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СРАВНИТЕЛЬНОЕ ИССЛЕДОВАНИЕ АГРЕГАЦИИ СУЛЬФО-ЗАМЕЩЕННЫХ ИК ФОТОСЕНСИБИЛИЗАТОРОВ НА ОСНОВЕ ИНВЕРТИРОВАННОГО ПОРФИРИНОИДА И КРАСИТЕЛЯ ИНДОЦИАНИНОВОГО ЗЕЛЕНОГО НОВОГО В ВОДНЫХ РАСТВОРАХ

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Поиск новых водорастворимых малотоксичных ИК фотосенсибилизаторов и их применение в биомедицине является актуальной задачей современной медицинской химии. В данной работе мы сравниваем агрегацию двух сульфосодержащих соединений карбоцианинового и инвертированного порфириноидного рядов в водных растворах с использованием электронной абсорбционной и флуоресцентной спектроскопии, а также метода динамического рассеяния света (DLS). Оба рассматриваемых соединения относятся к ИК-красителям, поглощающим излучение, в зависимости от полярности, кислотно-основных и дононо-акцепторных свойств растворителя, в длинноволновой области при 700-850 нм и характеризующимся относительно высокими логарифмами коэффициентов экстинкции полос - от 3,8-3,9 у порфириноида до 4,4-5,0 в случае цианинового красителя. Сделан вывод о том, что сульфосодержащие красители, независимо от структурных особенностей хромофора, склонны к гидрофобным взаимодействиям в водных растворах, и в зависимости от концентрации растворенного вещества образуют разноразмерные агрегаты J- и H-типа в случае соединений макрогетероциклического и линейного строения, соответственно. Показано, что по мере снижения концентрации красителей в интервале 10^{-3}-10^{-6} ***моль/кг распределение агрегатов по размерам становится более узким, а диаметр наночастиц уменьшается. Так, для красителя Индоцианинового зеленого нового размер (нм) снижается в следующем ряду (***m_{PS}***, моль/кг): 615 (***10^{-3}***) > 255 (***10^{-4}***) > > 105 (***10^{-5}***) > > 79 (***10^{-6}***). При этом склонность карбоцианинового красителя к агрегации намного выше, поскольку она контролируется гидрофобным вкладом органического π-хромофора. Наноагрегаты изученных соединений малостабильны в водном растворе неионогенного поверхностно-активного вещества Твин 80, в то время как субначастицы сульфосодержащих красителей сохраняются в этих условиях даже при большом избытке солюбилизатора.***

Ключевые слова: инвертированный порфирин, карбоцианиновый краситель, гидрофобная агрегация, электронная абсорбционная спектроскопия, метод динамического рассеяния света, неионогенный ПАВ Твин 80

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COMPARATIVE STUDY OF THE AGGREGATION OF SULFOSUBSTITUTED IR PHOTOSENSITILIZERS BASED ON THE INVERTED PORPHYRINOID AND DYE IN-DOCYANINE GREEN NEW IN AQUEOUS SOLUTIONS

