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.