Induction of iNOS gene expression by alpha-Hederin in macrophages

Choi ChulYung°, Jeong HyeGwang

Department of Pharmacology, Chosun University, Kwangju, South Korea

Alpha-Hederin, a triterpene saponin, is reported to have antitumor activities, however, the mechanism underlying its therapeutic effects is not known. In this study, we examine the effects of alpha-Hederin on the release of nitric oxide (NO) and the level of inducible nitric oxide synthase (iNOS) gene expression in mouse macrophages. Alpha-Hederin elicited a dose-dependent increase in NO secretion. Reverse-transcription polymerase chain reaction showed that the increased NO secretion was due to an increase in iNOS mRNA. Since the promoter in iNOS gene contains binding motifs for NF-kB, the effect of alpha-Hederin on the inactivation of this transcripts factor was determined by transient transfection assay. Employing a transfection and reproter gene expression system with p(NF-kB)3-Luciferase, the treatment of alpha-Hederin produced a dose-dependent increase of luciferase activity in RAW 264.7 murine macrophages cell line. These results demonstrate that alpha-Hederin stimulates NO release and is able to upregulate iNOS expression through NF-kB transactivation, which may be a mechanism, whereby alpha-Hederin elicits its biological effects.

[PD2-37] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Up-regulation of inducible nitric oxide synthase expression by 18b-glycyrrhetinic acid in macrophages

Kim JiYoung°, Jeong HyeGwang

Department of Pharmacology, Chosun University, Kwangju, South Korea

Glycyrrhizin, a triterpenoid saponin fraction of licorice, is reported to have anti-viral and anti-tumor activities and is metabolized to 18b-glycyrrhetinic acid (GA) in the intestine by intestinal bacteria. However, the mechanism underlying its effects is poorly understood. To further elucidate the mechanism of GA, the aglycone of glycyrrhizin, we investigated the effects of GA on the release of nitric oxide (NO) and at the level of inducible nitric oxide synthase (iNOS) gene expression in mouse macrophages. We found that GA elicited a dose-dependent increase in NO production and in the level of iNOS mRNA. Since iNOS transcription has been shown to be under the control of the transcription factor NF-kB, the effects of GA on NF-kB activation were examined. Transient expression assays with NF-kB binding sites linked to the luciferase gene revealed that the increased level of iNOS mRNA, induced by GA, was mediated by the NF-kB transcription factor complex. By using DNA fragments containing the NF-kB binding sequence, GA was shown to activate the protein/DNA binding of NF-kB to its cognate site, as measured by electrophoretic mobility shift assay. These results demonstrate that GA stimulates NO production and is able to upregulate iNOS expression through NF-kB transactivation in macrophages.

[PD2-38] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Monoamine Oxidase Inhibitory Component from the Fructus of Piper longum (II)

Lee SeonA°, Choi WooHoi, 1Oh GabJin, Son GunMai, Hong SeongSu, Hwang JiSang, Lee MyungKoo, Lee KyongSoon, Ro JaiSeup

College of Pharmacy, Chungbuk National University, Cheongju 361-763, and 1SamJin Pharm. Co. LTD., Hwasung 445-920

Monoamine oxidase(MAO) [EC 1.4.3.4] is flavin-containing enzyme, and catalyzes the oxidative deamination of endogenous neurotransmitter amines as well as exogenous amines. It exists in two subtypes, MAO-A and MAO-B, on the basis of their different specificities toward substrates and inhibitors. We had screened medicinal plants to search for novel MAO inhibitors from medicinal plants, and we discovered that the MeOH extract of the Fructus of Piper longum showed high inhibition against MAO. The MeOH extract was therefore subjected to the bioactivity-guided fractionation. Compound 1 was isolated from CH2Cl2 fraction. Compound 1 showed significant inhibitory effect against MAO-B(IC50 : 0.37 μg) than

MAO-A(IC50 : 6.3 μg). Compound 1 was also revealed to inhibit competitively MAO-B.

[PD2-39] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Free Radical Scavenging and Hepatoprotective Activities of Traxacum mongolicum

Jun JungYang°, Ko EunKyung, Oh MyungHun, Kim MiHee, Park SungUk, Kim YounChul

College of Pharmacy, Wonkwang University, Spela Co. Ltd.

There is now increasing evidence that free radicals and active oxygen species are involved in a variety of pathological events. Free radical-mediated cell damage and free radical attack on polyunsaturated fatty acids result in the formation of lipid radicals. These lipid radicals react readily with molecular oxygen to produce peroxy radicals responsible for initiating lipid peroxidation. The peroxidation of cellular membrane lipid can lead to cell necrosis and considered to be implicated in a number of pathophysiological conditions as well as in the toxicity of many xenobiotics. Therefore, substantial efforts have been made in recent years to identify both natural and synthetic antioxidants. In the course of screening for free radical scavenging activity from plants, the MeOH extract and its fractions of *Taraxacum mongolicum* (Compositae) were examined for their scavenging effects on DPPH and superoxide radicals, and hepatoprotective effects on tacrine-induced cytotoxicity in human hepatoma cell line, Hep G2 cells. Both CH_2Cl_2 and BuOH soluble fractions of the MeOH extract showed the free radicals scavenging and hepatoprotective effects. From these results, it is suggested that hepatoprotective effect of these fractions rely on the free radical scavenging activity in some extent.

[PD2-40] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Anti-inflammatory compounds from Patrinia saniculaefolia

An RenBo°[1], Jung Hyejin [2], Chang HyeunWook[2], Son KunHo[3], Kim HyunPyo[4], Kang SamSik [5], Bae KiHwan [1]

Chungnam National University[1], Yeungnam University[2], Andong National University[3], Kangwon National University[4], Seoul National University[5]

Two new iridoids, patridoid I , patridoid II , and other constituents nardostachin, squalene, β-farnesene which were isolated from the whole plant of *Patrinia saniculaefolia* Hemsley (Valerianaceae) have been evaluated for their in vitro anti-inflammatory activity.
Anti-inflammatory activity was evaluated by leukotriene C4 (LTC_4)-assay which was tested in cellular system generating 5-lioxygenase (5-LOX) pathways of arachidonate metabolism.
As a result, patridoid I , patridoid II and squalene showed a significant effect with IC_{50} values of 46.98 μM, 41.73 μM and 36.27 μM, respectively.

[PD2-41] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Antioxidative activity of flavonoid compounds from Cudrania tricuspidata root bark

Lee Seung Jae°, Ham Inhye, Chon In Ju, Kim Hohyun, Sung Whan Gil, Whang Wan Kyunn*

College of Pharmacy, Chung-Ang University

Cudrania tricuspidata have been used for anti-inflammatory, anti- hepatotoxic, anti-hypertensive and anti-diabetic activities.
In this study, isolation of chemical constituents of *Cudrania tricuspidata* were carried out by extracting with