

Green Synthesis of CdTe Quantum Dots and Their Effect on Human and Animal Cells

L. Garmanchuk^a, M. Borova^c, O. Kapush^b, V. Dzhagan^b, M. Valakh^b, Y. Blume^c, and A. Yemets^{c, *}

^a Educational and Scientific Center—Institute of Biology and Medicine,
Taras Shevchenko National University of Kyiv, Kyiv, 03022 Ukraine

^b Lashkarev Institute of Semiconductor Physics, National Academy of Sciences of Ukraine, Kyiv, 03028 Ukraine

^c Institute of Food Biotechnology and Genomics, National Academy of Sciences of Ukraine, Kyiv, 04123 Ukraine

*e-mail: yemets.alla@nas.gov.ua

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Abstract—Since the nanoscale in combination with luminescent properties and prospective applications in different fields of optoelectronics and biomedicine is stimulating a growing interest towards research in the area of cadmium telluride (CdTe) quantum dots (QDs), the method of “green” synthesis of CdTe QDs with the use of the *Pleurotus ostreatus* mycelium culture as a biological matrix has been developed. The study of their physical and chemical characteristics has shown that the synthesized CdTe QDs are characterized by a crystalline structure and a predominantly spherical morphology and are 3–8 nm in size with the luminescence maximum within the 340–370 nm range. The study of their effects on different types of mammalian cells has shown that CdTe QDs have dose-dependent effects on mouse endothelial cells and human and rat erythrocytes, T- and B-lymphocytes, colorectal cancer cells (Colo 205), and human breast cancer cells (MCF-7). In particular, suppression of proliferative indices of endotheliocytes and an increase in the count of dead cells were observed, which indicates the cytotoxic action of nanocrystalline CdTe and its antiproliferative effect on endothelial cells. At the 5 μM concentration, CdTe QDs exhibited hemolytic activity, due to their action on erythrocytes, and affected adhesive contacts and cancer cell survivability. At the same time, human breast cancer cells (MCF-7) were more sensitive to their action. The data obtained are exclusively important for the understanding of mechanisms underlying the toxicity of CdTe QDs and for their future application in biological and biomedical research.

Keywords: green synthesis, quantum dots, CdTe, toxicity, human cells, animal cells, cancer cell culture

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INTRODUCTION

Development of nanoscale materials, including semiconductor nanocrystals, is one of the main areas in contemporary materials science. Considering the growing interest in the application of nanoparticles in scientific research and development, one of the priority areas in nanotechnologies continues to be associated with the development of “green” synthesis of quantum dots (QDs) suitable for biological and medical applications (Borovaya et al., 2015a). Among those highest in demand are stable biocompatible QDs with various spectral characteristics applicable for bioimaging (Zhang et al., 2007; Matea et al., 2017; Sahoo et al., 2019), i.e., for the labeling of cells and intracellular determinants, and for therapies of some types of cancer (Fatima et al., 2021) and intracellular delivery of certain biomolecules and compounds, in particular, those with antitumor activity (Zhao et al., 2016; Matea et al., 2017; Jha et al., 2018; Ruzicka-Ayoush et al., 2021). The use of QDs as fluorescent probes to create conjugates with the corresponding antibodies (Sahoo

et al., 2019; Yemets et al., 2022) is a contemporary alternative to the routine indirect immunofluorescence microscopy methods to detect different intracellular structures, in particular, those involving in cell division, intracellular transport, and cell architecture and proliferation (Yemets et al., 2008; Blume et al., 2010, 2013).

It is the CdTe QDs that are distinguished among the known synthesized nanoparticles with a variety of chemical structures as the most promising agents for photo-sensory and biomedical studies (Chen et al., 2012; Fan et al., 2014; Chang et al., 2019; Kadim, 2019; Kumar, 2022) since they are photostable and have a relatively narrow spectrum of emission and a high quantum output of luminescence compared to the popular tests. There are now widespread methods for the chemical synthesis of CdTe QDs, including metal-organic synthesis and water synthesis (Chen et al., 2012); however, these approaches will require specific oxygen-free conditions and expensive toxic stabilizers, such as trioctylphosphine or trioctylphos-

phine oxide (Talopin et al., 2001; Pei et al., 2012). Attempts are now actively undertaken to solve the problem of excessive toxicity characterizing conventional synthesis methods through developing some alternative technology based on the use of different types of biological objects as matrices for stabilizing and obtaining nanoparticles, such as Cd-containing quantum dots. It is important to note that the biological objects, as well as the matrices obtainable on their basis, play, in the first place, the role of natural stabilizers preventing the aggregation of the formed CdTe nanocrystals, regulating their sizes and forming their protective organic coating (Bao et al., 2010a, 2010b; Syed et al., 2013; Green et al., 2015; Jigyasu et al., 2020), thus reducing the toxic effect exerted by the obtained QDs on a surrounding medium (Nel et al., 2006). Therefore, the aim of the study was to develop a method for the “green” synthesis of CdTe quantum dots using a biological matrix (mycelium cultures of the basidial fungus *Pleurotus ostreatus*), to investigate their physicochemical characteristics and their effect on various types of animal and human cells.

