

The bacterial infections comprise serious epidemiologic threat mainly due to the wide-spread resistance to the commonly used antibiotics. Moreover, transfer of genetic traits between bacterial species by horizontal gene transfer leads to the occurrence of super-pathogenic strains (super-bugs), multidrug-resistant and containing various virulent factors.

Enteropathogenic *Escherichia coli* (EPEC) strains are common source of food poisoning and hospital infections, leading to the severe complications. One of the most virulent bacterial group among those pathogens are Shiga toxin producing strains. The infections with enterohaemorrhagic *Escherichia coli* (EHEC) may lead to developing of serious life threatening complications such as hemolytic uremic syndrome, hemolytic colitis and acute renal failure. The complex molecular mechanisms underlying the regulation of Shiga toxin synthesis explain the lack of effective and safe therapy of EHEC infections.

The decreasing efficiency of standard antibiotics and the emergence of drug resistance among bacterial pathogens indicate the strong need to develop new antimicrobial factors and therapeutic strategies. Phytoncides are natural, plant-based compounds. Biodiversity of plant world makes it an excellent source of potentially beneficial natural compounds. Some of them can exhibit antibacterial effects which indicate their potential use to combat pathogen infections. However, establishing and registering of new drugs and therapeutics require complex and thorough studies of their mechanisms of action and potential toxicity for humans.

The research performed by our team showed that compounds produced by cabbage family of plants (*Brassicaceae*), isothiocyanates, exhibit antimicrobial effects against EHEC strains. Moreover, in the contrary to many antibiotics, they do not lead to increasing of synthesis of dangerous Shiga toxins. The mechanism of isothiocyanates effect, revealed by our team, involves the induction of the bacterial stress mechanism, called the stringent response, which typically happens in the conditions of starvation.

In the proposed project we plan to extend our current studies to fully elucidate the molecular mechanisms of antibacterial effects of these compounds, and most importantly, to verify their potential therapeutic effects using animal model of EHEC infection. For this, we plan to answer following questions: (i) how isothiocyanates induce stress and the stringent response, (ii) what antibacterial effect could be obtained using the mixtures of these compounds and their combinations with standard antibiotics, (iii) are there any *E. coli* strains naturally resistant to these compounds, (iv) how isothiocyanates affect the regulation of virulent factors production in other pathogenic *E. coli* strains (such as EAEC, UPEC, EIEC) (v) whether isothiocyanates can be safely and efficiently used to combat EHEC infections. These studies will provide indispensable basis for the future use of isothiocyanates as potential therapeutic factors which could be essential for antibacterial therapy of infections with pathogenic *E. coli* strains.