

†Anticancer Agents Research Laboratory, Korea Research Institute of Bioscience and Biotechnology, ‡College of Pharmacy, Chungnam National University, Korea

Nuclear factor  $\kappa$ B (NF- $\kappa$ B) represents a family of eukaryotic transcription factors participating in the regulation of various cellular genes. Since aberrant regulation of NF- $\kappa$ B has been implicated in the pathogenesis of various diseases including inflammation, asthma, atherosclerosis, AIDS, septic shock, arthritis, and cancer, this transcription factor has been shown to be an interesting target of new drug discovery. While searching for NF- $\kappa$ B modulators from natural resources, we found that an ethyl acetate extract of the culture broth of fungi B000527 activated NF- $\kappa$ B activity as assessed by a NF- $\kappa$ B reporter assay. Two closely related trichothecenes, Harzianum A (1) and a new compound Harzianum B (2), were identified as the active principles by activity-guided fractionation. The structure of 1 and 2 was determined by extensive spectral analyses including EI-MS,  $^1\text{H}$  and  $^{13}\text{C}$ -NMR, HMQC. Compound 2 contains a (*E*, *Z*, *E*)-2, 4, 6-octatriendioic acid esterified on the 4 beta-hydroxyl group of trichodermol. These two compounds significantly increased NF- $\kappa$ B activity in RAW264.7 cells transfected with NF- $\kappa$ B reporter construct in a dose-dependent manner with ED<sub>50</sub> values of 0.01  $\mu\text{g}/\text{ml}$  and 0.1  $\mu\text{g}/\text{ml}$ , respectively, without affecting cell viability. Furthermore, treatment of compound 1 to RAW264.7 cells induced the degradation of I $\kappa$ B $\alpha$  as well as DNA-binding activity of NF- $\kappa$ B.

[PC1-26] [ 10/17/2002 (Thr) 13:30 - 16:30 / Hall C ]

The effects of some natural products on mouse melanoma cells in vitro

Cha EunJung<sup>O</sup>, Kim AnKeun

Sookmyung Women's University

To identify inhibitors of melanogenesis, we compared the effect of some natural products on mushroom tyrosinase, human melanocytic tyrosinase activity and melanin content. The cytotoxicity of the component were also tested on cultured mouse melanoma cells. Each extract significantly inhibited tyrosinase activity and melanin synthesis in vitro and B 16 melanoma cell lines. In B 16 cell lines, watermelon's inner shell extract inhibited tyrosinase activity as strong as kojic acid at 150  $\mu\text{g}/\text{ml}$  concentration. And morning glory's seed extract inhibited melanin synthesis more than kojic acid at 150  $\mu\text{g}/\text{ml}$  concentration. Each extract were strong inhibitors of tyrosinase activity and total melanin synthesis in B 16 mouse melanoma cell lines at less than 100  $\mu\text{g}/\text{ml}$  concentration. These result show that extract of watermelon's inner shell, lettuce, morning glory's seed and licorice root could be developed as skin whitening component of cosmetics.

[PC1-27] [ 10/17/2002 (Thr) 13:30 - 16:30 / Hall C ]

Inhibitory effects of a new iridoids, patridoid I and II on TNF, iNOS and COX-2 expression in cultured murine macrophages

Ju HyeKyung<sup>O</sup>, Jung Hyejin, Moon TaeChul, Lee Eunkyung, Baek SukHwan, An RenBo, Bae KiHwan, Son KunHo, Kim HyunPyo, Kang SamSik, Chang HyeunWook

College of Pharmacy Yeungnam University

Possible role of anti-inflammatory effects of a new iridoids, patridoid I, II and II-A which were isolated from *Patrinia saniculaefolia*, examined by assessing their effects on tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) and 2 enzymes, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in the lipopolysaccharide (LPS)-stimulated murine macrophage-like cell line RAW 264.7. Among them, patridoid II consistently inhibited the production of TNF $\alpha$  and NO production in a dose dependent manner. But patridoid I and patrioid II isomer patrioid II-A, these compounds very weakly inhibited NO production. Moreover, treatment of macrophage with these compounds, the decrease in NO products was accompanied by a decrease in iNOS protein level as assessed by Western Blot. But these compounds did not affect COX-2 protein expression in LPS-stimulated macrophage. Our results suggest that patridoid II could become a leading compound for developing a novel type of anti-inflammatory drugs.

[PC1-28] [ 10/17/2002 (Thr) 13:30 - 16:30 / Hall C ]