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Spectral Characterization of Complexes of Tetra– and Tricationic Porphyrins with DNA Duplex

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Dedicated to the memory of Prof. G. V. Ponomarev, Prof. A. F. Mironov, and Prof. T. S. Kurtikyan

A systematic spectral study of the interaction of DNA with a number of tetra- and tricationic porphyrins, in which the N-methyl group is located in the para- or meta-position of the pyridyl substituent, has been carried out. The conditions for the formation of intercalation complexes of DNA with the studied porphyrins were established. It was shown that DNA exhibits greater affinity for porphyrins with an N-methyl group in the para-position of the peripheral substituent, compared to porphyrins with an N-methyl group in the meta-position. Intercalation complexes of DNA with porphyrins with the meta-position of the N-methyl group are characterized by spectral features, such as a slight bathochromic shift of the Soret band in the UV-Visible spectrum and the absence of band inversion in the fluorescence spectrum of intercalated porphyrins. For DNA complexes with monohetaryl-substituted porphyrins, a "semi-intercalation" binding model has been proposed.

Keywords: Porphyrins, DNA, fluorescence.

Спектральные характеристики комплексов тетра– и трикатионных порфиринов с двухцепочечной ДНК

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Памяти проф. Г. В. Пономарева, проф. А. Ф. Миронова и Т. С. Куртикян

Проведено систематическое спектральное исследование взаимодействия ДНК с рядом тетра- и трикатионных порфиринов, в которых N-метильная группа расположена в пара- или мета-положении пиридильного заместителя. Установлены условия образования интеркаляционных комплексов ДНК с изученными порфиринами. Показано, что ДНК проявляет большую аффинность к порфиринам с N-метильной группой в пара-положении периферийного заместителя, по сравнению с порфиринами с N-метильной группой в мета-положении. Интеркаляционные комплексы ДНК с порфиринами с мета-положением N-метильной группы характеризуются спектральными особенностями, такими как: небольшой батохромный сдвиг полосы Соре, спектр излучения интеркалированных порфиринов без инверсии полос. Для комплексов ДНК с моногетарилзамещенными порфиринами предложена модель связывания – «полуинтеркаляционная».

Ключевые слова: Порфирины, ДНК, флуоресценция.

Introduction

Macroheterocyclic compounds of the porphyrin series are widely used in medical practice as drugs for the diagnosis and treatment of oncological diseases by the method of photodynamic therapy. Interest in porphyrin compounds is not limited to these tasks. The annually increasing resistance of pathogenic microorganisms to the action of antibiotics necessitates the development of new methods and new medicinal compounds (preparations) that do not cause adaptation of pathogens and provide the required bactericidal action. In this context, tetrapyrrole macroheterocyclic compounds are considered the most promising. Their virucidal and antibacterial activity against pathogenic microorganisms have already been proven.[1,2] Currently, a scientific direction is actively developing, associated with the targeted synthesis of compounds of the porphyrin series, capable of showing their biological effect due to intercalation binding with the DNA double helix of pathogens. Intercalation was first discovered 40 years ago when analyzing the spectral changes of 5,10,15,20-tetrakis(methylpyridin-4-yl)porphyrin during DNA titration. The scientific experience accumulated over the past period in the study of DNA intercalation complexes makes it possible to give a clear characteristic description of the spectral manifestations of intercalation. Control effects of intercalation include: significant long-wavelength shift of the Soret band up to 10–30 nm, hypochromicity of the Soret band up to 50 %, negative signals of induced circular dichroism,[3] DNA elongation caused by its unwinding,[4] an increase in the viscosity of DNA intercalate solutions, a decrease in DNA melting temperature, high kinetic and thermodynamic stability of intercalation complexes. Intercalation interaction of DNA with porphyrins also causes a characteristic downfield shift of the phosphate peak of DNA in the ^{31}P NMR spectrum.[5]

