



HYBRID COMPOSITES BASED ON CHITOSAN MODIFIED BY CONJUGATES OF Ag AND Cu NANOPARTICLES WITH DIHYDROQUERCETIN

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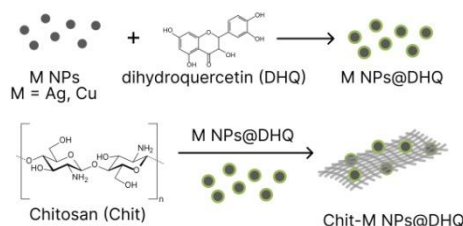
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Abstract

New hybrid materials based on chitosan modified with conjugates of metal nanoparticles (silver and copper) and dihydroquercetin, a biologically active flavonoid with antioxidant and anti-inflammatory properties, were obtained. The metal nanoparticles were prepared by the environmentally safe metal-vapor synthesis. The resulting materials exhibit biological activity against bacteria *Bacillus cereus* and *Escherichia coli*.

Key words: chitosan, copper and silver nanoparticles, dihydroquercetin, biological activity, metal-vapor synthesis.



Introduction

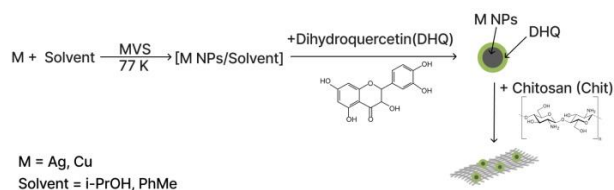
The creation of new metal-containing materials based on biopolymers for medical applications is one of the most relevant and intensively developing areas. The interest to this field is caused by an increase in the number of microorganism strains resistant to most antibiotics. It was established that biologically active nanoparticles of metals and their oxides do not cause resistance in microorganisms. The introduction of metal nanoparticles into the biopolymer structure can ensure an increase in the antimicrobial activity and impart new functional properties to the resulting composite. Owing to their biological and physicochemical properties, the materials based on natural polymers (chitosan, cellulose, *etc.*), flavonoids and metal nanoparticles can meet the basic requirements for medical materials [1]. **Chitosan (Chit)** is a polyaminosaccharide derived from crustacean shell chitin. Owing to the presence of amino and hydroxy groups, this polymer possesses chelating properties and can stabilize metal nanoparticles [2, 3]. A significant number of studies demonstrated the high biological activity of silver and copper nanoparticles (NPs), which stimulates their use in the creation of new functional materials [4, 5]. Dihydroquercetin (DHQ) is a flavonoid with high antioxidant, capillary-protective and anti-inflammatory activity [6]. Flavonoids can regulate the immune response, reduce inflammation and prevent angiogenesis. It can be expected that the materials obtained on the basis of a combination of quercetin, metal nanoparticles, and chitosan will promote activation of regenerative processes in damaged tissues and increase the antimicrobial and antibacterial activity of the system as a whole. Herein, we report on the synthesis of new Ag- and Cu-containing hybrid materials based on chitosan modified by dihydroquercetin conjugates with silver or copper nanoparticles, which were obtained by the environmentally safe method of metal-steam synthesis.

Results and discussion

The properties of materials containing metal nanoparticles are determined not only by the composition, particle sizes, and nature of the specific interaction with the matrix stabilizing them, but also by the method of obtaining the material. Metal-vapor synthesis (MVS) is effective for the synthesis of metal nanoparticles and allows one to avoid or significantly reduce contamination introduced into biomedical materials [7–11]. Using the MVS method, the materials based on chitosan modified by dihydroquercetin conjugates with silver (AgNP@DHQ) and copper (CuNP@DHQ) nanoparticles were obtained. The resulting materials were characterized using scanning electron microscopy (SEM) and powder X-ray diffraction (PXRD).

