

Nanocomposites Based on Gold Nanostars with a Hollow Silica Shell for Controlled-Release Drug Delivery

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Abstract. Recently, there has been a significant development of targeted drug delivery methods using various nanomaterials. This has opened up new opportunities for the therapeutic use of drugs with pronounced side effects. The use of targeted delivery and controlled release systems provides an opportunity to reduce the negative effect on the whole organism and improve the effectiveness of treatment. In this work, nanocomposites based on gold nanostars with a hollow organosilica shell were studied as carriers for drug delivery. Two types of drugs, docetaxel and doxorubicin, were loaded into the cavities formed after silica etching. To implement controlled unloading, the nanocomposites were coated with a molecular gate based on tetradecanol. It was found that the drug was retained in the nanocomposites until an external stimulus was received. © 2024 Journal of Biomedical Photonics & Engineering.

Keywords: gold nanostars; hollow shell; organosilica; drug delivery; docetaxel; doxorubicin; tetradecanol; cytotoxicity.

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1 Introduction

Recently, the treatment of cancer has become an important area of research in the field of medicine and biotechnology [1]. One of the main methods of treating such diseases is chemotherapy using antitumor drugs [2]. For example, the drug docetaxel is a clinically proven anti-tumor agent for inhibiting breast cancer [3]. However, despite their high efficiency, antitumor drugs have many side effects, affecting not only tumor cells, but also healthy cells of the body [4]. The most common side effects include bone marrow suppression, nausea and vomiting, fatigue, and hair loss. To solve this problem, targeted drug delivery using various nanocarriers is currently of great practical interest. The use of nanocarriers helps reduce side effects and increase the effectiveness of chemotherapy due to the fact that they can be delivered directly to the tumor, minimizing their impact on other organs and tissues of the body. In addition, encapsulating the drug in a carrier helps reduce its interaction with other substances and overcome various physiological barriers [5]. Such carriers may

include protein-based conjugates [6], liposomes [7], dendrimers [8], magnetic nanoparticles [9], etc. Among the numerous nanocarriers for drug delivery, it is worth noting silica nanoparticles, which have favorable physicochemical properties [10, 11]. Firstly, they have a large surface area, which ensures high drug loading. This way, more active substance can be delivered to its destination. Secondly, due to their chemical structure, silica nanoparticles are not broken down by the body's enzymes, which ensures that the drug will be delivered to the right place and maintain its effectiveness for a long time. Another important advantage of silica nanoparticles is the controlled release of drugs [12]. By using various surface modification methods, it is possible to control the rate of drug release from nanoparticles. Slow release of the drug ensures maintenance of a therapeutic concentration of the drug at the site of localization, which allows achieving maximum therapeutic effect with minimal side effects and reducing the frequency of drug administration.

In addition to chemotherapy, photothermal therapy can be used to treat tumor diseases. It is based on the use

of light-absorbing agents, which, by absorbing light, heat up and destroy cancer cells [13, 14]. Of particular interest here are gold nanoparticles that exhibit plasmon resonance. Plasmon resonance of nanoparticles can be tuned to a specific wavelength by changing the shape and size of the nanoparticles, which is important for biomedical applications. Of great interest in biomedicine is the near infrared range with wavelengths from 650 to 950 nm, called the first therapeutic “optical window” [15]. The “optical window” corresponds to the wavelength range where absorption by water and biological tissues is minimal and laser penetrating power is maximal. Therefore, non-spherical gold nanoparticles with high absorption within the “optical window” can act as effective agents for photothermal therapy on their own or even as part of composites [16]. In addition, gold is a noble and inert metal that is non-toxic and ideal for use in biomedicine. In addition, the surface of gold nanoparticles has adsorption capacity. Coating gold nanoparticles with silica shells offers an alternative strategy where drugs incorporated into the shell can be co-delivered with photothermal agents [17]. On the one hand, heating can directly destroy cancer cells. On the other hand, increasing the temperature promotes the release of the drug, thereby initiating chemotherapy. In a number of studies, gold nanostars were coated with a mesoporous silica shell and loaded with doxorubicin. After drug encapsulation, a molecular layer, such as paraffin heneicosane [18] or hyaluronic acid [19], was applied to the surface of the composite to seal the channels of the mesoporous silica shell. The drug was contained within these composites and release was initiated either by heating under laser irradiation, or by changing the pH, or by exposure to an enzyme. In addition, hollow silica shells are of great interest [20]. Due to their hollow structure, they are able to accommodate a larger number of encapsulated substances, which in turn are protected from the effects of the environment. Nanocomposites for drug delivery are also created based on the hollow shell. Various types of gold nanoparticles are used as cores. Thus, in the work [21], gold nanocages were used, which acted both as a sensitive substrate for SERS and as an effective photothermal converter for localized hyperthermic cancer therapy due to strong absorption of near-infrared light. In addition, coating the nanocages with a hollow SiO₂ shell prevents the aggregation of metal particles, preserving their optical properties. Such nanocomposites can be effectively used for drug delivery and photothermal therapy. Gold nanorods were also used as cores for the nanocomposites [22]. They were used to synthesize a hollow silica shell, which was loaded with doxorubicin and then the pores were closed. This structure allowed the drug to be preserved inside with virtually no losses. In addition, they were able to demonstrate that combined chemo-photothermal therapy was more effective in killing cancer cells than either chemotherapy or photothermal therapy alone. Also in 2021, it was shown [23] that gold nanotriangles, nanorods, and other types of particles can act as cores for

the synthesis of nanocomposites with a hollow silica shell.

