72 to 144 sec and 19 to 27 sec, respectively. With 0.5 M NaCl eluted fraction, we observed prolongation in clotting time (aPTT) in a dose-dependent manner and approximately three times prolongation was obtained at 200 μg/150 μl.

[PC1-6] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Differentiation Inducer Activity of Magnolialide, a 1β-Hydroxyeudesmanolide Isolated from Cichorium intybus on Human Leukemia Cells

Lee KT1°, Park HJ2, Han YN3

1College of Pharmacy, Kyung Hee University, Seoul 130-701, 2Department of Botanical Resources, Sangji University, Wonju 220-702 , 3Natural Products Research Institute, Seoul National University, Seoul 110-460, Korea

Cichorium intybus contained two 1β-hydroxyeudesmanolides, magnolialide and artesin together with several constituents. Magnolialide exhibited a growth-inhibitory activity against several tumor cells and it appeared to induce differentiation of human leukemia HL-60 and U-937 cells to monocyte/macrophage-like cells, Another 1β-hydroxyeudesmanolide, artesin, and other constituents were not active. The content of magnolialide was shown to be highest in the leaves of Inje cultivar among the investigated cultivars in this study.

[PC1-7] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Inhibitory effect of sophoricoside analogs on proinflammatory cytokines

Yun J°, Lee HK, Min KR, Kim Y

College of Pharmacy, Chungbuk National University & Korea Research Institute of Bioscience and Biotechnology

IL-5, IL-3 and GM-CSF are known to be involved in allergic inflammation, and their receptors are composed of ligand-specific alpha subunits associated with a common beta subunit. IL-1, TNF and IL-6 are well known as proinflammatory cytokines. Inhibitory effects of soporicoside and its analogs (genistin, genistein and orobol), which were isolated from S. japonica, on the cykokine bioactivity have been invesigated. Sophricoside showed inhibitory effects on IL-5, IL-3 and IL-6 bioactivities but did not inhibit the GM-CSF, IL-1 and TNF bioactivities. Genistin inhibited the IL-5 and IL-3 bioactivities but not on the other cytokine bioactivities. Genistein and orobol showed inhibitory effects on IL-5, IL-3, GM-CSF and IL-6 bioactitivies but did not inhibit the IL-1 and TNF bioactivities. Among the compounds, sophoricoside showed the highest inhibitory effects on IL-5, Il-3 and IL-6 bioactivities with IC50 values of 1.9 uM, 6.9 uM and 6.0 uM, respectively and orobol did show on GM-CSF bioactivity with an IC50 value of 18.0 uM. The result would provide an additional mechanism by which the compounds exert immunosuppressive and anti-inflammatory effects.

[PC1-8] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

NO Produced by iNOS Mediates KH-1-Induced Differentiation In a Human Neuroblastoma Cell Line SH-SY5Y

Kim H°, Choung SY

College of Phrmacy, Kyung Hee University, Hoegidong, Dongdaemunku, 130-701, Seoul, Korea

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

Jang JW1°, Sohn IC1, Park HJ2, Kwon SH2, Lee KT1

1College of Pharmacy, Kyung Hee University, Seoul 130-701, 2Department of Botanical Resources, Sangji University, Wonju 220-702, Korea

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

Lee SH(1), Choi JH(1), Park HJ(3), Park JH(2), Lee KT(1)

College of pharmacy(1) and College of medicine(2), Kyung Hee University, Seoul, Korea, Departmant of Botanical Resources(3), Sangi University, Wonju, Korea.

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.