MATERIALS AND METHODS

Green synthesis of CdTe QDs. The synthesis of CdTe QDs was performed according to the methods described in (Bao et al., 2010a) with some modifications. In particular, we used a mycelium culture of a basidial fungus *Pleurotus ostreatus* (Jacq.) P. Kuman (strain 551) from the fungi collection of the Kholodny Institute of Botany, the National Academy of Sciences of Ukraine, as the biological matrix for the synthesis of the nanoparticles (we described its obtaining in detail in Borovaya et al., 2015b), and the following agents: cadmium chloride, CdCl₂ (Acros, United States, purity at 98%); sodium telluride, Na₂TeO₂ (Alfa Aesar, Germany, purity at 99.5%); and sodium borohydride, NaBH₄ (Acros, United States, purity at 98%) as a reducing agent. The synthesis was performed as follows: the flask with the beforehand grown mycelium of *P. ostreatus* was sequentially supplemented with a water solution of 0.1 M CdCl₂ followed by 0.1 M Na₂TeO₂ and 50 mg of NaBH₄. When the reducing agent was added, the solution was observed to gradually change its color from transparent to dark orange/brown, and the obtained sample was subsequently centrifuged at 5000g for 10 min to remove remains of the fungal matrix and residues of nonorganic salts. After centrifugation, we carefully separated the supernatant (cadmium telluride solution) for the further analysis.

Study the properties of QDs. The optical properties of the obtained CdTe nanocrystals were studied by the photoluminescence spectroscopy (PL) method. The PL spectra were excited at the 325 nm line of He-Cd-laser (10 mW) and recorded using an automated

MDR-23 spectrometer equipped with uncooled FEU-100 photomultiplier.

The QDs were characterized by transmission electron microscopy using a JEOL JEM-2100F electron microscope (Japan). Its accelerating voltage reached 200 kV. At first, the ultrasound mixing of samples was made, and drops of sample solutions were further placed on a silica-coated copper lattice. The postevaporated precipitate was used for further investigation.

Cell lines, obtaining of cells, and culture conditions. Possible toxicity of CdTe QDs were assessed using different cell lines, in particular, the mouse aortal endothelial cell line (MAECs); erythrocytes, primary cultures of rat and human T- and B-lymphocytes; MCF-7, human breast cancer cells; and Colo 205, cells of colon cancer line.

The studied cells of the MAEC line cryopreserved in liquid nitrogen were promptly unfrozen at 37°C on a water bath for culture. The cell suspension in a volume of 1–2 mL was further introduced, stirring carefully, into 25 mL of the culture medium. The cells were precipitated by centrifugation at 800g for 2–3 min, the supernatant was separated and subsequently resuspended in a whole DMEM or RPMI-1640 medium (Sigma, United States), which contained 5–20% of fetal bovine serum (FBS) (Sigma, United States), and the total amount and the ratio between viable and dead cells was counted after coloring the latter with trepan blue. The cells with the death count not exceeding 15% were used for the culture.

Toxicological effects on lymphocytes were determined relative to the primary rat and human lymphocyte culture. Lymphocytes were isolated from the periphery blood of healthy donors through the ficoll-verographin density-gradient centrifugation ($\rho = 1.077 \text{ g/cm}^3$) at 1000g during 40 min. To isolate T- and B-lymphocytes from the spleen of experimental animals, the tissue was first fragmented and filtered through capron filters unless a homogeneous mixture was obtained, and the isolation of lymphocytes was performed with the gradient, as described above. Effects of the studied nanoparticles on the primary lymphocyte cultures were determined by culturing the latter at a concentration of $1 \times 10^6/\text{mL}$ at 37°C and 5% CO₂ during 3 days in a whole RPMI-1640 nutrient with the addition of 10% FBS, glutamine 200 mmol/L, penicillin 100 U/mL, and L-streptomycin 100 U/m. T- and B-lymphocytes were separated using the methods for T-lymphocyte rosette-creation with sheep erythrocytes. The mixture of lymphocytes was incubated with sheep erythrocytes in the ratio of 1 : 10 at +4°C for 1 h, and the mixture was further placed on the ficoll : verographin gradient and centrifuged for 40 min. B-lymphocytes were left on the gradient, whereas T-lymphocytes creating rosettes with erythrocytes were precipitated. The erythrocytes conjugated with T-lymphocytes were removed from this fraction through lysis using a two-fold saline solution.

