

The oral administration of *Lotus corniculatus* L. attenuates acute and chronic pain models in male rats

ABSTRACT

Ethnopharmacological relevance: *Lotus corniculatus* L. (Fabaceae) traditionally used in Persian folk medicine to heal peritoneal inflammation and back pain. Aim of the study: To explore the antinociceptive (acute pain) and anti-neuropathic (chronic pain) activities of *Lotus corniculatus* leaves essential oil (LCEO) in addition to uncovering the possible mechanisms of antinociception. Materials and methods: LCEO as well as the pure oleanolic acid (OA) compound, were assayed for their effects on acute (formalin induced paw licking test or FIPT) and chronic (cervical contusion injury models on the fifth cervical vertebra or CCS; 14-day intervals) pain. The possible involvements of NO-cGMP-K⁺ channel, TRPV, dopamine, cannabinoid, PPAR, adrenergic, and opioid mechanisms in the antinociceptive activity of LCEO have studied by formalin test. The levels of p53 and inflammatory markers were measured using a streptavidin biotin immune peroxidase complex and ELISA methods, respectively. Results: The LCEO and OA exerted antinociceptive activity in the first-phase of FIPT. Pretreatment with antagonists of TRPV1, dopamine D2, cannabinoid type1 and 2, and NO-cGMP-K⁺ channel blockers (glibenclamide, LNAME and methylene blue) attenuated the antinociceptive effect of LCEO in FIPT. In addition, LCEO and OA meaningfully reduced hyperalgesia (days 6–14) and mechanical allodynia (days 2–14) in the CCS model. LCEO suppressed the apoptotic marker (p53) in CCS model and also ameliorated IL-2, TNF- α , and IL-1 in the spinal cord. Conclusion: Finally, LCEO inhibited acute (possibly via the modulation of opioid, TRPV, dopamine, cannabinoid mechanisms as well as NO-cGMP-K⁺ channel) and chronic pain (via suppressing apoptotic and inflammatory markers) in male rats. The results also suggest that OA has analgesic activity against acute and chronic pain conditions.