

Project goal

The aim of the project is to develop modern research methods that will allow for the rapid and accurate detection of bacterial resistance to polymyxins—potent antibiotics used in the treatment of the most severe infections. The project will focus particularly on Gram-negative bacteria, which are increasingly resistant to multiple drugs and are responsible for hard-to-treat hospital infections. A key aspect of our research is the analysis of lipid A—a component of the bacterial outer membrane—as its structural modifications are directly linked to antibiotic resistance. The project will employ advanced techniques such as mass spectrometry to better understand how bacteria defend themselves against antibiotics and how they can be effectively targeted.

The fundamental research

The first phase of the research involves optimizing the cultivation conditions of Gram-negative bacteria isolated from clinical samples (saliva, swabs, urine) to obtain material for further analysis. Factors influencing the cultivation process, such as the type of medium, incubation time, aerobic and anaerobic conditions, and sample preparation methods, will be assessed.

In subsequent stages, rapid methods for detecting resistance to polymyxins will be developed, utilizing proteomic, lipidomic, and genomic techniques. The minimum inhibitory concentration (MIC) will be evaluated using the broth microdilution (BMD) method, which will allow the classification of strains based on their resistance to polymyxins, along with biofilm analysis. Detailed analyses of lipid A structure will be conducted using MALDI-TOF MS and LC-MS/MS techniques, along with the detection of resistance genes, such as *mcr-1*, by real-time PCR. The goal of these studies is to develop a protocol enabling strain identification, resistance assessment, and understanding of resistance mechanisms.

The reasons for attempting the research topic

The motivation for undertaking this research is the growing resistance of Gram-negative bacteria to polymyxins, which are among the last effective drugs for treating severe infections. This phenomenon poses a serious public health threat, particularly in hospitals. The aim of the research is to develop faster methods for detecting resistance mechanisms, enabling earlier diagnosis and more effective treatment, as well as a better understanding of the molecular basis of resistance.

Substantial results expected

The expected outcomes of the research include the development of faster and more precise methods for detecting polymyxin resistance, which will enable earlier detection of resistant strains and quicker adjustment of treatment. By using advanced proteomic, lipidomic, and genomic techniques, it will be possible to more accurately diagnose resistance in Gram-negative bacteria and gain a better understanding of the molecular mechanisms of resistance, particularly through the analysis of lipid A and resistance genes such as *mcr-1*. The development of a comprehensive protocol for strain identification and resistance assessment will aid in controlling the spread of resistant bacteria, and the research results may provide a foundation for developing new treatment strategies and preventing antibiotic resistance.