STUDY OF ENERGY TRANSFER PROCESSES BETWEEN RARE EARTH IONS AND PHOTOSENSITIZER MOLECULES FOR PHOTODYNAMIC THERAPY WITH IR-EXCITATION

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Abstract

Today, photodynamic therapy is one of the most promising minimally invasive methods of treatment of various diseases, including cancer. The main limitation of this method is the insufficient penetration into the tissue of laser radiation used to activate photosensitizer molecules, which makes it difficult to carry out therapy in the treatment of large or deep-seated tumors. In this regard, there is a great interest in the development of new strategies for photodynamic therapy using infrared radiation for excitation, the wavelengths of which fall into the "transparency window" of biological tissues. In this work, it was proposed to use upconversion $NaGdF_4$:Yb:Er nanoparticles (UCNP), which absorb infrared excitation and serve as a donor that transfers energy to the photosensitizer. Photosens and phthalosens were chosen as the most promising photosensitizers for the study. The aim of this work was to study the energy transfer processes between upconversion nanoparticles doped with rare-earth ions and photosensitizer molecules. in order to excite photosensitizers with IR radiation and carry out photodynamic therapy of deep-seated neoplasms. Using spectroscopic and time-resolved methods, it has been demonstrated that there is an efficient energy transfer between upconversion particles and photosensitizers phthalosens and photosens. The calculated efficiency of energy transfer by the Foerster mechanism was 41% for the UCNP + photosens system and 69% for the UCNP + phthalosens system. It has been experimentally and theoretically proved that there is a binding of photosensitizer molecules with UCNP by means of surfactants, leading to a reduction in the distance between them, due to which effective nonradiative energy transfer is realized. The generation of singlet oxygen by the phthalosens photosensitizer upon excitation by means of energy transfer from UCNP, excited at 980 nm wavelength of, has been demonstrated.

Key words: photodynamic therapy, infrared range, upconversion nanoparticles, photosensitizer, rare earth ions, resonant energy transfer.

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ИССЛЕДОВАНИЕ ПРОЦЕССОВ ПЕРЕДАЧИ ЭНЕРГИИ МЕЖДУ РЕДКОЗЕМЕЛЬНЫМИ ИОНАМИ И МОЛЕКУЛАМИ ФОТОСЕНСИБИЛИЗАТОРОВ ДЛЯ ЗАДАЧ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ С ВОЗБУЖДЕНИЕМ В ИК-ДИАПАЗОНЕ

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Резюме

На сегодняшний день фотодинамическая терапия (ФДТ) является одним из самых перспективных минимально инвазивных методов лечения различных заболеваний, включая злокачественные новообразования. Основным ограничением применения этой методики является недостаточная проникающая способность в ткань лазерного излучения, используемого для активации молекул фотосенсибилизатора (ФС), что затрудняет проведение терапии при лечении объемных или глубокозалегающих опухолей. В связи с этим наблюдается большой интерес к разработке новых стратегий ФДТ с использованием для возбуждения инфракрасного (ИК) излучения, длины волн которого попадают в «окно прозрачности» биологических тканей. В работе было предложено использовать ап-конверсионные наночастицы (АКНЧ) $NaGdF_4$:Yb:Er, которые поглощают инфракрасное возбуждение и служат донором, передающим энергию ФС. В качестве наиболее перспективных ФС для исследования были выбраны фотосенс и фталосенс. Исследованы процессы передачи энергии между АКНЧ, легированными редкоземельными ионами, и молекулами ФС для верификации возможности возбуждения ФС ИК-излучением и проведения ФДТ глубокозалегающих новообразований. При помощи спектроскопических и время-разрешенных методов продемонстрировано, что наблюдается эффективная передача энергии между АКНЧ и ФС фталосенс и фотосенс. Расчётная эффективность передачи энергии по механизму Фёрстера составила 41% для системы АКНЧ + фотосенс и 69% для АКНЧ + фталосенс. Экспериментально и теоретически доказано, что наблюдается связывание молекул ФС с АКНЧ посредством поверхностно-активного вещества, приводящее к сокращению расстояния между ними, за счет чего реализуется эффективная безызлучательная передача энергии. Продемонстрирована генерация синглетного кислорода молекулами фталосенса при возбуждении посредством передачи энергии от АКНЧ, возбуждаемых длиной волны 980 нм.

Ключевые слова: фотодинамическая терапия, инфракрасный диапазон, ап-конверсионные наночастицы, фотосенсибилизатор, редкоземельные ионы, резонансный перенос энергии.

