Antinociceptive activity of methanolic extract of Clinacanthus nutans leaves: possible mechanisms of action involved

ABSTRACT

Methanolic extract of Clinacanthus nutans Lindau leaves (MECN) has been proven to possess antinociceptive activity that works via the opioid and NO-dependent/cGMP-independent pathways. In the present study, we aimed to further determine the possible mechanisms of antinociception of MECN using various nociceptive assays. +e antinociceptive activity of MECN was (i) tested against capsaicin-, glutamate-, phorbol 12-myristate 13-acetate-, bradykinin-induced nociception model; (ii) prechallenged against selective antagonist of opioid receptor subtypes (β-funaltrexamine, naltrindole, and nor-binaltorphimine); (iii) prechallenged against antagonist of nonopioid systems, namely, α2-noradrenergic (yohimbine), β-adrenergic (pindolol), adenosinergic (caffeine), dopaminergic (haloperidol), and cholinergic (atropine) receptors; (iv) prechallenged with inhibitors of various potassium channels (glibenclamide, apamin, charybdotoxin, and tetraethylammonium chloride). +e results demonstrated that the orally administered MECN (100, 250, and 500 mg/kg) significantly ($p < 0.05$) reversed the nociceptive effect of all models in a dose-dependent manner. Moreover, the antinociceptive activity of 500 mg/kg MECN was significantly ($p < 0.05$) inhibited by (i) antagonists of μ-, δ-, and κ-opioid receptors; (ii) antagonists of α2-noradrenergic, β-adrenergic, adenosinergic, dopaminergic, and cholinergic receptors; and (iii) blockers of different K+ channels (voltage-activated-, Ca2+-activated, and ATP-sensitive-K+ channels, resp.). In conclusion, MECN-induced antinociception involves modulation of protein kinase C-, bradykinin-, TRVP1 receptors-, and glutamatergic signaling pathways; opioidergic, α2-noradrenergic, β-adrenergic, adenosinergic, dopaminergic, and cholinergic receptors; and nonopioidergic receptors as well as the opening of various K+ channels. +e antinociceptive activity could be associated with the presence of several flavonoid-based bioactive compounds and their synergistic action with nonvolatile bioactive compounds.