The rat and human blood was heparinized and different cell subpopulations, including erythrocytes, were further isolated. Erythrocytes were thrice washed with a saline solution (NaCl 0.15 mol/L, 0.01 mol/L phosphate buffer, pH 7.4) through centrifuging at 1500–2000g for 5 min. The supernatant was separated and the precipitate was used to prepare a 1% erythrocyte suspension on a saline solution. The erythrocyte suspension was supplemented with the nanocrystalline CdTe in a wide range of concentrations. The erythrocytes used for the study were obtained from human donor blood and the rat blood prepared with Glugicir, a blood preserving agent. After separating the plasma, the erythromass was thrice washed through centrifuging (OPn-3U4.2 centrifuge, at 3000g, for 3 min) using a tenfold saline solution (NaCl 0.15 mol/L, phosphate buffer 0.01 mol/L, pH 7.4). The leukocyte film and the supernatant were removed by aspiration. Erythrocytes were preserved as a dense precipitate at 0°C for no longer than 4 h.

The cells were treated using different CdTe concentrations through mixing the cell suspension (the suspension volume was 1 mL) at room temperature (22°C). After 1 h of incubation, the level of erythrocyte hemolysis was spectrographically studied at a wavelength of 543 nm. The absorption of the probe with the added triton X-100 (0.1%) was set as 100%. All manipulations were conducted according to the state and international bioethics standards.

Study of the CdTe QDs toxicity. The survivability of cells after treatment with CdTe QDs (1–20 µM) was evaluated using the vital trepan blue coloring agent (0.4% solution prepared with 0.1 M PBS, pH 7.2). To count the ratio between viable and dead cells, using Goryaev's camera, two probes were sampled from each well of the plate. An equal volume of a 0.4% trepan blue solution was added to the cell suspension, and the cells were counted in five large quarters after 5 min and the mean value, as well as the number of cells per mL, was also determined, assessing the cell dilution and incubation volume.

The cytotoxic/proliferative effect of the studied QDs was determined in vitro using the colorimetric MTT assay based on the ability of mitochondrial enzymes of a viable cell to restore 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl-tetrazolium bromide (MTT) (Sigma, United States), a yellow salt, dissolved in physiological solutions to the crystalline purple MTT-formazan (Mosmann et al., 1983). We added 20 µL MTT to the culture medium to the final concentration of 0.6 mM 4 h before the end of the cell incubation with the studied agents. After the incubation with MTT, the formazan crystals formed in cells were dissolved in 100 µL of dimethyl sulfoxide and the plate was measured using a photometer at a wavelength of 540 nm. The cells were analyzed using an inverted Axio-Vert-40 microscope (Carl Zeiss) and the Axio Vision software.

Statistical analysis. The data were statistically treated using Statistics 8.0 standard software. The significance of the difference between the compared groups was assessed by Student's *t*-test. A difference $p < 0.05$ was considered statistically significant for all indices.

RESULTS AND DISCUSSION

To develop a method for the green synthesis of CdTe QDs, a series of studies has been performed on selecting efficient concentration of initial compounds, i.e., CdCl₂, NaTeO₂, and NaBH₄, assessing the data on obtaining cadmium telluride nanocrystals with the use of yeasts (Bao et al., 2010a). A mycelium culture of *Pleurotus ostreatus* (*P. ostreatus*), a basidial fungus, served as a biological matrix for the synthesis CdTe QDs since we had already used it earlier to synthesize cadmium sulfide (CdS) QDs (Borovaya et al., 2015b), which were characterized by low toxicity compared to nonorganic cadmium (Garmanchuk et al., 2019). To confirm the nanoscale properties of CdTe, we analyzed the spectral and structural-morphological characteristics of the synthesized nanoparticles. It has been established that a characteristic shift was observed in the photo luminescence spectra towards the short-wave region of the spectrum, and the luminescence maximum of CdTe QDs was within the 340–370 nm range (Fig. 1a). The shift towards the short wavelength spectrum was probably associated with a diminishment in the diameter of nanoparticles and was probably caused by the specific features of the biological matrix.

The most accurate method for assessing the sizes of cadmium telluride QDs is a direct visualization of their structure using an electron microscope (both scanning and light one). This method allows us to determine not only the distribution by sizes but also to assess the degree of agglomeration among nanoparticles. Figure 6b represents the electron-microscopic image of synthesized CdTe QDs. It has been established that they predominantly had a spherical morphology with sizes varying between 3 and 8 nm and a crystalline structure typical of cadmium telluride. The X-ray spectral analysis showed that the synthesized samples had a definite number of chemical admixtures, in particular, elements such as K, I, Si, Cl, in the quantity not exceeding 10–15%.

