Abstract

The global problem of increasing resistance of bacterial pathogens to antimicrobials and the associated failures in treating infections are prompting the search for new alternative therapies. Research on the effects of magnetic field (MF) on the functional parameters of bacteria is being conducted by many research teams around the world. Relatively new line of research is the analysis of the effect of MF on the effectiveness of antimicrobials against bacteria. However, often such studies are conducted in a way that does not include in the analysis some of the factors that can affect the observed effects, and thus, the results obtained do not provide a satisfactory explanation of the observed phenomena. Therefore, it seems advisable to conduct further research in this area, as well as to systematize conducting the research.

The main objective of the dissertation was to analyze the effect of rotating magnetic field (RMF) on the effectiveness of antibiotics against *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) strains. In addition, the doctoral dissertation was an attempt to systematize the methodological approaches for analyses on the effects of MF on various functional parameters of bacteria.

All experiments carried out as part of the scientific achievement described herein were performed using RMF bioreactors made of a three-phase electric motor stator and a process chamber in which cultures of bacteria were placed during exposure. Both clinical and reference bacterial strains belonging to 8 species (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis*, *Enterobacter cloacae*, *Moraxella catarrhalis* and *Bacillus cereus*) were used in the study, with experiments related to antibiotic efficacy carried out exclusively with *S. aureus* strains (including MRSA and MSSA strains). Various parameters related to RMF exposure (e.g. RMF frequency ranging from 5 to 50 Hz and exposure time ranging from 1 to 18 hours) and antibiotics from different groups, characterized by different mechanisms of action, as well as different electrical charges. The analyses carried out were related to the effect of RMF on the growth kinetics and cellular metabolic activity of bacteria and the effectiveness of antibiotics.

The results obtained showed that the effect of RMF on parameters such as growth kinetics and cellular metabolic activity does not depend solely on the parameters described so far in the literature (e.g. bacterial species, cell shape, cell wall structure, or the type and parameters of MF and exposure time), but also, to a significant extent, on the diversity of bacterial strains within a species (including even strains belonging to a single clonal type). It was also found that the efficacy of antibiotics from different groups, including aminoglycosides, β-lactams, fluoroquinolones, glycopeptides, macrolides lincosamides and tetracyclines against *S. aureus* increases under influence of the RMF. Particularly significant changes were observed for antibiotics whose mechanism of action is related to inhibition of bacterial wall synthesis (β-lactams and glycopeptides). Changes in the effectiveness of β-lactams were shown to be due to structural weakening of bacterial cells. Among the changes observed were deformations in cell shape and changes in cell size, as well as cell wall collapse and loss of cell turgor.

The analyses also demonstrated that changes in the effectiveness of antibiotics against bacteria exposed to RMF are influenced by factors such as RMF frequency, exposure time and antibiotic concentration. It was further shown that changes in antibiotic efficacy under RMF

are, like growth kinetics and cellular metabolic activity, also closely related to strain variation within species. It has also been shown that changes in the efficacy of β-lactam antibiotics against bacteria are only manifested in the presence of RMF and do not remain fixed in cells after exposure. It has also been shown that, although RMF affects the release of antibiotics from the carrier and their diffusion in the agar, it is not a significant determinant of the effectiveness of antibiotics against bacteria.

The results obtained in the course of this dissertation have significantly advanced the knowledge of changes in the effectiveness of antibiotics under the influence of RMF against *S. aureus* bacteria. In addition, this is the first time when the effect of RMF on bacterial cells has been analyzed in such a detailed and comprehensive manner. An important achievement, resulting from the analyses, is the creation of a consistent methodological basis that can enable the systematization of studies related to the effects of MF on various functional parameters and the effectiveness of antimicrobials against bacteria.

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