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Introduction

Today, high-tech methods of theranostics are actively being developed. One of the most promising areas is the development of laser spectral-fluorescent methods for diagnostics and therapy. Luminescent diagnostics is currently the only method that allows obtaining information both at the tissue and subcellular levels with high sensitivity. In the last few decades, photodynamic therapy (PDT) has been actively used as an alternative to chemotherapy and radiation therapy for the treatment of various diseases, including cancer [1-5]. A typical PDT process involves three key components: excitation light (laser radiation is most commonly used), photosensitizer (PS) molecules, and oxygen. After absorption of light, the PS passes from the ground state to an excited state, then energy is transferred to neighboring oxygen molecules, which leads to the formation of singlet ($^1O_2$) or other reactive oxygen species (ROS). ROS generated during PDT cause destruction of tumor tissues through multifactorial mechanisms, including necrosis and/or apoptosis of tumor cells [6] or destruction of blood vessels that supply the tumor [7]. PDT is considered a minimally invasive procedure compared to chemotherapy and radiotherapy [8, 9]. The advantages of PDT also include the possibility of its local application, high selectivity and minor toxic and side effects [10-13], as well as stimulation of the immune system to recognize and remove the remaining tumor cells [14].

Despite the aforementioned advantages of PDT, one of the main limitations of the applicability of this treatment technique in clinical applications is the insufficient penetration of laser radiation used to activate PS molecules into the tissue. The limited penetration depth of laser radiation into biological tissues [15, 16] makes it difficult to perform PDT in the treatment of bulk or deep-seated tumors [17]. Therefore, there is a need to search for and develop new PDT strategies based on the use of infrared (IR) radiation for excitation, the wavelengths of which fall into the "transparency window" of biological tissues. It is believed that IR radiation (in the spectral range of 700–1000 nm) not only has a greater penetration depth into biological tissues compared to visible light [18], but also has low phototoxicity for cells and tissues [19]. In addition, IR radiation scatters less and does not excite autofluorescence of biological tissues, which makes it possible to obtain images with high contrast [20, 21].

Among the promising approaches to the development of new PDT strategies that use IR radiation for excitation of PSs, it is worth highlighting PDT using two-photon excitation [22, 23] and the use of up-conversion nanoparticles (UCNPs) [24]. When using UCNPs to deliver light to deep layers of biological tissues, it is necessary to create such nanostructures with fluorophores, where UCNPs act as absorbers of IR radiation and transfers energy to the fluorophore (both PS and organic dye molecules or quantum dots can be used as a fluorophore) acting as an acceptor.

UCNPs are nanocrystals doped with rare earth ions (REIs), one of which is a sensitizer that absorbs excitation radiation (Yb^{3+} is most often used), and the other is an activator (for example, Er^{3+}, Tm^{3+}, Ho^{3+}). In UCNP, the energy is transferred from the sensitizer to the activator and added up with the involvement of intermediate metastable energy states of the activator, as a result of which UCNPs emit high-energy photons when excited by low-energy IR radiation. UCNPs have low phototoxicity, high photostability, and good biocompatibility, and also exhibit narrow luminescence bands in the entire visible spectral range upon IR excitation [25]. Due to these unique properties, UCNPs have been widely studied in recent years as new nanoprobes for medical bioimaging [26-28], including multimodal luminescent diagnostics in combination with magnetic resonance imaging (MRI), positron emission tomography (PET), and computed tomography (CT) with additional introduction of boron and/or gadolinium ions into the UCNP composition [29, 30]. In addition, UCNPs are being actively studied as therapeutic agents, especially for PDT [31, 32]. When using UCNPs as PS carriers, it is possible to increase the selectivity of drug accumulation in tumor due to the different vascular permeability of normal tissues and tumors for nanoobjects [33]. The surface of the UCNPs can be functionalized by attaching hydrophilic molecules and targeting agents for selective accumulation in certain cells.

Several groups of researchers have demonstrated UCNP-mediated PDT *in vitro* and *in vivo* [34–38]. UCNPs were first used for *in vivo* PDT in 2011 in mice with a 4T1 mammary tumor [33]. The chlorin e6 PS was adsorbed onto the surface of the $NaYF_4$:Yb,Er UCNPs via hydrophobic interactions with the oleic acid layer. UCNPs coated with CaF_2 and functionalized with 5-aminolevulinic acid (5-ALA) were studied in [35], where the high efficiency of using such a complex with excitation radiation at 980 nm and an increase in the depth of therapeutic action were shown. Several studies have shown that PDT can activate the immune system. The combination of PS with immune adjuvants, which can be nanoparticles, can additionally enhance the immune response. X. Duan et al. [39] showed that PDT using nanoparticles can activate the immune response, causing immunogenic death of cancer cells.