The method of obtaining the composite is shown in Scheme 1. An organosol containing Ag or Cu NPs and DHQ in isopropanol or toluene was used to modify chitosan. The analysis of the surface of the AgNPs–Chit composite by SEM revealed minor morphological changes in the structure of the material compared to the original Chit (see Fig. S1 in the Electronic supplementary information (ESI)).

Transmission electron microscopy was used to study the microstructure of metal nanoparticles obtained by MVS. As can be seen from the micrographs (Fig. S2 in the ESI), Cu and Ag



Scheme 1. Production of a chitosan-based composite modified with dihydroquercetin conjugate with silver or copper nanoparticles.

NPs are present in these products with particle sizes of 3 nm and 6 nm, respectively.

The diffraction patterns of the initial chitosan and products of its modification with metal nanoparticles are shown in Fig. 1. In addition to the broad asymmetric reflections at $2\theta \sim 10.5^\circ$ and $\sim 20^\circ$ characteristic of chitosan, the patterns of silver-containing composites exhibit reflections in the region $2\theta > 35^\circ$. The positions of these reflections correspond to the phase of metallic silver (sp. gr. Fm-3m, $a = 4.0862 \text{ \AA}$): 38.11° (111), 44.3° (002), 64.44° (022), 77.4° (311), 81.54° (222). The Rietveld refinement of the diffraction profile in the specified region using the Ag metal phase allows for a sufficiently reliable description of the diffraction data, the divergence factor (R_{wp}) being 1.6% and 3.4% in the case of Chit-AgNPs@DHQ and Chit-AgNPs, respectively. The evaluation of the crystallite sizes (D) of the Ag phase by the broadening of the diffraction reflections using the Scherrer method showed that this phase is significantly more dispersed in the Chit-AgNPs@DHQ composite ($D = 9 \text{ nm}$) than in Chit-AgNPs ($D = 24 \text{ nm}$).

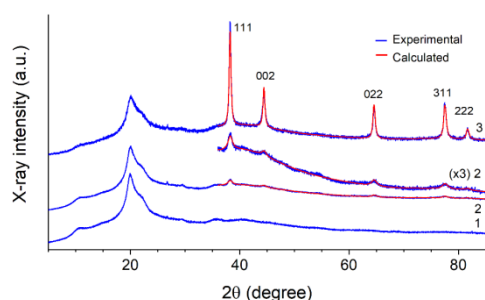


Figure 1. Experimental (blue) and calculated (red) powder diffraction patterns of initial chitosan (1), Chit-AgNPs@DHQ (2), and Chit-AgNPs (3). The reflection indices of the silver metal phase are indicated.

In the case of the Chit-CuNPs composite, the diffraction patterns of the initial and modified chitosan do not differ markedly from each other (see Fig. S3 in the ESI), which indicates an amorphous nature of the copper-containing compounds in this material.

The bacteriostatic activity of DHQ, AgNPs and AgNP@DHQ was studied against gram-positive (*Bacillus cereus*) and gram-negative (*Escherichia coli*) bacteria (Table 1).

Table 1. Minimum inhibitory concentrations of the samples explored

Sample	<i>B. cereus</i>	<i>E. coli</i>
AgNPs	10 mg/mL	10 mg/mL
DHQ	0.156 mg/mL	1.25 mg/mL
AgNP@DHQ	0.16 mg/mL	0.625 mg/mL

The results obtained suggest that AgNP@DHQ nanoparticles exert stronger inhibitory effects than AgNPs.

Conclusions

New biologically active hybrid materials based on chitosan modified by conjugates of metal silver or copper nanoparticles with dihydroquercetin were obtained by the metal-vapor synthesis using $^i\text{PrOH}$ and toluene as the reaction medium. Their compositions, surface, and antibacterial properties were

investigated. The results obtained can be used in the creation of medical materials.

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Electronic supplementary information

Electronic supplementary information (ESI), available online: [the materials and methods, SEM and TEM images, XRD patterns](#). For information about ESI, see DOI: 10.32931/ioXXXXx.

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