International Research Journal of Pharmacy and Pharmacology
ISSN 2251-0176
2020
Vol.8 No.4

Amelioration of chemically induced nociception & inflammation by 7-hydroxy coumarin through the modulation of COX-2, iNOS and inflammatory cytokines

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Abstract

Aim: The objective of the current investigation was to explore the analgesic effect of naturally occurring coumarin and the involvement of inducible cyclooxygenase (COX-2), inducible nitric oxide synthase (iNOS) and cytokines in the observed effect.

Materials and methods: Acute toxicity of 7-hydroxy coumarin was evaluated according to OECD guidelines. Anti-nociceptive effect was explored by inducing chemical hyperalgesia using acetic acid and formalin in mice. ED50 of 7-hydroxy coumarins was calculated in acetic acid model. Modulation of cyclooxygenase and nitric oxide pathway by 7-hydroxy coumarin was examined by stimulator/precursor challenge with substance P and L-arginine respectively and quantification of COX-2 and iNOS expression by immunohistochemical analysis in spinal tissues. Involvement of inflammatory cytokines TNF-α and IL-1β was investigated using LPS challenge and subsequent ELISA analysis of these inflammatory mediators in serum. Carrageenan inflicted paw edema was employed to explore the anti-inflammatory activity of 7-hydroxy coumarin.

Results: Acute toxicity studies revealed almost unremarkable viscera. A significant reduction in the nociceptive behaviour was observed with 7-hydroxy coumarin treatment. ED50 of 7-hydroxy coumarins was found to be 7.62 mg/kg. Pre-treatment with substance P and L-arginine significantly attenuated the anti-nociceptive activity of 7-hydroxy coumarin. Immunohistochemical findings revealed marked decrease in spinal COX-2 and iNOS expression. 7-hydroxy coumarin administration significantly downregulated LPS induced rise in levels of TNF-α and IL-1β dose dependently. In carrageenan test, maximum possible anti-inflammatory effect of 7-hydroxy coumarin was evident at 120 min of carrageenan administration.

Conclusion: Current investigation revealed that anti-nociceptive and anti-inflammatory potential of 7-hydroxy coumarin is probably mediated through the attenuation of COX-2, iNOS and reduction in circulatory cytokines.

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30th AnnualEuropeanPharmaCongress; Berlin, Germany-May 18-19, 2020

Abstract Citation:

Kirtika Madan,Amelioration of chemically induced nociception & inflammation by 7-hydroxy coumarin through the modulation of COX-2, iNOS and inflammatory cytokines, Pharma Europe 2020, 30th Annual European Pharma Congress; Berlin,Germany-May18-19,2020 (https://europe.pharmaceuticalconferences.com/abstract/2020/amelioration-of-chemically-induced-nociception-inflammation-by-7-hydroxy-coumarin-through-the-modulation-of-cox-2-inos-and-inflammatory-cytokines)