Our data somewhat differ from the reports on the synthesis of CdTe nanoparticles by other authors. In particular, it was shown in the study presenting the method of extracellular biological CdTe synthesis with the use of *Fusarium oxysporum* that the symmetrical maximum in the luminescence spectrum of these QDs was observed at the wavelength of 475 nm, and the sizes of nanoparticles reached 15–20 nm (Syed et al., 2013). The study with *Saccharomyces cerevisiae* for obtaining cadmium telluride QDs reported that they characterized by a luminescence maximum within the

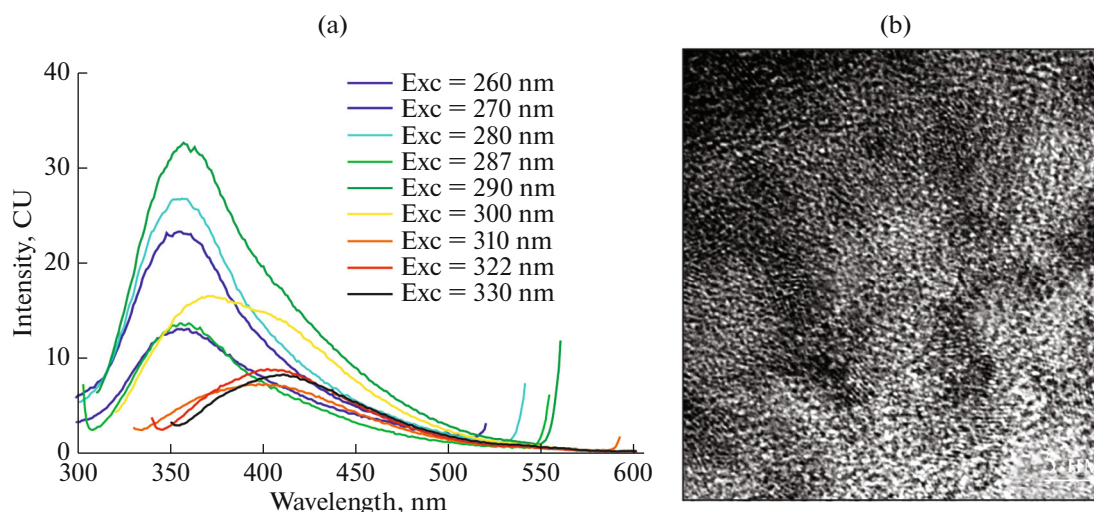


Fig. 1. (a) Spectrum of photoluminescence and the (b) structure of CdTe quantum dots obtained using *P. ostreatus*.

490–560 nm range and had a crystalline structure and sizes within 2–4 nm. The authors confirmed that the obtained nanoparticles have a high degree of intensity in luminescence, are water-soluble, very stable, biocompatible, and could be used as fluorescent probes (Bao et al., 2010a). Similar data on the synthesis of CdTe QDs using *S. cerevisiae* were recently obtained by other authors who showed their antiproliferative activity towards the PC-3 cell lines of human prostatic adenocarcinoma (Jigyasu et al., 2020). Comparing between the spectra of synthesized CdTe QDs, such as with those stabilized with thioglycolic acid (Kapush et al., 2014), the luminescent maximums of these CdTe nanoparticles were shifted towards the region of visible light and corresponded to the wavelengths of 550–580 (the orange region of visible light). These optic parameters are, in particular, characteristic of

colloidal cadmium telluride nanocrystals (Osovsky et al., 2007).

It should be noted that three main components may be specified in the process of biological synthesis of nanoparticles: selecting a biological object as an initial matrix or a medium (extract) for performing the synthesis, selecting initial chemical agents, and selecting the reaction conditions. The quantum dots obtained using the green synthesis method is usually less toxic and has unarguable advantages over those synthesized using ordinary physicochemical methods (Borovaya et al., 2015a). In particular, the green approach is ecologically friendly and will not require the use of any expensive and unsafe chemical substances, keeps power costs lower, and is more accessible under laboratory conditions. Thus, green nanobiotechnology is a novel promising approach enabling us to obtain biocompatible stable nanomaterials. With the green synthesis, we usually use an approach when the synthesis is mediated by reducing and stabilizing compounds. A special interest in this synthesis is given to the choice of a safe and accessible biomaterial as a capping-agent to stabilize synthesized nanoparticles and make them biocompatible (Alvand et al., 2019).

