* species have been also used to treat other diseases (Amalraj and Ignacimuthu, 2002; Ayissi et al., 2011). Thus, *Mimosa púdica* is used in the treatment of a variety of medical problems including headaches (migraine), insomnia, depression and anxiety (Ayissi et al., 2011; Del Amo, 1979; Mendieta and Del Amo, 1981); *Mimosa tenuiflora* is a popular remedy utilized in Mexico for the treatment of skin burns and wounds (Rivera-Arce et al., 2007; Sánchez-León and Yashté, 1991) and *Mimosa fragrifolia* is an acrid astringent. In addition, *Mimosa linguis* is a diuretic, *Mimosa humilis* is used against rheumatism (Grieve, 1931 in Molina et al., 1999), and *Mimosa hostilis* is employed as a hallucinogenic compound (Evans and Hofmann, 2008).

It has been shown that aqueous extracts from *Mimosa albida* Humb. & Bonpl. ex Willd exhibit a scant toxicity as determined by the brine-shrimp assay (Bussmann et al., 2011) but no other pharmacological and biochemical properties of this plant have been reported. In this work, we have investigated in mice the effects of aqueous extracts from the roots of *Mimosa albida* both in pain models and on anxiety-like behavior. In addition their potential effects on general activity (open field test) and motor coordination (rotarod test) were also studied.

2. Materials and methods

2.1. Plant material

Fresh plants of *Mimosa albida* were collected in april 2010, from the Highlands of Chiapas, México. The collected specimens were identified and authenticated by Dr. Miguel Angel Pérez Farrera,

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Curator of Eazi Matuda (HEM) herbarium of the University of Arts and Sciences of Chiapas, Mexico, where a voucher specimen with the number 26581 was deposited.

2.2. Extract preparation

Chopped roots of *Mimosa albida* were dried in a shade room for a month before being powdered. For extraction, 35 g of powder were dissolved in 1:1 of purified water and heated to boiling under stirring. After cooling, the mixture was filtrated and freeze-dried yielding 0.725 g of dried powder (2.07%) from the original plant material.

2.3. Animals

Male ICR mice (25–30 g) where used. Mice were housed in groups of six within boxes of polycarbonate (44/21/21 cm) and were kept in a controlled environment (temperature 23 °C ± 1, lights on 07:00–19:00 h) with water and food (Harlan, México) available *ad libitum*. Animals were donated by the biotherium of Laboratorio Estatal de Salud, Chiapas, Mexico. All the experiments of this project were done at the Laboratorio Experiemental de Farmacobiología, Chiapas, Mexico. The experimental protocol was approved (11/06/2010) by the local ethical committee (Bioethical allowance number 120/010) whose guidelines are based on the recommendations laid down by the United States Institutes of Health for the care and use of laboratory animals.

2.4. Drugs

The chemicals and drugs used in this study were acetic acid (Merck, Darmsted, Germay), sodium dipyrone (Hoechst, México), naloxone hydrochloride (Sigma Chemical Co., St Louis, Mo), fentanyl (Janssen-Cilag, México) and diazepam (Hoffmann-La Roche, México). Drugs and extracts were dissolved in 0.9% NaCl solution, with the exception of diazepam, which was dissolved in a mixture of polyethylenglycol 400/citric acid · H_2O (4 g/5 mg) in 10 ml sterile water (Rejón-Orantes et al., 2011). Stock solutions of each compound were prepared, and from there working solutions with a proper concentration were obtained to inject the animals. Although the traditional use of this extract is by the oral route the *Mimosa albida* extract was administered i.p. in this study to have a better control of the dose administered and to eliminate the risk of traumatic effects during oral cannulation. In addition i.p. administration was chosen to avoid that part of the dose was regurgitated or accidentally introduced into the animal airways. All other compounds used in this study were also injected intraperitoneally (i.p.) in a total volume of 10 ml/kg. Animals from the control group received an equal volume of the corresponding vehicle.

