

Current medical literature pays special attention to the interdependence between the state of human health and the composition of **gastrointestinal microbiota**. This huge bacterial mass, colonizing the intestines of an adult human can act as another human organ, affecting the integrity of the intestinal barrier, the functioning of the immune system, or the regulation of many life processes occurring in the intestinal lumen under the influence of bacterial metabolites. Microorganisms colonizing human intestines are involved, among others, in the metabolism of carbohydrates, amino acids, xenobiotics, the production of isoprenoids and vitamins. Therefore, qualitative and quantitative changes in the normal composition of intestinal microbiota must lead to deregulation of many life processes occurring in the lumen of the intestine, also including carcinogenesis processes. The substances produced by the gastrointestinal microbiota also include vitamins mainly from group B and K2 (menaquinone) that can be synthesized directly in the lumen of the digestive tract, or on its outside during the fermentation of some food products.

Vitamin K2 includes several homologues, which in their structure contain a ring of 2-methyl-1,4-naphthoquinone and various lengths of side chains, with bacteria colonizing the human gastrointestinal tract which synthesize short-chain homologs of these vitamins ($n \leq 7$). Oral supplementation with vitamin K2 is responsible for healthy bones, prevents vascular calcification and the development of cardiovascular disease, and it is even predicted that due to the presence of a vitamin in the chemical structure of the quinone ring (a functional group that is also present in many chemotherapeutics), it can be used in prevention and even in the treatment of selected cancers. This seems almost impossible, but based on preliminary in vitro studies conducted by a team of Japanese scientists on the human tumour lines of the stomach and liver, pro-apoptotic effect of the synthetic K2-MK4 homologue was demonstrated, and this action was strongly dose-dependent.

The **K2-MK7** homologue is relatively little known, and is synthesized in the largest amount naturally by Gram positive aerobic rods, and by fermentation of various food products. Based on our preliminary research conducted on the human tumor line (Caco-2), the synthetic form of the K2-MK7 homologue also showed an extremely strong pro-apoptotic effect on intestinal epithelial cells, which was slow and increasing over time.

In our project, we plan to check what **species of bacteria** that colonize the healthy human digestive tract will be able to produce the largest amounts of vitamin K2-MK7 by fermentation of selected products (AdSV and HPLC will be used for this study). In addition, based on human intestinal epithelial cancer lines and macrophage lines, research will be carried out to find the answer to the question: will the **natural** form of vitamin K2-MK7 (bacterial origin) be in a comparable manner (like the synthetic homologue) affecting the phenomena of apoptosis, necrosis, prostaglandin secretion and inflammatory cytokines (TNF- α , IL-6, IL-8, INF- γ , IL-12).

Next, based on the **mouse colorectal carcinoma model**, we will compare the anti-inflammatory and anti-cancer effects of the synthetic form K2-MK7 administered orally, relative to the digested extract containing the largest amounts of the natural form of K2-MK7 along with probiotic bacteria carrying out this fermentation process. The changes observed in the histopathological image of the large intestine and the general health of animals will answer the question: do we observe the **anti-cancer effect** of vitamin K2-MK7 in vivo, and whether there will be biological differences between the **synthetic and natural** form K2-MK7. The answer to these questions is very important at the moment, because we are seeing an avalanche increase in the amount of synthetic vitamin K2-MK7 consumed.