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

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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 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

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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㎍/㎖ 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]

Cytotoxicity and apoptosis inducing effects of phenylpropanoids.

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This study was carried out to determine cytotoxicity and apoptosis inducing effects of the seven pheylpropanoids. We have determined cytotoxocity by MTT(3-(4,5-dimethyl-thiazol-2-yl)-2,5-dipheryl-2H-tetrazo-liumbromide)assay and investigated the extendency of apoptosis by DAPI assay. The IC50s (ug/ml) of each phenylpropanoids by MTT(HL-60 cell) are 10.3(KYS50046), 15.9(KYS50047), >100 (KYS50049), >100 (KYS50050), 50.9(KYS50051), 52.3(KYS50153) and 48.36(KYS50154). Based on this result KYS50046 and KYS50047 showed significant cytotoxicity. When we observe Structure-activity relationship(SAR) of these compounds, KYS50049-51 which are unefficient in the cytotoxicity have methoxy group instead of hydroxy group on the phenol ring (ortho-form) compared to KYS50046-7. There is no sugar ring in KYS50153-4 which are also unefficient in cytotoxicity, whereas KYS50046-7 have sugar ring on the ring. So we suppose that the existences of hydroxy group on the phenol ring and sugar ring are *essential moiety* for cytotoxicity and apoptosis inducing effects.

[PC1-22] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Hydroquinone from Coffee Modulates Reactivity of Peroxynitrite and Nitric Oxide Production

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Peroxynitrite (ONOO-), a potent cytotoxic oxidant formed by the reaction of nitric oxide (.NO) and superoxide radical (.O2-), may be rapidly lethal in a cellular mileu if left unchecked due to oxidization and nitration process. In the present study, we investigated ONOO- scavenging effect of hydroquinone from coffee, consisting of both beneficial and hazardous biochemical substances, and its biological effect on NO metabolism in the murine macrophage RAW 264.7.
Hydroquinone strongly scavenged ONOO--induced dihydrorhodamine 123 (DHR123) oxidation not by electron donation but by nitration of the compound itself in a dose-dependent manner. The compound also decreased ONOO--induced nitrotyrosine of GSH reductase, suggesting that hydroquinone directly neutralizes ONOO- and may prevent ONOO--induced damage of GSH reductase. Furthermore, hydroquinone also suppressed NO production, which is one of upstream sources via inhibition of inducible NO synthase (iNOS) expression in lipopolysaccharide (LPS)-activated RAW 264.7 cells. The inhibitory effect of hydroquinone was mediated through blocking LPS-induced signaling pathway, since hydroquinone potently inhibited nuclear factor-kB (NF-kB), and phosphorylation of extracellular signal related kinases 1 and 2 (ERK 1/2), a member of the MAPK family. Our results suggest that hydroquinone may be regarded as a potent regulator of ONOO--mediated diseases via both directly scavenging and indirectly blocking ONOO- production pathways, such as NO synthesis.

[PC1-23] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Long-term Evaluation of the Mouse Model for Validity of Studying the Effects of Helicobacter pylori Infection on Gastric Carcinogenesis

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This study was aimed at evaluating the effect of *H. pylori* infection on gastric carcinogenesis. Four-week-old pathogen free C57BL/6 mice (n=115) were infected with SS1, the mouse-adapted *H. pylori* strain. *H.*