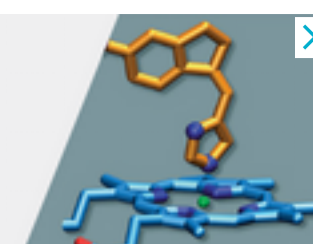
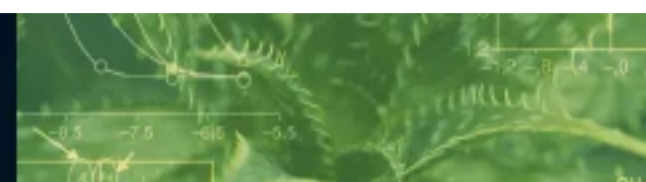




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Research Article

Molecular Targets of the Antiinflammatory *Harpagophytum procumbens* (Devil's claw): Inhibition of TNF α and COX-2 Gene Expression by Preventing Activation of AP-1

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Abstract

Harpagophytum procumbens (Hp) is often used in the supportive treatment of inflammatory and degenerative diseases of the skeletal system. Although the clinical efficacy in osteoarthritis has been demonstrated in clinical trials, the molecular target(s) of Hp are unclear. This study quantified the effects of the ethanol Hp extract (60% v/v ethanol, sole active ingredient of Pascoe®-Agil), on the expression and release of the major pro-inflammatory mediators in LPS-stimulated human monocytes and the intracellular signalling pathways involved in inflammation. The Hp extract dose-dependently inhibited the release of TNF α as well as that of interleukin (IL)-6, IL-1 β and prostaglandin E₂ (PGE₂). The Hp prevented TNF α and IL-6 mRNA expression in human monocytes and cyclooxygenase-2 (COX-2) in RAW 264.7 cells. Furthermore, the Hp extract inhibited LPS-stimulated AP-1-mediated gene transcription activity and binding to the AP-1 response elements. The extract had no effect on the LPS-induced binding of nuclear factor- κ B in RAW 264.7 cells, on LPS-induced degradation of I κ B α or on LPS-induced activation of mitogen-activated protein kinases (MAPK), p38MAPK and JNK in human monocytes. The data indicate that a standardized ethanol Hp extract inhibits induction of pro-inflammatory gene expression, possibly by blocking the AP-1 pathway. This is novel evidence of a possible mechanism of action of this antiinflammatory drug. Copyright © 2011 John Wiley & Sons, Ltd.

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