

Impact of Nanoparticles on Bacteria and Mycobacteria

Josef Jampilek¹, Martin Pisarcik²

¹Faculty of Natural Sciences, Comenius University, Ilkovicova 6, 842 15 Bratislava, Slovakia; josef.jampilek@gmail.com

²Faculty of Pharmacy, Comenius University, Kalinciakova 8, 832 32 Bratislava, Slovakia; pisarcik@fpharm.uniba.sk

Extended Abstract

Bacterial infections represent an increasing worldwide threat. The number of untreatable diseases decreased after the 1950s due to the introduction of antimicrobial agents. However, since the 1980s, morbidity has risen again, and mortality due to respiratory infections, AIDS, COVID-19 and tuberculosis now represents about 85% of world mortality from infections. The increase in the number of new infections is caused by general immunosuppression (primarily by tumour treatment, administration of immunosuppressive agents, wide-spectrum antibiotics and corticoids), a significant increase in the number of diabetic, HIV or SARS-CoV-2 positive patients and development of resistance to commonly used drugs. The resistance of common pathogens to first-line drugs increased by up to 100% during the last decade. Moreover, the resistance of some strains to second- or third-line drugs can be found. Development of cross-resistant or multidrug-resistant strains is also a great problem [1–4].

Selection of resistant microorganisms is especially caused by irrational and unavailing application of antimicrobial agents in human, veterinary medicine and in agriculture. Among the most frequent resistant bacterial strains there are methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *S. aureus*, vancomycin-resistant enterococci, penicillin- and macrolides-resistant *Streptococcus pneumoniae*, cotrimoxazol-resistant *Escherichia coli*, the 3rd generation of cephalosporin-resistant *E. coli* and *Klebsiella pneumoniae* and carbapenem-resistant *E. coli*, *K. pneumoniae* and *Pseudomonas aeruginosa* [3]. In addition, tuberculosis (TB) caused by *Mycobacterium tuberculosis* remains one of the world's deadliest communicable diseases. Multidrug-, extensively drug- and totally drug-resistant TB strains are a serious worldwide problem [5].

Thus, it can be stated that significant resistance to antimicrobials can be found at both Gram-positive and Gram-negative bacteria that cause serious infections. Bacterial resistance may complicate the treatment of infections regardless of how mild these infections were at the early stage. The consequence can be a prolonged disorder, treatment failure and patient's death [6–9].

It is increasingly complicated to design new classes of antimicrobial compounds suitable for following rational development, therefore R&D of new antimicrobials imply risks, and thus many pharmaceutical originator companies have continued in development of me-too drugs but which does not solve the basic problem of resistance. Thus increasing bacterial resistance refers to the urgency to design new effective antibacterial drugs [10].

Application of nanotechnology represents an excellent alternative for improvement of existing antimicrobial drugs. Nanomaterials are an alternative approach to treating and mitigating infections caused by resistant bacteria. Microbial cells are unlikely to develop resistance to nanomaterials, because, in contrast to conventional antibiotics, they exert toxicity through various mechanisms [11–14]. Using nanoformulations, enhanced bioavailability of active substances can be ensured and route of administration can be modified. Specific nanoformulations also provide a controlled released system or targeted biodistribution. Due to these facts, smaller amount of substance can be used, i.e. dose-dependent toxicity and various side effects decrease. An increase of the efficacy of individual agents can be ensured by fixed-dose drug combinations or antimicrobially active matrices. In addition, many formulations also protect drugs from degradation [15–19].

This contribution deals with the biological activity of various types of nanoparticles/nanomaterials against bacteria and mycobacteria species.

This study was supported by the Slovak Research and Development Agency (Grant No. APVV-17-0373).

