In vitro and in vivo anti-inflammatory activities of columbin through the inhibition of cyclooxygenase-2 and nitric oxide but not the suppression of NF-κB translocation.


Source

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Abstract

Columbin, a diterpenoid furanolactone, was isolated purely for the first time from the plant species Murraya koenigii. The anti-inflammatory effects of columbin were studied in vitro, in silico and in vivo. The effect of columbin on nitric oxide was examined on lipopolysaccharide-interferon-gamma (LPS/IFN) induced RAW264.7 macrophages. In vitro and in silico cyclooxygenase-1 and cyclooxygenase-2 inhibitory activities of columbin using biochemical kit and molecular docking, respectively, were investigated. Mechanism of columbin in suppressing NF-kappaB-translocation was tested using Cellomics®NF-κB activation assay and ArrayScan Reader in LPS-stimulated RAW264.7 cells. Moreover, effects of columbin in vivo that were done on carrageenan-induced mice paw-oedema were tested. Lastly, the in vitro and in vivo toxicities of columbin were examined on human liver cells and mice, respectively. Treatment with columbin or N(ω)-nitro-l-arginine methyl ester (l-NAME) inhibited LPS/IFN-γ-induced NO production without affecting the viability of RAW264.7. Pre-treatment of stimulated cells with columbin did not inhibit the translocation of NF-κB to the nucleus in LPS-stimulated cells. COX-1 and COX-2 inhibitory activities of columbin were 63.7±6.4% and 18.8±1.5% inhibition at 100μM, respectively. Molecular docking study further helped in supporting the observed COX-2 selectivity. Whereby, the interaction of columbin with Tyr385 and Arg120 signifies its higher activity in COX-2, as Tyr385 was reported to be involved in the abstraction of hydrogen from C-13 of arachidonate, and Arg120 is critical for high affinity arachidonate binding. Additionally, columbin inhibited oedema formation in mice paw. Lastly, the compound was observed to be safe in vitro and in vivo. This study presents columbin as a potential anti-inflammatory drug.

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