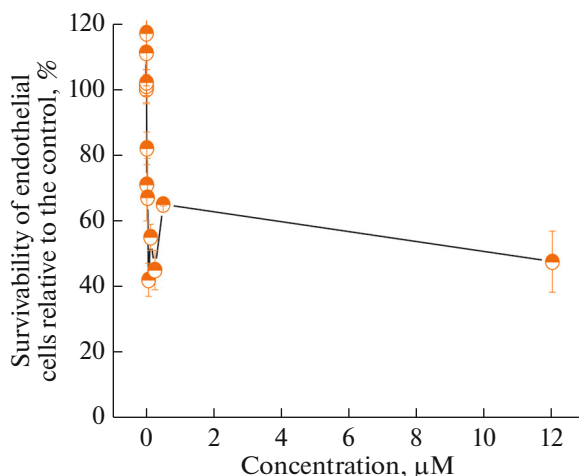


Fig. 2. Effect of CdTe quantum dots on the survivability of endothelial cells.

Nanomaterials are known for their unique properties at the nanoscale level and great prospects for applications in biological and biomedical studies and clinical practice (Aslan et al., 2008; Borovaya et al., 2015a; Yemets et al., 2022). Therefore, the safety assessment of nanomaterials with respect to cells of different genesis is a very important aspect in these studies. The cell lines with standard parameters characterized by proliferative, metabolic, and differentiation indicators, as well as the primary cultures of different cell populations, are used for these purposes (Liu and Tang, 2020). For example, peripheral blood as a source of leukocytes, thrombocytes, and erythro-

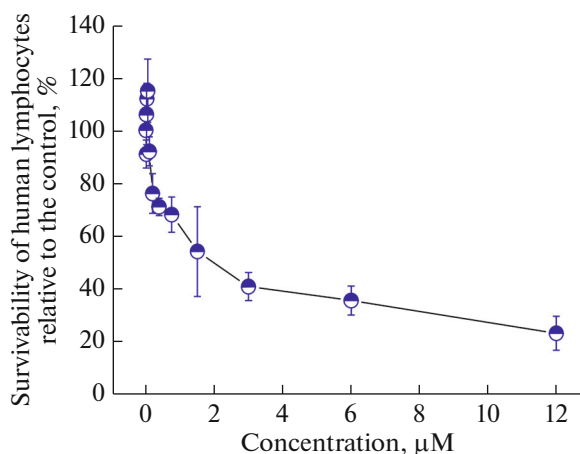


Fig. 3. Effect of CdTe quantum dots on the survivability of human lymphocytes.

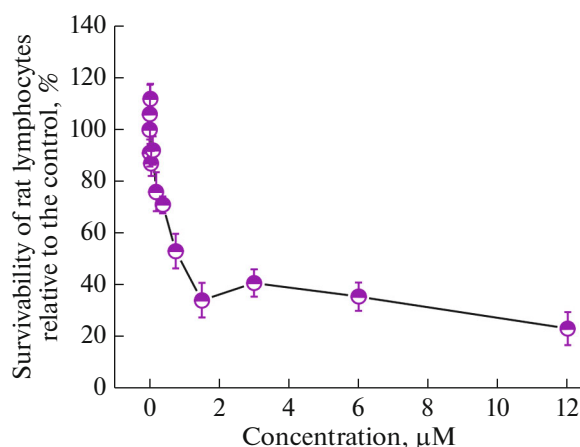


Fig. 4. Effect of CdTe quantum dots on the survivability of rat lymphocytes.

cytes allows us to determine different effects of nanomaterials for the purpose of their probable subsequent systemic effect on a multicellular organism (de la Harpe et al., 2019). Endothelial cells are also important cell targets for effects of nanomaterials (Cao, 2018). It should be noted that QDs as novel bioimaging agents (Kairdolf et al., 2013; Gil et al., 2021; Yemets et al., 2022) and drug delivery carriers (Matea et al., 2017; Jha et al., 2018; Badilli et al., 2020; Jan et al., 2022) being introduced into the vascular system directly by injection can directly produce effects on vascular endothelial cells (Xu et al., 2021). Therefore, the first important object of research into the possible toxic effects of biologically synthesized CdTe QDs was to study their effect on the endothelial cells. Therefore, we used mouse aortic endothelial cells able to manifest traits of differentiation in an immortalized culture under the conditions of measuring their growth characteristics by the substrate and the presence of nutrient substrates. The manifestation of their differentiated phenotypes is expressed in the formation of streaks in the endothelium, which reflects the blood vessel formation phase. The MTT assay has shown, in determining the effects of nanocrystalline CdTe on the cultured endotheliocytes, that the proliferative indicators of the latter began to be suppressed (by 50% against the control) from the 5 mM concentration (Fig. 2).