References

- [1] WHO. (2021, April 10). Antimicrobial resistance 2020. [Online]. Available: <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>
- [2] WHO. (2021, April 10). World health statistics 2020. [Online]. Available: <https://apps.who.int/iris/bitstream/handle/10665/332070/9789240005105-eng.pdf>
- [3] European Centre for Disease Prevention and Control. (2021, April 10). [Online]. Available: <https://www.ecdc.europa.eu/en>
- [4] C. J. Clancy, I. S. Schwartz, B. Kula, M. H. Nguyen, “Bacterial superinfections among persons with coronavirus disease 2019: A comprehensive review of data from postmortem studies,” *Open Forum Infect. Dis.*, vol. 8, no. 3, ofab065, 2021.
- [5] WHO. (2021, April 10). Global tuberculosis report 2020, [Online]. Available: <https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf>
- [6] B. Li and T. J. Webster, “Bacteria antibiotic resistance: new challenges and opportunities for implant-associated orthopaedic infections,” *J. Orthop. Res.*, vol. 36, no. 1, pp. 22-32, 2018.
- [7] B. Aslam, W. Wang, M. I. Arshad, M. Khurshid, S. Muzammil, M. H. Rasool, M. A. Nisar, R. F. Alvi, M. A. Aslam, M. U. Qamar, M. K. F. Salamat, Z. Baloch, “Antibiotic resistance: a rundown of a global crisis,” *Infect Drug Resist.*, vol. 11, pp. 1645-1658, 2018.
- [8] S. B. Kumar, S. R. Arnipalli, O. Ziouzenkova, “Antibiotics in food chain: The consequences for antibiotic resistance,” *Antibiotics*, vol. 9, no. 10, 688, 2020.
- [9] L. Serwecinska, “Antimicrobials and antibiotic-resistant bacteria: A risk to the environment and to public health,” *Water*, vol. 12, no. 12, 3313, 2020.
- [10] J. Jampilek, “Design and discovery of new antibacterial agents: Advances, perspectives, challenges,” *Curr. Med. Chem.*, vol. 25, no. 38, 4972-5006, 2018.
- [11] P. Singh, A. Garg, S. Pandit, V. R. S. S. Mokkalpati, I. Mijakovic, “Antimicrobial effects of biogenic nanoparticles,” *Nanomaterials*, vol. 8, no. 12, 1009, 2018.
- [12] N. E. Eleraky, A. Allam, S. B. Hassan, M. M. Omar, “Nanomedicine fight against antibacterial resistance: An overview of the recent pharmaceutical innovations,” *Pharmaceutics*, vol. 12, no. 2, 142, 2020.
- [13] M. F. Gomez-Nunez, M. Castillo-Lopez, F. Sevilla-Castillo, O. J. Roque-Reyes, F. Romero-Lechuga, D. I. Medina-Santos, R. Martinez-Daniel, A. N. Peon, “Nanoparticle-based devices in the control of antibiotic resistant bacteria,” *Front. Microbiol.*, vol. 11, 2987, 2020.
- [14] F. Amaro, A. Moron, S. Diaz, A. Martin-Gonzalez, J. C. Gutierrez, “Metallic nanoparticles – friends or foes in the battle against antibiotic-resistant bacteria?,” *Microorganisms*, vol. 9, no. 2, 364, 2021.
- [15] J. Jampilek and K. Kralova, “Nano-antimicrobials: Activity, benefits and weaknesses,” in: *Nanostructures for Antimicrobial Therapy*, A. Fikai, A.M. Grumezescu, Eds. Amsterdam: Elsevier 2017, pp. 23-54.
- [16] J. Jampilek and K. Kralova, “Nanoweapons against tuberculosis,” in: *Nanoformulations in Human Health – Challenges and Approaches*, S. Talegaonkar, M. Rai. Eds. Cham: Springer 2020, pp. 469-502.
- [17] M. Pisarcik, J. Jampilek, M. Lukac, R. Horakova, F. Devinsky, M. Bukovsky, M. Kalina, J. Tkacz, T. Opravil, “Silver nanoparticles stabilised by cationic gemini surfactants with variable spacer length,” *Molecules*, vol. 22, no. 10, 1794, 2017.
- [18] M. Pisarcik, M. Lukac, J. Jampilek, F. Bilka, A. Bilkova, L. Paskova, F. Devinsky, R. Horakova, T. Opravil, “Silver nanoparticles stabilised with cationic single-chain surfactants. Structure-physical properties-biological activity relationship study,” *J. Mol. Liq.*, vol. 272, pp. 60-72, 2018.
- [19] M. Pisarcik, M. Lukac, J. Jampilek, F. Bilka, A. Bilkova, L. Paskova, F. Devinsky, R. Horakova, T. Opravil, “Phosphonium surfactant stabilised silver nanoparticles. Correlation of surfactant structure with physical properties and biological activity of silver nanoparticles,” *J. Mol. Liq.*, vol. 314, 113683, 2020.