For a long time it was believed that there can be only one mechanism leading to the disruption of the basic functions of DNA due to the formation of intercalation complexes with porphyrins, and it is associated with DNA photooxidation. However, the data obtained[6] suggest that porphyrins can act not only as artificial nucleases,[7] but can alter the energy profiles of DNA repair, modification and recombination processes due to the so-called "semi-intercalation" binding. This term was proposed in 1996 based on the results of X-ray diffraction analysis of copper(II) complexes of *meso*-tetra(N-methyl-4-pyridyl)porphyrin with DNA. This cationic porphyrin, upon intercalation, causes a distortion of one of the DNA helices, while one of the nitrogenous bases, cytosine, is turned out of the spiral stack. Thus, the intercalation of porphyrin occurs with only one DNA strand, and the porphyrin bound in this way causes distortion of the second DNA strand. The authors of this work attribute this mechanism to the large size of metal complexes of tetrapyridylporphyrins, which is larger than traditional intercalates, such as, for example, ethidium bromide. This work inspired us, since the displacement of the nitrogenous base from the DNA stack was known only under the action of some repair proteins (5-methyltransferases,[8] uracil-DNA glycosylase[9]). We hypothesized that, since the meta-isomers of the peripheral substituents of porphyrins, due to steric distortions, increase the volume of porphyrin,[10] as compared to porphyrins with para-isomeric cationic groups, it is possible that the interaction of meta-isomeric porphyrins with DNA will be unusual intercalation. The transition from tetracationic porphyrins to tricationic ones containing a bulky hetaryl substituent may lead to "semi-intercalation" binding, and the heteroatom itself may specifically interact with the displaced nitrogenous base. Therefore, the purpose of this work was a comparative study of the intercalation processes of cationic porphyrins containing 3- and 4-N-methylpyridyl groups at the *meso*-positions of porphyrins in DNA, as well as monohetaryl substituted porphyrins, which will allow us to assess the effect of both the position of the cationic substituent and monohetaryl substitution on the ability of porphyrins to form intercalates with DNA.

Experimental

The studied porphyrins – 5-[4'-(1'',3''-benzothiazol-2''-yl) phenyl]-10,15,20-tri(*N*-methyl-3'-pyridyl)porphyrin triiodide (triMPyP3S), 5-[4'-(1'',3''-benzoxazol-2''-yl)phenyl]-10,15,20-tri(*N*-methyl-3'-pyridyl)porphyrin triiodide (triMPyP3O) and 5-[4'-(*N*-methyl-1'',3''-benzoimidazol-2''-yl)phenyl]-10,15,20-tri(*N*-methyl-3'-pyridyl)porphyrin triiodide (triMPyP3N) were synthesized in the same way.[11]

Tetra(4-pyridyl)porphyrin (TPyP4). A mixture of 10 mL (0.144 mol) of pyrrole and 13.7 mL (0.144 mol) of 4-pyridylcarboxaldehyde was gradually added under reflux to a mixture of 500 mL of acetic acid, 150 mL of nitrobenzene and 27 mL (0.286 mol) of acetic anhydride. The mixture was boiled for 1.5 h, and then cooled, acetic acid was distilled off, the residue was diluted with 150 mL of water, nitrobenzene was distilled off with steam. The residuum was filtered off, the precipitate was washed with water and dried in air. Then the precipitate was boiled with stirring with 100 mL of methanol, the precipitate was filtered off, washed with methanol and dried. Yield 16.2 g. The precipitate was extracted with chloroform in a Soxhlet apparatus until colorless flow. The extract was evaporated to 200 mL and the precipitate that formed was filtered off. The solution was chromatographed on a column with Al_2O_3 (activity II according to Brockmann). The eluate was evaporated to a minimum volume, TPyP4 was precipitated with 50 mL of methanol. TPyP4 was filtered off, washed with 50 mL of methanol and dried at 70 °C to constant weight. Yield 6.3 g (25.1 %). R_f 0.80 (silufol, $CHCl_3$:MeOH – 5:1). UV-Vis ($CHCl_3$) λ_{max} nm (logε): 643 (3.43); 589 (3.82); 546 (3.79); 514 (4.30); 417 (5.62). ^{1}H NMR ($CDCl_3$) δ_H ppm: 8.87s (8H, *β*-H); 9.08 d (8H, 2.6-H); 8.18 d (8H, 3.5-H); –2.92 s (2H, NH). *m/z* (Found / Calculated): $[M+H]^+$ 619.27 / 618.70.