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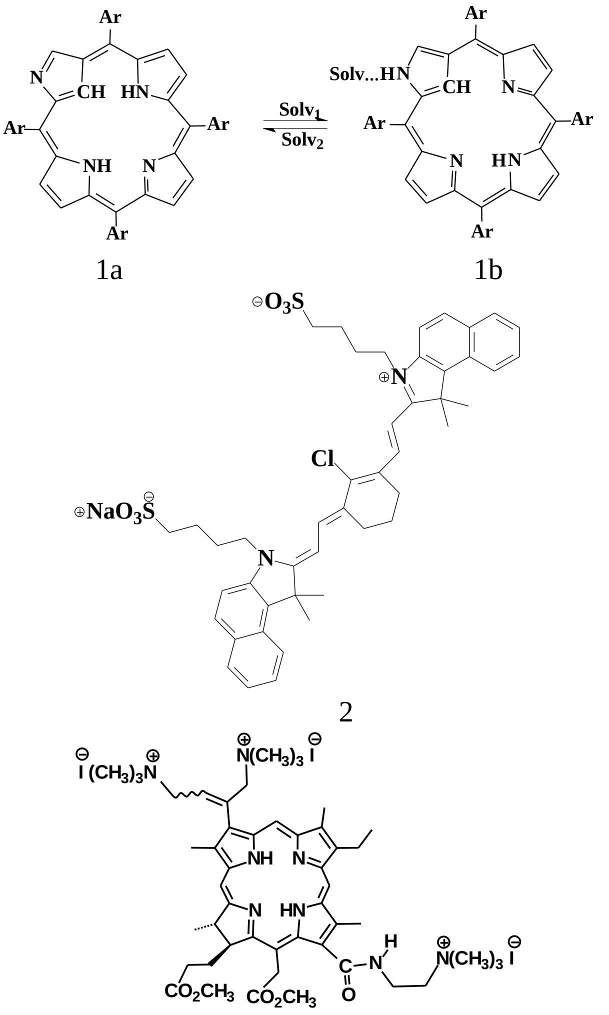
The search for new water-soluble low-toxic IR photosensitizers and their application in biomedicine is an actual task of the modern medicinal chemistry. In this work we compare the aggrega-tion of two sulfo-containing compounds of the carbocyanine and inverted porphyrinoid series in aqueous solutions using electron absorption and fluorescence spectroscopy, as well as the dynamic light scattering (DLS) method. Depending on the polarity, acid-base and donor-acceptor properties of the solvent both IR-dyes absorb the light in the long-wave region at 700-850 nm and are characterized by relatively high values of logarithms of the extinction coefficients of the absorption bands varying from 3.8-3.9 for the porphyrinoid to 4.4-5.0 in the case of the cyanine dye. It is concluded that sulfo-containing dyes, regardless of the structural features of the chromophore, are prone to the hydrophobic interactions in aqueous solutions and, depending on the solute concentration, form different sized J- and H-type aggregates in the case of compounds of macroheterocyclic and linear structure, respectively. Decline of the dyes concentration in the range of 10^{-3}-10^{-6} mol/kg is accompanied by the reduction of the diameter and narrowing of nanoparticles distribution of aggregates by size. Thus, for the dye Indocyanine green new, the size of aggregates (nm) decreases in the following series (m_{PS}, mol/kg): 615 (10^{-3}) > 255 (10^{-4}) > 105 (10^{-5}) > 79 (10^{-6}). The tendency of the carbocyanine dye to aggregate is much higher, as it is controlled by the hydrophobic contribution of the organic π-chromophore. Nanoaggregates of the studied compounds are unstable in an aqueous solutions of the nonionic surfactant Tween 80, while subnano particles of sulfo-containing dyes are preserved under these conditions even at high excess of solubilizer.

Keywords: inverted porphyrinoid, carbocyanine dye, hydrophobic aggregation, UV-Vis spectroscopy, dynamic light scattering method, nonionic surfactant Tween 80

INTRODUCTION

A number of compounds based on indocyanine, phthalocyanine, inverted and expanded porphyrinoid, BODIPY and other molecular platforms are considered as an IR-photosensitizers (PSs), perspective substances for biomedical photonics [1-10]. These dyes intensively absorb visible light close to the IR-region demonstrating strong emission at higher wavelengths or conversion of the electron excitation into the heat energy. Such a valuable photophysical features of the molecules combined with their ability to the selective accumulation in certain kind of biological tissues are attractive for the application in photodiagnostics (PD) and biosensors construction [11, 12], as well as in photo- (PDT) and thermotherapy (PTT) both oncological and infectious diseases [4, 13-15].



