## Induction of Apoptosis in HL-60 cells by Cinnamaldehyde Isolated from the Stem Bark of Cinnamomum cassia through Depletion of Intracellular Glutathione

Ka h, Choi JH, Park HJ, Han YN, Lee KT

*College of Pharmacy, Kyung-Hee University, Seoul 130-701, Korea **Division of Applied Plant Sciences, Sangji University, Wonju 220-702, Korea ***Natural Products Research Institute, Seoul National University, Seoul 110-460, Korea

Cinnamaldehyde showed a significant cytotoxic activity against various tumor cells. These concentration-dependent anti-proliferative activity was observed that appears to be due to induction of apoptosis. Cinnamaldehyde-induced apoptosis was evaluated by increasing of hypodiploid nuclei and a nucleosomal ladder. In order to explore the possible mechanism involved in cinnamaldehyde-induced apoptosis, the effect of cinnamaldehyde on intracellular reduced glutathione and the effect of N-acetylcystein (NAC) on cinnamaldehyde-induced cytotoxicity and apoptosis were investigated. NAC significantly alleviated cinnamaldehyde-induced cytotoxicity and apoptosis. These results suggest that cinnamaldehyde induces apoptosis in HL-60 cells, probably through depletion of intracellular glutathione.

[PC1-7] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Differentiation-Inducing Activity of Taxanic acid in HL-60 Human Promyelocytic Leukemia cells

Choi JH°, Kim NY, Sin KM, Lee YS, Kim HJ, Lee KT

Division of Life Sciences, KIST, P.O. Box 131, Cheongryang, Seoul(1), College of Pharmacy, Kyung Hee University, Seoul.

Taraxinic acid-1'-O-β-D-glucopyranoside isolated from Taraxacum coreanum and its aglycon taraxanic acid were examined for differentiation-inducing activity in U-937 cells. Aglycon taraxinic acid showed potent cytotoxic activity in contrast to taraxinic acid-1'-O-β-D-glucopyranoside. We investigated whether these cytotoxic and growth inhibitory effects were associated with differentiation induction. Taxanic acid was found to be a potent inducer of differentiation in human leukemia derived HL-60 cells by examination of differentiation marker, as assessed by reduction nitroblue tetrazolium (NBT) and expression of CD14 and CD66b surface antigens. These events were accompanied by a decline in expression of the c-myc protein. These results suggest that taraxanic acid induces differentiation in human leukemia cells to granulocyte and monocytes/macrophages lineage.

[PC1-8] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Inhibitory Effect of Prosapogenins Obtained from Kalopanax pictus on Tumor Necrosis Factor-α and Nitric Oxide Production in Raw 264.7 Murine Macrophage Cells

Kim YG, Park SJ, *Park HJ, **Choi JW, Lee KT

College of Pharmacy, Kyung-Hee University, Seoul, 130-701, Korea , *Division of Applied Plant, Sangji University, Wonju, 220-702, Korea , **College of Pharmacy, Kyungsung University, Pusan 608-736, Korea

In order to elucidate the anti-inflammatory effect of hederagenin monodesmosides, by which anti-

rheumatoidal arthritis could be deeply associated, the experiments on inhibitory effects of tumor necrosis factor (TNF)-α production, nitric oxide (NO) induction and cyclooxygenase-2 (COX-2) expression were undertaken in lipopolysaccharide (LPS) - activated macrophage cells. Hederagenin monodesmosides such as hederagenin, δ-Hederin, kalopanaxsaponin A, kalopanaxsaponin I, sapindoside C, inhibited the TNF-α and NO production, and the COX-2 expression. These biomarkers are deeply related with inflammatory phenomena. Kalopanaxsaponin A expressed the most significant inhibition among the other hederagenin monodesmosides. These results present the first report that saponin could inhibits the TNF-α, NO production and COX-2 expression in LPS-activated macrophage cells.

[PC1-9] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Exomethylene Group of Costunolide Induces Intracellular Thiol Depletion and is Essential for Apoptosis

Choi JH°, Seo BL, Park JH, Lee JY, Lee YS, Park HJ, Kwon SH, Lee KT

Division of Applied Plant Science, Sangji University, Wonju(1), Division of Life Sciences, KIST, P.O. Box 131, Cheongryang, Seoul(2), College of Pharmacy, Kyung-Hee University, Seoul.

In the prevoius study, we demonstrated that costunolide (1) caused apoptosis via reactive oxygen species-mediated mitochondrial membrane potential loss in human leukemia HL-60 cells. In pursuit to find functional exomethylene group on costunolide, we synthesized two new costunolide-derived products, dihydrocostunolide (2) and saussurea lactone (3). Costunolide showed strong cytotoxic and apoptotic activities in contrast to compound 2 and 3. Reversal of its effects on cytotoxicity was obtained with pretreatment by various sulfur containing compounds such as 2-mercaptoethanol, dithiothreotil, glutathion. In order to explore the possible mechanism involved in costunolide-induced cytotoxiciry and apoptosis, the effect of costunolide on intracellular thiol concentrations including reduced glutathione (GSH) and protein thiols was determined. It was found that costunolide rapidly concentration - and time - dependent depleted intracellular GSH and protein thiols, moreover, the depletion preceded the occurrence of apoptosis. Taken together, the present study demonstrated that apoptosis inducing effect of costunolide is through rapid depletion of intracellular thiols due to cross-reactivity with costunolide and the formation of adducts.

[PC1-10] [ 04/19/2001 (Thr) 15:30 - 16:30 / Hall 4 ]

## Chemical Degradation of Chondroitin Sulfate by Free Radical Process Induced by Hydrogen Peroxide in the Presence of Cupric Ions

Sim JS°, Kim JS, Kim YS*

Natural Products Research Institute, Seoul National University

Chondroitin sulfates (CS) are mainly composed of an alternate β1→3 and β1→4 glycosidic linkages of D-glucuronic (GlcA) acid and N-acetyl-D-galactosamine (GalNAc). The sulfate group is usually unsubstituted or substituted at the 4 and 6 positions of GalNAc. They are ubiquitous components of al connective tissues, where they are mainly covalently attached to core proteins in the form of proteoglycans. Recently, CS has been used as a chondroprotective agent for human osteoarthritis. In order to get the degraded CS, it was usually degraded by chemical or enzymatic methods. In this presentation, chondroitin sulfate A was degraded by free radicals induced by hydrogen peroxide in the presence of cupric ions. Degraded chondroitin sulfate fractions with different molecular weights were analyzed by GPC-HPLC and polyacrylamide gel-electrophoresis. These results suggest that a controlled free radical process is an effective method for chemical degradation of chondroitin sulfate.