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Cu/Dioxidine Hybrid Nanocomposites: Cryochemical Synthesis and Antibacterial Activity

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Abstract—Hybrid nanocomposites consisting of an antibacterial drug, dioxidine, and copper nanoparticles are obtained by cryochemical synthesis. It is shown by UV spectroscopy, X-ray diffraction, PAM, and low temperature argon adsorption that the obtained hybrid systems represent dioxidine particles with a size of 100 to 400 nm, including copper particles with the size of 50 to 150 nm. The resulting composites possessed higher antibacterial activity against *E. coli* 52 than the initial dioxidine and copper nanoparticles.

Keywords: copper nanoparticles, dioxidine, cryochemical synthesis, hybrid materials, nanocomposites, antibacterial activity

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INTRODUCTION

Interest in hybrid materials, consisting simultaneously of organic and inorganic components, has increased in the past few years [1, 2]. The inclusion of metal nanoparticles in the organic matrix allows us to impart to it new optical [3], sensory [4], catalytic [5], and biological properties [6] or to modify the existing ones. The bactericidal properties of silver and copper nanoparticles stipulate their inclusion in organic matrices (polymeric [7], cellulose [8], chitosan [9]) to impart antibacterial activity to them or to enhance it. Notably, copper nanoparticles just as silver nanoparticles possess (due to the gradual release of ions) prolonged antibacterial activity, including against bacterial strains resistant to antibiotics; however, they are much cheaper, which makes the development of hybrid antibacterial drugs containing nanoparticles not only silver [10] but also copper, in addition to antibiotics, promising.

The aim of this work is the cryochemical synthesis of nanocomposites based on the antibacterial drug dioxidine and copper nanoparticles, as well as the determination of their antibacterial activity.

EXPERIMENTAL

The dioxidine substance corresponding to the pharmacopoeial monograph (PM) 42-2308-97 and the basic copper carbonate and aqueous formic acid solution qualified as *p.a.* were used without further purification. Finely dispersed anhydrous copper formate was prepared according to the procedure [11]. Copper nanoparticles were obtained by the thermal decomposition of anhydrous copper formate in hydrogen stream at the temperature of 200°C for 30 min. Dioxidine nanocomposites were synthesized with copper as follows: 0.005 g of copper nanoparticles and 1 g of dioxidine were dissolved in 100 mL of distilled water, placed in an ultrasonic bath for 30 min, sprayed into liquid nitrogen through a pneumatic nozzle, and subjected to freeze-drying for 24 h. A finely dispersed dioxidine powder, for comparative microbiological analysis, was obtained by the procedure described in [12, 13].

X-ray diffraction analysis (XRD) of the samples was performed on a Rigaku D/MAX-2500 diffractometer (Japan) under CuK_α radiation (λ = 1.54056 Å). A SPECORD M 40 UV spectrometer (Carl Zeiss, Germany) was used to obtain the spectra of the aqueous solution of the samples in the range of 200 to 900 nm. The specific surface area (S_s) of the samples was determined by the method of thermal desorption of argon in an installation based on a Chrom 5 chromatograph. The preadsorbed gases were removed from the surface of the samples on a vacuum installation. The average particle size (d) was calculated by the formula

$$d = 6/\rho S_s,$$

where ρ is the density of dioxidine.

Photomicrographs of the sample were obtained by transmission electron microscopy (TEM) using a JSM 6380 LA electron microscope with magnification of ×1000 to ×20000.

