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Synthesis and characterization of magnetite/silver/antibiotic nanocomposites for targeted antimicrobial therapy

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ABSTRACT

The article is devoted to preparation and characterization of magnetite/silver/antibiotic nanocomposites for targeted antimicrobial therapy. Magnetite nanopowder was produced by thermochemical technique; silver was deposited on the magnetite nanoparticles in the form of silver clusters. Magnetite/silver nanocomposite was investigated by XRD, SEM, TEM, AFM, XPS, EDX techniques. Adsorptivity of magnetite/silver nanocomposite towards seven antibiotics from five different groups was investigated. It was shown that rifampicin, doxycycline, ceftriaxone, cefotaxime and doxycycline may be attached by physical adsorption to magnetite/silver nanocomposite. Electrostatic surfaces of antibiotics were modeled and possible mechanism of antibiotic attachment is considered in this article. Raman spectra of magnetite, magnetite/silver and magnetite/silver/antibiotic were collected. It was found that it is difficult to detect the bands related to antibiotics in the magnetite/silver/antibiotic nanocomposite spectra due to their overlap by the broad carbon bands of magnetite nanopowder. Magnetic measurements revealed that magnetic saturation of the magnetite/silver/antibiotic nanocomposites decreased on 6–19 % in comparison with initial magnetite nanopowder. Pilot study of antimicrobial properties of the magnetite/silver/antibiotic nanocomposites were performed towards *Bacillus pumilus*.

1. Introduction

Magnetite nanoparticles, due to their magnetic and biocompatible properties, are being intensively investigated for their application in the medical field. Magnetite is used for magnetic field guided drug delivery, tumor treatment via hyperthermia, biomolecular separation, diagnostic imaging, etc.[1–3]. The great advantage of magnetite particles are their magnetic properties that allow direct delivery of the matters into pathogen zone without influencing the whole organism. The other advantage of magnetite nanoparticles is their ability to solve in human organism [4–6], where magnetite particles are biotransformed into iron ions, captured by proteins like ferritine and transferrine, and involved in tissue metabolism. As is known [7], iron is one of the "biological" metals. Since iron is primarily required for hemoglobin, dissolution of magnetite particles could help to prevent iron deficiency anemia — the primary clinical manifestation of iron deficiency. For targeted drug delivery, antibiotics with anticancer and antimicrobial properties are typically used [8,9]. As is known the most important problem in antibiotic therapy is the resistance of pathogens to antibiotic actions. Presently, there is no alternative to antibiotic therapy, it is thus a very timely issue [10–12].

The development of magnetic drug carriers is connected with some technological difficulties. In particular, biofunctionalization of nanoparticles often causes worsening of their magnetic properties. Another difficulty is connected with antibiotic attachment to the magnetic carrier. Using supporting materials (like biocompatible polymers and surfactants) for nanoparticle coating is reasonable from a technological point of view whereas from therapeutic point of view it is useless. In our synthesis we tried to avoid therapeutically useless substances by using silver as platform for antibiotic attachment to magnetic nanocomposite. It is known that silver is one of the oldest antimicrobial agents and may reveal therapeutic activity simultaneously with antibiotic. Silver/antibiotic combination was shown to be promising for its use against drug resistant pathogens [13–15]. In previous works it was also reported about creation of magnetite/silver nanocomposites and their successful action against antibiotic-resistant biofilms [16,17]. We suggest to combine antimicrobial activity of silver with that of antibiotic in magnetic nanocomposite. To our knowledge, this is the first study devoted to the creation of magnetic silver/antibiotic nanocomposites. We also expect that silver/antibiotic combination may prolong the

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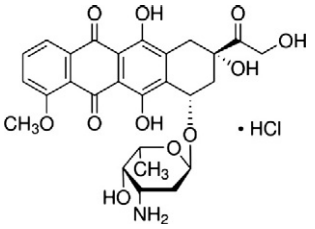
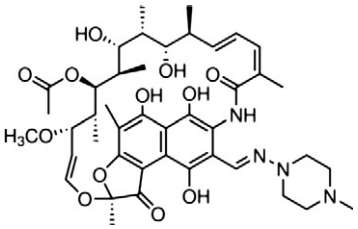
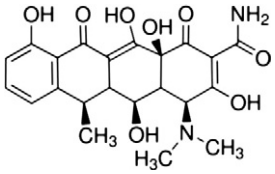
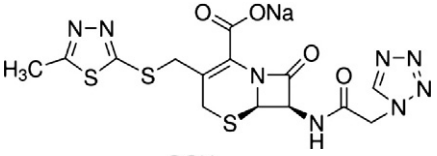
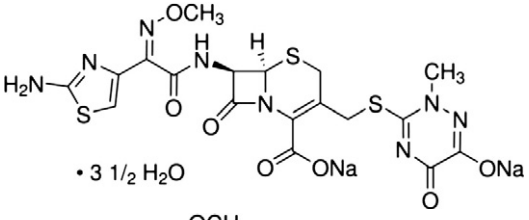
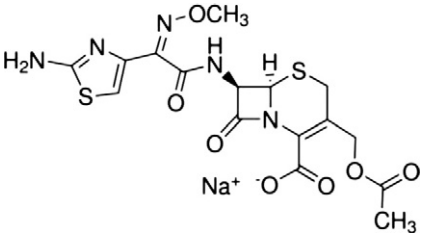
therapeutic action of nanocomposite due to the difference in silver and antibiotic solubility and make the spectrum of antimicrobial activity wider due to overlap of both silver [18–23] and antibiotic antimicrobial spectra.

The other technological problem is connected with magnetic properties; silver coating on magnetite nanoparticles is known to drastically decrease the magnetic properties of the magnetite nanopowder [21–23]. Silver may also reveal a toxic effect [20]. To avoid significant worsening of magnetic properties and toxicity, we decided to introduce rather low amount of silver into magnetite powder — less than 3 mass%.

This study is devoted to technology of magnetite/silver/antibiotic nanocomposites, their physico-chemical characterization and preliminary antimicrobial tests. For the purpose of this study, there were seven antibiotics used from five different groups (rifamycin, anthracycline, fluoroquinolone, tetracycline, and cephalosporin). Produced magnetite/silver/antibiotic nanocomposites are very promising for targeted

Table 1
Structural and chemical formulas of the antibiotics used.

Antibiotic	Pharmacological group	Chemical formula	Structural formula
Doxorubicin hydrochloride	Anthracyclines	$C_{27}H_{30}ClNO_{11}$	
Rifampicin	Rifamycin derivatives	$C_{43}H_{58}N_4O_{12}$	
Doxycycline hydrochloride	Tetracyclines	$C_{22}H_{25}ClN_2O_8$	
Cefazolin sodium	Cephalosporins	$C_{14}H_{13}N_8NaO_4S_3$	
Ceftriaxone disodium	Cephalosporins	$C_{18}H_{16}N_8Na_2O_7S_3$	
Cefotaxime sodium	Cephalosporins	$C_{16}H_{16}N_5NaO_7S_2$	
Ciprofloxacin hydrochloride	Fluoroquinolones	$C_{17}H_{21}ClFN_3O_4$