In the previous study, we have reported that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone (NQ304), a vitamin K derivative, had potent inhibitory effects on human platelet aggregation *in vitro* and *ex vivo*, and on animal pulmonary thrombosis. In the present study, the effect of NQ304, an antithrombotic agent, on platelet aggregation and arachidonic acid (AA) metabolism was investigated using by rabbit washed platelets. Measurements of AA liberation and generation of thromboxane B_2 (TXB_2) and prostaglandin D_2 (PGD_2), through cyclooxygenase pathway, or 12-hydroxyeicosatetraenoic acid (12-HETE), through lipoxygenase pathway, from [^{3}H]AA were evaluated by radio-chromatographic analysis with washed rabbit platelets *in vitro*. Collagen-, AA, or U46619-stimulated platelet aggregation were inhibited dose-dependently by NQ304. The IC_{50} values of NQ304 on collagen-, AA- and U46619-induced rabbit platelet aggregation were calculated to be 3.9, 1.2 and 4.3 μM, respectively. Furthermore, NQ304 potently suppressed the AA liberation from [^{3}H]AA-labeled rabbit platelets exposed to collagen, indicating that it may affect phospholipase A_2 (PLA_2) activation on collagen-induced AA liberation from membrane phospholipids. However, NQ304 didn't suppress the TXB_2 generation induced by addition of [^{3}H]AA in intact rabbit platelets, whereas PGD_2 and 12-HETE generation were enhanced by NQ304. These results suggest that NQ304 may affect PLA_2 activation and which stimulate PGD_2 or 12-HETE generation from AA, thus eliciting the inhibition of platelet aggregation.

[PC1-4] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Upregulation of NF-kappaB Expression by Alkylating Carcinogens in Human Transfectant Keratinocytes

Moon Ki-Young°, Lee YoungJong, Kim Seung-Kyoon, Choi Young-Kuk, Kim JungEun, Kim YeongShik[1]

Department of Clinical Pathology, Bioindustry and Technology Research Institute, Kwangju Health College, Kwangju, 506-701 and [1]Natural Products Research Institute, Seoul National University, Seoul 110-460, Korea kmoon@www.kjhc.ac.kr

Effect of alkylating carcinogens, e.g., *N*-nitroso-*N*-methylurea, *N*-nitroso-*N*-ethylurea, ethyl iodide and benzyl bromide on the activation of NF-kappaB was evaluated in human transfectant HaCaT and SCC-13 cells in order to investigate the possible correlation of NF-kappaB expression with chemical carcinogenesis. Human HaCaT and SCC-13 cells transfected with pNF-kappaB-SEAP-NPT plasmid were used to determine the NF-kappaB expression induced by alkylating agents. These transfectants release the secretory alkaline phosphatase (SEAP) as a transcription reporter in response to the NF-kappaB activity and contain the neomycin phosphotransferase (NPT) gene conferring resistance to the geneticin. Alkylating carcinogens significantly upregulated the NF-kappaB activations in a time-dependent manner until 72h at concentrations of 0.5 ~ 5 μ , M in both keratinocytes cell lines. This results suggest that carcinogenic activities of alkylating chemicals may be associated with their ability to increase NF-kappaB activation at the genetic molecular basis and NF-kappaB activation in response to chemical carcinogens may provides some of the molecular levels of regulatory activities of carcinogenic chemicals in human skin cells on carcinogenecity.

[PC1-5] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Anti-inflammation activity of the organoseleniums : inhibition of iNOS and COX-2 protein level.

