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

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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.

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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