1a 1b

2

3

Fig. 1. Molecular structures of the compounds considered:
1 - 2-Aza,21-carba-5,10,15,20-tetra-(4-sulfophenyl)porphyrin tetrasodium salt ($[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$, Ar = 4-$NaSO_3Ph$) presented in tautomeric forms a and b ($Solv_1$ and $Solv_2$ are low polar aprotic (weakly proton do-nating) and dipolar aprotic solvents, respectively); **2** - Indocyanine green new (IR820);
3 - Chlorin e_6 3(1),3(2)-*bis*-(N,N,N-trimethylammoniomethyl iodide)-13(1)-N'-(2-N'',N'',N''-trimethyl-ammonioethyl iodide) amide 15(2),17(3)-dimethyl ester

Рис. 1. Молекулярные структуры рассматриваемых в работе соединений: **1** - 2-Аза,21-карба-5,10,15,20-тетра-(4-сульфофенил)порфирин тетранатриевая соль ($[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$), представленный в таутомерных формах a и b ($Solv_1$ и $Solv_2$ - слабополярный апротонный / слабо протонодонорный) и диполярный апротонный растворитель, соответственно); **2** - Индоцианиновый зеленый новый (IR820); **3** – Хлорин e_6 3(1),3(2)-*бис*-(N,N,N-триметиламмонийметилйодид)-13(1)-N'-(2-N'',N'',N''-триметиламмонийэтил йодид) амид 15(2),17(3)-диметиловый эфир

Amphiphilicity of the photosensitizer appropriate for biomedical application is one of most important requirements provided by the presence of hydrophobic and hydrophilic parts in the molecule. A widely used way to synthesize water-soluble PSs is to bring some charged or neutral hydrophilic groups into the structure of mainly hydrophobic organic molecule. Usually they are low toxic carboxylic or sulfonic functions to prepare anionic PSs, alkylammonio- or alkylpyridil groups in the case of cationic dyes and glycol or carbohydrate fragments in neutral compounds [16, 17]. Similar synthetic ways to solubilize the molecule are more or less applicable for every class of PSs.

The main disadvantage on the way of using sulfo-derivatives in photodiagnostics and phototherapy is a pronounced aggregation of these compounds in water [6, 8, 18-20]. However, the statement regarding negative ascendant of hydrophobic aggregation on the photophysical parameters of the photosensitizer is mostly controversial [6, 21, 22], as a luminescence quenching hampering one of the transformation routes of the excitation energy can release an alternative relaxation pathway. Nevertheless, PSs aggregation caused by cooperative hydrophobic interactions of their molecules usually results in dramatic decline of key photophysical characteristics including quantum yields of fluorescence and reactive oxygen species (ROS) generation [23, 24] on the one hand, and able to cause problems with a PS biocompatibility, on the other one. That is why the study of the concentration and medium control of the aggregates formation for PSs of the different structure in water and solutions modeling biological environment is of a great importance.

Here we present the results of our investigation devoted to the comparative study of the aggregation behavior of two water-soluble photosensitizers containing more than one sulfonic group to stress the specificity of this substitution pattern. Aqueous solutions study of tetrapyrrolic inverted porphyrinoid 2-aza,21-carba-5,10,15,20-tetra-(4-sulfophenyl)porphyrin disodium salt ($[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$, comp. **1*ab***) and non-macroheterocyclic tricarbocyanine dye "Indocyanine green new" (IR820, comp. **2**) presented in Fig. 1 is carried out. Some previously published results on the aggregation of the sulfo-containing compounds of phthalocyanine series [8] and multicationic chlorin dye [19] (comp. **3**) are also discussed for comparison.

EXPERIMENTAL PART

Materials

Pyrrole (98%), benzaldehyde (99%), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 98%), methanesulfonic acid (99%), sodium hydroxide (99%) purchased from Sigma-Aldrich and dye Indocyanine Green New (IR820, **2**) of 95% purity from Alfachem (China) were used without further refining. Tween 80 (Panreac, chemical purity) as well as ethanol (EtOH, Sigma Aldrich, >99.5%), dichloromethane (DCM, 99.8%, Ekos-1), hexane (95%, Kriochrom), N,N-dimethylformamide (DMF, 99%, Khimsnab) and sulfuric acid (99%, Vekton) were used as supplied. Water was distilled twice.

