Effects of sphondin, isolated from Heracleum laciniatum, on IL-1b-induced cyclooxygenase-2 expression in human pulmonary epithelial cells

林建煌;李文森
Yang LL;Liang YC;Chang CW;Lee WS;Kuo CT;Wang CC;Lee HM and Lin CH

Abstract

Recently, under large-scale screening experiments, we found that sphondin, a furanocoumarin derivative isolated from Heracleum laciniatum, possessed an inhibitory effect on IL-1beta-induced increase in the level of COX-2 protein and PGE(2) release inA549 cells. Accordingly, we examined in the present study the action mechanism of sphondin on the inhibition of IL-1beta-induced COX-2 protein expression and PGE(2) release in a human pulmonary epithelial cell line (A549). Pretreatment of cells withsphondin (10-50 microM) concentration-dependently attenuated IL-1beta-induced COX-2 protein expression and PGE(2) release. The IL-1beta-induced increase in COX-2 mRNA expression was also attenuated by sphondin (50 microM). The selective COX-2 inhibitor, NS-398 (0.01-1 microM), inhibited the activity of the COX-2 enzyme in a concentration-dependent manner, while sphondin (10-50 microM) had no effect. Sphondin (50 microM) did not affect the IL-1beta-induced activations of p44/42 MAPK, p38 MAPK, and JNK. Treatment of cells with sphondin (50 microM) or the NF-kappaB inhibitor, PDTC (50 microM) partially inhibited IL-1beta-induced degradation of IkappaB-alpha in the cytosol and translocation of p65 NF-kappaB from the cytosol to the nucleus. Furthermore, IL-1beta-induced NF-kappaB-specific DNA-protein complex formation in the nucleus was partially inhibited by sphondin (50 microM) or PDTC (50 microM). Taken together, we demonstrate that sphondin inhibits IL-1beta-induced PGE(2) release in A549 cells; this inhibition is mediated by suppressing of COX-2 expression, rather than by inhibiting COX-2 enzyme activity. The inhibitory mechanism of sphondin on IL-1beta-induced COX-2 expression may be, at least in part, through suppression of NF-kappaB activity. We conclude that sphondin may have the therapeutic potential as an anti-inflammatory drug on airway inflammation