activity and expression of COX-2. There are multiple lines of evidence supporting that the induction of COX-2 is regulated by the eukaryotic transcription factor NF-κB. TPA stimulated both NF-κB DNA-protein binding and COX-2 promotor activity. However, genistein did not inhibited TPA- or TNF-α-induced NF-κB DNA-protein binding, but suppressed the transcriptional activity of NF-κB induced by TPA. Immunofluorescence staining also demonstrated that increased nuclear translocation of the active NF-κB p65 subunit was not abolished by genistein. Genistein treatment attenuated TPA- or TNF-α-induced activation of ERK1/2. Above findings, taken together, suggest that genistein inhibits COX-2 expression and PGE_2 production in MCF10A cells by acting at the transcription initiation complex via a tyrosine kinase- or ERK-dependent pathway.

[PC1-19] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Differential inhibitory effects of sophoricoside and its analogs on COX isozymes

Kim Byung Hak°, Min Kyung Rak, Kim Youngsoo

College of Pharmacy, Chungbuk National University

Cyclooxygenase (COX), COX-1 and 2 catalyzes the conversion of arachidonic acid to prostaglandin H2, rate-limiting step of prostanoid biosynthesis. COX-1 is constitutive expressed in most tissues under physiological conditions, whereas COX-2 is induced by some cytokines, mitogens, and endotoxin presumably in pathological conditions, such as inflammation. In this study, inhibitory effects of sophoricoside and its analogs on COX-1 and COX-2 activities has been evaluated. Microsomal fraction of bovine seminal vesicles was used as the COX-1 source, and lysate of LPS-stimulated murine macrophages Raw 264.7 as the COX-2 source. COX activity was measured by chemiluminescence emitted for 30 sec in the presence of arachidonic acid and luminol. Inhibitory potencies of the compounds on COX-2 were in the order of orobol (IC50=0.8 uM) > genistein (IC50=7.7 uM) > genistin (IC50=8.7 uM) > sophoricoside (IC50=9.3 uM). Selective COX-2 inhibitor NS-398 showed an IC50 value of 0.23 uM on COX-2 activity and 48.9 uM on COX-1 activity. Orobol and genistein exhibited IC50 values of 7.9 uM and 72.6 uM on COX-1 activity, respectively, and sophoricoside and genistin of >100 uM. All of the compounds did not affect the expression and synthesis of COX-2 in the LPS-stimulated murine macrophages Raw 264.7, which was analyzed by RT-PCR. These pharmacological findings will be helpful to analyze protective mechanisms of flavonoid compounds against inflammatory conditions.

[PC1-20] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Spiciformisin-b and Moncyclicsqualene Induce Differentiation and Apoptosis of Human Leukemic cell HL-60

Jeong SeungHee° Koo SungJa Park HeeJun Lee KyungTae

Department of Food & Nutrition, Kyung Hee University, Seoul 130-701, Korea

From the leaves of Ligularia Fischery var. spiciformis, a new terpenoids named spiciformisin-b and moncyclicsqualene were isolated. These compounds have a antitumor activity by induction of cell differentiation and apoptosis in HL-60. Spiciformisin-b and moncyclicsqualene were found to be a potent inducer of differentiation toward granulocyte and monocyte/
macrophage lineages. The effect of differentiation has been detected by esterase activity, phagocytosis, NBT reduction and CD14, CD66b surface antigen. Moreover, they showed apoptosis inducing effect at a concentration of 40㎍/㎖ These apoptotic features were identified by increasing of hypodiploid nuclei and nucleosomal ladder. These results suggest that spiciformisin-b and moncyclicsqualene induce differentiation and apoptosis in HL-60 cells.

[PC1-21] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]