In this work, we synthesized nanocomposites based on gold nanostars coated with a hollow organosilica shell for drug delivery. These nanocomposites have a number of advantages, making them ideal candidates for controlled drug delivery. First, gold nanostars have wide tuning ranges of localized surface plasmon resonance [24]. Secondly, among other forms of gold nanoparticles, they are the most photostable [25]. Third, the organosilica shell contains two different functional groups: Si–OH and –SH. The thiol residue provides a more convenient way of covalently linking to target molecules: fluorescent molecules, proteins or single-stranded DNA (ssDNA) with isothiocyanate, succinimidyl ester or maleimide groups [26]. Thus, the surface of nanocomposites is convenient for functionalization. The resulting cavities were loaded with drugs: doxorubicin and docetaxel after etching the organosilica shell. The cytotoxicity of the obtained nanocomposites was also studied for their further use in biomedicine.

2 Materials and Methods

2.1 Chemicals

The following reagents were used in the synthesis without further purification: hydrogen tetrachloroaurate(III) trihydrate (HAuCl₄*3H₂O; 99%), sodium citrate trihydrate (Na₃C₆H₅O₇*2H₂O), sodium borohydride (NaBH₄), hydrochloric acid (HCl, high purity grade), L-ascorbic acid (99.9%), silver nitrate (AgNO₃; 99.9%), 3-mercaptopropyltriethoxysilane (MPTES), polysorbate 20 (Tween 20), docetaxel (DOC, purum, ≥97.0% (HPLC)) all purchased from Sigma-Aldrich (Darmstadt, Germany). Adriamycin hydrochloride (doxorubicin, DOX, 98%) purchased from Macklin (China). Polyethylene glycol thiol (Mw=5000, Creative PEGWorks, Chapel Hill, North Carolina, USA), sodium hydroxide (NaOH, analytical grade; Dia-M, Russia), 25% ammonia solution (Vekton, Russia). MilliQ ultrapure water (18 mΩ×cm; Millipore, Merck KGaA, Darmstadt, Germany) was used in all experiments. All glassware and magnets were cleaned with freshly prepared aqua regia (a mixture of HNO₃ and HCl, in a ratio of 1:3 by volume) followed by rinsing with plenty of water.

2.2 Equipment

To measure the extinction spectra of colloidal solutions of nanoparticles and nanocomposites, a high-speed spectrophotometer Specord S300 (Analytik Jena, Germany) was used. Measurements were carried out in the wavelength range of 320–1100 nm using a 2 mm thick quartz cuvette. To measure the extinction spectra of drugs, in particular docetaxel, and drug-loaded nanocomposites, a Specord 250 dual-beam spectrophotometer (Analytik Jena, Germany) was used. It is additionally equipped with a UV lamp and allows

measurements in the wavelength range of 190–1100 nm. The measurements were carried out in a 1-mm thick quartz cuvette.

To describe the morphological properties of the synthesized nanoparticles and nanocomposites, we used transmission electron microscopy (TEM) images obtained using a Libra-120 microscope (Carl Zeiss, Germany) at the Simbioz Center for the Collective Use of Research Equipment of the Institute of Biochemistry and Physiology of Plants and Microorganisms – Subdivision of the Federal State Budgetary Research Institution Saratov Federal Scientific Centre of the Russian Academy of Sciences (IBPPM RAS).

2.3 Synthesis of Gold Nanostars

Gold nanostars were synthesized from gold seeds using a two-step protocol [27]. For this purpose, in the first stage, using the citrate reduction method of HAuCl_4 described by Frens [28], gold nanospheres with an average diameter of 25 nm were synthesized, which were used as seeds for the synthesis of gold nanostars. To do this, 145.95 ml of water was poured into an Erlenmeyer flask and brought to a boil with a reflux water condenser while stirring on a magnetic stirrer. 1.5 ml of 1% HAuCl_4 and 2.55 ml of 1% sodium citrate were added. The solution was stirred for 15 min. The color of the solution changed from colorless to red. The second step involved the actual synthesis of nanostars. Briefly, to a mixture (“growth solution”) containing 40 ml of water, 1 ml of 1% HAuCl_4 , 120 μl of 1 M HCl, different amounts of a colloid of 25 nm gold nanospheres (“seeds”), 600 μl of 4 mM AgNO_3 and 600 μl of 100 mM ascorbic acid were quickly alternately added.

2.4 Synthesis of Organosilica Shell

The organosilica shell was synthesized using the method described in the article [26]. Briefly, after the gold nanostars were synthesized, they were coated with SH-PEG-COOH. Then, different amounts of 3-mercaptopropyltriethoxysilane (MPTES) were added to the particle colloid to synthesize shells of different thicknesses and a 25% ammonia solution as an initiator for the hydrolytic condensation reaction.

2.5 Etching of Organosilica Shell

To load the drugs into the synthesized nanocomposites, an internal cavity was created using a protocol that has been described in detail for the etching of silica nanoparticles [29]. For this purpose, the inner part of the organosilica shell was etched in an alkaline medium using NaOH with a final concentration of 0.75 M. Before etching, the organosilica-coated nanoparticles were coated with polyvinylpyrrolidone (PVP) to protect the surface. In this case, the PVP polymer performs the important function of preserving the surface of the nanoparticles, and this process is called the surface-protecting etching method. It is also important to note here that coating with PVP does not prevent the

penetration of drug molecules and other substances into the nanoparticles [22, 29]. The degree of etching is defined in our work by analogy with the work [29] as a decrease in the extinction intensity at a certain wavelength in percent relative to the initial value. The fact is that during etching the colloid becomes more transparent and a decrease in extinction can be an easily measured characteristic of the etching degree. In the work of Zhang Q. et al. [29] the extinction value at a wavelength of 700 nm was used, which was convenient for silica nanospheres. In our work, starting from approximately 550 nm, the spectrum exhibits a characteristic maximum of gold nanostars, which act as nanocomposite cores. And the characteristic spectral contribution of silica is observed as a pronounced shoulder in the region of 350–600 nm. Therefore, for our nanocomposites, the degree of etching is conveniently determined by the decrease in the extinction value at a wavelength of 400 nm.

