Nanoformulations of Antimicrobial Chemotherapeutics

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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 and tuberculosis now represents about 85% of world mortality from infections [1,2]. 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 or HIV-positive patients and development of resistance to commonly used drugs. The resistance of common pathogens to first-choice drugs increased by up to 100% during the last decade. Moreover, the resistance of some strains to second- or third-choice drugs can be found. Development of cross-resistant or multidrug-resistant strains (*Mycobacterium* spp., *Staphylococcus*, *Enterococcus*, *Salmonella*, *Pseudomonas*, *Klebsiella*, *Candida* spp., *Aspergillus* spp. and *Cryptococcus* spp.) is a great problem [3,4]. Selection of resistant microorganisms is especially caused by irrational and unavailing application of antimicrobial agents in human, veterinary medicine and in agriculture [1,5–8]. Bacterial resistance may complicate the treatment of infections regardless of how mild these infections were at the early stage [9]. Infections caused by these MDR bacterial strains have been responsible for the increase in additional healthcare costs and productivity losses [3,4,7,10].

Although it is not difficult to discover microbicidal agents, it is increasingly complicated to design new classes of antimicrobial compounds suitable for following rational development [11], therefore R&D of new antimicrobials imply risks, and thus many pharmaceutical originators have continued in development of me-too drugs. Increasing bacterial resistance refers to the urgency to design new effective antibacterial drugs [12–14].

Application of nanotechnology represents an excellent alternative for improvement of existing antimicrobial drugs. Nanomaterials are an alternative approach to treatment and mitigation of infections caused by resistant strains. Microbial cells are unlikely to develop resistance to nanomaterials, because, in contrast to conventional antibiotics, they exert toxicity through various mechanisms [15]. Using nanosystems/nanoformulations, enhanced bioavailability of active substance can be ensured, and the 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 in the efficacy of individual agents can be ensured by fixed-dose drug combinations or antimicrobially active matrices – polymers physically destroying cell membranes of the organism and rendering them ineffective that could be applied in the prevention of developing drug-resistance microbes. In addition, many formulations also protect drugs from degradation [16–22].

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