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J Ethnopharmacol. 2023 Aug 4;117004. doi: 10.1016/j.jep.2023.117004. Online ahead of print.

Himalayan *Pyracantha crenulata* (D.Don) M.Roem. leaf and fruit extracts alleviate algesia through COX-2 and Mu-opioid receptor mediated pathways

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PMID: 37544342 DOI: 10.1016/j.jep.2023.117004

Abstract

Ethnopharmacological relevance: *Pyracantha crenulata* (D.Don) M.Roem., a plant of high nutritional and medicinal value is traditionally employed for its analgesic property for joint and body pain in Kumaun region of Western Himalaya.

Aim of the study: To validate the traditional claims for analgesic property of *Pyracantha crenulata*.

Methods: Hydroethanolic extract of *P. crenulata* leaves and fruits were tested for their analgesic potential in rodent models for algesia by tail immersion test, tail flick test, Eddy's hot plate model, and formalin induced paw irritation test in Wistar rats.

Results: Both *P. crenulata* fruit extract and leaf extract exhibited significant amelioration in all the tested experimental models of algesia acting through central and peripheral mechanisms. The efficacy in reducing nociception was found comparable to diclofenac that was used as a reference standard. Molecular docking and dynamic simulation studies further established binding affinity of gallic acid (confirmed to be present in *P. crenulata* leaf extract through HPTLC profiling) with cyclooxygenase-2 (COX-2) and mu-opioid receptors, suggesting the modulatory effect of these extracts on COX-2 and mu-opioid receptors in combating algesia.

Conclusion: *P. crenulata* extracts produce analgesic effects plausibly through COX-2 and mu-opioid receptor mediated pathways.

Keywords: Gallic acid; Ghingharu; Himalaya; Molecular dynamics; Pain; Simulation.

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