2-aza,21-carba-5,10,15,20-tetra-(4-sulfophenyl)porphyrin tetrasodium salt (comp. **1**, see Fig. 1) was obtained according to the known two-staged synthetic procedure [25, 26] using the condensation of pyrrole and benzaldehyde in DCM in the presence of methanesulfonic acid and the subsequent oxidation of the reaction mixture with DDQ followed by intermediate product heating in concentrated sulphuric acid.

MEASUREMENTS

^{1}H NMR spectra were recorded on Bruker AVANCE 500 MHz instrument using a deuterated solvent as a standard. MALDI-TOF MS data were collected using a Shimadzu AXIMA Confidence instrument with dihydroxybenzoic and cinnamic acids as a matrix. UV-Vis (see Fig. 2) and fluorescence (Fl) spectra were measured from 300 nm to 900 nm using spectrofluorimeter CM-2203 (Solar, Belarus’). Size distribution of nanoaggregates was controlled by dynamic light scattering using a Zetasizer Nano instrument from Malvern Instruments Ltd (UK).

The spectrophotometric study of the PSs association in the ethanol-water system

The stock solutions of the compounds studied were prepared by dissolving a dye in an appropriate amount of water, ethanol or their binary mixtures. Then solutions were diluted to reach the desirable solute concentration of $7\text{-}25\cdot10^{-6}$ mol/kg appropriate for spectrophotometric measurements and $1.1\text{-}2.5\cdot10^{-6}$ mol/kg for fluorescence (Fl) experiments. The series of solutions with a different mass ratio of EtOH and H_2O was prepared by the gravimetric method and their UV-Vis spectra were recorded at 298 K. The analytical wavelength equal 438 nm was chosen in the case of inverted porphyrinoid **1** and 825 nm for the carbocyanine dye **2**. Aggregation curves obtained in an ethanol/water system are represented in Fig. 3.

Dynamic light scattering measurements

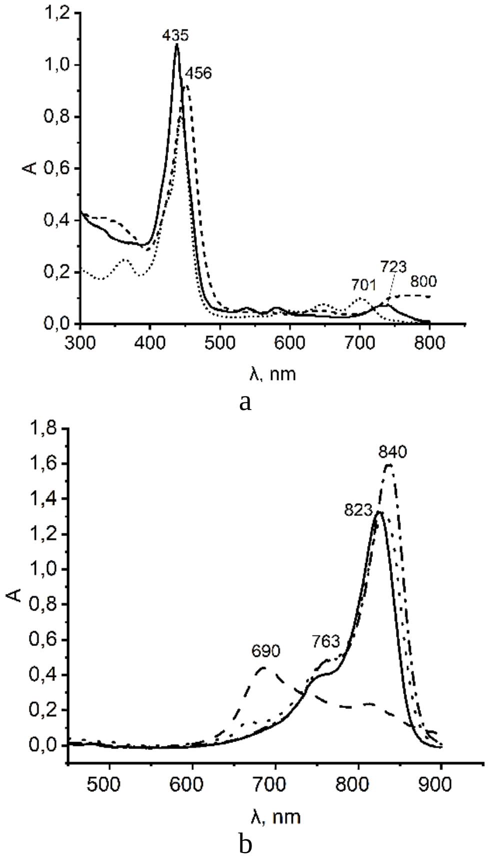
The diameter of the aggregates formed by PSs in an aqueous solution and these particles size distribution were studied by the DLS method using a Zetasizer Nano ZS ZEN3600 analyzer supplied with the $\lambda = 633$ nm laser and the non-invasive backscatter technology (NIBS) of the optical registration system. The scattered light detector was located at the angle of 173° to incident light. Coefficients of the dynamic viscosity and the refractive index of water ($\eta = 0.8872$ mPa/s and $n = 1.330$) as a dispersion medium were chosen. The PS solutions were prepared by the gravimetric method, filtered with a cellulose filter (Jetbiofil, 0.22 μm) and stored in a dark place for several days before the DLS experiments. The results are represented in Fig. 4.

