Title: The influence of free and immobilized bacteriophages on a bacterial cellulose-based carrier on human cells and the possibility of their application in the treatment of wounds covered with biofilm

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Antimicrobial resistance is one of the most important global threats to public health. In 2019, 1.27 million people died due to increasing resistance to antibiotics. The World Health Organization warns that if appropriate preventive measures will be not taken, this number will increase to 10 million per year by 2050. Therefore, for years there has been an intensive search for treatment methods that could be an alternative to traditional antibiotic therapy. Phage therapy is a leading candidate among the proposed solutions.

Phagotherapy is a form of antibacterial therapy carried out using specific viruses (bacteriophages) that lyse only bacterial cells, both Gram-positive and Gram-negative. In this kind of therapy uses bacteriophages that have the ability to multiply and lyse specific strains of bacteria responsible for the infection. It has been confirmed that phage-based therapies are effective in the treatment of chronic wounds caused by multidrug-resistant strains such as *Pseudomonas aeruginosa* or *Staphylococcus aureus* and also biofilm eradication. There is also great interest in combining phages with various types of carriers in order to improve and expand their potential applications, e.g. as dressings for difficult-to-heal wounds or burns. It has been suggested that applying immobilized phages directly to the wound surface can significantly improve the effectiveness of the healing process. An example of a biomaterial that meets all the requirements of an ideal dressing is bacterial cellulose (BC). It is a natural polymer synthesized, among others, by non-pathogenic bacteria of the *Komagataeibacter* genus. BC is characterized by high purity, crystallinity, mechanical strength and water retention capacity. Moreover, it is a biodegradable and, above all, biocompatible material. BC has been used in many industries, including biomedicine, where it can be used as a skin substitute, an artificial blood vessel, various types of implants or a dressing for difficult-to-heal wounds. Due to its three-dimensional structure, BC can be an ideal carrier for the immobilization of bioactive substances and various types of human cells, bacteria and viruses.

Currently, phage therapy as a treatment method is only available as an experimental therapy. However, more and more countries are showing interest in introducing phage therapy as a legal, standardized treatment method. However, it should be noted that in recent years there have been more and more reports that bacteriophages, after being administered to a patient, can spread throughout the body, penetrate other organs, and interact with the patient's immune system. Recent publications suggest that bacteriophages can influence the biochemical and physiological parameters of human cells. There is nothing that disqualifies phage therapy, but it is necessary to carefully analyze the safety of bacteriophages in various research models before they are used as a medicine.

The main goal of the project is to assess the impact of free and immobilized bacteriophages on the physiology of human fibroblasts and macrophages. An additional goal of the project is to assess the effectiveness of the obtained dressing based on bacterial cellulose (BC) containing immobilized bacteriophages in the treatment of wounds covered with biofilm.

This project includes basic research aimed at providing information on the interactions between free and immobilized bacteriophages and human cells. These data are necessary so that phage therapy can be introduced in the future as a parallel method of treating bacterial infections with antibiotics. The results of the obtained research will allow to assess the effectiveness of the use of a BC-based dressing containing immobilized phages, which will support the treatment of infections caused by *P. aeruginosa* and *S. aureus* bacteria, and thus support the process of antibiotic therapy. This project is characterized by high cognitive value and is an environmentally friendly solution with a significant economic and social impact.