

[PA3-3] [10/19/2000 (Thr) 10:00 – 11:00 / [Hall B]]

Antiplatelet and antithrombotic activities of CP201, [2-(3,5-di-tert-butyl-4-hydroxy)-3-chloro-1,4-naphthoquinone]

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The possibility of CP201, 2-(3,5-di-tert-butyl-4-hydroxy)-3-chloro-1,4-naphthoquinone, as a synthetic antithrombotic agent was investigated. Effects of CP201 on platelet aggregation in human in vitro, murine pulmonary thrombosis in mouse in vivo, and the mechanism of antithrombotic activity were examined. CP201 inhibited collagen-, thrombin-, thapsigargin- and calcium ionophore A23187-induced aggregation of human platelets with the IC50 values of 3.42 ± 0.39 , 3.93 ± 0.03 , 1.45 ± 0.25 and 3.17 ± 0.10 μ M. In the vivo study, CP201 prevented murine pulmonary thrombosis dose-dependently. CP201 did not alter the activated partial thromboplastin time (APTT), prothrombin time (PT) and thrombin time (TT) in human plasma. The LDH activity released from CP201-treated platelets did not change compared with control (DMSO). These results suggest that CP201 may be a promising antithrombotic agent, and the antithrombotic activity of CP201 may be due to the antiplatelet aggregation activity not to anticoagulation.

[PA3-4] [10/19/2000 (Thr) 10:00 – 11:00 / [Hall B]]

Effects of Zinc on the Cytokine Production induced by Lipopolysaccharide in the Tumor Bearing Mice

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Zinc levels in plasma are decreased in malignant patients with endotoxemia or other infections. These low zinc levels may be restored by zinc administration. In this study, we investigated effects of zinc chloride (Zn) on the TNF- α , IL-1 β , IL-2 and IFN- γ production induced by lipopolysaccharide (LPS) in tumor bearing ICR mice.

The results estimated by ELISA in serum and supernatants were the following: Zn treatment significantly increased IFN- γ levels in supernatants compared with those in controls; LPS treatment significantly increased TNF- α and IL-1 β levels in serum and TNF- α , IL-1 β and IFN- γ levels in supernatants compared with those in controls; combination of Zn and LPS significantly increased TNF- α and IL-1 β levels in serum and IFN- γ levels in supernatants compared with those in controls; combination of Zn and LPS significantly decreased IL-1 β levels in supernatants compared with those in LPS group and significantly increased IL-2 levels.

These results suggest that zinc might attenuate the inflammation of malignant patients with endotoxemia and enhance resistance to tumor.

[PA3-5] [10/19/2000 (Thr) 10:00 – 11:00 / [Hall B]]

Effects of Phellius linteus on nitric oxide production from peritoneal macrophage in normal and cyclophosphamide-treated mice.

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The purpose of this research was to investigate effects of *Phellius linteus* methanol extract (PL-M) on nitric oxide production from peritoneal macrophage in normal and cyclophosphamide (CY)-treated mice. PL-M was administered p.o. single (400, 800, 1600 mg/kg) or once a day for 5 days to normal and CY (20mg/kg, i.p.)-treated mice. Peritoneal macrophages were obtained from mice after 2 days and cultured for 48 hours with LPS. Also, normal mouse peritoneal macrophages (1×10^6 cells/ml) were incubated in the presence of various concentration of PL-M (0.5, 1.0, 2.5, 5mg/ml) and/or CY (6mM/ml) for 48 hours. Nitric oxide production was affected by treatment PL-M in vitro and in vivo. And this effect was dependent on the dose of PL-M. PL-M showed inhibition of suppression of nitric oxide production induced by CY.

[PA3-6] [10/19/2000 (Thr) 10:00 – 11:00 / [Hall B]]

Screening of natural product inhibitors on the UVA phototoxicity of Chlorpromazine

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15 Natural products known to contain antiinflammatory effect were screened whether they have UVA phototoxicity inhibitory effect or not by two methods – RBC photohemolysis and MTT assay. Samples were obtained by the process of 80% methanol extraction and then concentration under vacuum. And we made these concentration powder with freeze-dryer at -50°C ~ -60°C . In RBC photohemolysis method, effects of the test compounds on RBCs were monitored with a spectrophotometer by the method of Kahan et al. And in MTT assay we used human fibroblast cell. UVA 3 J/cm^2 and 2.5 J/cm^2 were irradiated respectively.

[PA3-7] [10/19/2000 (Thr) 10:00 – 11:00 / [Hall B]]

Vasorelaxation and Antiproliferation of Apigenin

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Apigenin, a flavone, has showed hypotensive effect in vivo and relaxant effect in vitro. However, the mechanisms remain incompletely understood. This study aimed to determine whether the relaxant effect of apigenin was endothelium-dependent and to examine the possible antiproliferative effect of apigenin on cultured aortic smooth muscle cells. Apigenin relaxed the 65.4 mM K^+ and 10^{-7} M phorbol 12,13-dibutyrate-induced contraction of endothelium-denuded rat aortic rings with respective IC₅₀ values of $12.0 \pm 1.1 \times 10^{-6} \text{ M}$ and $34.6 \pm 1.2 \times 10^{-6} \text{ M}$. Apigenin also relaxed phenylephrine-precontracted endothelium intact aortic rings with IC₅₀ values of $3.7 \pm 0.5 \times 10^{-6} \text{ M}$ and removal of a functional endothelium significantly attenuated the apigenin-induced relaxation (IC₅₀ = $8.2 \pm 0.9 \times 10^{-6} \text{ M}$) without affecting the maximum relaxant response. Pretreatment with 30 and 100 μM N-nitro-L-arginine methyl ester (L-NAME) reduced the relaxant effect of apigenin and the IC₅₀ values of apigenin were decreased to $6.9 \pm 1.2 \times 10^{-6} \text{ M}$ and $8.7 \pm 0.6 \times 10^{-6} \text{ M}$, respectively. Pretreatment of apigenin significantly potentiated relaxant effect of acetylcholine on phenylephrine-induced contraction. In addition, apigenin significantly inhibited [³H]thymidine incorporation into primary cultured rat aortic smooth muscle cell DNA in a dose-dependent manner. These findings suggest that nitric oxide from endothelium may account primarily for the apigenin-induced endothelium-dependent relaxation and mechanisms related to protein kinase C activation may also be involved in hypotensive activity. Both vasorelaxant and antiproliferative effects may contribute to a benefit of apigenin in the vascular system.