Induction of iNOS gene expression by alpha-Hederin in macrophages

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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.

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

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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.

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

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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