Tetra(4-N-methylpyridyl)porphyrin tetraiodide (TMPyP4). A mixture of tetra(4-pyridyl)porphyrin and 2 mL (3.25 mmol) of methyl iodide in 30 mL of DMF was refluxed for 1 hour while passing 0.4 g (0.65 mmol) of argon. The solution was cooled to room temperature, diluted with 30 mL of benzene. The precipitated porphyrin (TMPyP4) was filtered off, washed sequentially with 5 mL of benzene and 5 mL of acetone, and dried at room temperature to constant weight. Yield 0.7 g (90 %). UV-Vis (H_2O) λ_{max} nm (logε): 641 (3.58); 585 (3.93); 555 (3.88); 519 (4.23); 423 (5.39). ^{1}H NMR (DMSO-d_6) δ_H ppm: 9.51 s (4H, 2′-H), 9.12 dd (4H, J_{ab} = 5.0 Hz, J_{ac} = 1.3 Hz, 6′-H), 8.91s (8H, β-H), 8.57 d (4H, J = 7.6 Hz, 4′-H), 7.82 d (4H, J_{ab} = 7.4 Hz, J_{ac} = 5.0 Hz, 5′-H), –2.78 s (2H, NH).

Tetra(3-pyridyl)porphyrin (TPyP3) was obtained similarly to TPyP4 using 3-pyridylcarboxaldehyde. Yield 5.6 g. (25 %). R_f 0.92 (silufol, $CHCl_3$:MeOH 5:1). UV-Vis ($CHCl_3$) λ_{max} nm (logε): 647 (3.53); 590 (3.79); 550 (3.88); 516 (4.26); 419 (5.64). ^{1}H NMR

($CDCl_3$) δ_H ppm: 9.50 s (4H, 2-H-Py); 9.10 dd (4H, ^1J = 5.6 Hz, ^2J = 1.4 Hz, 6-H-Py); 8.90 s (8H, *β*-H); 8.56 d (4H, ^1J = 5.6 Hz, 4-H-Py); 7.81 t (4H, ^1J = 5.6 Hz, 5-H-Py); –2.80 bs (2H, NH). *m/z* (Found / Calculated): $[M+H]^+$ 619.32/618.70.

Tetra(3-N-methylpyridyl)porphyrin tetraiodide (TMPyP3) was obtained similarly to TMPyP4 using tetra(3-pyridyl)porphyrin. Yield 0.73 g (94 %). UV-Vis (H_2O) λ_{max} nm (logε): 653 (3.40); 581 (3.89); 513 (4.28); 416 (5.52). ^{1}H NMR (DMSO-d_6) δ_H ppm: 10.04 bs (4H, 2-H-Py); 9.60 d (4H, J = 6.2 Hz, 4-H-Py); 9.35 d (4H, J = 7.6 Hz, 6-H-Py); 9.30 bs (8H, βH); 8.66 t (4H, 2 J = 7.0 Hz, 5-H-Py); 4.72 s (12H, CH_3-N); –3.12 bs (2H, NH).

DNA from salmon sperm and ethidium bromide were bought in Acros Organics (Thermo Fisher Scientific, Belgium). DNA concentrations were determined spectrophotometrically using molar extinction coefficient: ε = 6600 $cm^{-1}·M^{-1}$ at 260 nm. All investigations were performed in Tris-HCl buffer. Tris-HCl buffer was prepared by adding 0.1 N HCl to 0.2 M tris(hydroxymethyl) aminomethane (Merck, USA) up to p*H* 7.4.

Ethidium Bromide (EtBr), (Sigma-Aldrich) ~95 % was used as received.

UV–Vis and fluorescence spectra were registered using an AvaSpec-2048 spectrophotometer (Avantes BV, Netherlands), with a temperature-controlled cell at 25 °C. The monochromatic LEDs UVTOP-295 (Sensor Electronic Technology, Inc. USA) and VL425-5-15 (Roitner Lasertechnik Gmbh., Germany) were used as excitation light sources for fluorescence study. ^{1}H NMR spectra were recorded with spectrometer Bruker-500 (Germany) using operating frequency of 500 MHz in $CDCl_3$ with TMS as the internal reference. The MALDI-TOF mass-spectra of the positive ions were registered on Shimandzu AXIMA Confidence, a time-of-flight mass spectrometer with matrix-associated laser desorption and a Bruker Daltonics Ultraflex apparatus.