Different degrees of etching are achieved by adjusting the exposure time of nanocomposites in the NaOH solution. The longer the exposure time, the greater the etching degree. The etching degree is determined in real time by measuring the extinction using a high-speed spectrophotometer Specord S300 by the extinction value at 400 nm. To stop etching, the same volume of water is added to the colloid, which reduces the NaOH concentration. After this, the nanocomposites are washed by three-fold centrifugation at 800 g for 20 min with redispersion in water.

2.6 Drug Loading

The drugs used were doxorubicin and docetaxel. Two methods were used to load the drug. In the first method, the composite nanoparticles were concentrated to a concentration of 375 $\mu\text{g}/\text{ml}$, which was determined by drying and weighing a portion of the sample. The drug (doxorubicin or docetaxel) was then added to the nanoparticles to bring its final concentration to 200 $\mu\text{g}/\text{ml}$. The mixture was incubated for 24 h and then measurements were taken of the spectra of the colloid of nanoparticles with the drug and the supernatant after centrifugation.

The second method of drug loading was used to close the pores with a molecular gate [22]. The temperature-sensitive material 1-tetradecanol was used as such a molecular gate. This method consists of drying the particles and adding a high concentration solution of the drug to them – 8 mg/ml. The mixture was stirred while heating at 60 °C for 1 h, then tetradecanol and hot water were added successively. After this, the samples were washed from excess drugs and tetradecanol, first in hot water and then in cold water. This method allowed the tetradecanol to harden and close the pores.

2.7 Determination of the Concentration of Loaded and Released Drug

The concentration of the loaded and released drug was determined as follows. First, calibration curves were

constructed for each drug using the two-fold dilution method and the formula for the dependence of extinction on concentration was determined. Docetaxel was dissolved in ethanol and the concentration was determined by the intensity of the maximum at a wavelength of 231 nm. Doxorubicin hydrochloride was dissolved in water and the concentration was determined at a wavelength of 480 nm. After incubation of the nanocomposites with the drug, the samples were centrifuged and the concentration of the drug in the supernatant was measured. The amount of loaded drug was determined as the difference between the initial concentration and the concentration in the supernatant. The concentration of the released drug was determined similarly by measuring the concentration of the drug in the supernatant after centrifugation of nanocomposites.

2.8 Cytotoxicity Test

The toxicity test of the synthesized nanocomposites was based on measuring the metabolic activity of cells. Quantitative assessment of cell viability was measured by a spectrofluorometric method using Alamar blue reagent (ThermoFisher, USA). Alamar blue is resazurin, a cell-permeable dye that can be reduced by mitochondrial dehydrogenases in living cells to the fluorescent compound resorufin. The integrated fluorescence intensity of resorufin at a wavelength of 600 nm is directly proportional to the number of cells and their metabolic activity. The Chinese hamster ovary cell line (CHO II) was chosen as the object of study. This cell line is considered one of the most sensitive cell lines for cytotoxicity studies [30]. The cells were cultured in DMEM/F-12 (1:1) nutrient medium supplemented with 20% fetal calf serum, L-glutamine and 1% penicillin in an atmosphere of 5% CO₂ at 37 °C until a monolayer was formed. When the cell monolayer reached 70–90%, the old nutrient medium was removed and a new one containing the studied nanocomposites was introduced. Cytotoxicity assessment was performed for samples of gold nanostars coated with an organosilica shell without drug loading. The preparations were preliminarily washed 3 times from the reaction mixture. Next, the solution with nanoparticles was diluted with DMEM nutrient medium to a final gold concentration of 0.8 to 25 µg/ml. The resulting solution was poured into a 96-well plate at 190 µl. The plate was placed in an

Innova CO-14 CO₂ incubator (New Brunswick Scientific, USA) at 37 °C with 5% CO₂. For each obtained gold concentration, the test was performed in 4 replicates. The duration of the cytotoxicity test was chosen to be 72 h based on the observation of cell growth without nanocomposites in the wells of the plate 24, 48 and 72 h after the introduction of the seed dose. At the growth time of 72 h, the cells filled about 80% of the well bottom area, which was a favorable control for careful measurement of the cytotoxicity of the nanocomposites. After 72 h of incubation of cells with nanoparticle samples, the culture medium was removed and a resazurin solution was added to a final concentration of 0.01 mg/ml. The incubation time with the dye was 1 h. Next, spectrofluorometric measurements were performed on a Cary Eclipse microplate fluorimeter (Agilent Technologies, USA). The excitation wavelength was 530 nm. The emission wavelength range was 590–610 nm. To assess the cytotoxicity of gold nanoparticle samples, the metabolic activity value was calculated:

$$MA = \frac{I}{I_0} * 100, \quad (1)$$

where *MA* is the metabolic activity, *I* is the fluorescence intensity value of the experimental sample, *I*₀ is the fluorescence intensity value of the control sample.