The key process involved in the upconversion transformation is the energy transfer between the sensitizer ion and the activator ion [40]. In the case of hybrid nanostructures consisting of UCNP and PS, the pair of sensitizer-activator ions, in turn, acts as a sensitizer for PS in the case of IR-mediated PDT. Despite the fact that there are a fairly large number of examples in the literature of using combinations of UCNPs and dye molecules, they are mainly focused on the direct practical application of the obtained structures *in vitro* and *in vivo* [41–47]. At the same time, there have been relatively few studies on the optimization of energy transfer between UCNP and PS molecules in such systems [48 – 51].

The aim of this work is to study the processes of energy transfer between nanoparticles doped with REIs and dye molecules for excitation of PS by IR radiation and PDT of deep-seated neoplasms.

Materials and methods

$NaGdF_4$:Yb:Er UCNPs (Yb:Er = 20:2) coated with an inert $NaYF_4$ shell were synthesized by the anhydrous method in oleic acid. The synthesis procedure is described in detail in [52, 53]. The ligand exchange method was used to transfer hydrophobic nanoparticles into the aqueous phase. Polyvinylpyrrolidone (PVP) (Sigma Aldrich, USA) was used as a surfactant.

For the studies, we selected the clinically approved PS Photosens ("NIOPIK", Russia), Fotoditazin (Belmedpreparaty, Belarus), Temoporfin (Sigma-Aldrich, USA) and PS Phthalosens not yet used in clinical practice ("NIOPIK", Russia).

The absorption of aqueous solutions of PS in the concentration range from 1 mg/mL to 20 mg/L in the spectral wavelength range of 350 – 900 nm was measured on a Hitachi U-3410 double-beam spectrophotometer (Hitachi, Japan). Spectral fluorescence studies were carried out using a LESA-01 "BIOSPEC" spectrometer. A laser with a wavelength of 980 nm (Biospec, Russia) was used as a source of laser radiation for excitation of the UCNP luminescence with 1 W/cm^2 power density. To record the spectrum of upconversion luminescence in the visible range, an optical filter FESH900 (Thorlabs, USA) was used, which suppresses radiation with wavelengths greater than 900 nm. UCNP colloids with the addition of phthalosens PS were additionally examined using a Carl Zeiss LSM 710 NLO laser scanning microscope (Carl Zeiss, Germany). A colloid drop was dried on glass, and then its luminescence image and spectrum were recorded using a 32-channel GaAsP PMT spectral detector in the range 410 – 750 nm under excitation by a pulsed femtosecond laser Chameleon Ultra II (Coherent, USA) at a wavelength of 980 nm.

The kinetic characteristics of the upcconversion luminescence were recorded in the range from 1 ns to 10 ms using a C9300-508 streak camera and a Hamamatsu Photonics streak scope C10627-13 (Hamamatsu, Japan) in the spectral range of 300–900 nm with wavelength resolution of 1.4 nm. As a source of laser radiation, a LSR980H IR laser with a wavelength of 980 nm operating in the modulation mode was used. A Hamamatsu C10647-01 delay generator was used as a source of trigger pulses. We measured the decay time of the upconversion luminescence in the green and red spectral ranges, corresponding to the radiative transitions of Er^{3+} ions $^2H_{11/2}$, $^4S_{3/2}$–$^4I_{15/2}$, and $^4F_{9/2}$–$^4I_{15/2}$, respectively.

The efficiency of singlet oxygen generation for a system consisting of UCNP with a PS was calculated