The affinity constants, R (DNA/Porphyrin Ratio) and a number of binding sites (n) were estimated according to Scatchard method[12] from spectral data.

Results and Discussion

The interaction of the studied porphyrins with DNA was studied by electron absorption and fluorescence spectroscopy. Figure 1 shows typical change in the UV-Vis spectrum during titration of triMPyP3S with deoxyribonucleic acid as an example. Titration of porphyrin with DNA leads to stepwise changes in the UV-Vis spectra of porphyrins, regardless of the nature of the peripheral porphyrin substituents and their position. For example, triMPyP3S with a molar ratio of DNA base pairs:porphyrin equal to 1:(15÷3), a slight decrease in all absorption bands of porphyrin is recorded. Isosbestic points are recorded on the spectra. For triMPyP3S in the Soret band region, the isosbestic point is fixed at 430 nm. In the range of DNA:porphyrin molar ratios of 1:(2.5÷0.8), a bathochromic shift of the Soret band occurs, a significant decrease in its intensity, and an isosbestic point is found at 425 nm.

The initial spectral changes during titration of porphyrins with DNA are associated with the formation of a rather labile external complex. The driving forces of its formation are electrostatic and hydrophobic interactions, due to which cationic porphyrins are oriented relative to the negatively charged phosphate backbone of DNA, and form π-stacking structures, minimizing contact with an aqueous medium. Therefore, the spectral manifestation of the outer complex is similar to π-π aggregation of porphyrins. An increase in the concentration of DNA in porphyrin-containing solutions leads to the formation of intercalation complexes, which are recorded spectrally. With a significant increase in the concentration of DNA in solution, the equilibrium is almost completely shifted towards the formation of intercalates (Table 1). It should be noted that, in general, the amount of DNA required to shift the equilibrium towards the formation of intercalates with porphyrins with N-methyl groups in the meta-position is less than the required amount of DNA when titrating porphyrins with N-methyl groups in the para-position (Table 1). The reasons for this phenomenon probably lie in the lower stability of external complexes of DNA with porphyrins with meta-isomers of peripheral substituents. As we have shown earlier,[10] by the example of TMPyP3 and TMPyP4, TMPyP3 with a meta-substituent has a much larger volume than TMPyP4 with a para-substituent, mainly due to steric hindrances caused by the meta-substituent and leading to an increase in the angle of deviation of the pyridyl rings of porphyrin from the main plane of the macroring. Apparently, this

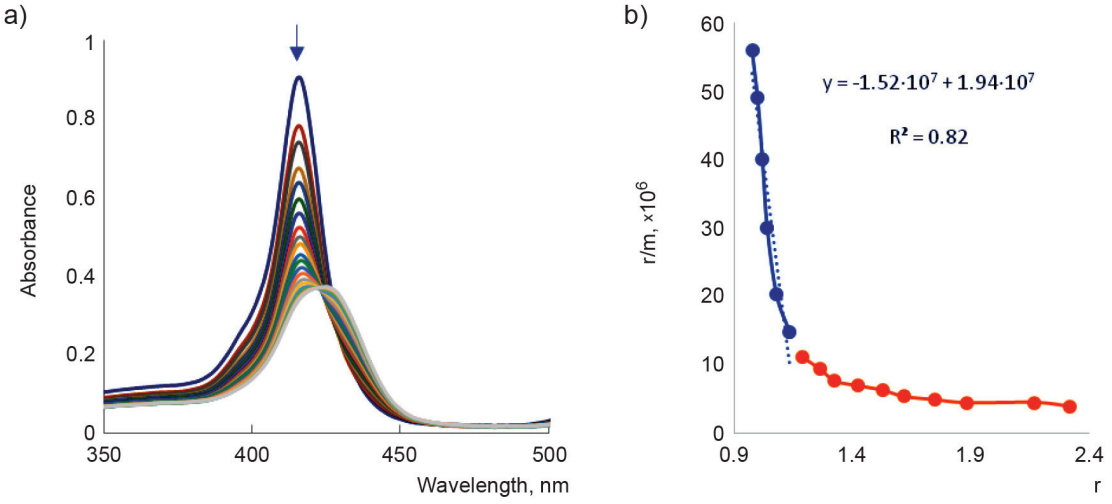

Figure 1. UV-Vis spectra (a) and Scatchard plot (b) of titration of triMPyP3S ($8.6·10^{-6}$ M) with DNA (0–$1.3·10^{-5}$ M) in Tris-HCl buffer at 25 °C.