RESULTS AND DISCUSSION

UV-Vis and fluorescence spectra. The UV-Vis (Fig. 2) and fluorescence spectra of comps. **1** and **2** are typical of tetrapyrrolic and carbocyanine type of the dye, respectively. It is believed that π-electronic structure of the porphyrin-like macrocycles including inverted (or N-confused) porphyrinoids is described by four-electron quantum-chemical Gouterman model and its later modifications [18, 27]. The absorption spectra of the comp. **1** is represented by the intense B-band (Soret) at about 440 nm with the molar extinction coefficient logarithm ($\log\varepsilon$) exceeding 5 and four less pronounced ($\log\varepsilon \leq 4.3$) Q-bands with the absorption maxima ranging from 540 to 800 nm in dependence on the solvation and aggregation state of the molecule. Both long-wave Q_x(0-0) and Soret bands of the inverted porphyrinoid **1** induced by a π-π*-electron transfers within the 18π-electronic macroheterocyclic chromophore are red shifted as compared with common *meso*-aryl substituted porphyrins by 50-80 nm owing to the molecule polarization [28, 29].

In contrast, the UV-Vis spectra of the dye “Indocyanine green new” (comp. **2**) demonstrate only two bands with the absorption maximum in the near IR-region (see Fig. 2) assigned to the aggregated (690-760 nm) and non-aggregated (810-840 nm) solution state of the dye [30]. Both sulfo-containing compounds studied are characterized by the weak fluorescence, especially in water. The bands in the fluorescence spectra of comps. **1** and **2** are characterized by significant Stokes shifts ranging from 12 to 30 nm for the inverted porphyrinoid and from 15 to 20 nm for the carbocyanine dye. Normally, the Stokes shifts typical for most of the porphyrins are rather moderate and seldom exceed 10 nm [31, 32]. For dyes adopted to the linear structure of the chromophore and possessed by the higher conformation flexibility higher shifts are usually found [32, 33].

Usually porphyrins, free of powerful centers of solvation at the periphery of the molecule or in the macrocyclic core, demonstrate slight dependence of the absorption bands position on the nature of solvent media [31, 33], but this is not the case for the compounds studied here. The validity of this statement is illustrated in Fig. 2. Since the tautomeric transformation **1*a*** → **1*b***, presented in Fig. 1, usually accompanied by the aromaticity loss [29, 34], the maximum position of the long-wavelength Q_x(0-0)-band is predictably shifted to the blue region by about 25 nm on the solute transfer from weakly proton donor EtOH towards highly polar aprotic DMF (Fig. 2). The exocyclic location of the nitrogen atom in the molecule of the comp. **1** favors to the strong solvent-dependent tautomeric equilibrium shifted to the $^2N^{21}CH$-tautomer (*a*) formation in non-polar or weakly proton-donating solvents (if acceptor number (AN) exceed donor one (DN)) and towards to *b*-form (^2NH-), when the molecule is dissolved in polar electron-donor media (dipolar aprotic solvents) [34-37]. So, pronounced solvatochromism of the comp. **1** is mainly explained by both tautomeric and aggregation processes common for these dyes [13, 28-30].



a

b

Fig. 2. UV-Vis spectra of $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ (comp. **1**, *a*) and IR820 (comp. **2**, *b*) in solution of: EtOH (*solid line*); DMF (*dotted line*); H_2O (*dashed line* and 1%Tween-H_2O ($m_{Tween} = 7.7\cdot10^{-3}$ mol/kg, *dash-dotted line*), $C_{PS} = 2.5\cdot10^{-5}$ mol/l

Рис. 2. Электронные спектры поглощения $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ (соед. **1**, *а*) и красителя IR820 (соед. **2**, *b*) в растворе: EtOH (*сплошная линия*); ДМФА (*пунктирная линия*); H_2O (*штриховая линия*) и 1%Tween-H_2O ($m_{Tween} = 7{,}7\cdot10^{-3}$ mol/kg, *штрих-пунктирная линия*), $C_{PS} = 2{,}5\cdot10^{-5}$ моль/л

