Bacterial resistance to antibiotics is becoming an increasingly widespread problem in the modern world. New multi-drug-resistant strains are emerging, effectively hindering the actions of existing therapeutic agents. The incidence of infections and the number of deaths caused by them continue to rise. Consequently, there is an immense need for the introduction of new, effective antibacterial therapies.

The aim of the doctoral project was to investigate new potential antibacterial strategies using nucleic acids and peptidomimetics. The dissertation presents three approaches that may lead to the inhibition of bacterial growth or involve the transport of molecules into the interior of microbial cells.

The first strategy uses ribozymes - catalytically active RNA enzymes. Ribozymes can hydrolyze phosphodiester bonds at specific sites in the sequence of other RNA molecules. A hammerhead ribozyme was modified to interact with messenger RNA (mRNA) encoding the sequence of acyl carrier protein (ACP). ACP, which is a cofactor in fatty acid biosynthesis, is essential for bacteria to sustain life. Hydrolysis of the mRNA encoding the ACP sequence at the appropriate site should lead to inhibition of bacterial growth. Ribozymes of different arm lengths were designed and the stability of their complexes with an mRNA fragment as a substrate and its hydrolysis were tested *in vitro*. Subsequently, the ribozyme sequences were incorporated on a plasmid and introduced into *E. coli* cells, where the ribozyme catalytic activity leading to growth inhibition was observed. Additionally, synergy between one of the ribozymes and the antibiotic tetracycline was demonstrated. The design and testing of ribozymes as potentially mRNA-hydrolyzing enzymes in cells pave the way for the investigation of catalytic RNAs as antibacterial compounds or adjuncts.

The second strategy involved membrane-active peptides. It was demonstrated that stabilizing their secondary structure improves their interaction with bacterial membranes and enhances their antibacterial potential. Peptides, including anoplin, with weak antibacterial properties, were modified using hydrocarbon stapling technique. This stapling stabilized their helical membrane-active structure, enabling them to interact more effectively with cell membranes than unmodified peptides. The effectiveness of such peptidomimetics varied depending on the bacterial strain. Gram-negative strains showed greater sensitivity to the action of more hydrophilic peptidomimetics, while Gram-positive strains showed sensitivity to hydrophobic derivatives. The results showed that chemical stabilization of the membrane-active structure of natural peptides significantly increased their antibacterial activity, often without causing hemolysis.

The third strategy involved using vitamin B_{12} (cyanocobalamin) as a carrier of peptide nucleic acid (PNA) to *E. coli* bacteria and determining the pathway of this transport. PNA is a synthetic DNA analog that can act as an antisense oligonucleotide. PNA sequences can be designed to bind complementarily and block mRNA essential for bacterial life. However, they need transporters, as free PNA is not taken up by cells. The transport pathway of vitamin B_{12}-PNA conjugates to *E. coli* bacteria was determined. It turned out that PNA bound to vitamin B_{12} is transported through the same receptors in the outer and inner membranes as free vitamin B_{12}. This opens the way for the use of this transport pathway by other PNA molecules covalently attached to vitamin B_{12}.