Table 1. Scatchard and spectral parameters of DNA-porphyrins binding.

Porphyrin	R, DNA/ Porphyrin	Δλ of Soret band, nm	From UV-Vis data			From fluorescence data		
			Affinity constant	n	R^2	Affinity constant	n	R^2
TMPyP3	2.2	10	$1.81 \cdot 10^7$	0.7	0.879	$1.64 \cdot 10^7$	0.8	0.846
TMPyP4	3.9	15	$3.64 \cdot 10^7$	0.4	0.787	$4.99 \cdot 10^7$	0.3	0.935
triMPyP3N	2.3	3	$9.16 \cdot 10^6$	0.6	0.952	$8.08 \cdot 10^6$	0.5	0.579
triMPyP3O	1.6	7	$2.21 \cdot 10^7$	0.7	0.914	$1.92 \cdot 10^7$	0.6	0.672
triMPyP3S	1.3	8	$1.52 \cdot 10^7$	1.3	0.815	$1.36 \cdot 10^7$	1.1	0.831

distortion leads to a decrease in the stability of π-stacking structures in the external complex of porphyrins with DNA. On the other hand, the parameter R (Table 1) also depends on the stability of the resulting intercalation complex.

The results of competitive titration of DNA complexes with ethidium bromide provide additional confirmation of the formation of intercalation complexes of porphyrins with DNA. Ethidium bromide is a fluorescent marker for double-stranded DNA.[13–15] During intercalation between pairs of nitrogenous bases, ethidium bromide intensely fluoresces with a maximum of about 600 nm. Judging by the literature data, the binding constant of ethidium bromide with deoxyribonucleic acid is about $6.58 \cdot 10^4$ M^{-1}.[14] Porphyrins, as a rule, form more stable complexes; therefore, substitution titration was carried out as follows: the previously obtained intercalation complex of EtBr with DNA was titrated with the studied porphyrins. Typical changes in the fluorescence spectra of EtBr with DNA upon photoexcitation with light with a wavelength of 295 nm during titration with porphyrins are shown in Figure 2. As can be seen from the data presented (Figure 2), the addition of porphyrin to the DNA-EtBr intercalate leads to quenching of the fluorescence of ethidium bromide. The fluorescence quenching of EtBr intercalated in DNA upon the addition of porphyrin may be due not only to the substitution of EtBr with porphyrin, but also to the porphyrin reabsorption of light emitted by EtBr. However, the optical density of porphyrin in the 600–700 nm range does not exceed 0.1, which makes it possible to ignore reabsorption. It should be noted that, theoretically, the fluorescence of EtBr can be quenched by porphyrins also in the composition of the external complex. This idea was voiced by Pasternak,[16] who suggested the possibility of energy transfer between ethidium cation to porphyrins in the presence of DNA. In this case, an isoemission point should appear in the fluorescence spectra.[16,17] In our studies, it was not detected for all studied systems; therefore, energy transfer between the ethidium cation and cationic porphyrins is unlikely. The recorded quenching of fluorescence during titration of the intercalate with DNA-EtBr porphyrins is associated with the displacement of the ethidium cation from double-stranded DNA and their replacement with porphyrins.

Thus, the performed spectral studies allow us to conclude that all the studied porphyrins form intercalation complexes with DNA when the molar ratio R is reached, as indicated in Table 1.