Shin KyungMin°, Park ByungGyu, Jang JungAn, Kim RyungGyu, Shen LiuLan, Lee KyungTae, Jeong JinHyun

College of Pharmacy, Kyung Hee University, Seoul 130-701, Korea

Nitric Oxide (NO) has been known as multifunctional mediator produced by iNOS in inflammatory process and acting on various cells, and PGs are also called inflammatory mediator, produced by COX-2 in inflammatory tissues. In this point of view modulation of iNOS and COX-2 expression level represent a new treatment of inflammtory and autoimmune disease.
The present study examined effect of di- 3-hydroxyphenyl diselenide, di-4- hydroxyphenyl diselenide, and

dipyridyl diselenide on iNOS and COX-2 expression induced LPS(lipopolysaccharide) in Raw 264.7 murine macrophages. This organoselenium compounds inhibited NO production, iNOS expression, and COX-2 expression in a concentration-dependent manner. These findings suggest that this organoselenium compounds exert anti-inflammtory effect by inhibiting expression of iNOS and COX-2.

[PC1-6] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Development of Protein Chip for Osteoporosis Diagnosis

Kim So Young°, Yun Mi Yong, Chang Dong Il, Lee Nam Taek, Choi Myung Ja

Bioanalysis & Biotransformation Research Center, Korea Institute of Science & Technology, Department of Chemistry, Korea Military Academy

Osteoporosis has been characterized by its low bone mass and architectural deterioration of bone tissue. We performed noncompetitive enzyme immunoassay (EIA) for the detection of osteoprotegerin (OPG) and transforming growth factor β3 (TGFβ3) as osteoporotic biomarkers. Sensitive EIA calibration curves were obtained for OPG and TGFβ3 with detection limits of 0.05 ng/mL and 0.1 ng/mL, respectively, under optimized condition. To develope a solid matrix of protein chip, we initially treated a silica-based glass with 3-aminopropyltriethoxysilane (APS), and additionally with either glutaraldehyde or sulfo-EGS (Ehyleneglycol bis(sulfosuccinimidyl-succinate)) to activate the amino group of APS. The antibody of osteoporotic biomarkers were immobilized on the chip surfaces and calibration curves for OPG and TGFβ3 using a microchip were compared with those obtained from EIA. We found that detection limits performed with microchip considerably correlated with those of EIA. These results promisingly indicate that the microchip can be applied for the diagnositic tool of osteoporosis as EIA.

[PC1-7] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Alpha-viniferin: paw dema reduction and down-regulation of inflammatory mediators

Chung Eun Yong°, Min Kyung Rak, Kim Youngsoo

College of Pharmacy, Chungbuk National University

Anti-inflammatory activity of alpha-viniferin, a polymeric compound of resveratrol, has been demonstrated in an animal model, and inhibitory effect of the compound on inflammatory mediators has been investigated in order to elucidate mode of the action. When administered orally with >30 mg/kg or injected intravenously with >3 mg/kg, alpha-viniferin showed significant anti-inflammatory activity on carrageenin-induced paw edema in mice. Alpha-viniferin showed IC50 values of 4.9 uM on cyclooxygenase (COX)-2 activity, 2.7 uM on production of nitric oxide in lipopolysaccharide (LPS)-stimulated murine macrophages Raw264.7, and 8.5-9.8 uM on production of superoxide anions in unopsonized zymosan-stimulated human monocytes and neutrophils. The compound showed very weak inhibitory effect on COX-1 and myeloperoxidase activities. Alpha-viniferin showed differential inhibitory effects on proinflammatory cytokines with IC50 values of 10.4 uM on interleukin (IL)-3 bioactivity, 18.9 uM on IL-5 bioactivity, and 18.8 uM on IL-6 bioactivity. Alpha-viniferin showed an IC50 value of 9.8 mM on tumor necrosis factor (TNF) production in LPS-stimulated Raw264.7 cells, but did not inhibit the IL-1 and TNF bioactivities. These pharmacological findings expand the importance of alpha-viniferin as a beneficial agent to human health, and will help to clarify protective mechanisms of the compound against inflammatory conditions.

[PC1-8] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Antioxidant Effect of Flavonoids and Phenolic Acids on Early Phase of Cu2+-Catalyzed LDL Oxidation

Kim JuRyoung°, Jeong Taesuk, Sok DaiEun