Abstract

The increased use of antibiotics, antifungal agents and disinfectants in the last decades has resulted in development of microbial resistance to these drugs. *Candida* species are the fourth most common cause of hospital-acquired bloodstream infection and kill 40% of those patients. Natural antimicrobial peptides are promising candidates for the development of new agents to treat yeast and bacterial infections, as their presumed mechanism of action differs significantly from the mechanism of action of current drugs. This work is focused on several peptides isolated from the venom of wild bees and their synthetic analogues and the identification of the most effective ones against non-pathogenic *Saccharomyces cerevisiae* and several pathogenic *Candida* species.

Antifungal activity of eight cationic antimicrobial peptides was tested and compared under various conditions. The overall susceptibility of pathogenic yeast species to currently used antifungal drugs and the antimicrobial peptides was screened with the aim to identify potential synergistic and species-specific effects.

The effect of antimicrobial peptides on membrane potential was measured by a fluorescent probe (diS-C_3(3)), and the relative hyperpolarization of plasma membrane was shown for each peptide. The effect of antimicrobial peptides on yeast viability was established, depending on specific conditions, such as concentration of the peptides, pH or concentration of ions in the environment. In addition, the combination of antimicrobial peptides with conventional antifungal drugs was tested, and positive or negative effect of various combinations and different ratios of concentrations of the peptides to the drugs were demonstrated.

As an advanced level of testing of antimicrobial peptides, *in vivo* system was used to assess the efficiency under an interaction with an immune system. Larvae of *Galleria mellonella* were infected by the most drug-resistant yeast strains and treated by one selected peptide acting the best in the previous experiments.