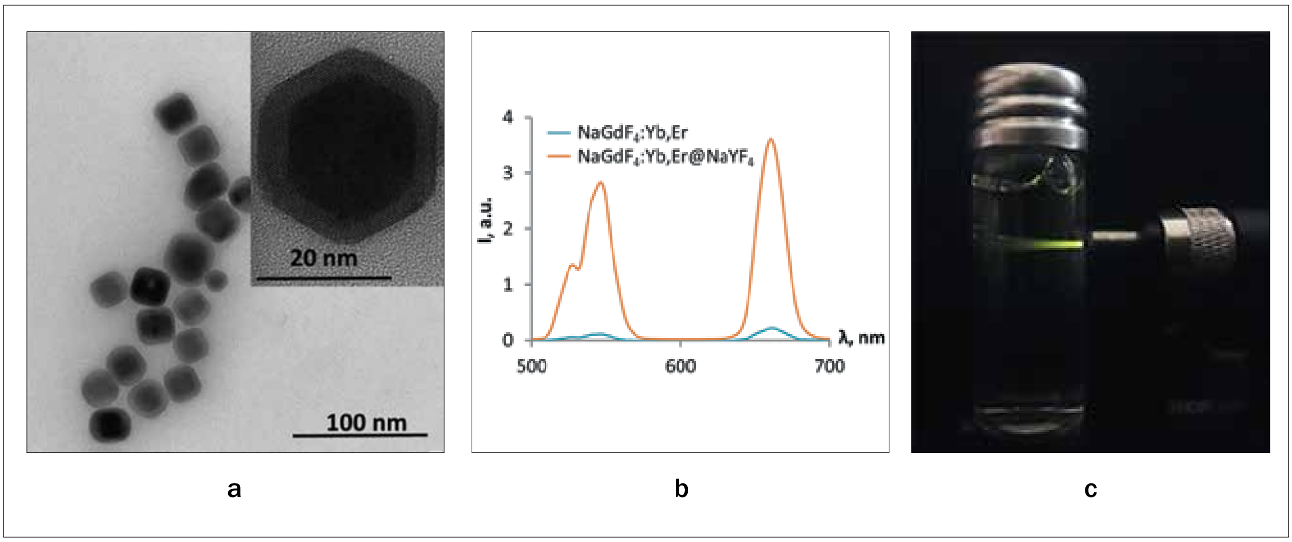

Рис. 1. a – просвечивающая электронная микроскопия полученных наночастиц $NaGdF_4$: Yb, Er (соотношение концентраций легирующих примесей Yb: Er = 20:2); b – спектры ап-конверсионной люминесценции наночастиц $NaGdF_4$: Yb, Er (соотношение концентраций легирующих примесей 20:2) до и после покрытия инертной оболочкой; c – фото люминесценции полученного коллоида при возбуждении длиной волны 980 нм.

Fig. 1. a – TEM of the obtained $NaGdF_4$: Yb, Er nanoparticles (the ratio of the dopant concentrations Yb: Er = 20:2); b – the up-conversion luminescence spectra of the $NaGdF_4$: Yb, Er nanoparticles (the ratio of the dopant concentrations 20:2) before and after coating with an inert shell; c – luminescence of the obtained colloid upon excitation with a 980 nm wavelength.

from a decrease in the optical absorption of a chemical “trap”, a molecule of sodium tetra-a, a` (anthracene-9,10-diyl)- bis-methylmalonate (ADMA, produced by "NIOPIK", Russia) [54]. The ADMA molecule absorbs in the range of 350–400 nm, however, interacting with singlet oxygen, ADMA is oxidized. The oxidized form of the molecule is optically transparent. Optical density measurements were carried out on a Hitachi U-3400 double-beam spectrophotometer; a decrease in the ADMA absorption peak was recorded in the wavelength range 350 – 410 nm. The studied colloids were a mixture of UCNPs with a concentration of 0.3 mg/ml with phthalosens at concentrations of 1, 2, and 5 mg/L in cuvettes with an optical path length of 10 mm. A mixture of UCNPs with a concentration of 0.3 mg/mL and a photosens with a concentration of 5 mg/L was used as a sample for comparing the efficiency of singlet oxygen generation. ADMA was added to the investigated colloids immediately before irradiation, the concentration was 0.025 mg/mL. The studied samples were irradiated by a continuous wave diode laser with a wavelength of 980 nm, focused into a spot with an area of 1 cm^2 with 2 W/cm^2 power density. The samples were irradiated for 5 min, for the total light dose of 600 J (5 min, 2 W/cm^2). A mixture of PS with ADMA without the addition of UCNPs was used as a control.

Results and discussion

As a result of the synthesis, aqueous colloids of $NaGdF_4$:Yb, Er@$NaYF_4$ UCNPs stabilized with PVP were obtained, the particle size was about 30 nm (Fig. 1a).

The coating of UCNPs with an inert shell made it possible to significantly increase the intensity of upconversion luminescence (Figs. 1b, 1c).

An analysis was made of the overlap between the upconversion luminescence spectra of the UCNP colloidal solution and the absorption spectra of the studied PS. For this purpose, solutions of photosens, fotoditazin and temoporfin at concentrations of 2, 8, and 4 mg/L, respectively, and phthalosens (concentration 2 mg/L), were prepared, and their absorption spectra were recorded (Fig. 2).

Among the studied PSs, the strongest overlap of the upconversion luminescence in the red part of the spectrum (transition $^4F_{9/2} – ^4I_{15/2}$, wavelength 665 nm) was observed with the absorption spectrum of photosens and phthalosens in the red region (wavelength 680 nm), so further studies were carried out with them.

The concentration dependence of the upconversion luminescence intensity of UCNP colloids with photosens and phthalosens upon excitation of colloids at a wavelength of 980 nm was studied. To study the possibility of energy transfer from UCNPs to PS molecules, UCNP colloids were prepared with the PS concentration of 1, 2, 5, 10, and 20 mg/L. The spectra exhibited characteristic peaks corresponding to the upconversion luminescence of Er^{3+} ions in green (transitions $^2H_{11/2}$, $^4S_{3/2} – ^4I_{15/2}$, wavelengths 525, 545 nm) and red (transitions $^4F_{9/2} – ^4I_{15/2}$, wavelength 665 nm) parts of the spectrum (Fig. 1b).

