

## Abstract

# Effect of Fermented Food Products as Vitamin K Dietary Sources on the Development of Atherosclerotic Lesions in ApoE/LDLR<sup>-/-</sup> Mice<sup>†</sup>

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**Abstract:** The term vitamin K refers to a group of similarly structured fat-soluble compounds. One of the vitamin K forms is phyloquinone, known as vitamin K1. The main nutritional sources of vitamin K1 are green, leafy vegetables like kale, beetroot, spinach and broccoli. Other forms of vitamin K are menaquinones (vitamin K2) that can further be divided into a few subtypes depending on the number of isoprenoid residues in the side chain (MK-n). Besides MK-4, bacteria synthesize all menaquinones. As such, the main dietary sources of vitamin K2 are natto, dairy (especially fermented products, e.g., cheese), meat and eggs. Until recently, vitamin K was associated with the regulation of the coagulation system. Interest in the biological activity of these compounds increased once it was discovered that vitamin K2 affects the processes of the calcification of both bones and soft tissues. Vitamin K can reduce oxidative stress and inflammation. The objective of the present study was to verify the hypothesis about the effectiveness of dietary vitamin K2 as an anti-atherosclerotic agent. An in vivo experiment on ApoE/LDLR<sup>-/-</sup> mice was conducted to verify this hypothesis. Two month-old mice were fed AIN-93G modified diets containing vitamin K-rich products, i.e., natto, cheese (Munster), sauerkraut and synthetic vitamin K2 MK-7 (100 µg/kg b.w./day) for 8 weeks. The body weight, weight of organs and glucose concentration were determined. Blood was taken and the aorta dissected. The investigation included both the area of lesions and biochemical parameters such as lipid profile. Quantification of the atherosclerotic area in entire aorta was performed by an en face method. The lipid profile was determined automatically by ABX Pentra 400 (Horiba Medical, Kyoto, Japan). The concentration of vitamins K was determined using UHPLC-MS/MS technique in faeces. Body weights of mice fed MK-7 and Munster were significantly decreased compared to Control (respectively, 20.01 and 19.98 vs 21.45 [g]). Liver's weight of mice fed Munster was significantly increased in comparison to other groups (5.70 vs 4.53 [g/100g] in Control). Glucose concentration was unchanged. Significant changes in plasma lipid profile of mice fed modified diets, especially in groups fed Munster and Sauerkraut, were observed. Total cholesterol and LDL concentrations were significantly increased in Munster and Sauerkraut compared to Control (respectively, for TC 20.45 and 19.80 vs 15.95 [mmol/L]; for LDL 17.15 and 11.94 vs 7.85 [mmol/L]). Moreover, TAG level was significantly increased in Sauerkraut in comparison to Control (2.87 vs 2.23 [mmol/L]). The main forms of vitamin K identified in mouse faeces were menaquinones MK-6. Nutritional factors with an alleviating effect on the development of atherosclerotic plaques are still being investigated.

**Keywords:** vitamin K; fermented products; atherosclerosis; ApoE/LDLr<sup>-/-</sup> mice



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