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In the previous study, we reported the differentiation effects of the KH-1 isolated from *Vitis vinifera* on human neuroblastoma cell line SH-SY5Y.
The KH-1 decreased cell proliferation and increased neuritogenesis, neurite length, NO and L-citrulline production at the concentration range of 0.1~1uM.
The aim of the present work is to investigate whether the NO production is generated from inducible NO synthase(iNOS) which is one of the three different NOS isoforms: ncNOS, ecNOS and iNOS Aminoguanidine(AG) was used as a selective inhibitor of the iNOS. There were two AG treatment groups; The AG(0.3mM) and KH-1(0.1~1uM) added to the cells simultaneously and AG was added to the KH-1 treated cells at day 4. The morphological and functional parameters to determine a change occurring in the KH-1 treated cells by the AG showed similar patterns with the previous investigation in neuritogenesis, neurite length, NO and L-citrulline production.
Use of the AG inhibited decreasing cell proliferation in the both groups. The neuritogenesis, NO and L-citrulline generation levels were declined to the control levels or showed some what lower values. These findings indicate that the KH-1 induced differentiation of human neuroblastoma cells is associated with NOS through iNOS induction. Furthermore, NO may play by acting as a signal molecule of the human neuroblastoma cell line SH-SY5Y during differentiation

[PC1-9] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Induction of Apoptosis in U937 Human Leukemia Cell by Kalopanaxsaponin A

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In previous study we screened that triterpenoids, kalopanaxsaponin A, B, I, kaikasaponin III and hederagenin, isolated from kalopanax pictus showed different cytotoxicity against various cancer cells. This study was purposed to describe the mechanism of kalopanaxsaponin A which selective cytotoxicity on cancer cells. 20㎍/㎖ of kalopanaxsaponin A induced significant apoptosis through inhibition of PTK, Bcl-2, topoisomerase II-α and activation of PKC-α and caspase-3. Furthermore, kalopanaxsaponin A increased hypodiploid nuclei and caused a nucleosomal ladder. From these result we suggest that kalopanaxsaponin A induces apoptosis through multi target signal transduction in U937 human leukemia cell.

[PC1-10] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Mechanism of Costunolide-Induced Apoptosis in Human Leukemia Cell Lines

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The present work was carried out to examine the mechanism of costunolide-induced apoptosis in HL-60 human leukemia cell line. Costunolide is a sesquiterpene lactone compound isolated from leaf of Magnolia sieboldii and differentiated HL-60 and U937 cells to monocyte/macrophage-like cells. Costunolide produced a potent protein tyrosine kinase inhibition in vitro and in vivo dependant on concentration in HL-60. PTK inhibition is associated with the increase of intracellular ROS level. Treatment of HL-60 cells with costunolide induced PARP cleavage accompanied with DNA fragmentation. These results suggest that induction of apoptosis by costunolide resulted in the activation of caspase-3 proteases, which are interleukin-1β-converting enzyme family protease.

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

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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-ɣ-induced Nitric Oxide Synthase expression and production of PGE2 in RAW 264.7 cell

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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 E_2 (PGE_2) through the activation the cyclooxygenase-2 (COX-2) in macrophage. PGE_2 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