The dependence of the up-conversion luminescence intensity in the green and red parts

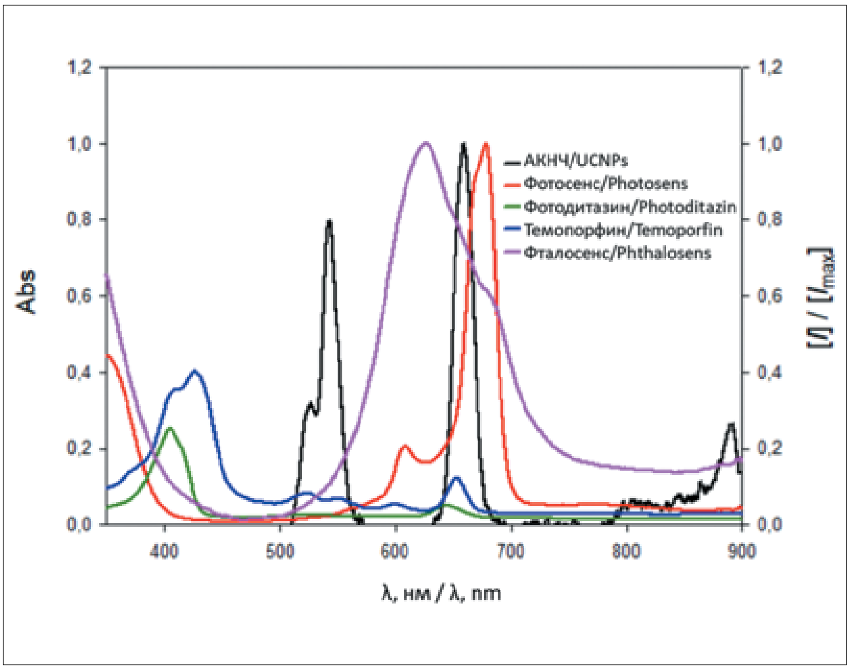

Рис. 2. Спектр люминесценции коллоида АКНЧ и спектры поглощения фотосенса, фотодитазина, темопорфина и фталосенса.

Fig. 2. The luminescence spectrum of the UCNPs colloid and the absorption spectra of photosens, photoditazin, temoporfin and phthalosens.

of the spectrum on PS concentration was analyzed. Graphs of the dependence of the integral area under the green (525, 540 nm) and red (660 nm) peaks on the concentration of photosens and phthalosens are shown in Fig. 3.

The intensity of the green component, both for colloids with photosens and for colloids with phthalosens, first increases and then decreases. It is assumed that the enhancement of green luminescence is caused by the interaction with the PS and with the transfer of energy from the PS triplet state to the REI. The dependences obtained show that the intensity of the red peak decreases with increasing concentrations of photosens and phthalosens. It is assumed that this occurs as a result of the absorption of part of the red luminescence of the PS, as well as a result of energy transfer between the UCNP and the PS molecules. Over time, a precipitate formed in the colloids of UCNP with phthalosens, which was examined using a laser scanning microscope. Images of the precipitate are shown in Fig. 4.

Aggregation of UCNP and phthalosens is observed, the aggregates are colored blue due to the addition of PS. The precipitate was excited at a wavelength of 980 nm (into the absorption band of UCNPs); the obtained upconversion luminescence spectra are shown in Fig. 4b. The spectra show peaks of upconversion luminescence at wavelengths of 525 and 540 nm and a small peak at a wavelength of about 690 nm, which is the luminescence of phthalosens. The study of a sample with a precipitate using laser scanning microscopy allows us to conclude that the PS and UCNPs are unevenly distributed in the solution and bond with each other, as a result of which the distance between the UCNPs and the PS molecule is small, which makes possible nonradiative energy transfer between them.

To study the processes of energy transfer and quantify their efficiency, we investigated the decay characteristics of the upconversion luminescence for UCNPs colloids with the addition of photosens and phthalosens using the method of single photon counting. The measured upconversion luminescence lifetimes in the green (525, 545 nm) and red (660 nm) spectral ranges are given in Table 1.

A significant decrease in the lifetime of upconversion luminescence in the red range is observed for UCNPs acting as a sensitizer, which indicates the presence of nonradiative energy transfer. The calculated efficiency of energy transfer by the Foerster mechanism was 41% for the UCNP + photosens system and 69% for the UCNP + phthalosens system. The increase in the lifetime in the green part of the spectrum confirms the earlier assumption that there is an additional energy transfer between PS and the $^2H_{11/2}$, $^4S_{3/2}$ states, from which the upconversion luminescence occurs in the green part of the spectrum.

