

Bcl-2 levels was concentration -dependant decreased by costunolide and further we found that antioxidant, N-acetyl cystein(NAC) treatment attenuated costunolide-induced cytotoxicity and apoptosis. These results suggest that ROS and caspase-3 protease mediated signal transduction are essential for costunolide-induced apoptosis.

[PC1-11] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

CURCUMIN INHIBITS EXPRESSION OF CYCLOOXYGENASE-2 AND INDUCIBLE NITRIC OXIDE SYNTHASE AND ACTIVATION OF NF-kappaB AND AP-1 TRANSCRIPTION FACTORS

Chun Kyung-Soo, Keum Young-Sam, Han Seong-Su, Seo Hyo-Joung, Lee Jeewoo, and Surh Young-Joon

College of Pharmacy, Seoul National University, Seoul, Korea

Recently, considerable attention has been focussed on identifying edible and medicinal phytochemicals that retain chemopreventive activities. Spices and herbs contain phenolic substances with potent antioxidative and anti-inflammatory properties. Curcumin, a yellow colouring ingredient of turmeric (*Curcuma longa* L., Zingiberaceae), has been shown to inhibit experimental carcinogenesis and mutagenesis, but molecular mechanisms underlying its chemopreventive effects remain unclear. In the present work, we have examined the effects of curcumin on expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) which play a important role in mediating inflammatory responses. Topical application of the tumor promoter, 12-O-tetradecanoylphorbol-13-acetate (TPA) onto shaven backs of female ICR mice induced epidermal expression of COX-2 and iNOS proteins and their mRNA in a time-related manner. Curcumin, when topically given 30 min prior to TPA, significantly suppressed TPA-induced COX-2 and iNOS expression at both transcriptional and translational levels. Yakuchinone A and Yakuchinone B, pungent diarylheptanoids derived from *Alpinia oxyphylla* Miquel (Zingiberaceae) also exhibited inhibitory effects on epidermal expression of COX-2 and iNOS in mice treated with TPA. Curcumin pretreatment resulted in attenuation of TPA-induced activation of NF-kappa B in mouse epidermis. Curcumin-mediated inactivation of NF-kappa B appears to be associated with its suppression of I-kappa B degradation and subsequent nuclear translocation of the functionally active subunit, p65 as well as direct interference with DNA binding of NF-kappa B. Likewise, TPA-stimulated activation of another transcription factor, activator protein-1 (AP-1) was inhibited by curcumin pretreatment. Similar down-regulation of NF-kappa B and AP-1 by curcumin was observed in cultured human promyelocytic leukemia (HL-60) cells stimulated with TPA. Taken together, the results of this study may provide molecular basis of cancer chemopreventive properties of curcumin.

[PC1-12] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Zaluzanin-C and Estafiatone from *Anisliaea acerifolia* inhibit of LPS and IFN-gamma-induced Nitric Oxide Synthase expression and production of PGE2 in RAW 264.7 cell

Yoon JW^o, Ahn SH, Shin SK, *Hong SY,[#] Lee HY, Zee OP, Lee KR, Han JW, Lee HW

College of Pharmacy, *Department of Genetic Engineering, Sungkyunkwan University, #Department of Medicine Konyang University

Nitric Oxide (NO) is an important regulator and effector molecule in various inflammatory disease states. High output of NO during inflammation is generated by the inducible NO Synthase (iNOS) and increases production of prostglandin E₂ (PGE₂) through the activation the cyclooxygenase-2 (COX-2) in macrophage. PGE₂ is important mediators of inflammation, vasodilatation, pain and pyrexia. Thus inhibitors of iNOS could be a novel candidate as anti-inflammatory drug. In this study, we