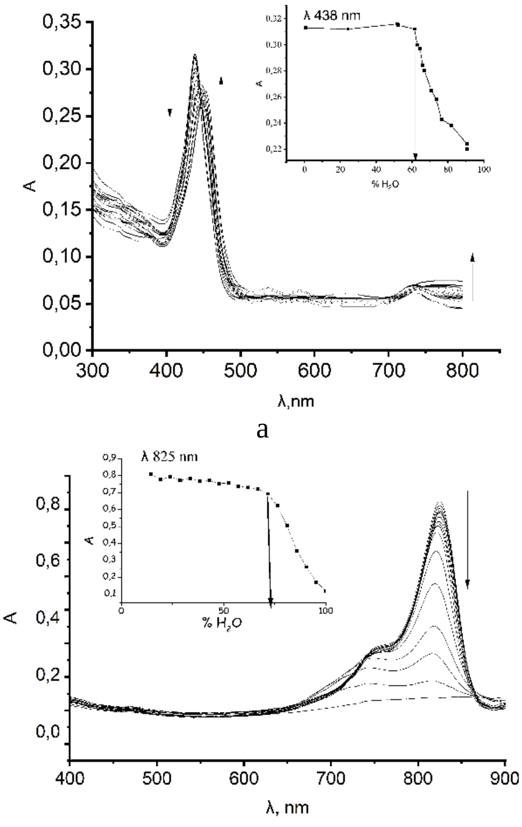
Carbocyanine dyes are also can be exposed to the isomerism [38] which is, however, substantially blocked by the insertion of carbocyclic chlorine-containing fragment into the molecule of well-known vital dye and drug for fluorescent diagnostics “Indocyanine green” (ICG) to form the comp. **2**. This substitution pattern in IR820 molecule results in higher chemical stability including photostability of the chromophore compared to ICG [39].

Aggregation of the sulfo-containing PSs in water-rich solutions. Water is known to be a solvent with a pronounced polarity and high donor number. Meantime, its proton donating ability is also very high. That is why $^2N^{21}CH$-tautomer (*a*) of the inverted porphyrinoid is expected to be found in an aqueous solution. However, dissolution of the comp. **1** in water leads to the broadening and strong red shift of the absorption bands due to a significant hydrophobic aggregation of the *a*-form of the molecule (Fig. 1). The aggregation-induced bathochromic shift revealed for the comp. **1** when moving from EtOH to H_2O and estimated of about 75 nm is explained by *J*-supramolecular nanoparticles formation [18]. The formation of nanoaggregates in water is confirmed by the dynamic light scattering method (DLS). Meantime, at the addition of an appropriate surfactant like Tween 80 nanoaggregates are mainly destroyed and the typical UV-Vis spectra of the non-associated tautomeric form absorbing at 723 nm [29, 34, 37] is appeared (Fig. 2).

Carbocyanine dyes like “Indocyanine green” are also found to be prone to form aggregates [30]. On the contrary to the comp. **1** the UV-Vis spectra of the dye **2** undergoes to the essential blue shift under aggregation. Especially it is concerned to the absorption band assigned to the aggregated form of the dye which is moved from 760 to 690 nm (see Fig. 2). The absorption maxima broadening of the IR820 and their high hypsochromic shift in combination with the dramatic fluorescence quenching are observed and can be considered as a satisfactory conditions indicating *H*-aggregates formation [18, 40].

The spectrophotometric titration curves (Fig. 3) are also clearly demonstrate the aggregation of both PSs in the ethanol – water system even at low concentration (about 10^{-5} mol/kg) of the solute. The mass content of water corresponding to the initiation of IR820 aggregation is much greater compare to most of water-soluble porphyrins and chlorins studied [19, 41, 42]. For instance, tricationic chlorin **3** is exposed to the aggregation in aqueous ethanol already at 60 percent of water [43]. For comparison, the aggregation of tetrapyrrolic (comp. **1**) and carbocyanine (comp. **2**) photosensitizers is initiated at the mass content of water equal 62 and 76 percent, respectively indicating more hydrophilic nature of the later although this dye contains fewer number of sulfonic groups.

