THE ANTI-INFLAMMATORY POTENTIAL OF DIETARY VITAMIN K_2 IN ATHEROSCLEROSIS PROGRESSION

The purpose of this project is to evaluate the impact of natural dietary vitamin K_2 on the development of atherosclerosis being main cause cardiovascular diseases (CVD). Chronic noncommunicable diseases including atherosclerosis and other CVD, diabetes, obesity, and cancer are now one of the major health problems in developed and developing societies, also in Poland. World Health Organization (WHO) suggested that from these disorders, CVD are the leading cause of death worldwide. It is estimated that by 2030 CVD will cause 23,6 million deaths. Geographical differences and an increased incidence of CVD indicate that life style plays a major role in the development of these diseases. Number of modifiable atherosclerosis risk factors can be eliminated by appropriate dietary habits.

Until recently vitamin K was thought to be associated only with regulation of coagulation system, hence its name from Danish Koagulations vitamin. Term vitamin K refers to the group of lipophilic compounds mainly vitamin K_1 (of plant origin) and vitamin K_2 which consist of several forms depending on length of isoprene side chain. The increased interest in biological activity of these compounds was noticed after discovery, that vitamin K_2 modulates calcification, both bones and soft tissues. The blood vessels calcification process accompanies atherosclerosis. That is why it seems necessary to investigate the effects of vitamin K_2 on atherogenesis.

According to the data on dietary intake of vitamin K, in western diet vitamin K_1 covers 90% of total intake of this compound. Due to the fact that vitamin K_2 (excluding MK-4) is produced by bacterial synthesis, the richest source of these compounds for Europeans may be soft cheeses or sauerkraut consumed in the eastern regions of Europe.

In order to determine the effect of dietary vitamin K_2 on the development of atherosclerosis as well as inflammation, ApoE/LDLR$^{-/-}$ mice will be fed diet supplemented with high-vitamin K_2 products (natto, cheese, sauerkraut). The project involves also in vitro studies in cultured murine macrophages. Methods, such as histological examination, immunohistochemistry, cell culture and gene expression analysis will be used to assess the quantitative development of atherosclerosis, plaque structure and potential molecular mechanisms of dietary vitamin K_2.

The current dietary recommendations included only vitamin K_1. Recent study show, that this recommendation level of vitamin K is rather low, and is enough only to maintain coagulation homeostasis. Unfortunately to use this compound for diseases prevention, highest level of vitamin K should be used. Additionally, not vitamin K_1 but rather vitamin K_2 and its biological functions should be taken into consideration. However, to change current recommendations more studies, describing vitamin K molecular mechanism, are needed. Therefore results of this project may have significant impact on the present state of knowledge and help to inhibit global epidemic of cardiovascular diseases.