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ORIGINAL ARTICLE

The potential effects of *Melicope ptelefolia* root extract as an anti-nociceptive and anti-inflammatory on animal models

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Abstract The demand of herbal medicine has been increasing for the purpose of reducing the side effects of modern medicine. *Melicope ptelefolia* (*M. ptelefolia*) is a local Malaysian plant claimed to have many benefits for health. This study was performed to evaluate the potential of *M. ptelefolia* root extract as anti-nociceptive and anti-inflammatory agents in rats. The anti-nociceptive activity of *M. ptelefolia* root extracts (50 and 100 mg/kg) was evaluated using acetic acid-induced writhing and tail immersion test, while the anti-inflammatory activity was studied using carrageenan-induced paw edema test. *M. ptelefolia* root extract significantly inhibited the pain stimulant in acetic acid-induced writhing test, however it did not exert any significant change in the tail immersion test. Nevertheless, the mean reaction time in tail immersion test of *M. ptelefolia* root extract increased as the doses of extract increased. Furthermore, *M. ptelefolia* root extract at both doses showed significant anti-inflammatory activity by reducing paw edema volume ($p < 0.05$). In conclusion, methanol root extract of *M. ptelefolia* possesses anti-inflammatory effects and anti-nociceptive effects in rats.

1. Introduction

The use of contemporary medicines as anti-inflammatory and anti-nociceptive agents is becoming controversial due to their multiple side effects such as gastro-intestinal bleeding and ulcers, renal disorders[1,2] and adverse cardiovascular events.[3]

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Therefore, herbal medicines are currently in demand and their popularity as health supplements has been increasing throughout the world.[4] *Melicope ptelefolia* (*M. ptelefolia*) is from the Rutaceae family which is commonly found in several Asian countries as well as in Malaysia.[5] Locally it is known as 'tenggek burung', 'pauh-pauh', 'medang beberas', 'cabang tiga' and 'tapak itik'. As for Javanese people in Indonesia, they called it 'sampang' while the Siamese called it as 'Uam, Sam Ngam'.[6]

M. ptelefolia is claimed to have many advantages in terms of health care. The leaves of *M. ptelefolia* have gained a great deal of popularity over the years as a traditional fresh vegetable among Malaysians.[7] *M. ptelefolia* leaf extract was reported to have anti-inflammatory, antipyretic, analgesic and antioxidant properties[8] as well as antimicrobial activities.[9] Besides, other parts of this plant have also been used traditionally to treat pathological conditions such as fever, wounds, stomach ache and rheumatism.[10] To our knowledge, no research has been done on the potential of anti-nociceptive and anti-inflammatory effect of *M. ptelefolia* root extract. Therefore, this study was done to evaluate the anti-nociceptive and anti-inflammatory activity of *M. ptelefolia* methanolic root extract.

2. Materials and methods

2.1. Chemicals

Indomethacin was bought from ChemLab, USA and other chemicals were bought from Sigma Chemical Co, USA.

2.2. Plant materials and extraction

The plant was obtained from Institute of Bioscience, UPM, Serdang, Selangor, Malaysia with reference number UPM/IBS/UB/H14-13. The extraction method with slight modification is based on Sulaiman et al.[11] Briefly, freshly collected roots of *M. ptelefolia* were air-dried for 48 h and ground into a fine powder. The powder was extracted with methanol with the ratio of 1:5 (sample/solvent) (w/v). The mixture was allowed to stand for 24 h, filtered and evaporated using rotary evaporator (Rotavapor® R-210, BUCHI, Switzerland) under controlled temperature of 55 °C. The resultant extract was then dried using freeze dryer (Alpha 1–2 LD plus freeze dryer, SciQuip, UK) for 24 h. Dry extract was stored in a refrigerator at 4 °C until further use.

2.3. Animals

Adult female Sprague Dawley rats ($n = 48$), weighing approximately between 180 and 230 g were used in this study. All rats were maintained at room temperature 22 ± 2 °C (12 h light/12 h dark) cycle during the experiment[12], housed in polypropylene cages with access to standard pellet and water *ad libitum*. The rats were acclimatized for at least seven days prior to environmental adaption period. All the experiments were conducted in accordance with the ethical guidelines on animal experimentation with resolution number: UPM/FPPSK/PADS/BRUUH/00221 by Institution Animal Care and Use Committee (IACUC) FMHS, Universiti Putra Malaysia (UPM), Malaysia. All rats were randomly divided into four groups which consist of six animals per group for each antinociceptive and anti-inflammatory effect. Normal saline group: The negative control rats received 5 ml/kg of 0.9% normal saline solution; 50 mg/kg mp group: rats received 50 mg/kg of methanol root extract of *M. ptelefolia*; 100 mg/kg mp group: rats received 100 mg/kg of methanol root extract of *M. ptelefolia*; aspirin group: rats received 100 mg/kg of aspirin as a positive control for antinociceptive effects and indomethacin group: rats received 10 mg/kg of indomethacin as a positive control for anti-inflammatory effects. All substances were given orally before 30 min prior to test.

2.4. Acetic acid-induced writhing test

The peripheral analgesic activity was tested by glacial acetic acid-induced writhing test in rats.[13] Writhes were induced by intraperitoneal injection of 0.6% (v/v) 10 ml/kg acetic acid.[8] The number of abdominal constrictions, which consist of constriction of abdominal part together with full stretching of both hind limbs were counted and recorded over a period of 20 min, starting 5 min after acetic acid injection.[11] The percentage inhibition of writhing was calculated and evaluated statistically.

2.5. Tail immersion test

The central analgesic activity was tested by tail immersion test in rats.[13] Basal reaction time was taken by immersing the tip (last 2 cm) of the tail in one liter of water at 55 ± 2 °C.[14] Reaction times were chosen as the time when the animals completely withdraw their tails from the hot water. The tails should only allow to be immersed for not more than 10 s to prevent tissue damage to the tail of the animals.[8] The initial reading was taken immediately before administration of extracts and 90 min after the administration. The mean difference of reaction time was calculated and evaluated statistically.

2.6. Carrageenan-induced paw edema method

Inflammation was induced by injecting 0.1 ml of 1% (w/v) carrageenan into the sub-plantar area of the right hind paw of rats. The increase in paw edema volume was measured by plethysmometer (Ugo Basile, Canada) every hour for five hours. The edema volume and the percentage inhibition of paw edema was calculated and evaluated statistically.

2.7. Statistical analysis

The obtained data were statistically analyzed using statistical package for social science (SPSS) version 20. After confirming the normality and homogeneity of variance of data, the mean differences were established by a one-way analysis of variance (ANOVA) followed by Fisher's LSD post hoc multiple comparisons. The results were statistically significant if $p < 0.05$. All data were expressed as mean ± standard error (SEM).

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