In our recent publications we have shown [19, 41, 42] that the UV-Vis spectroscopy of organic dyes is able to reveal both types of macroheterocyclic aggregates like nanosized and subnanosized, although these particles can not be distinguished using this method. Under combination of UV-Vis spectroscopy and dynamic light scattering (DLS) methods we have demonstrated here that both sulfo-containing PSs studied here despite their good water solubility are prone to the nanoaggregation even in diluted aqueous solutions – from the millimolar down to the micromolar concentration range (see Fig. 4).



a

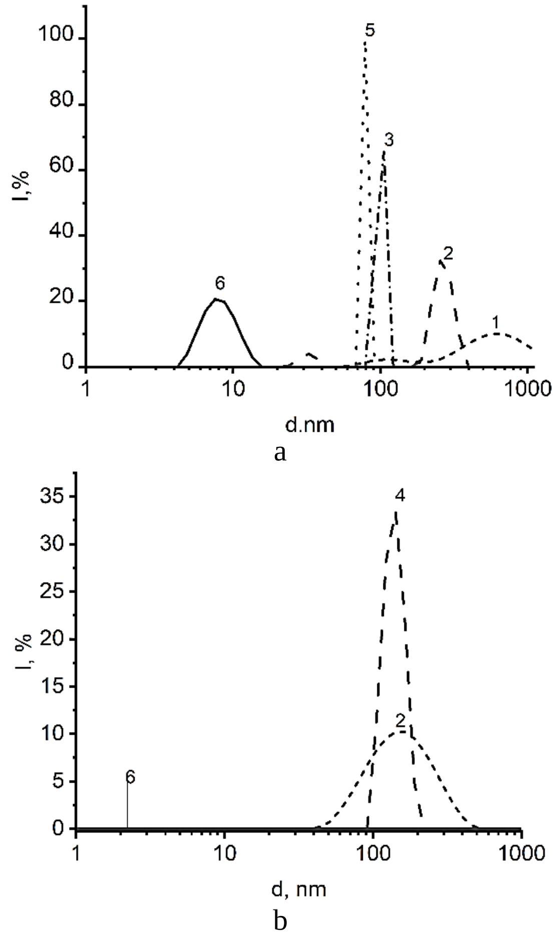
b

Fig. 3. Spectrophotometric titration curves of $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ (comp. **1**, *a*) and IR820 (comp. **2**, *b*) in ethanol – water binary solvent, $C_{PS} = 7\cdot10^{-6}$ mol/l

Рис. 3. Кривые спектрофотометрического титрования $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ (соед. **1**, *a*) и IR820 (соед. **2**, *b*), полученные в бинарном растворителе этанол – вода, $C_{PS} = 7\cdot10^{-6}$ mol/l

The size distribution of nanoaggregates is predominantly monomodal in the case of both $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ and IR820 aqueous solutions. Gradual decrease in the concentration of the dyes leads to the narrowing and more intense modes in the photocorrelation spectra (DLS). And in opposite, the hydrophobic nature of the massive organic molecules promotes the formation of larger aggregates with a broader size distribution at higher PS concentration. So, the following series of nanoparticles scattering maximum (nm) is observed for comp. **2** (Fig. 4, m_{PS}, mol/kg): 615 (10^{-3}) > 255 (10^{-4}) > 105 (10^{-5}) > 79 (10^{-6}).

Comparison of DLS data for the tetraanionic macrocycle **1** and recently studied naturally derived chlorin containing three positively charged alkylammonia groups (comp. **3**) shows [43, 44] that in spite of a smaller number of polar groups cationic PS is significantly less prone to nanoaggregation. The latter compound is found to be nanoaggregated in aqueous solutions only at millimolar concentrations with the only scattering peak at 200 nm (m_{PS} = 1.75 mmol/kg), while in the micromolar range this PS generate subnano particles not observed by the DLS techniques and seeable by the UV-Vis or Fl spectroscopy only [17, 41, 42].



a

b

Fig. 4. Diameter (d) and size distribution of dyes aggregates in an aqueous solution measured for IR820 (comp. **2**, *a*) and $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ (comp. **1**, *b*) at 10^{-3} (1), 10^{-4} (2), 10^{-5} (3), $5\cdot10^{-6}$ (4); 10^{-6} (5) and at 10^{-4} mol/kg in the presence of 1% amount of Tween 80 (6)

