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저밀도지단백질 수용체 결손 마우스에서 동맥병변 형성을 억제하는 콩잎 주정추출물의 항동맥경화 효과

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Anti-atherosclerotic Effects of Ethanol Extract of Soy Leaves (*Glycine max*) Supplementation on Suppression of Atherogenic Lesion Formation in LDL Receptor-Deficient Mice

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실험목적 (Objectives)

Atherosclerosis is a chronic vascular inflammatory response. The cascade of leukocyte - endothelial cell interactions and leukocyte infiltration are crucial processes in atherogenesis. For a long time, dietary soy (*Glycine max* L. Merr.) products have been known to have beneficial effects on the atherosclerosis, hypercholesterolemia, and lipoprotein peroxidation. The extracts of soy leaves contain well known active compounds, genistin and kaempferol glycosides. Although there were many studies about the health benefits of soybean, there was no report about the biological effect of soy leaves in the diet-induced atherosclerosis using mouse model. The objective of this study was to investigate the inhibitory effects of ethanolic extracts of *Glycine max* leaves (EGML) on development of early atherosclerosis. We also examined the expression of adhesion molecules and inflammatory factors in $LDLR^{-/-}$ mice and in TNF-α-stimulated human umbilical vein endothelial cells (HUVECs).

재료 및 방법 (Materials and Methods)

The dried soy leaves were collected from Jinju, Korea. Homozygous LDL receptor deficient ($LDLR^{-/-}$, C57BL/6J background) mice were purchased from The Jackson Laboratory (Bar Harbor, ME) and housed at the Korean Research Institute of Bioscience and Biotechnology (KRIBB). Ten-week-old male $LDLR^{-/-}$ mice (n=24) were randomly divided into three groups. The control group (n=8) was fed a Western diet of 0.15% cholesterol and 21% fat by weight

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(Dyets Inc., PA) while the EGML experimental group (n=10) was fed a Western diet supplemented with 1% wt/wt diet EGML for 12 weeks. Additionally, we used chow diet-fed $LDLR^{-/-}$ mice (n=6, CD group) as negative control. Plasma levels of lipid parameters were measured using an automatic blood chemical analyzer. All samples were embedded in a Tissue-Tek OCT compound, and were placed on a cryotome model AS620. Cryostat sections of aortic roots (10 μm) were collected and stained with oil red O. Macrophage infiltration was detected with MOMA-2, a mouse macrophage specific antibody. To investigate the change in the expression of inflammation-related gene by EGML, we examined real time RT-PCR analysis.

실험결과 (Results)

In this study, the EGML significantly reduced TNF-α-induced expression of adhesion molecules, chemokines, and proinflammatory cytokines in HUVECs. Especially, EGML improve the suppression of Krüppel-like factor 2 (KLF2), a novel regulator of endothelial gene expression in TNF-α-stimulated HUVECs. In vivo experiment using $LDLR^{-/-}$ mice, EGML supplementation with a Western diet slightly lowered plasma total cholesterol and triglyceride levels as compared to the control group. Atherosclerotic lesions in a Western diet fed-$LDLR^{-/-}$ mice had significantly positive oil red O staining noted in examination of tissue cross-sections. However, EGML supplementation reduced the presence of atherosclerotic plaque by up to 70% in the proximal aortic sinus (oil red O-stained lesions was 141.4±56.3 x 10^3 μm^2 in control group versus 58.2±32.9 x 10^3 μm^2 in the EGML-supplemented group, $p<0.01$) and reduced in the ascending aorta lesion formation compared with control group. Moreover, the mRNA and protein levels of VCAM-1, ICAM-1, Fractalkine, TNF-α, IL-1β, and MCP-1 were significantly suppressed in aorta.

These data suggest that EGML may have potential as a safe and effective anti-atherogenic agent via the inhibition of lesion formation and vascular inflammation.