[PA1-27] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## Inhibitory mechanism of rat aortic vascular smooth muscle cell proliferation by apigenin

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Apigenin, a plant flavone, derived from the chinese herb *Apium graveolens* L. *Var. dulce DC* has a variety of pharmacological activities including hypotensive, anti-inflammatory, anti-spasmotic and anti-diarrhoeal effects. The objective of this study was to investigate the effects of apigenin on the growth factor-induced proliferative responses, mitogen-activated protein kinase (MAPK) and its down stream c-fos mRNA expression of rat aortic vascular smooth muscle cells (VSMCs). Apigenin significantly inhibited 5% fetal bovine serum- and 50ng/ml platelet derived growth factor-BB-induced proliferation in a concentration-dependent manner in cultured rat aortic VSMCs. In addition, we also found that apigenin resulted in a significant inhibition of the fetal bovine serum-induced phosphorylation of extra cellular signal-regulated kinase 1/2 (ERK 1/2). Moreover, apigenin potently inhibited fetal bovine serum-induced c-fos mRNA level. These results showing the inhibitory effect of apigenin on cell proliferation with down regulation of ERK 1/2 signal and c-fos pathway response in rat aortic VSMCs suggest that apigenin may be a useful preventive agent for cardiovascular disease including atherosclerosis.

[PA1-28] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## Effect of SPP002 on the contraction of the isolated rat uterus

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The SPP002 is a mixture of extracts from Cervi parvum Cornu, Angelicae gigantis Radix and Cnidii Rhizoma. The objective of this study was to characterize in vitro the effect of SPP002 on the contractility of the non-pregnant and pregnant rat uterus. Pregnancy was confirmed by presence of the deep vaginal plug at 12 hr after mating. The uterus from pregnant rats on day 17 or 18 was removed and the fetuses were gently expelled. Non-pregnant rats were excited by pretreatment of 6-estradiol benzoate for 2 days. The isometric contractile force and frequency of uterus were recorded with a force transducer and a polygraph. The SPP002 (1-300μg/ml) selectively elevated uterine contractile force in pregnant rat uterus while the oxytocin (0.1-10 mU/ml) elevated uterine contractile force and frequency in both pregnant and non-pregnant rat uterus, respectively. We conclude that SPP002 produces an increase in the pregnant rat myometrial activity in vitro, independent of oxytocin.

[PA1-29] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## Free Radical Scavenging Effects of MeOH extracts of various Cacti

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The MeOH extracts of 42 species of cacti were examined for their *in vitro* antioxidative activity. The antioxidative activity was determined by scavenging effects of 1-diphenyl-2-picrylhydrazyl (DPPH) radical, and then was compared to L-ascorbic acid. The approximate flavonoid aglycone contents were also determined spectrometrically at 425nm with the aid of aluminium chloride ($AlCl_3$). Almost all cactus

extracts tested showed more or less antioxidative activity. *Crassula cv. himaturi* showed the stongest antioxidant activity ($EC_{50}$, 10.45 ug/ml), followed by *Euphorbia mill var. splendens, Euphorbia ingens, Euphorbia submammillaris (Bgr.) Bgr* ( $EC_{50}$, 45.31, 72.07, 96.29, respectively). The approximate flavonoid aglycone content ranged from 0.5 % up to 6.1 %. No significant relationship was observed between the antioxidant activities and the flavonoid contents.

[PA1-30] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## New Acetylenic Compound, Montiporyne A, from the Stony Coral Montipora sp. Induced Apoptosis in Human Skin Cancer Cells

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The antiproliferative effect of a new acetylenic compound, Montiporyne A, from the stony coral Montipora sp. on human skin cancer cells was investigated. As determined by MTT assay, Montiporyne A decreased cell viability in a concentration dependent manner. To test if the growth inhibitory effect of Montirporyne A was derived from apoptosis induction, general evaluation focusing on apoptosis was conducted. Characteristic manifestations of apoptosis, such as nuclear changes, the increased ratio of proapoptotic protein Bax to antiapoptotic protein Bcl-2, and cleavage of a specific subset of protein, poly(ADP-ribose) polymerase, via activation of caspase-3, were demonstrated. Human Fas ligand and its membrane receptor Fas, which trigger apoptosis, were induced. Hence, these results suggest that the newly isolated Montiporyne A are capable of inhibiting cell proliferation and inducing apoptosis in human skin cancer cells.

[PA1-31] [ 10/18/2001 (Thr) 14:00 - 17:00 / Hall D ]

## Protective effects of quinic acid derivatives on tetrahydropapaveroline- induced cell death in C6 glial cells: Possible role of a MAP kinase during cell death

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Tetrahydropapaveroline (THP) is biosynthesized in plant by Pictet-Spengler condensation of dopamine with dopaldehyde. THP was reported to inhibit mitochondrial respiration and thought to be a contributing factor in developing Parkinson's disease. THP was toxic to C6 cells in a dose-dependent manner. When cells were exposed to 10 □, M of THP, the activities of JNK and p38 kinase rapidly increased whereas the activity of ERK decreased significantly. Furthermore, pretreatment of C6 cells with 8-(4-chlorophenylthio)-cAMP or SB203580 prevented THP-induced cell death, while exposure to either PD98059 or LY294002 did not protect cells from THP-induced death, indicating the involvement of JNK and p38 kinase in THP-induced cell damage. The neuroprotective effects of quinic acids from Aster scaber on THP-induced cell toxicity were evaluated to see whether quinic acid derivatives are beneficial for neurodegenerative diseases. Quinic acid derivatives significantly diminished THP-induced cell toxicity. Among the quinic acid derivatives tested, (-) 4,5-dicaffeoyl quinic acid exhibited the highest protection effect against THP-induced cell toxicity. Preincubation of cells with quinic acid prior to THP exposure elevated the cell survival rate and the activities of glutathione peroxidase and catalase, but decreased the level of MDA and SOD activity. Types of cell death caused by THP were assessed by morphological observation of cells after staining with Propidium iodide and Hoechst 33342. Taken together, the results indicate that THP-induced cell death is likely to be mediated through the activation of JNK and p38 kinase and that quinic acid might be a potential agent for treating neurodegenerative diseases including Parkinsonism.