

One of the biggest breakthroughs in modern medicine took place in 1928, when Alexander Fleming discovered that *Penicillium* fungi produce a substance that can inhibit growth of pathogenic bacteria in a very effective way. It took 10 more years to isolate an active antibacterial compound from *Penicillium* culture: penicillin, which was introduced in a very short time as an effective drug for treating life-threatening infectious diseases. Since then, a peculiar arms race goes on, including pathogenic microorganisms from the one hand, and scientists from the other, who have been trying to develop new, sophisticated ways of bacteria elimination. However, after introduction of new antibiotics, which are at first effective, bacteria in a relatively short time can defend themselves by acquiring so called antibiotic resistance, which makes antibiotic no more active.

Nowadays epidemiologists pay more and more attention to the fact that it is not necessarily cancer, viral pandemics (such as bird flu, SARS, Ebola virus infections), cardiovascular or autoimmune diseases (such as diabetes, multiple sclerosis) that can be the most serious threats for humankind. This role is in turn ascribed to pathogenic, multidrug-resistant bacteria, that had been assumed as harmless, or at least possible to defeat with 'wonder drugs' – antibiotics.

Within the project we plan to test and check the rationale of a different approach to fighting with pathogenic bacteria. Instead of developing next substance with antibacterial properties (which sooner or later will lose its effectiveness and will have to be displaced with a subsequent one), we want to apply the combination of conventional antibiotics with an additional compound that would increase their antimicrobial action. When two compounds – representing diverse modes of action – are used against bacteria instead of a single one, bacteria are less prone to defend from such a treatment. Compounds that we intend to look at within the project are xanthine derivatives: caffeine – commonly consumed as a component of popular beverages, such as tea or coffee, and pentoxifylline – used as a drug improving blood circulation. Caffeine and pentoxifylline have been thoroughly analyzed concerning their safety in humans. They have been classified as safe compounds even if consumed in relatively large doses, reaching half a gram a day in the case of caffeine (drinking a single cup of strong coffee you absorb about 200 mg of pure caffeine). Much less is known about their influence on bacteria. It has been observed earlier that caffeine is capable of inhibiting bacterial growth, but only at high doses. The results of the studies conducted by our group revealed that caffeine in moderate doses (similar to those which we consume drinking tea or coffee) can significantly influence the growth of pathogenic *Staphylococcus aureus* bacteria. We intend to look at this phenomenon in details – we plan to determine conditions in which xanthines enhances antibiotics action the most effectively, especially toward bacteria isolated directly from patients who suffer from difficult to treat bacterial infections, and to get to know the way in which xanthines alter drug activity. Additionally, we want to check caffeine influence on so called virulence factors – the ways of bacteria action allowing them to colonize inside our bodies, causing dangerous infections.

We believe that the outcomes of this study will constitute the first step toward developing a new, efficient antibacterial therapy that will combine the commonly used antibiotics with caffeine or pentoxifylline as compounds significantly potentiating their action.