College of Pharmacy, Kangwon National University

Flavonoids from plant origin show anti-inflammatory activity in vitro and in vivo. In addition to inhibition of inflammation-associated enzymes such as cyclooxygenases and lipoxygenases, they have been found to regulate the expression of inflammation-associated proteins from in vitro experiments. In order to prove in vivo behavior and the potential for beneficial use against inflammatory skin disorders, the effect of wogonin (5,7-dihydroxy-8-methoxyflavone) on in vivo expression of several inflammation-associated genes was examined in the intact as well as in the inflamed mouse skin by reverse transcriptase-polymerase chain reaction analysis. When applied topically on the intact skin, only a high dose treatment of wogonin (1000 mg/ear/3 days) slightly increased cyclooxygenase-1 and fibronectin m-RNA. On the other hand, wogonin at the doses of 250 – 1000 mg/ear/3 days potently lowered m-RNA levels of cyclooxygenase-2 and tumor necrosis factor-a with less effect on intercellular adhesion molecule-1 and interleukin-1b in a sub-chronic skin inflammation model of tetradecanoylphorbol 13-acetate-induced ear edema (multiple treatment). The decrease of prostaglandin E_2 concentration (27.3 – 34.3%) was concomitantly observed in the wogonin-treated groups. A similar effect was also observed in an acute inflammation model of arachidonic acid-induced ear edema. From the present study, wogonin was proved to differentially regulate the expression of inflammation-associated genes in vivo and to become a useful therapeutic agent for skin inflammatory diseases mainly due to its modulation of the expression of proinflammatory molecules.

[PC1-37] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

The roles of ceramide on the cellular signal transduction in RAW 264.7 murine macrophages activated with lipopolysaccharide and interferon-gamma.

Park Sung Sik°, Chun Young Jin
Department of Immunology, College of Pharmacy, Chung-Ang University, Seoul 156-756, Korea

Ceramide acts as a lipid second messenger in the cellular signal transduction and is involved in mediating a variety of cell functions such as proliferation, differentiation, growth arrest, and apoptosis. In the present study, we have investigated the effect of ceramide on cellular cytotoxity and reactive oxygen species (ROS) to understand the relationship between them. Ceramide treatment significantly increased cell death in RAW 264.7 murine macrophages activated with lipopolysaccharide (LPS) and interferon-g (IFN-g). Interestingly, cotreatment with C_6-ceramide and LPS/IFN-g highly enhanced the production of ROS in cells. It is also shown that the production of NO and iNOS are inhibited by ceramide treatment in activated RAW cell, but the level of COX-2 was unaffected. The elevated level of ROS production was reduced by the presence of an NO donor S-nitroso-N-acetylpenicillamine (SNAP). These findings illustrate that the enhanced ROS generation may modulate the ceramide-mediated apoptosis and the cross-talk between NO and ROS-dependent transduction pathway will be possible. Understanding of the detailed mechanism will elucidate the pathway of ceramide-mediated cell death in murine macrophages.

[PC1-38] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Inhibition of nitric oxide and TNF-α production by propenone compound through blockaded of NF-κB activation in cultured murine macrophages

Ju Hye Kyung, Lee Eunkyung, Jahng Yurngdong, Lee Eung-Seok, Chang Hyeun Wook
College of Pharmacy, Yeungnam University

Lipopolysaccharide (LPS)-stimulated macrophages produced a large amounts of nitric oxide (NO) by inducible nitric oxide synthase (iNOS). This is an important mechanism in macrophages-induced septic shock and inflammation. In the present study, we tested a synthetic propenone compound, 1-furan-2-yl-3-pyridin-2-yl-propenone (FPP-3) for its ability to inhibit the production of tumor necrosis factor-a (TNF-α) and an inducible enzyme, iNOS, in the LPS-stimulated murine macrophage-like cell line, Raw264.7. FPP-3 consistently inhibited nitric oxide (NO) and TNF-α αproduction in a dose dependent manner, with IC_{50} values of 10.0 and 13.1 μM, respectively. Western Blotting probed with specific anti-iNOS antibodies showed that the decrease in the quantity of the NO product was accompanied by a decrease in the iNOS