3 Results and Discussion

3.1 Synthesis of Nanocomposites

The general scheme for the synthesis of nanocomposites based on gold nanostars with a hollow silica shell for controlled-release drug delivery is shown in Fig. 1. The first step involves the synthesis of gold nanostars. It is carried out using a seed protocol that includes the synthesis of spherical seeds and their subsequent growth, which includes the formation of sharp spikes. Next, a shell of organosilica is formed on the surface of the nanoparticles. To ensure controlled drug delivery, a cavity is created inside the organosilica shell. The resulting pores on the outside of the shell are closed with a heat-sensitive gate – tetradecanol. This system allows the drug to be kept inside the nanocomposite at room temperature. The drug is released by heating.

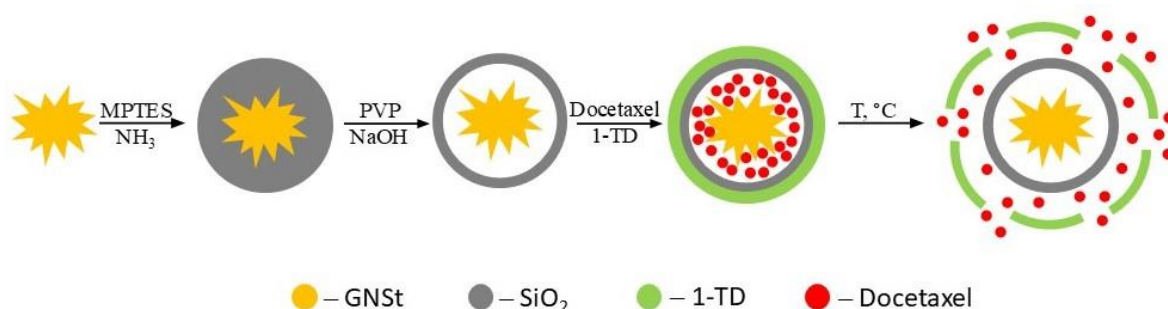


Fig. 1 Scheme for the synthesis of nanocomposites based on gold nanostars with a hollow silica shell for controlled drug delivery.

3.2 Characteristics of Gold Nanostars

By varying the amount of added 25-nm seeds, the plasmon resonance was tuned in the range from 700 to 1000 nm. When the amount of added seed solution was reduced from 400 to 150 μl per 5 ml of growth solution, the plasmon resonance shifted to a longer wavelength region of the spectrum from 758 to 853 nm (Fig. 2a). This is explained by the fact that as the number of seeds decreases, the amount of HAuCl_4 per nanoparticle increases. It is known that in such cases the average size of the core and the length of the spikes of nanostars increase [31]. Accordingly, the length of the spikes increases on average from 36.3 ± 6.7 nm (Fig. 2b) to 91.7 ± 15.6 nm (Fig. 2d). Also, with a decrease in the number of seeds, the diameter of the core of the nanostars increases from 52.9 ± 7.4 nm (Fig. 2b) to 86.8 ± 11.5 nm (Fig. 2d). In further experiments, nanostars with a plasmon resonance of 853 nm were

used, where 150 μl of seeds per 5 ml of growth solution were added during synthesis (Fig. 2d).

3.3 Synthesis of Organosilica Shell

Using this method, 3 samples with an organosilica shell with an average shell thickness of 170 ± 24.6 , 90 ± 10.2 and 28 ± 3.5 nm were synthesized (Fig. 3a–c). Spectral changes are shown in Fig. 3d. When a shell is formed on the surface of nanoparticles, a shift in plasmon resonance occurs to the long-wave region as a result of a change in the local dielectric environment of the nanoparticles. Also, with an increase in the thickness of the organosilica shell, a significant increase in the short-wave shoulder in the spectrum is observed. For all subsequent experiments on silica shell etching and drug loading, a sample of nanocomposites with a maximum silica shell thickness of 170 ± 24.6 nm was used (Fig. 3a).

