B31

Antioxidant effects of quinoline alkaloids and 2,4-di-tert-butylphenol isolated from Scolopendra subspinipes

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Objectives

During the last decade, it has been determined that ox-LDL contributes to the development of atherosclerosis by several mechanisms. Oxidative modification of plasma LDL enhances its atherogenic potency and promotes its accumulation in monocyte-macrophages in the vascular wall, which lead to vascular lipidosis at the early stages of atherosclerosis. Thus, the prevention of LDL oxidation by antioxidants may arrest the progression of atherosclerosis. Many antioxidants have been developed to exhibit the anti-atherogenic activities by inhibiting foam cell formation in an animal model. Several antioxidants such as probucol, N,N'-diphenylphenylenediamine, and butylated hydroxy-toluene (BHT) have been shown to decrease the degree of LDL oxidation and the extent of atheromatous lesions in animal models of atherosclerosis, but they had various side effects.

In this study, we describe the isolation and antioxidant activities against LDL oxidation of the compounds **1-3**.

Materials and Methods

○ Material

The dried centipede, S. subspinipes, was purchased from a market of traditional Asian medicine in Daejeon, Korea.

○ Methods

The IR spectra were taken on a FT-IR spectrometer MB-100 (Bomen Co.) instrument with KBr pellets. ^{1}H-NMR, ^{13}C-NMR, and 2D-NMR (^{1}H-^{1}H COSY, HMBC, and HMQC) spectra were recorded on a Bruker AM 500 FT-NMR [FT 500 MHz NMR spectrometer AMX-500 (Bruker Co.)] with CD_3OD. HREI-MS was recorded on a JMS-700 (Jeol, Japan). Silica gel (230 400 mesh) and Lichroprep RP-18 (40-63 μM) for column chromatography and silica gel 60 F254 for TLC were supplied by Merck Korea Ltd..

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Results and Discussion

The oxidized loe-density lipoprotein (ox-LDL) plays a critical role at the early stages of atherosclerosis. Two quinoline alkaloids, 3,8-dihydroxyquinoline (**1**) and 2,8-dihydroxy-3,4-dimethoxyquinoline (**3**), and 2,4-아-tert-butylphenol (**2**) were isolated from the dried body of Scolopendra subspinipes. Compounds **1-3** exhibited antioxidant activities on copper-mediated (**1**: IC_{50} = 2.6 μM, **2**: IC_{50} = 8.2 μM, **3**: IC_{50} = 63.0 μM), AAPH-mediated oxidation (**1**: IC_{50} = 3.9 μM, **2**: IC_{50} = 9.9 μM, **3**: IC_{50} = 71.8 μM), and SIN-mediated oxidation (**1**: 70%, **2**: 52%, **3**: 29% at 5.0 μM) in the TBARS assay. The antioxidant activities of compounds **1-3** were tested with respect to other parameters, such as the lag time of conjugated diene formation, relative electrophoretic mobility (REM) of ox-LDL, and apoB-100 fragmentation on copper-mediated LDL-oxidation, In addition, compounds **1-3** showed 1,1-diphenyl-2-picrylhydrasyl (DPPH) radical scavenging activity and compound **1** also exhibited metal chelation activity. Also, methanolic extracts of *S. subspinipes* showed an inhibitory effect on the NO production and iNOS expression in RAW264.7 cell.