To confirm this assumption about the binding of PS molecules to UCNPs by means of surfactants, we studied the lifetime for UCNP colloids prepared without the use of surfactants by dispersing UCNP powders thoroughly washed to remove oleic acid

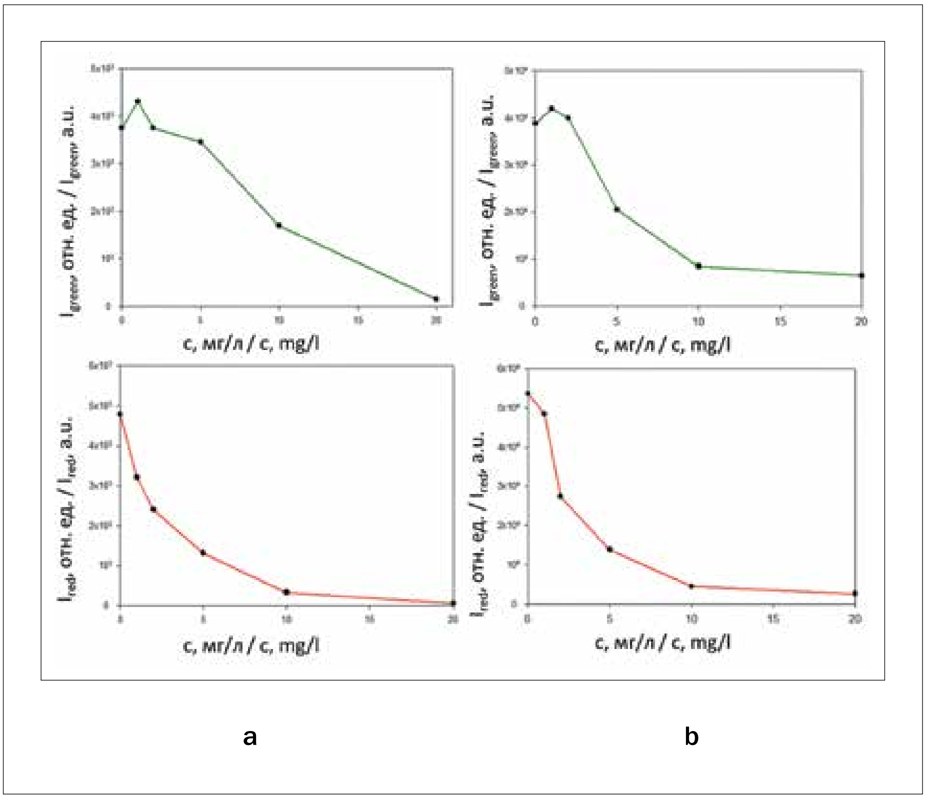

Рис. 3. Графики зависимости площади под зеленым (525, 540 нм) и красным (660 нм) пиком ап-конверсионной люминесценции от концентрации фотосенса (a) и фталосенса (b) при возбуждении длиной волны 980 нм.
Fig. 3. Dependence of the area under the green (525, 540 nm) and red (660 nm) peak of upconversion luminescence on the concentration of photosens (a) and phthalosens (b) under excitation with a 980 nm wavelength.