As has been found in determining the ratios between viable and dead cells due to the effect of CdTe QDs at different concentrations, a $20.7 \pm 3.5\%$ increase in dead cells and a decrease in the total endotheliocyte concentration to $3.6 \pm 0.04 \times 10^4$ cells/mL against the control $4.7 \pm 0.02 \times 10^4$ cells/mL occurred only at the 5 mM concentration, which points not only to the cytotoxic effect of nanocrystalline CdTe at the given concentration but also to the cytostatic (antiproliferative) effect of CdTe QDs on mouse endothelial cells in the immortalized culture.

The toxic effect of chemically synthesized CdTe QDs on endothelial cells was also demonstrated earlier. In particular, the potential vascular endothelial toxicity of water-soluble CdTe QDs covered (capped) with mercaptosuccinic acid was investigated in an in vitro study based on human umbilical vein endothelial cells (HUVECs). As has been established, CdTe QDs applied at concentrations of 0.1–100 µg/mL decreased the viability of HUVECs in a dose-dependent manner, inducing a significant endothelial toxicity at high concentrations. It has, in particular, been established that cadmium telluride QDs at a concentration of 10 µg/mL cause oxidative stress, the fragmentation of mitochondrial network, and the destruction of mitochondrial potential as well as an increase in the number of apoptotic HUVECs by more than 400%. The data reliably demonstrate a toxic effect of chemically synthesized CdTe QDs on human vascular endothelial cells, which, as the authors of the study state, may lead to developing cardiovascular diseases in case of their practical use (Yan et al., 2011).

Determining the effect of CdTe QDs on lymphocytes was also performed using primary human and rat lymphocyte cultures. We have established that the effect of CdTe QDs on rat and human lymphocytes has a similar dependence. It has been found that when a lymphocyte population was separated into T- and B-lymphocytes, a higher level of toxicity was manifested towards B-lymphocytes (the data is not given). A dose-dependent effect was observed in the action of CdTe QDs on human lymphocytes (Fig. 3), whereas a peak with an insignificant increase in the activity was present at the CdTe 3.2 µM concentration in the effect on rat lymphocytes; however, a decrease in proliferative activity was subsequently observed at higher concentrations of QDs (Fig. 4). Thus, the toxic effects towards endothelial cells and lymphocytes, which were determined in the MTT assay and by estimating directly the ratio between viable and dead cells

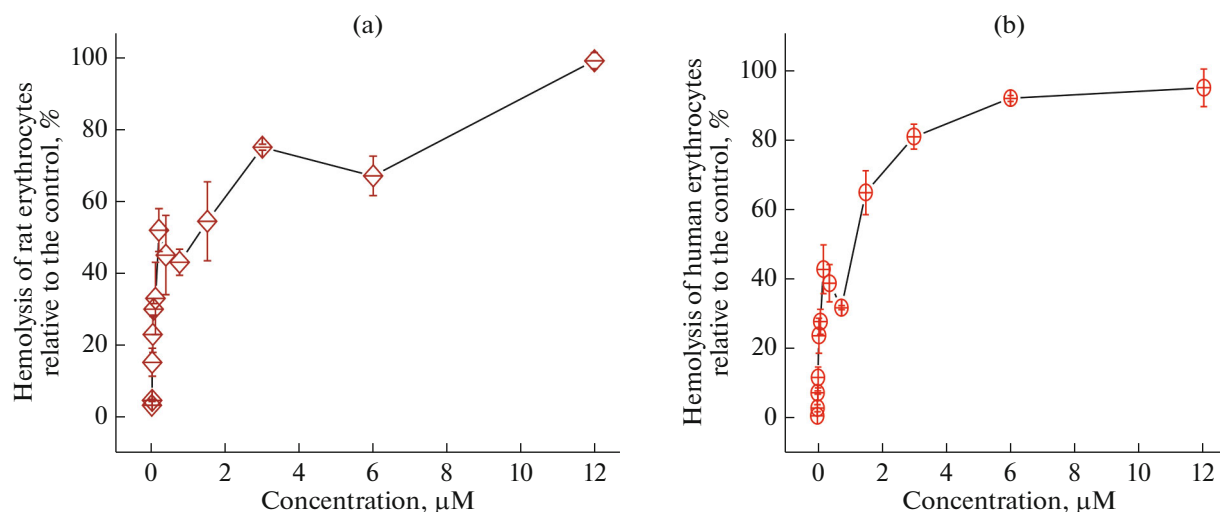


Fig. 5. Effect of CdTe quantum dots on the hemolysis of (a) rat and (b) human erythrocytes.

as an effect of synthesized CdTe QDs, were manifested within similar ranges of concentrations of these nanostructures.

