Antinociceptive activity of methanolic extract of Muntingia calabura leaves: further elucidation of the possible mechanisms

Abstract

Background: Muntingia calabura (Elaecoparceae) is a medicinal plant traditionally used, particularly, by the Peruvian people to alleviate headache and cold, pain associated with gastric ulcers or to reduce the prostate gland swelling. Following the recent establishment of antinociceptive activity of M. calabura leaf, the present study was performed to further elucidate on the possible mechanisms of antinociception involved. Methods: The methanol extract of M. calabura (MEMC) was prepared in the doses of 100, 250 and 500 mg/kg. The role of bradykinin, protein kinase C, pottasium channels, and various opioid and non-opioid receptors in modulating the extract's antinociceptive activity was determined using several antinociceptive assays. Results are presented as Mean ± standard error of mean (SEM). The one-way ANOVA test with Dunnett's multiple comparison was used to analyze and compare the data, with $P < 0.05$ as the limit of significance. Results: The MEMC, at all doses, demonstrated a significant ($p < 0.05$) dose-dependent antinociceptive activity in both the bradykinin- and phorbol 12-myristate 13-acetate (PMA)-induced nociception. Pretreatment of the 500 mg/kg MEMC with 10 mg/kg glibenclamide (an ATP-sensitive K+ channel inhibitor), the antagonist of μ-, δ- and κ-opioid receptors (namely 10 mg/kg β-funaltrexamine, 1 mg/kg naltrindole and 1 mg/kg nor-binaltorphimine), and the non-opioid receptor antagonists (namely 3 mg/kg caffeine (a non-selective adenosinergic receptor antagonist), 0.15 mg/kg yohimbine (an α2-noradrenergic antagonist), and 1 mg/kg pindolol (a β-adrenoceptor antagonist)) significantly ($p < 0.05$) reversed the MEMC antinociception. However, 10 mg/kg atropine (a non-selective cholinergic receptor antagonist), 0.15 mg/kg prazosin (an α1-noradrenergic antagonist) and 20 mg/kg haloperidol (a non-selective dopaminergic antagonist) did not affect the extract's antinociception. The phytochemicals screening revealed the presence of saponins, flavonoids, tannins and triterpenes while the HPLC analysis showed the presence of flavonoid-based compounds. Conclusions: The antinociceptive activity of MEMC involved activation of the non-selective opioid (particularly the μ-, δ- and κ-opioid) and non-opioid (particularly adenosinergic, α2-noradrenergic, and β-adrenergic) receptors, modulation of the ATP-sensitive K+ channel, and inhibition of bradikinin and protein kinase C actions. The discrepancies in MEMC antinociception could be due to the presence of various phytochemicals.

Keyword: Muntingia calabura; Elaecocarpaceae; Methanol extract; Antinociceptive activity; Mechanisms of action