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ORIGINAL PAPER

Specific effects and features of a combination of amine-containing antibacterial agents and silver nanoparticles stabilized by dicarboxylic acid copolymers

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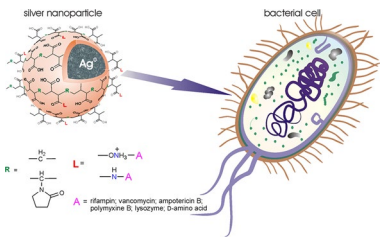
Abstract

Various types of combinations of amine-containing antibacterial agents (heterocyclic and macrocyclic antibiotics, protein and peptide antibiotics, D-amino acids) and silver nanoparticles stabilized by dicarboxylic (maleic) acid copolymers (AgNPs) are obtained. The study demonstrated the specific action of the conjugates on the planktonic form of gram-positive and gram-negative microorganisms, and fungi. The antimicrobial properties of the conjugates depend on the structures of the AgNPs stabilizing shell, antibacterial agent, and the cell membrane of the pathogen. The polymer shell of the metal nanoparticles allowed to solubilize hydrophobic antibiotics due to the formation of covalent and non-covalent complexes. A pronounced synergistic antimicrobial effect was observed, when AgNPs were combined with hydrophobic amine-containing antibiotics: rifampin—against *Staphylococcus aureus* and amphotericin B—against *Candida albicans*. In these cases, the values of Fractional Inhibitory Concentration Indices were lower than 0.5. A pronounced positive bactericidal effect was observed, when using conjugates of AgNPs and a peptide antibiotic (vancomycin) against *Enterococcus faecalis*, as well as a protein (lysozyme) and D-amino acids against the variety of microorganisms.

Graphic abstract



Keywords Silver nanoparticles · Maleic acid copolymers · Antimicrobial activity · Antibiotics

Introduction

Pathogenic bacteria are able to cause serious disease and this is a major public health problem. This is complicated by the emergence of drug-resistant strains of microorganisms. Many strains of bacteria isolated from animals and humans, earlier sensitive to antibiotics, became resistant to almost all available antibiotics [1, 2]. Combination therapies coupling different antibiotic-enhancing substances with antibiotics are a promising antimicrobial strategy. One intervention to enhance the efficacy of antibiotics against bacterial cells is

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0.1 cm^3 was pipetted into the first well containing 0.1 cm^3 of broth. After mixing, 0.1 cm^3 of the mixture was pipetted to the second well, initially containing 0.1 cm^3 of broth. The procedure was repeated until a sufficient number of dilutions was made. For inoculation, a microbial suspension of test microorganisms prepared on a nutrient broth was used. 0.1 cm^3 of the inoculum was introduced into a well containing 0.1 cm^3 of the appropriate dilution of the NPs composite, as well as in the last well with a nutrient broth without the test preparation (positive control).

The suspension prepared was checked for purity by seeding on a solid nutrient media and culture growth in the broth without silver nanoparticle preparation (positive control) was monitored. The plates covered with a sterile film were incubated at 35 °C overnight (48 h for *C. albicans*). The culture growth in the presence of composite was compared with the one in a reference cell without composite (positive control) under visual control (wells in plates were viewed in transmitted light). The minimum inhibitory concentration was determined by the lowest concentration of composite in the cell, suppressing the apparent growth of the tested microorganism.

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