Рис. 4. Распределение агрегатов красителей в водном растворе по размерам (d – диаметр), измеренное для IR820 (соед. **2**, *a*) и $[^2N,^{21}CH]H_2(4\text{-}NaSO_3Ph)_4P$ (соед. **1**, *b*) и при 10^{-3} (1), 10^{-4} (2), 10^{-5} (3), $5\cdot10^{-6}$ (4); 10^{-6} (5) и при 10^{-4} моль/кг в присутствии 1% Твин 80 (6)

One of the simplest ways to avoid the aggregation of PSs is to apply an appropriate carrier preventing this kind of hydrophobic interactions [8, 18-20]. The dynamic light scattering study demonstrate disappearance of a dye nanoparticles in aqueous solutions in the presence of micellar carrier Tween 80 (Fig. 4), sometimes taken even in the same amount with PS. However, according to the UV-Vis spectra the subnanoaggregates of the comp. **1** and **2** are kept in aqueous solution even in a large excess of the surfactant. So, comp. **1** is not completely disaggregated even in the presence of 200-fold excess of Tween 80 (see Fig. 5). Meantime, apparently, nanoaggregates of the organic dyes containing sulfonic groups are not very stable and destroyed readily [45]. The same situation was observed in our recent study concerned to the disaggregation of sulfo-containing phthalocyanines in Tween 80 solutions [8].

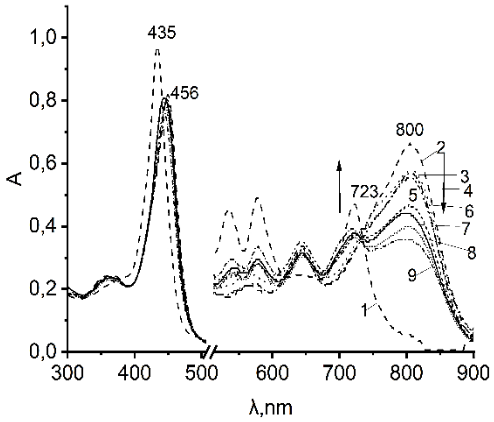


Fig. 5. UV-Vis-spectra for the comp. **1** ($7.3 \cdot 10^{-6}$ mol/kg) in EtOH (1), H_2O (2) and aqueous solutions with an addition of Tween 80 with a surfactant/PS ratio: 5 (3), 10 (4), 30 (5), 50 (6), 100 (7), 175 (8) and 200 (9)

Рис. 5. ЭСП соед. **1** в EtOH (1), H_2O (2), а также в водных растворах с добавками Твин 80 при соотношении ПАВ/ФС: 5 (3), 10 (4), 30 (5), 50 (6), 100 (7), 175 (8) and 200 (9)

Fig. 5 clearly demonstrates the gradual formation of the typical spectra of the comp. **1** tautomeric *a*-form in the Tween-H_2O system, which is observed also in ethanolic solution. However, the Q-band at 723 nm corresponding to the *a*-form is broadened in aqueous solution of Tween compared to the UV-Vis spectra in ethanol which is presumably explained by the presence of the impurity of tautomer *b* formed in water as a highly polar coordinating solvent [29, 37].

CONCLUSIONS

Both the compounds studied (**1** and **2**) here give a different kind of aggregates assigned as *J*-type for macroheterocyclic compound **1** and *H*-type for the non-macroheterocyclic dye **2**. The tendency of the carbocyanine dye **2** to aggregate is found to be much higher despite the presence of only two sulfonic groups in the molecule compared to four ones in the porphyrinoid molecule **1**. The hydrophilicity degree of these molecules is controlled by the hydrophobic contribution of the organic π-chromophore. Nanoaggregates of the compounds **1** and **2** investigated by DLS method are unstable in the aqueous solution of non-ionic surfactant Tween 80 while subnano particles of sulfo-substituted dyes are preserved in a solution even at high excess of the solubilizer.

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