Abstract EN

The growing emergence of bacteria resistant to conventional antibiotics is very alarming. This has prompted an intensive search for alternative antimicrobial agents which kill bacteria with different modes of action than do traditional antibiotics and do not develop drug resistance. Among these, antimicrobial peptides (AMPs) are considered as promising compounds against resistant pathogens. These positively charged peptides permeabilize or disrupt bacterial cell envelope which leads to leakage of cytoplasmic components and cell death.

The aim of my dissertation thesis was the study of the action mechanism of novel antimicrobial peptides which I have isolated from the venom of different wild bees. I identified six novel AMPs which were named panurgines (PNG), codesane (COD) and antapines (ANTPs). These peptides were isolated from the venom of three different bee species (*Panurgus calcaratus, Collete daviesanus* and *Anthophora plumipes*). I was also involved in the structural studies of lasiocepsin (Las), the antimicrobial peptide identified in the venom earlier in our laboratory. All studied peptides possess activity against various strains of bacteria and low or moderate hemolytic activity. We prepared series of PNG, COD and ANTP analogs in order to study the effect of physicochemical properties such as cationicity, hydrophobicity, α-helicity and amphipathicity on their structure and biological activities. NMR measurements and molecular modeling of ANTPs and Las helped us to elucidate the effect of peptides secondary structure on their biological activity.

The main part of the dissertation focuses on the study of the interactions of these peptides with artificially made membrane – liposomes. For this purpose I constructed negatively charged liposomes, as a general model of bacteria membrane, and uncharged liposomes, as a model of eukaryotic cells membrane. These peptide-membrane interactions were also followed on the outer and inner membrane of *E. coli* cells, resulting in the permeation of outer as well as inner membrane. We have shown that all tested peptides have stronger potency to permeabilize bacteria-mimicking anionic membranes than those which mimic eukaryotic cell membrane. That is generally in good agreement with their antimicrobial and hemolytic activity. In summary we can conclude that the antimicrobial peptides discovered in our laboratory act specifically against bacterial cell membrane and their killing mechanism involve membrane disruption.