Antibiotic resistance crisis is currently one of the most serious challenges in public health. It is a process in which bacteria become resistant to the effects of antibiotics, making it difficult to effectively control and combat bacterial infections. This growing problem raises concerns among scientists and doctors worldwide. Inappropriate use of antibiotics, such as non-compliance with dosage recommendations or premature discontinuation of treatment, leads to incomplete elimination of bacteria. The surviving bacteria can develop resistance. Despite the increasing problem of drug resistance among bacteria, the discovery and introduction of new antibiotics to the market are challenging. The process of researching and developing new drugs is costly and complex, and many pharmaceutical companies have reduced their investments in this field. Therefore, alternative methods that could effectively combat bacterial infections caused by antibiotic-resistant bacteria are actively sought. One such alternative may be phage therapy, which utilizes bacteriophages (phages) - viruses whose hosts are bacterial cells. Bacteriophages are commonly found in nature, and municipal wastewater is a rich source of them. Importantly, bacteriophages do not attack human cells. Phages are very specific viruses, often attacking only specific strains within a species. The result of this high specificity is the preservation of the natural human microbiota in balance during potential therapy, as phages eliminate only the dangerous pathogen. This is undoubtedly a significant advantage of phage therapy, although it does not mean that it is without limitations and drawbacks. One of the more serious limitations arises somewhat from the aforementioned advantage. High specificity requires the acquisition and characterization of a large number of bacteriophages to effectively treat bacterial infections in the future. Another strategy for combating drug-resistant infections is the use of phage enzymes - depolymerases and endolysins that the phage produces during bacterial infection. Depolymerases are proteins that break down the bacterial capsule, while endolysins act on the bacterial cell wall. Scientists' attention is often focused on combination therapy, which utilizes the synergistic effects of both phages, their enzymes, and antibiotics.

Escherichia coli is one of the bacterial species in which a drastic increase in the number of strains resistant to most available antibiotics is observed. Many strains of *E. coli* occur naturally in the human gut microbiota and bring many benefits to the body. However, some strains of *E. coli* are dangerous extraintestinal pathogens. This includes uropathogenic *E. coli* (UPEC) strains, which cause urinary tract infections (UTIs). *E. coli* is the leading cause of both complicated and uncomplicated UTIs, accounting for approximately 50-65% and 75-85% of cases, respectively. Treating uncomplicated UTI cases usually does not pose significant difficulties. However, episodes of complicated infections, particularly those caused by multidrug-resistant UPEC strains, pose therapeutic challenges. It is estimated that the majority of complicated UTI cases are caused by UPEC strains that are resistant to multiple antibiotics, making the treatment of these infections more difficult. Due to their ability to form biofilms, UPEC bacteria become particularly challenging to combat in the hospital environment. A biofilm is a structure in which bacterial cells adhere to surfaces, forming a protective layer. Biofilms protect bacteria from chemical factors, antibiotics, and the host's immune system. Bacteria forming biofilms colonize not only the epithelium of the human urinary system but also abiotic surfaces, such as polymers used in clinical practice catheters. Prolonged catheter use, not only negatively affects the patient's quality of life but also increases the risk of serious urinary tract infections. It is estimated that the risk of developing a UTI associated with long-term catheterization increases by 5% each day.

The aim of this project is to examine the ability of a newly isolated bacteriophage, named vB_EcoS_10.1, its enzymes - depolymerases and endolysins, and antibiotics to combat biofilms formed on urological catheters by clinical UPEC strains. Considering the drastic increase in recent years in UPEC strains resistant to most known antibiotics and the limited number of scientific reports on bacteriophages and phage enzymes infecting these bacteria, these studies seem necessary for a better understanding of the interactions between phages and UPEC bacteria. To most accurately mimic the process of the natural formation of a biofilm, the studies will be conducted in synthetic urine using a catheter flow system. Clinical UPEC isolates were obtained from hospitalized patients with UTI symptoms. To test the ability to degrade the biofilm formed by these bacteria on the catheter, we will administer both the bacteriophage and its enzymes, as well as antibiotics, separately and in combination. We will try to answer the question of which of the applied therapies will be the most effective.