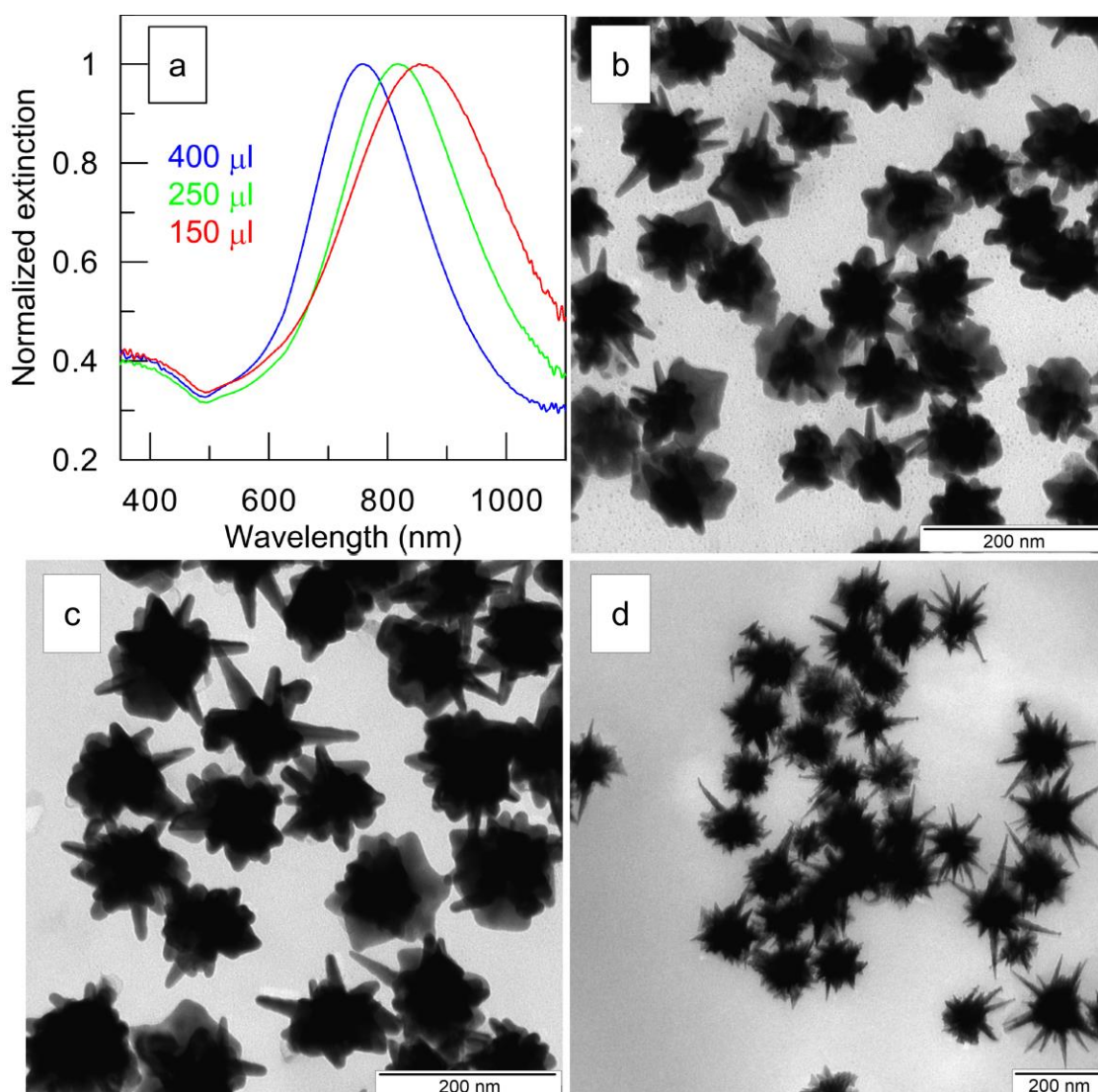


Fig. 2 (a) Extinction spectra of gold nanostar colloids after adding 400 (blue line), 250 (green line) and 150 μl (red line) of seeds to 5 ml of growth solution and TEM image of gold nanostars synthesized with the addition of (b) 400, (c) 250 and (d) 150 μl of seeds.

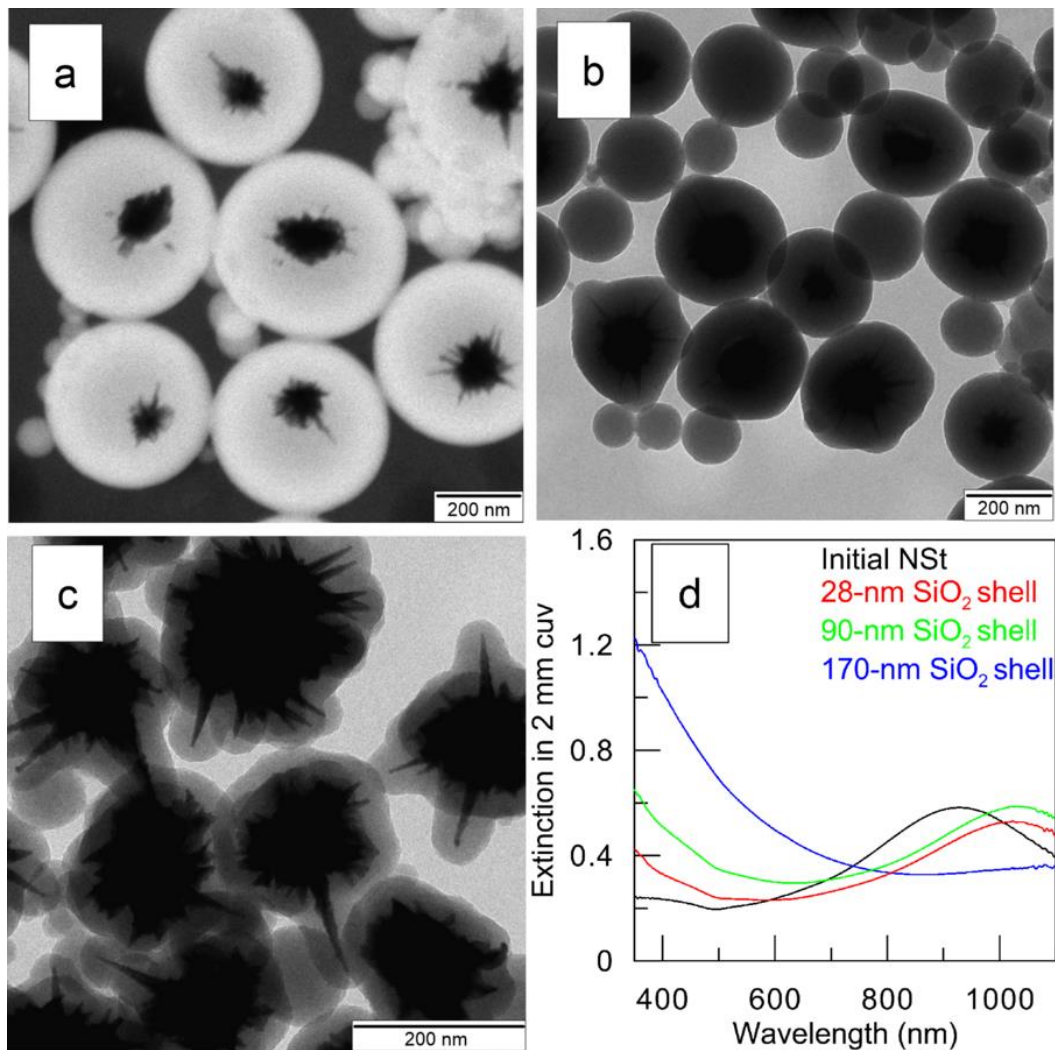


Fig. 3 TEM images of gold nanostars coated with an organosilica shell of (a) 170, (b) 90 and (c) 28 nm thickness. (d) Extinction spectra of gold nanostars before (black) and after the formation of an organosilica shell with a thickness from 28 nm (red) to 170 nm (blue).

