Antinociceptive effect of semi-purified petroleum ether extract derived from crude methanol extract of muntingia calabura and its possible mechanisms of action

ABSTRACT

Muntingia calabura L., Muntingiaceae, is a medicinal plant for various pain-related diseases. The aims of the present study were to determine the antinociceptive profile and to elucidate the possible mechanisms of antinociception of petroleum ether partition obtained from crude methanol extract of M. calabura leaves using various animal models. The antinociceptive profile of petroleum ether fraction (given oral; 100, 250 and 500 mg/kg) was established using the in vivo chemicals (acetic acid-induced abdominal constriction and formalin-induced paw licking test) and thermal (hot plate test) models of nociception. The role of glutamate, TRPV1 receptor, bradykinin, protein kinase C, potassium channels, and various opioid and non-opioid receptors in modulating the partition's antinociceptive activity was also determined. The results obtained demonstrated that petroleum ether partition exerted significant ($p < 0.05$) antinociception in all the chemicals-, thermal-, capsaicin-, glutamate-, bradykinin, and phorbol 12-myristate 13-acetate (PMA)-induced nociception models. The antinociceptive activity was reversed following pretreatment with opioid antagonists (i.e. naloxone, β-funaltrexamine, naltrindole and nor-binaltorphimine), and the non-opioid receptor antagonists (i.e. pindolol (a β-adrenoceptor), haloperidol (a non-selective dopaminergic), atropine (a non-selective cholinergic receptor), caffeine (a non-selective adenosinergic receptor), and yohimbine (an α2-noradrenergic)). In addition, pretreatment with L-arginine (a nitric oxide (NO) donor), NG-nitro-L-arginine methyl esters (L-NAME; an inhibitor of NO synthase (NOS)), methylene blue (MB; an inhibitor of cyclic-guanosine monophosphate (cGMP) pathway), or their combination failed to inhibit petroleum ether partition's antinociception. In conclusion, petroleum ether partition exerts antinociceptive activity at the peripheral and central levels via the modulation of, partly, the opioid (i.e. μ, κ and δ) and several non-opioids (i.e. β-adrenergic, dopaminergic, cholinergic, adenosinergic, and α2-noradrenergic) receptors, glutamatergic, TRPV1 receptors, PKC and K+ channels systems, but not L-arg/NO/cGMP pathway.

Keywords: Muntingia calabura; Petroleum ether partition; Antinociceptive activity; Mechanisms of antinociception