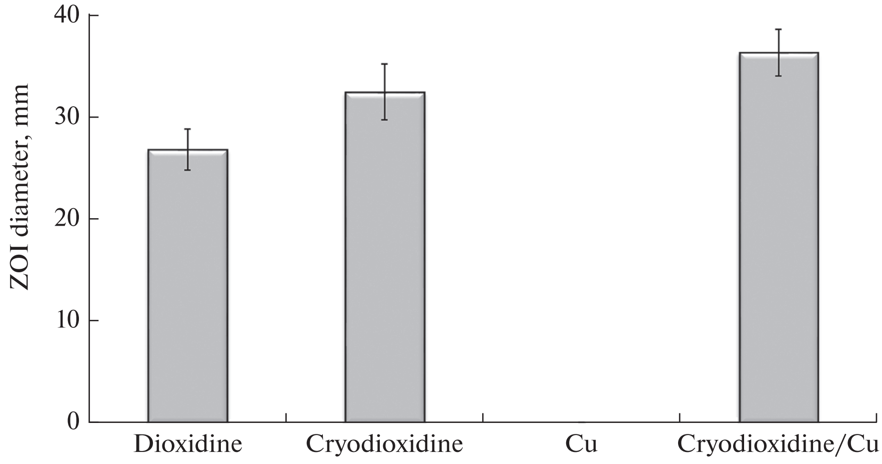

Fig. 1. ZOI of *E. coli* 52 growth around tablets of initial and cryomodified dioxidine after 20 h of incubation

The antibacterial activity of the samples was determined by the disk diffusion method using pressed tablets of the obtained composites, pharmacopoeial and cryomodified dioxidine (weight 100 mg, diameter 0.5 cm), as well as filter paper discs (diameter 0.5 cm), impregnated with a colloidal solution of copper nanoparticles (copper content on the disk was 0.0005 g). The *E. coli* 52 bacteria, obtained from the culture collection of the Department of Biology, Moscow State University, were used as the test cultures. The experiments were carried out in Petri dishes, in 20 mL of an agar medium, and dried for 24 h (thickness of medium layer 4 mm). The zones of inhibition (ZOI) of the test cultures were measured after 20 h of incubation.

RESULTS AND DISCUSSION

In order to establish the chemical composition of the obtained composites, the latter were characterized by XRD and UV spectroscopy. In the UV spectrum of an aqueous solution of the sample (0.1% by weight), peaks with maxima at 241, 259, and 376 nm, typical for dioxidine, are present [12, 13]. In the obtained spectrum, the peak corresponding to the plasmon resonance of the copper nanoparticles is absent, which is probably associated with its low content (0.5%) in the sample.

The set of interplanar distances (d, Å) and the corresponding intensities, calculated based on the X-ray diffractogram of the obtained composites, corresponds to the set of interplanar distances and intensities of nanocrystallites of dioxidine [12, 13] and copper (d, Å – I, %: 8.740–100; 8.026–94.2; 7.546–22.3; 6.899–57.8; 6.681–24.4; 6.274–50.9; 5.978–43.4; 5.177–17.1; 4.952–29.5; 4.498–19.4; 4.470–19.3; 4.345–23.9; 4.072–25.3; 4.013–17.6; 3.905–20.5; 3.678–28.4; 3.440–30; 3.358–99.3; 3.304–67.6; 3.206–31.6; 3.145–18.3; 2.091–6.43; 1.811–2.6; 1.282–1.3).

The specific surface area of the obtained hybrid material and the average particle size calculated based on it are 17 m^2/g and 240 nm, respectively. The TEM photomicrographs and electronic diffractograms of the resulting powder indicate that it represents organic particles with the size of 100 to 400 nm, in which copper nanoparticles with the size of 50 to 150 nm are enclosed.

The activity of the obtained composites against *E. coli 52* was assessed by the disc diffusion method in comparison with dioxidine and copper nanoparticles (see Fig. 1). The size of the ZOI around the pressed tablets of the resulting composites exceeded the size of the inhibition zones around the tablets of pharmacopoeial and finely dispersed dioxidine obtained by cryochemical synthesis [12]. Discs of filter paper impregnated with a solution of copper nanoparticles with the copper concentration similar to that in the pressed tablets of the composites were found to be inactive against *E. coli* 52.

Thus, Cu/dioxidine hybrid nanocomposites with a higher activity against *E. coli* 52 compared to dioxidine and copper nanoparticles were obtained by cryochemical synthesis.

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