3.4 Etching of Organosilica Shell

Three samples with different degrees of etching of the organosilica shell were obtained, when the decrease in optical density at a wavelength of 400 nm was 35, 64 and 75% (Fig. 4). These etched samples were designated as ENC1, ENC2 and ENC3, respectively.

The spectrum shows a significant decrease in the intensity of the short-wave shoulder, indicating a decrease in the amount of silica. There is also a shift in the plasmon resonance of gold nanostars toward shorter wavelengths due to a change in the local dielectric environment of the nanoparticles.

Electron microscope images confirm spectral changes (Fig. 5). With a spectrum reduction of 64% (ENC2), nanocomposites exhibit irregularities along the perimeter of the shell. Light areas also appear, indicating thinning of the shell (Fig. 5c). With further etching, the number of light areas increases and, accordingly, the amount of silica decreases (Fig. 5d).

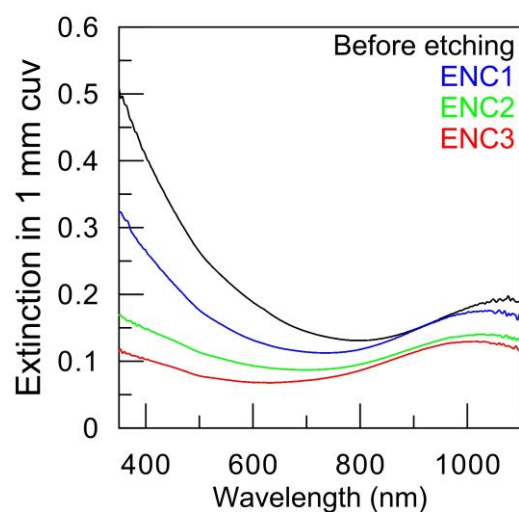


Fig. 4 Extinction spectra of gold nanostars coated with an organosilica shell before (black line) and after etching, where the extinction at 400 nm is reduced by 35% (ENC1, blue line), 64% (ENC2, green line), and 75% (ENC3, red line).

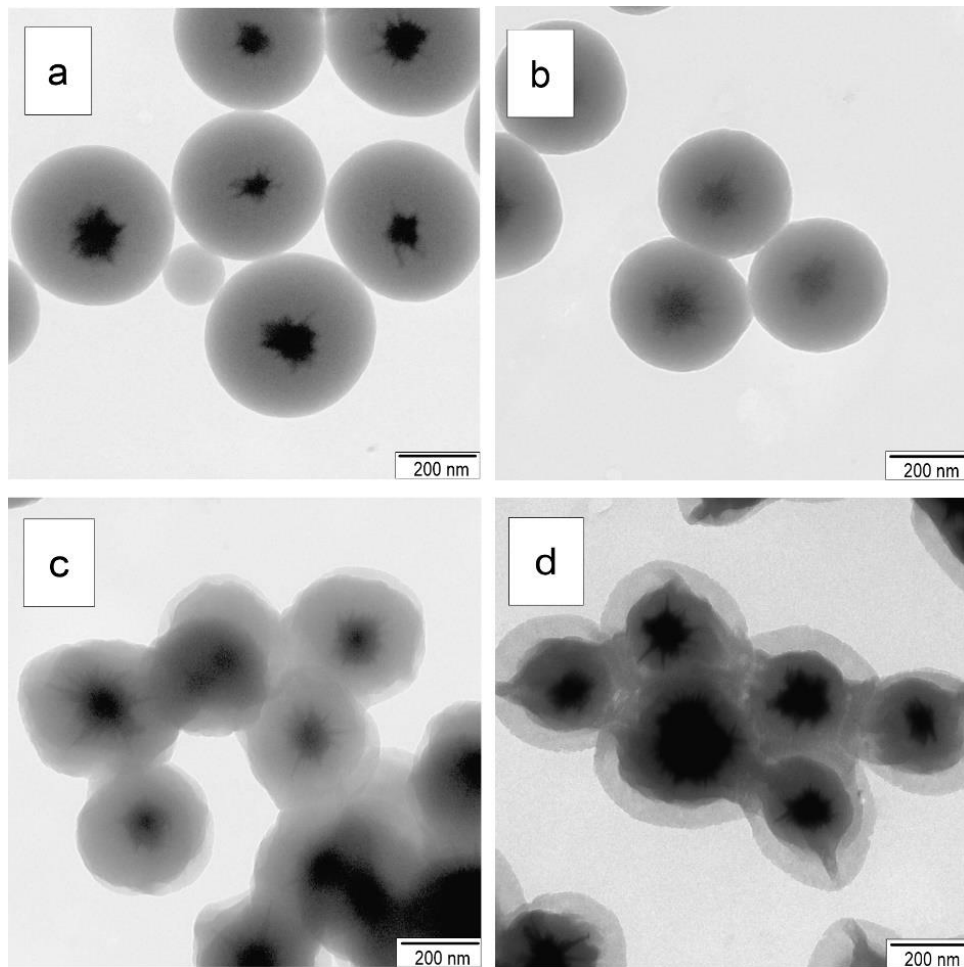


Fig. 5 TEM images of gold nanostars coated with a silica shell (a) before and after etching: (b) ENC1, (c) ENC2, and (d) ENC3.

