

**POPULAR SCIENCE DESCRIPTION OF THE PROJECT**

The increase of the occurrence of multi-drug bacterial resistance has now reached alarming levels, as confirmed by numerous reports of the World Health Organization (WHO). This situation is a significant threat to human health, because even seemingly trivial infections or wounds can result in serious complications, and in extreme cases even death. For this reason, there is an urgent need to look for new compounds with antibiotic activity whose mechanism of action would minimize the possibility of occurrence of resistance. Currently used antibiotics, in most cases, act quite specifically by affecting specific biochemical processes in the cells. Unfortunately, the abuse of antibiotic drugs has resulted in mutations in numerous bacterial strains, which developed defense mechanisms that impairs the effect of the drug. It is believed that in order to solve this problem, the antimicrobial action of the drug should be less specific. Such an effect can be achieved by the use of natural antibiotic peptides, which are produced by numerous living organisms as elements of their defense system. The action of this type of compounds is less specific because it is targeted at the destruction of the cell membrane, which makes the development of resistance mechanisms difficult. Natural antibiotic peptides have been studied by numerous groups of scientists for many years, and their bactericidal and fungicidal properties have been shown many times, and some of them seem to be good candidates for anticancer drugs as well. Nevertheless, they have their significant disadvantages, which often limit their clinical use. One of the key problems is the susceptibility of peptides to the action of a particular type of enzymes - proteases found in biological fluids such as saliva, blood or digestive juices. These enzymes have the ability to break down peptides, which in turn makes them inactive before they reach their target. Moreover, many antibiotic peptides display hemolytic effects, in other words, they destroy for example red blood cells, which is a highly undesirable effect. Therefore, there is a strong need to find new compounds that have similar properties to natural antibiotic peptides, but at the same time show none of their disadvantages. Accordingly, the major aim of this project is to develop and test a new class of synthetic antimicrobial compounds, which we have called lipo-oligoureas. These compounds are a combination of commonly known fatty acids and so-called foldamers, i.e. molecules that are able to imitate natural peptides with their structure. Oligourea is a special case of the mentioned group of foldamers and consists of linked urea units. The latter can possess the same side chain groups as those found in amino acids. The lipo-oligoureas proposed in this project seem to have great potential in the area of applications related to the antimicrobial agents, which results from the unique properties of the foldamers: they are resistant to the action of the aforementioned enzymes, and what is more, they can be designed in such a way that their structure mimics natural peptides with antibacterial properties. Hence, to achieve the goal assumed in the project, it will be necessary to properly design and synthesize a number of lipo-oligoureas. Preferably, their target is to be a cell membrane, and therefore we are planning to study their effect on artificial lipid membranes. This will allow us to determine the potential activity of lipo-oligoureas, and due to the use of model biomimetic bilayers with lipid composition representative for Gram-positive and Gram-negative bacteria, it will be possible to determine whether they act selectively on a given type of membrane. The use of modern spectroscopic and microscopic techniques will enable determination of the mechanism of action of lipo-oligoureas, i.e. how they are incorporated into the lipid membrane and how they change its properties. In addition to physicochemical characteristics, we are also planning to verify the biological activity of lipo-oligoureas by studying their effect on bacterial cell growth.