Since the dawn of history, medicine has been guided by the goal of saving human life and improving the functionality of damaged tissues or organs to increase the patient's quality of life as much as possible. The possibilities offered by modern medicine and biomaterial engineering mean that many serious diseases and dysfunctions of the body are no longer factors excluding a given person from a normal and full social life. The proposed solutions are very often based on the use of implants made of polymeric materials that ensure high biocompatibility. Because their structure is based on a carbon skeleton, polymeric substances are structurally more similar to human tissues than substances of inorganic origin. This fact allows them to be used in targeted therapies, where there are specific interactions between the biomaterial and the cells of the patient's body. Unfortunately, all foreign bodies implanted into the human body lack the natural protective barrier of the human immune system and are exposed to infections caused by a wide range of organisms classified as nosocomial pathogenic strains and from the natural microflora of human skin. These organisms include, among others bacteria *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas* sp., *Klebsiella* sp., *Enterobacter* sp. or yeasts *Candida albicans*. The greatest risk of infections occurs in the elderly and metabolically overloaded people, while the use of traditional antibiotic therapy becomes ineffective very often. Conducting inappropriate therapy may result in necessity of reoperation and even death of the patient. To increase the aseptic potential of biomaterials used in medicine, modifications with the use of silver nanoparticles or antibiotics have been developed, but even such an approach does not completely ensure lack of contamination in the implanted biomaterial. Moreover, due to the common phenomenon of antibiotic resistance among many bacteria, new substances with high antimicrobial potential are being sought.

The aim of the project is to **develop new two-component preparations consisting of an antimicrobial peptide molecule and an inhibitor of proteolytic enzymes** (as a component responsible for protection against the undesirable effect of proteolysis), **that would show antimicrobial properties against pathogenic microorganisms** - *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa and Candida albicans.* As part of the proposed research tasks, the impact of these preparations on the general metabolic activity of microorganisms and the formation of possible changes in cellular and membrane structures will be determined. Then, from among all two-component preparations characterized in this way, the one showing the highest antimicrobial activity will be selected in order to be immobilized on the surface of the polymeric biomaterial and to verify its biological usefulness in the immobilized form.

Planned scope of research include several stages of experiments. The first of them are FIC analyzes, the aim of which is to determine the synergy of action between antimicrobial peptide molecules and inhibitors of proteolytic enzymes, and to identify two-component preparations with the highest antimicrobial potential. The next stage of the experiments is checking the influence of the created mixtures on the overall metabolic activity of microorganisms, considering such analyzes as live/dead tests, the ability to produce biofilm, the continuity of biological membranes or the production of ATP and NADH, which are one of the main molecules that indicate the efficient functioning of living organisms. The research covering the next step is based on a wide range of microscopic analyzes that will allow to fully visualize potential changes in extracellular and intracellular structures, with particular emphasis on biological membranes (SEM, TEM, AFM, confocal microscopy). As part of the last task, the immobilization process of the selected two-component preparation on the surface of the polymer prosthesis will be carried out and the assessment of its biological usefulness in combating infections with pathogenic microorganisms will be implemented.

The experiments undertaken in this project are aimed at understanding and describing the mechanisms of action of two-component preparations on selected reference bacterial and yeast strains, which are the main etiological factors of infections within polymer biomaterials implanted into the human body.