

Anti-oxidant and Anti-atherosclerotic Effects of the Ethanolic Extracts of
Artemisia princeps Pamp. cv. Sajabal

¹NRL of Lipid Metabolism & Atherosclerosis, KRIBB, Daejeon, ²Ganghwa Agricultural Technology Service Center, Incheon, ³Graduate School of Biotechnology & Plant Metabolism Research Center, Kyung Hee University, Suwon, ⁴Department of Food Science & Nutrition, Kyungpook National University, Daegu, ⁵College of Pharmacy, Kyung Hee University, Seoul, Korea

Jong-Min Han¹, Sojin An¹, Min-Jung Kim¹, Yue-Jan Jin¹, Hae-Gon Chung²,
Nam-In Baek³, Myung-Sook Choi⁴, Kyung-Tae Lee⁵, and Tae-Sook Jeong^{1,*}

Objectives

Artemisia princeps has been widely used in traditional Korean medicine in treating of colic, vomiting and diarrhea, and irregular bleeding from the uterus. *Artemisia princeps* Pamp. cv. Sajabal is particularly cultivated in Ganghwa County, a place located in the west coast of Korea. They contain a high-content of flavonoids such as eupatilin and jaceosidin compared to the *Artemisia* herbs from other regions in east and south coast of Korea. The extracts of *A. princeps* Pamp. cv. Sajabal (ESJ) has been reported to anti-diabetic and antiallergic activities. In the current study, we investigated anti-oxidant and anti-atherosclerotic effects of ESJ in RAW264.7 cells and LDLr^{-/-} mice.

Materials and Methods

○ Material

The aerial parts of *A. princeps* Pamp. cv. Sajabal were provided from Ganghwa County Agricultural Technology Service Center, Incheon, Korea, which were harvested at Gangwha County in 2003 and stored for 3 years in the air. The aerial parts were ground and soaked in 95% ethanol for 8 h. The ethanolic extracts were filtered through Whatman No. 1 filter paper and concentrated under vacuum at 40 °C.

*Corresponding author: Tae-Sook Jeong E-mail: tsjeong@kribb.re.kr Tel: 042-860-4558

○ Experiments

Human monocyte THP-1 cells obtained from American Type Culture Collection, and the cells were incubated at 1×10^6 cells/well in the phorbol 12-myristate 13-acetate for 4 day to induce differentiation into macrophages. In the present studies, we describe anti-inflammatory effects of ESJ against production of NO, ROS, and inflammatory cytokines through NF- κ B activation in LPS-induced macrophages.

Homozygous LDL receptor deficient (LDLR^{-/-}, C57BL/6J background) mice were purchased from the Jackson Laboratory (Bar Harbor, ME) and C57BL/6J mice were purchased from the Dae Han Biolink, Inc. One negative control group (CD) was fed with a chow diet containing normal diet composition and other control group (HFHC) was fed with a Western diet containing 21% fat and 0.15% cholesterol. ESJ group was fed a Western diet supplemented with 1.0% ESJ (wt/wt diet) for 8 weeks. And we investigated anti-oxidant and anti-atherosclerotic effects of the ESJ.

Results and Discussion

We explored the effect of ESJ on Cu²⁺-mediated human LDL oxidation. ESJ showed the potent LDL-antioxidant activity in the thiobarbituric acid-reactive substances (TBARS) assay. ESJ inhibited the formation of conjugated diene during Cu²⁺-induced LDL oxidation as well as apoB-100 fragmentation by LDL oxidation.

Treatment of RAW264.7 macrophages with ESJ decreased the generation of reactive oxygen species (ROS) and nitric oxide (NO). Furthermore, ESJ suppressed this LPS-stimulated production of iNOS and IL-6 in a dose dependent manner. ESJ inhibited the degradation of I κ B α and the translocation of NF- κ B p65 as well as DNA binding activity of NF- κ B in LPS-stimulated RAW264.7 cells. From this results, we propose that ESJ can be attenuates atherosclerosis development by its antioxidant activity and inhibition of NF- κ B.

In vivo studies, ESJ reduced the aortic lesion formation and macrophage accumulation at 37% and 43%, respectively, compared to control. In aorta, ESJ decreased the transcriptional levels of CD36, LOX-1, ABCA1, ICAM-1, VCAM-1, TNF- α , IL-1, COX-2, and iNOS and increased the levels of CYP7 family. ESJ also reduced epididymal fat accumulation (28%) and plasma lipid peroxidation (16%).

These findings indicate that ESJ, may have an additional beneficial effect on inflammatory cascade as well as antioxidant properties, would provide useful approach for the prevention of inflammatory and atherosclerotic diseases.