

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- κ B. TPA stimulated both NF- κ B DNA-protein binding and COX-2 promoter activity. However, genistein did not inhibit TPA- or TNF- α -induced NF- κ B DNA-protein binding, but suppressed the transcriptional activity of NF- κ B induced by TPA. Immunofluorescence staining also demonstrated that increased nuclear translocation of the active NF- κ B 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 PGE₂ 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

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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 μ M) > genistein (IC₅₀=7.7 μ M) > genistin (IC₅₀=8.7 μ M) > sophoricoside (IC₅₀=9.3 μ M). Selective COX-2 inhibitor NS-398 showed an IC₅₀ value of 0.23 μ M on COX-2 activity and 48.9 μ M on COX-1 activity. Orobol and genistein exhibited IC₅₀ values of 7.9 μ M and 72.6 μ M on COX-1 activity, respectively, and sophoricoside and genistin of >100 μ M. 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

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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 μ g/ml. 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]