Diabetic foot is a serious health problem that affects many people with diabetes around the world. Diabetes affects ~422 million people in the world, and it is estimated that approx. 15-25% of them will experience problems resulting from foot problem, which, due to an impossible-to-cure bacterial infection, leads to foot amputation and even death. Today, we stand on the threshold of post-antibiotic era when simple infections will again kill people. This is due to a phenomenon called antibiotic resistance. Bacteria compete for resources and food, producing deadly compounds that they direct against each other. Other bacteria, to protect themselves, develop defensive mechanisms against such attacks. When we created antibiotics, we took these compounds to the laboratory and created our own versions, and bacteria reacted to our attack in the same way they always have. Penicillin was introduced in 1943, and by 1945 there were already bacteria resistant to it. The same was true for Vancomycin and Imipenem. Interestingly, bacteria even became resistant to one of the newest antibiotics just a year after its introduction. For nearly 100 years, we have been playing a game with bacteria - our drug and their resistance, then another drug, and then resistance again - and now the game is ending. Bacteria develop resistance so quickly that it is not profitable for pharmaceutical companies to look for new antibiotics, so infections are spreading around the world, against which out of over 100 antibiotics available on the market, two drugs, or one, or none may work. Can we prevent this? Bacteria birth a new generation every 20 minutes. Creating a new drug takes at least 10 years. Every time we use an antibiotic, we give bacteria billions of chances to break the codes of our constructed defense mechanisms. No drug has yet been invented that they cannot overcome. That's why we need a real breakthrough in game changing. Sugar is not just something we eat. On the contrary. Sugar is one of the most naturally occurring molecules, and all cells in the body are covered with a thick layer of sugar. In fact, almost 80% of all viruses and bacteria bind to sugars on the outside of our cells. Especially in the case of diabetics, elevated sugar levels provide the perfect conditions for bacteria to exist and invasive grow. That's why we propose in the project to combine synergistic antibiotics and adjuvant combinations in one natural polysaccharides-based nanodelivery system, which are a kind of “Trojan Horses” and “Pandora's boxes” for bacteria in the treatment of diabetic wounds infections. Although they do not naturally exhibit antibacterial properties, they will be used as scaffolds for the deposition of selected combinations of antibiotics and adjuvant molecules. Such combinations will be selected using artificial intelligence. AI, thanks to its ability to process huge amounts of data and recognize patterns that may escape the human eye, opens new possibilities in discovering drug combinations that may work better together than separately. AI can search existing drug databases, analyze their chemical structures, modes of action, and interactions with other drugs. Importantly, AI will help us predict how different drugs will interact to minimize the risk of unwanted interactions and side effects. Additionally, the best prepared nanoantimicrobials will be tested on highly advanced infection models such as animals or organoids - which will allow us to significantly reduce the number of used animals. And what are organoids? They can be compared to having miniature versions of human organs in the laboratory. It is a small, three-dimensional structure that mimics a real human organ, in our case, skin. These complex structures are grown from stem cells - versatile cells that can transform into different types of cells. This will allow us to better understand how infections develop, as well as test nanoantimicrobials in a way that is closer to the real conditions of the human body than traditional cell culture methods. The proposed in this project “Trojan Horses” - nanoantimicrobials, developed using highly innovative technologies, have the most promising potential in improving the treatment of not only diabetic foot ulcers but also setting the future direction of therapy for antibiotic-resistant bacterial infections