3.5 Loading Drugs

To determine the concentration of the loaded drug, calibration curves were constructed (Fig. 6) and formulas for the dependence of concentration on the maximum absorption of a specific drug were determined. For docetaxel, the concentration was determined by the intensity of the maximum at a wavelength of 231 nm, and for doxorubicin at 480 nm. The measurements were carried out in a 1 mm thick quartz cuvette; the graphs show the values recalculated for a 10 mm cuvette.

Fig. 7 shows the extinction spectra of solutions of gold nanostars coated with a silica shell after etching (ENC1, ENC2 and ENC3) with docetaxel (Fig. 7a) and doxorubicin (Fig. 7b). Depending on the degree of shell etching, 64.5 ± 0.11 to 77.3 ± 0.6 $\mu\text{g/ml}$ of docetaxel were loaded, which amounted to 32.23 ± 0.55 and $38.65 \pm 0.3\%$ of the initial drug concentration of 200 $\mu\text{g/ml}$, respectively. Doxorubicin was loaded in concentrations from 95.74 ± 0.13 to 106.25 ± 0.23 $\mu\text{g/ml}$, which amounted to 47.9 ± 0.07 and $53.1 \pm 0.11\%$ of the initial drug concentration of 200 $\mu\text{g/ml}$, respectively. The release of drugs from nanocomposites was also investigated. Without the use of a molecular gate,

doxorubicin was found to be completely released from the loaded nanoparticles into solution within 30 min. Docetaxel is released from loaded nanoparticles in less than 4 h. The increase in the release time of docetaxel compared to doxorubicin may be due to the fact that it is practically insoluble in water.

A second drug loading method using tetradecanol was used to load docetaxel into nanocomposites with a maximally etched shell (ENC3, 75% extinction decrease). It was performed as described in the Materials and Methods Section. This method caused tetradecanol to solidify and close the pores, thereby preventing the drug from escaping from the particles, as confirmed by measuring the extinction of the sample over 72 h when stored at room temperature. This stability ensures that the drug remains unchanged for a long time and, therefore, increases the likelihood of its delivery to its destination. To study the controlled release of drugs, tetradecanol-coated nanocomposites were heated to 50 °C after 72 h of storage, centrifuged, and the spectrum of the supernatant was measured (Fig. 8). Within 10 min of heating, the loaded drug docetaxel was released from the particles into solution and its maximum was clearly detected in the supernatant (Fig. 8, blue line).

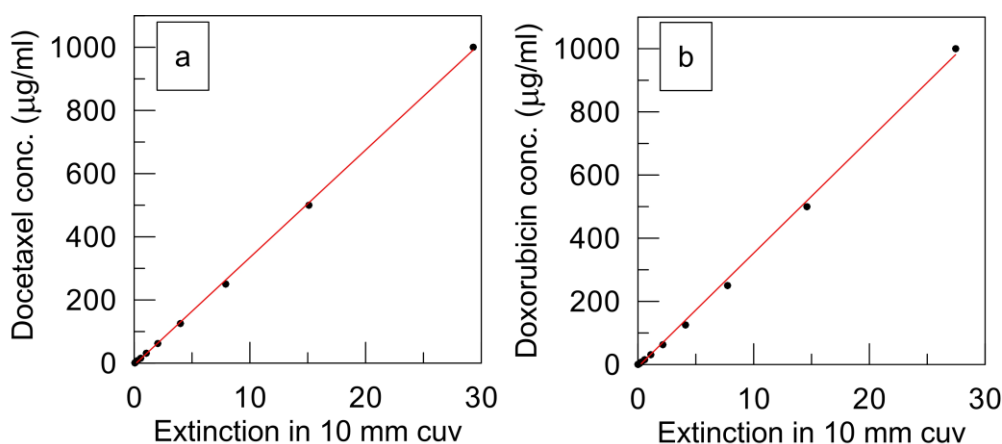


Fig. 6 Calibration curves of the dependence of the concentration of (a) docetaxel and (b) doxorubicin on the extinction value in a 10 mm cuvette at a maximum of 231 and 480 nm, respectively.

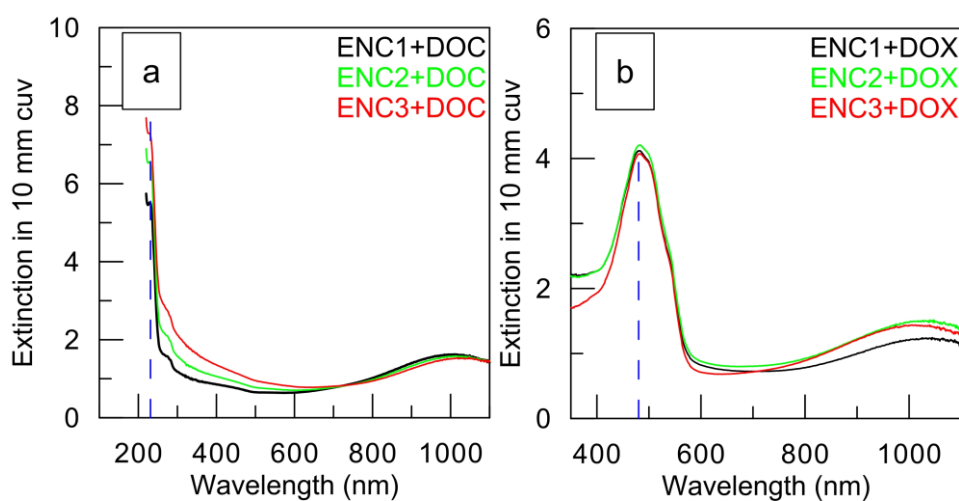


Fig. 7 Extinction spectra of colloidal solutions of gold nanostars coated with a silica shell after etching (ENC1, ENC2 and ENC3) loaded with (a) docetaxel and (b) doxorubicin, plotted for a 10 mm cuvette. The blue dotted line shows the major drug peaks: (a) 231 nm for docetaxel and (b) 480 nm for doxorubicin.

