Possible participation of ionotropic glutamate receptors and l-arginine-nitric oxide-cyclic guanosine monophosphate-ATP-Sensitive K+ channel pathway in the antinociceptive activity of cardamonin in acute pain animal models

ABSTRACT

The perception of pain caused by inflammation serves as a warning sign to avoid further injury. The generation and transmission of pain impulses involves various pathways and receptors. Cardamonin isolated from Boesenbergia rotunda (L.) Mansf. has been reported to exert antinociceptive effects in thermal and mechanical pain models; however, the precise mechanism has yet to be examined. The present study investigated the possible mechanisms involved in the antinociceptive activity of cardamonin on protein kinase C, N-methyl-d-aspartate (NMDA) and non-NMDA glutamate receptors, l-arginine/cyclic guanosine monophosphate (cGMP) mechanism, as well as the ATP-sensitive potassium (K+) channel. Cardamonin was administered to the animals intra-peritoneally. Present findings showed that cardamonin significantly inhibited pain elicited by intraplantar injection of phorbol 12-myristate 13-acetate (PMA, a protein kinase C activator) with calculated mean ED50 of 2.0 mg/kg (0.9–4.5 mg/kg). The study presented that pre-treatment with MK-801 (NMDA receptor antagonist) and NBQX (non-NMDA receptor antagonist) significantly modulates the antinociceptive activity of cardamonin at 3 mg/kg when tested with glutamate-induced paw licking test. Pre-treatment with l-arginine (a nitric oxide precursor), ODQ (selective inhibitor of soluble guanylyl cyclase) and glibenclamide (ATP-sensitive K+ channel inhibitor) significantly enhanced the antinociception produced by cardamonin. In conclusion, the present findings showed that the antinociceptive activity of cardamonin might involve the modulation of PKC activity, NMDA and non-NMDA glutamate receptors, l-arginine/nitric oxide/cGMP pathway and ATP-sensitive K+ channel.

Keyword: Cardamonin; Glutamate receptor; L-arginine nitric oxide pathway; cGMP; potassium channels; Acute pain