One of the most important effects is the effect of different toxicants on hemolysis of erythrocytes. In addition, one of the stages in the studies of different substances of natural or synthetic origin is to determine their action on isolated peripheral blood erythrocytes. Our studies have shown that the CdTe nanoparticles also showed hemolytic activity due to the action on both human and rat erythrocytes within a similar range of concentrations (Figs. 5a, 5b). The mechanism of toxicity of the Cd-based QDs is known to be explained through the oxidation reaction in the nucleus of cadmium. This reaction generates reactive oxygen species (ROS) and cadmium ions that are highly toxic for viable cells. The QDs of the cadmium telluride type may produce singlet oxygen, which leads to the formation of ROS via the photo-oxidation reaction. These ROS products cause the CdTe-induced cell death followed by a release of highly toxic free cadmium ions (Nguyen et al., 2013).

Through a significant degree of cytotoxicity of QDs, the composition of which includes ions of important metals, their use in clinical practice is somewhat limited. One of the ways to decrease the toxicity of these nanostructures is to coat their surface, for example, with SiO₂ (Sadaf et al., 2012). It has been shown in mouse that nephrotoxicity and hepatotoxicity were minimized at intravenous introduction of silicon dioxide-coated CdTe QDs, and the erythrocyte and thrombocyte counts did not increase, in contrast to leukocytes, which confirms the importance of these approaches for further applications of CdTe QDs (Sadaf et al., 2012).

We should note that CdTe QDs attract our interest for the possibility of their application in biomedical research since they possess definite antitumor properties, and the information on the oncogenic potential of CdTe in cancer progression is limited. We have also conducted the assessment of cytotoxicity in the synthesized QDs on human breast cancer cells (MCF-7). The checkup of sensitivity of tumor cells to the action of CdTe QDs was performed for several stages, including in the monolayer culture of human breast cancer cells and in the conditions of formation of multicellular tumor spheroids. After the treatment of cells with CdTe at a concentration of 20 μM, damages in the cell membrane and the destruction of cells were observed. At reducing the concentrations of CdTe nanoparticles, the count of dead cells was observed to decrease, but cell proliferation was observed to decrease compared to the control (MCF-7 cells without addition of CdTe nanoparticles). In particular, the cell growth inhibition was observed after treatment with 5 μM, whereas no suppression effects were observed in cell proliferation at 1 μM (Fig. 6). Similar studies were also recently conducted to assess the toxic effect of three types of CdTe QDs in the human breast cancer MDA-MB468 and MCF-7 cell lines (Naderi et al., 2018), and these studies have shown that these nanostructures decrease cell survivability and induce apoptosis in a dose-dependent manner. The accumulation of apoptotic bodies, as well as chromatin condensation and DNA fragmentation, was observed in cells.

A modification was also found in the extracellular matrix due to the effect of the studied CdTe nanoparticles compared to the control. For example, after the treatment with CdTe at a concentration of 5 μM, the cells were observed to detach from the substrate, which may point to a modifying effect of CdTe

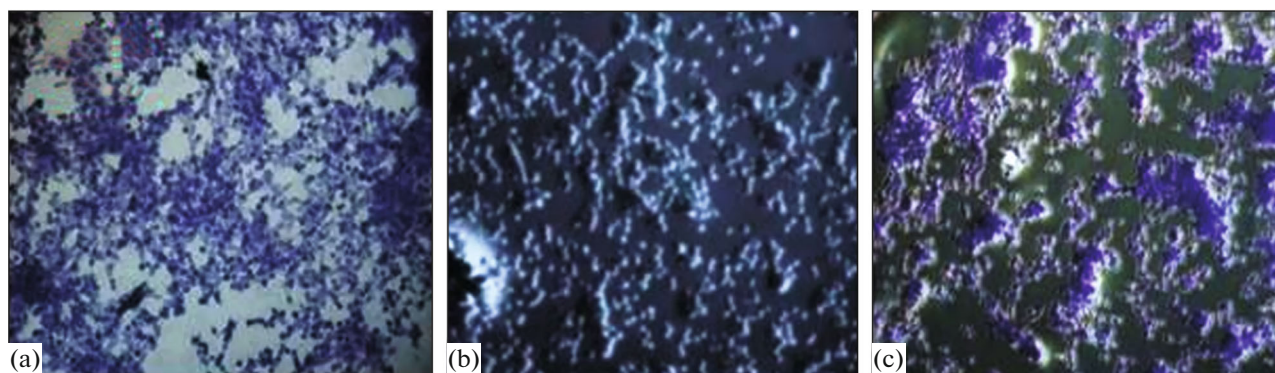


Fig. 6. Effect of CdTe quantum dots on the human breast cancer MCF-7 cells: (a) control, (b) 1, (c) 5 μM , 100 \times .