2.5. Behavioral evaluation

The behavioral experiments were carried out in the absence of any experimenter in a sound attenuated room. The room was illuminated with a 40 W red light bulb (Silvania et al., 2004) and was equipped with video recording facilities. In all cases, a video camera was placed above the setup used to evaluate behavior. The behavioral evaluation was carried out off-line in a manual way. All evaluations were conducted between 10:00 and 14:00 h. The apparatuses used for each behavioral test were cleaned with detergent and dried before each trial. Animals were assigned to each group at random. Behavioral evaluation was carried out by an observer blind to the experimental conditions. Animals were used only once.

2.6. Antinociceptive activity

2.6.1. Acetic acid-induced writhing

This test was performed as described by Fontenele et al. (1996). Acetic acid (0.6%) was administered (i.p.) at the beginning of the test in a volume of 10 ml/kg. Writhings, responses involving contraction of the abdominal wall and pelvic rotation followed by hind limb extension, were counted during the whole duration of the test (20 min). Both, *Mimosa albida* extract (12.5, 25 and 50 mg/kg; i.p.) and the reference analgesic drug (dypirone, 100 and 500 mg/kg; i.p.) (Kiliç and Erol, 2000) were administered 60 min before the acetic acid administration.

This model was also used to investigate whether the opioid system may be involved in the aninociceptive effects of the *Mimosa albida* extracts (Trentin et al., 1997). For this purpose, separate groups of mice were treated with fentanyl (0.1 mg/kg, i.p.), a synthetic μ-opioid agonist (Zhang et al., 2012) or *Mimosa albida* extract (50 mg/kg; i.p.). Naloxone (5 mg/kg; i.p.), an opioid antagonist (de Campos et al., 1997), was administered due to its short time-effects 30 min after *Mimosa albida* extract (Ngai et al., 1976), and 20 min following treatment with fentanyl. Separate groups of mice received either fentanyl (0.1 mg/kg; i.p.), *Mimosa albida* extract (50 mg/kg; i.p.) or vehicle (NaCl solution, 10 ml/kg; i.p.), either at 30 (fentanyl) or 60 min (*Mimosa albida* extract or vehicle) before testing.

2.6.2. Hot plate test

This test was performed according to the method described by Franzotti et al. (2000). Animals were placed on a hot plate set at 53 ± 0.5 °C and their pain responses (hind-paw licking and jumping) were observed. The time that elapsed between the placement of the animal in the platform of the apparatus and its pain reaction was recorded as the response latency. Such a latency was determined before testing and at 30 and 60 min after administration of either *Mimosa albida* extract, the reference drug (fentanyl 0.1 mg/kg, i.p.) or the vehicle.

2.7. Anxiolytic activity

2.7.1. Elevated plus-maze

The maze used in this work was similar to the one employed by Lister (1987) to measure anxiolytic activity in mice. The maze consisted of two open (30×5 cm^2) and two closed ($30 \times 5 \times 15$ cm^3) arms that intersected in a central platform (5×5 cm^2). The maze was built of opaque acrylic and was elevated 40 cm from the ground. The open arms were supplied with a 2 mm bulge that was extended along its periphery. At the beginning of the test the mice were placed on the central platform facing the open arms, and the number of entries into as well as the time spent in them were recorded for 5 min. An entry into any arms of the maze was considered only when the animal's four paws were placed in the respective arm (Pellow et al., 1985). The percentage of time spent on the open arms was calculated as (open arm time/(open arm+closed arm time) × 100). It has been shown that a decrease of the exploration of the open arms of the maze reflects the rodent's innate fear for open spaces devoid of thigmotactic cues (Treit et al., 1993).

2.7.2. Hole board test

The hole board apparatus used consisted of a wooden box ($40 \times 40 \times 25$ cm^3) with 16 holes (3 cm diameter) evenly distributed along the surface of its floor. The hole board was elevated to the height of 15 cm. Animals were placed on the apparatus and the number of head-dippings was registered for 5 min. A head-dipping is counted when the mouse introduces its head into any hole of the box up to the level of the ears. It has been shown that

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