

Activity-guided isolation of bioactive constituents with antinociceptive activity from *Muntingia calabura* L. leaves using the formalin test

ABSTRACT

The present study was conducted to determine the antinociceptive potential of methanol extract of *Muntingia calabura* L. (MEMC) and to isolate and identify the bioactive compound(s) responsible for the observed antinociceptive activity. The MEMC and its partitions (petroleum ether (PEP), ethyl acetate (EAP), and aqueous (AQP) partitions), in the dose range of 100, 500, and 1000 mg/kg, were tested using the formalin-induced nociceptive test. The PEP, which exerted the most effective activity in the respective early and late phase, was further subjected to the fractionation procedures and yielded seven fractions (labelled A to G). These fractions were tested, at the dose of 300 mg/kg, together with distilled water or 10% DMSO (negative controls); morphine and aspirin (positive controls) for potential antinociceptive activity. Of all fractions, Fraction D showed the most significant antinociceptive activity, which is considered as equieffective to morphine or aspirin in the early or late phase, respectively. Further isolation and identification processes on fraction D led to the identification of three known and one new compounds, namely, 5-hydroxy-3,7,8-trimethoxyflavone (1), 3,7-dimethoxy-5-hydroxyflavone (2), 2',4'-dihydroxy-3'-methoxychalcone (3), and calaburone (4). At the dose of 50 mg/kg, compound 3 exhibited the highest percentage of antinociceptive activity in both phases of the formalin test. In conclusion, the antinociceptive activity of MEMC involved, partly, the synergistic activation of the flavonoid types of compounds.

Keyword: Bioactive constituent; Antinociceptive activity; *Muntingia calabura* L. leaves; Formalin test