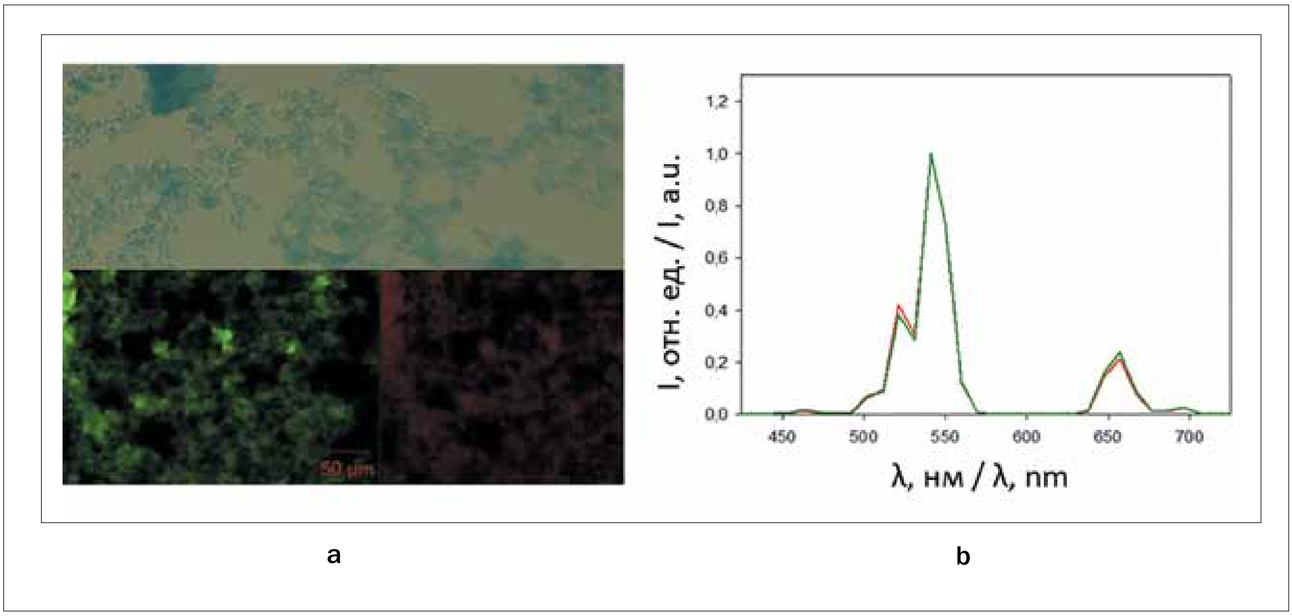

Рис. 4. а – микроскопическое изображение осадка, наблюдаемого в коллоидах АКНЧ с фталосенсом в концентрации 5 мг/л, полученное в проходящем свете в видимом диапазоне и люминесцентные изображения осадка в зеленом (525 нм) и красном диапазонах (660 нм) при возбуждении длиной волны 980 нм; b – спектры ап-конверсионной люминесценции осадка.
Fig. 4. a – microscopic image of the sediment observed in UCNPs colloids with phthalosens at a 5 mg/L concentration, obtained in transmitted light in the visible range and luminescent images of the sediment in the green (525 nm) and red ranges (660 nm) with excitation at a wavelength of 980 nm; b – upconversion luminescence spectra of the precipitate.

Таблица
Времена жизни люминесценции коллоидов АКНЧ в смеси с ФС
Table
UCNPs luminescence lifetimes of colloids mixed with PS

Образец Sample	τ_{green}, мкс τ_{green}, us	τ_{red}, мкс τ_{red}, us	Эффективность Фёрстеровской резонансной передачи энергии между АКНЧ и ФС (в красном диапазоне) FRET efficiency (red),%
$NaGdF_4$: Yb: Er@$NaYF_4$ (ПВП/PVP)	123	320	–
$NaGdF_4$: Yb: Er@$NaYF_4$ (ПВП/PVP) + Фотосенс 20 мг/л / Photosens 20 mg/l	144	189	41
$NaGdF_4$: Yb: Er@$NaYF_4$ (ПВП/PVP) + Фталосенс 20 мг/л / Phtalosens 20 mg/l	150	100	69
$NaGdF_4$: Yb: Er@$NaYF_4$ (вода / water)	215	428	–
$NaGdF_4$: Yb: Er@$NaYF_4$ (вода / water)+ Фотосенс 1 мг/л / Photosens 1 mg/l	221	419	2
$NaGdF_4$: Yb: Er@$NaYF_4$ (вода / water) + Фотосенс 10 мг/л / Photosens 10 mg/l	223	410	4

Примечание: τ_{green} – время жизни ап-конверсионной люминесценции в зеленом диапазоне; τ_{red}, мкс – время жизни ап-конверсионной люминесценции в красном диапазоне.
Note: τ_{green} – green upconversion luminescence lifetime; τ_{red} – red upconversion luminescence lifetime; FRET efficiency (red),% – Forster resonance energy transfer efficiency (in red range)

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residues in water. Photosens was added to the obtained colloids at concentrations of 1 and 10 mg/L. As can be seen from the obtained results, the trend towards a decrease in the lifetime in the red part of the spectrum, along with an increase in the lifetime in the green part of the spectrum, remains. However, the relative change in both components is much smaller than in the case of surfactant-coated nanoparticles. This fact confirms the presence of PS binding with UCNP via surfactants, which leads to more efficient nonradiative energy transfer between them due to the decreased distance. The increase in the lifetime of upconversion luminescence for colloids of nanoparticles obtained without the use of surfactants is due to their thorough washing from oleic acid residues, which can act as quenching ligands on the surface of nanoparticles.

To evaluate the efficiency of singlet oxygen generation upon excitation at a 980 nm wavelength (in the UNCP absorption band), the absorption spectra of the ADMA singlet oxygen trap added to the studied colloids of UCNPs with PS at various concentrations were recorded. The ADMA absorption spectra recorded before and after irradiation are shown in Fig. 5a.