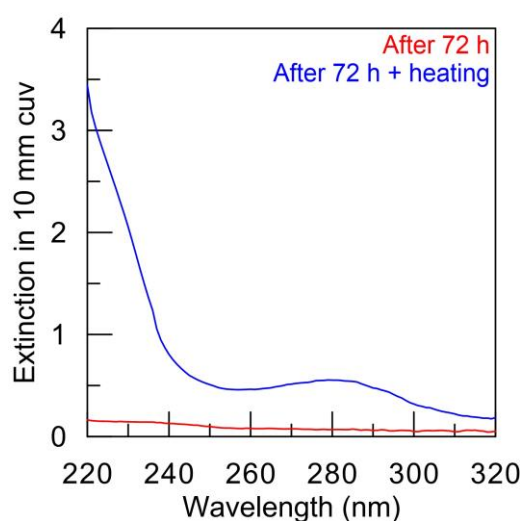


Fig. 8 Extinction spectrum of the supernatant of docetaxel-loaded nanocomposites after 72 h of incubation at room temperature without heating (red line) and after heating (blue line) plotted for a 10 mm cuvette.

3.6 Cytotoxicity Test

To test the possibility of using the synthesized nanocomposites based on gold nanostars coated with an organosilica shell in biomedicine for drug delivery, they were tested for cytotoxicity. Fig. 9 shows the results of the assessment of metabolic activity on the Chinese hamster ovary cell line (CHO II) after 72 h of incubation with the synthesized unloaded nanocomposites.

It was found that with an increase in gold concentration from 0.8 to 25 µg/ml, a decrease in metabolic activity occurs. At gold concentrations from 0.8 to 12.5 µg/ml, a sufficiently high metabolic activity was observed, above the threshold value of 70%. This indicates the absence of a cytotoxic effect of nanocomposites on the cell line. However, at a gold concentration of 25 µg/ml, the metabolic activity was $50.8 \pm 5.1\%$, which indicates an increase in the toxicity of the obtained nanocomposites. Thus, the fabricated nanocomposites in a certain concentration range may be favorable candidates for use in biomedical drug delivery.

applications, which will require further *in vitro* and *in vivo* studies.

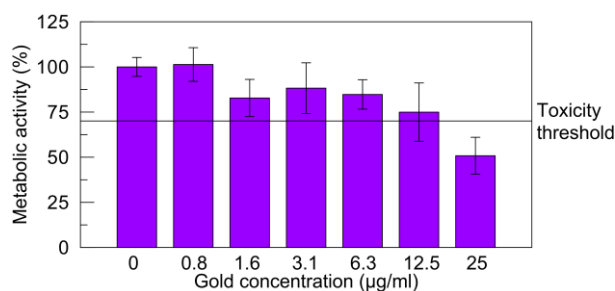


Fig. 9 Fluorometric quantification of the metabolic activity of Chinese hamster ovary cell line (CHO II) after 72 h incubation with synthesized nanocomposites based on gold nanostars coated with an organosilica shell.

4 Conclusions

This work demonstrated the development of innovative nanocomposites designed for targeted delivery of drugs. Gold nanostars, which have unique optical properties and high chemical stability, were chosen as the basis for these nanocomposites. Three samples with different degrees of etching of the organosilica shell were obtained, when the decrease in optical density at a wavelength of 400 nm was 35, 64 and 75%. Two antitumor drugs, doxorubicin and docetaxel, were loaded into the created cavity. Their amount loaded into the nanocomposites depended on the degree of etching of the shell. For example, doxorubicin was loaded from 95.74 to 106.25 µg/mL, which was 47.9 and 53.1%, respectively, of the initial concentration. Docetaxel was loaded from 64.5 to 77.3 µg/mL, which was 32.23 and 38.65% of the initial concentration. A

molecular gate was used to prevent premature drug release. It prevents the release of drugs from the nanocomposite for a long time. It has been experimentally proven that docetaxel is retained inside nanocomposites for 72 h at room temperature. We also demonstrated the possibility of initiating a controlled release of the drug docetaxel from nanocomposites by heating the solution to 50 °C, which was detected spectrophotometrically by the appearance of a characteristic absorption maximum in the supernatant. It is important to note that the developed nanocomposites demonstrated low toxicity to cells at gold concentrations from 0.8 to 12.5 µg/mL. This demonstrates the safety of using these nanocomposites in biomedical applications. In conclusion, it can be said that the results of the study indicate the possibility of using the developed nanocomposites as effective carriers for drug delivery.

Author Contributions

Methodology, investigation, data curation, V.A.K., A.V.S.; writing—original draft, A.V.S.; TEM study, A.M.B.; writing—review and editing, conceptualization, project administration, funding acquisition, V.A.K. All authors have read and agreed to the published version of the manuscript.

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Disclosures

The authors declare no conflicts of interest.

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