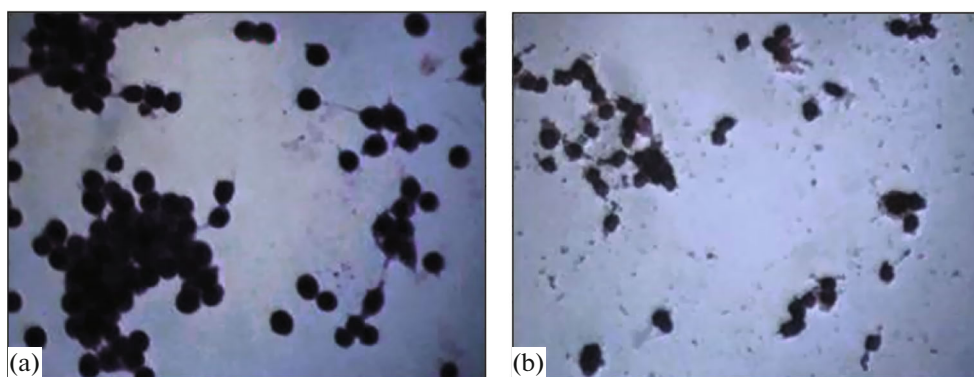


Fig. 7. Effect of CdTe quantum dots on the cells of the human colorectal cancer Colo 205 line: (a) 1, (b) 5 μM , 200 \times .

nanoparticles on the adhesion of cells to the extracellular matrix, whereas no similar effects were observed at the 1 μM concentration. Normal cells are known to support the tissue structure due to the binding of cells with other cells and with the extracellular matrix through interaction with cell adhesion molecules, which are divided into four main groups: cadherins, integrins, selectins, and immunoglobulins (Janiszewska et al., 2020). Damages in the intercellular adhesion lead to the emergence of various diseases, including cancer whose cause is a loss of intercellular adhesion, which may result in a collective migration of cancer cells (Janiszewska et al., 2020).

It has been found in the study of the effect of biologically synthesized CdTe nanoparticles on the Colo 205 colon cancer cell line (Fig. 7) that the treatment with 5 μM CdTe leads to damage in the cell membrane of these cells and significantly reduces their survivability. Researchers used to study only a possibility for using CdTe QDs conjugated with the ND-1 antibody for labelling the CCL187 colorectal cancer, giving more attention to the functioning of these nanostructures, their biocompatibility, fluorescent characteristics, in particular, optical stability (Yu et al., 2012), but not to a cytotoxic effect. As to the study of a toxic

effect of these nanoparticles on cancer cells, it has recently been clarified that the nanoscale cadmium telluride (at a concentration of 1–25 $\mu\text{g}/\text{mL}$) causes DNA destruction and induces apoptosis or necrosis in the human hepatocarcinoma cells (HuH-7) (Katubi et al., 2019). The authors of the work have found high cytotoxicity in the use of CdTe nanoparticles at 25 mg/mL , in particular, due to the treatment of cells at this concentration 48 h after the CdTe cytotoxicity indicator reached 62%. The treatment with CdTe QDs also caused intracellular generation of ROS, depolarization of mitochondria, and induced apoptotic cell death at higher concentrations (Katubi et al., 2019).

Research has recently been published on the problem of oncogenic potential of the CdTe QDs on the gene-expression profiles of the Chang cancer cell (Aldughaim et al., 2021). It has been established that a change in the gene-expression profiles had a dose-dependent nature. Changes in transcriptional profiles of several genes associated in some way with carcinogenesis occurred directly due to the CdTe effect. It has also been found that the CdTe QDs triggered the functional pathways associated by the authors with gene expression, cell proliferation, migration, adhesion, cell cycle progression, signal transmission, and

metabolism. The obtained results are exclusively important for the further research in vivo in carcinogenic transformation or cancer progression with the use of these nanoparticles (Aldughaim et al., 2021).

All these data, as well as the results of our studies, are also exclusively important for the understanding of toxicity mechanisms in the GdTe QDs synthesized via different pathways and will require taking the safety issues into consideration in the future use of nanostructures and manipulations with them in order to make them efficient and reliable instruments in biomedical research and nanomedicine.

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COMPLIANCE WITH ETHICAL STANDARDS

The authors declare that they have no conflicts of interest. This article does not contain any studies involving animals or human participants performed by any of the authors.

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