

[PD2-41] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Evaluation of induction of quinone reductase activity by natural products in cultured murine hepatoma cells

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NAD(P)H:quinone reductase, known as DT-diaphorase, is a kind of detoxifying phase II metabolic enzyme catalyzing hydroquinone formation by two electron reduction pathway from quinone type compounds, and thus facilitating excretion of quinoids from human body. With the usefulness of this assay system for modulation of toxicants, in the course of searching for cancer chemopreventive agents from natural products, the methanolic extracts of approximately two hundreds of oriental medicines were primarily evaluated using the induction potential of quinone reductase activity in cultured Hepa1c1c7 cells. As a result, several extracts including *Hordeum vulgare*, *Momordica cochinchinensis*, *Strychnos ignatii*, *Houttuynia cordata*, *Polygala japonica*, and *Uncaria sinensis* were found to significantly induce quinone reductase activity. Further study for isolation of active principles from these lead extracts is warranted for the discovery of novel cancer chemopreventive agents.

[PD2-42] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Effect of Lithospermi Radix on apoptosis of transplanted-L1210 cells in mice

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Cellular death by apoptosis is an active process, depending on gene transcription and protein synthesis. It was reported that cytokines can induce apoptosis in several cancer cell-lines. We have previously observed that apoptosis of transplanted-L1210 cells in BALB/c mice were induced by the administration of methylenechloride fraction of Lithospermi Radix. In the present study, the mechanism on apoptosis of transplanted-L1210 cells was examined. The fraction enhanced the production of gamma-interferon and the subpopulation of CD4+ cells in splenic T-lymphocytes. These findings suggest that the fraction activates Th1 cells in splenic T-lymphocytes. The fraction enhanced the production of tumor necrosis factor-alpha and nitric oxide in peritoneal macrophage. The apoptosis of transplanted-L1210 cells was enhanced by co-culture of the peritoneal macrophages of GL-administered mice and L1210 cells in vitro, and was inhibited by L-NMMA. These results suggest that the apoptosis of transplanted-L1210 cells is partly induced via the production of TNF-alpha and nitric oxide in macrophages activated by gamma-interferon secreted from Th1 cells.

[PD2-43] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Kalopanaxsaponin A from Kalopanax pictus, a Potent Antioxidant in the Rheumatoidal Rat Induced by Freund's Complete Adjuvant Reagent

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In patients with rheumatoid arthritis, it is well known that the aging associated with oxidative stress is accompanied. In the rheumatoid rat induced by Freund's complete adjuvant (FCA) reagent, we investigated hepatic lipid peroxide contents and hepatic drug-metabolizing system to demonstrate the inhibitory effect of hederagenin monodesmosides of *Kalopanax pictus* on oxidative stress. Kalopanaxsaponin (KPS) A significantly decreased malondialdehyde formation, and the activities of xanthine oxidase and aldehyde oxidase of hepatic non-microsomal systems in FCA reagent-treated rats. Increased activity levels of superoxide dismutase, catalase and glutathione peroxidase were also found. The effects of KPS-A were more potent than those of KPS-I. Because we have demonstrated the anti-inflammatory effects of KPS-A and -I in the present experimental model, it was suggested that *K. pictus* could reduce rheumatoid syndromes as the most important mechanism in the unique way of anti-inflammatory herbal medicines.

[PD2-44] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Analgesic Effect of *Kalopanax pictus* extract and Its Saponin Components, and Their Inhibitory Effect on Freund's Complete Adjuvant Reagent-Induced Rheumatoid Arthritis in Animal

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To elucidate active components for rheumatoid arthritis, the methanolic extract of *Kalopanax pictus* was fractionated to CHCl₃, ethylacetate (EtOAc) and n-butanol (BuOH) fraction. Further, the column chromatographic isolation of EtOAc fraction gave kalopanaxsaponin A and I (KPS-A and -I, hederagenin monodesmosides), and that on BuOH fraction gave kalopanaxsaponin B, -H and -J (KPS-B, -H and -J, hederagenin bisdesmosides), respectively. MeOH extract, EtOAc fraction (250, 500 mg/kg, p.o.) and KPS-A and -I (5, 10, 20 mg/kg, i.p.) exhibited significant analgesic effects on acetic acid-writhing method and hot plate method. On Freund's complete adjuvant reagent-induced rheumatoid arthritis in rats, the administration of EtOAc fraction and KPS-A and -I inhibited edema, agglutination, vascular permeability and trypsin inhibitor. In addition, LD₅₀ of the MeOH extract was shown to be 4,033 mg/kg. In conclusion, anti-rheumatoid effects of KPS-A and -I were suggested to be attributed to the inhibition of kinin formation by suppression of trypsin inhibitor activity. Further, it was suggested that *K. pictus* extract could be suitable for the treatment of rheumatoid arthritis, because the extract belonged to slightly toxic class.

[PD2-45] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Studies on the Development of Antihyperlipidemic Drugs from Oriental Herbal Medicines(III) -Antihyperlipidemic Effects of Herbal Prescriptions-

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In the previous study, we have found that several herbal medicines including *Trichosanthes Fructus*, *Pinelliae Tuber*, *Aurantii Immaturus Fructus*, *Magnoliae Cortex*, *Allii Macrostemis Bulbus*,