It can be seen that with an increase in the concentration of phthalosens in the colloid from 1 mg/L to 5 mg/L, the optical absorption of the trap decreases after irradiation compared to the value before irradiation, which indicates that with an increase in the phthalosens concentration, the amount of energy transferred from the UCNP to the phthalosens increases and, accordingly, the generation of singlet oxygen increases. The percentage change in optical absorption for various concentrations of phthalosens before and after irradiation is shown in Fig. 5b. With an increase in the PS concentration, an increase in the efficiency of singlet oxygen generation is observed, which indicates that UCNPs provide efficient energy transfer and PS excitation in the studied concentration range. The generation efficiency of singlet oxygen by phthalosens is comparable to the generation efficiency for photosens.

Conclusion

In this work, the processes of energy transfer from UCNPs (Er^{3+} ions act as a sensitizer of PS fluorescence) to PS molecules photosens and phthalosens and the possibility of PDT under IR excitation were studied. Using spectroscopic and time-resolved methods, it

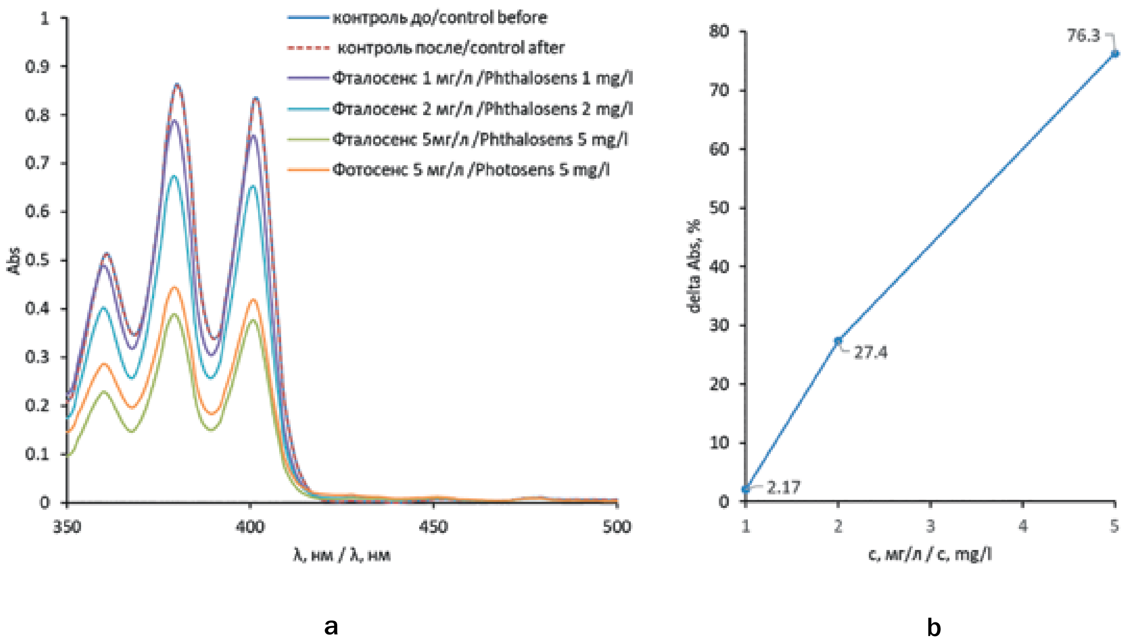

Рис. 5. a – оптическое поглощение ловушки на синглетный кислород ADMA до и после облучения коллоидов АКНЧ с различной концентрацией фталосенса и фотосенса для оценки генерации синглетного кислорода, контроль – смесь фталосенса с ADMA без добавления АКНЧ; b – процентное изменение оптического поглощения ловушки ADMA в зависимости от концентрации фталосенса в коллоиде.

Fig. 5. a – optical absorption of the singlet oxygen trap ADMA before and after irradiation of UCNPs colloids with different concentrations of phthalosens and photosens to assess the singlet oxygen generation, control – mix of phthalosens and ADMA without UCNPs; b – percentage change in the optical absorption of the ADMA depending on the Phthalosens concentration in the colloid.

was demonstrated that for phthalosens and photosens there is a strong overlap of the absorption spectra with the upconversion luminescence spectra, and an efficient energy transfer was also observed. The calculated efficiency of energy transfer by the Foerster mechanism was 41% for the UCNP + photosens system and 69% for the UCNP + phthalosens system. It has been established that the main mechanism of energy transfer is non-radiative. It has been experimentally and theoretically proved that there is a binding of PS molecules with UCNP by means of surfactants, leading to a reduction in the distance between them, due to which effective nonradiative energy transfer is realized. In addition, the generation of singlet oxygen by the phthalosens PS upon excitation by means of energy transfer from UCNP, excited at 980 nm wavelength, has been demonstrated. At the same time, with an increase in the PS concentration, an increase in the efficiency of singlet oxygen generation is observed, which indicates that UCNPs provide efficient energy transfer and PS excitation in the studied concentration range.

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