The spectrophotometric titration data of the studied porphyrins with deoxyribonucleic acid were processed using the Scatchard equation. The obtained parameters of the DNA affinity for the studied porphyrins are shown in Table 1. The DNA affinity constant for porphyrins increases in the following subsequence:

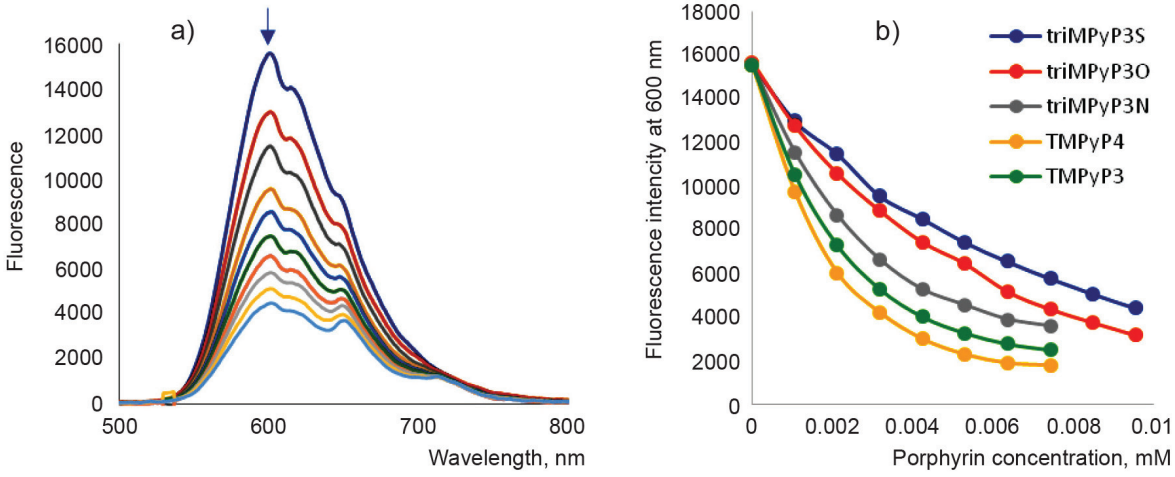

Figure 2. a) Fluorescence spectra of DNA-EtBr complex ($1.25 \cdot 10^{-5}$ M EtBr + $1.15 \cdot 10^{-4}$ M DNA) in Tris-HCl buffer at 25 °C while titration by triMPyP3S (0 – $2.15 \cdot 10^{-5}$ M), λ_{ex} = 295 nm. b) Fluorescence intensity at 600 nm of titration of DNA-EtBr ($1.25 \cdot 10^{-5}$ M EtBr + $1.15 \cdot 10^{-4}$ M DNA) complex with studied porphyrins.

triMPyP3N < triMPyP3S < TMPyP3 <
< triMPyP3O < TMPyP4 (1)

The highest affinity of DNA for TMPyP4 in comparison with TMPyP3 and monohetaryl-substituted porphyrins is due to the fact that the N-CH_3^+ groups in the para position have a much greater degree of freedom of rotation along the axis; therefore, the molecule can assume a more planar conformation when intercalated into DNA. In the case when the N-CH_3^+ group is in the meta position, it has a limited rotation around its axis and at the same time occupies a larger volume.[10,18] The dependence of the affinity of DNA for monohetaryl-substituted porphyrins on the nature of the heteroatom in the porphyrin substituent turned out to be unexpected. The distance of the heteroatom from the porphyrin aromatic system does not allow us to speak about the influence of the electronic effects of heteroatoms on the state of the π-system of the macroring, and, accordingly, to influence its π-π interaction with the nitrogenous bases of DNA. This, in particular, is evidenced by the dependence of the shift of the Soret band of porphyrins upon intercalation (Table 1):

triMPyP3N < triMPyP3O < triMPyP3S <
< TMPyP3 < TMPyP4 (2)

Subsequence (2) reflects the effect of the π-π interaction of the aromatic system of the porphyrin macrocycle with nitrogenous bases of DNA on the stability of the obtained complexes of porphyrins with DNA. Obviously, this contribution will be maximum for porphyrin with para-isomeric peripheral substituents, since this porphyrin is more planar (*i.e.*, the ability to π-π interaction is higher) and its intercalation between four nitrogenous bases of DNA will have less effect on DNA unwinding when porphyrin is included in the duplex compared to porphyrins with meta-isomeric peripheral substituents.

Replacement of one of the N-methylpyridyl substituents with a hetaryl-substituted one, in general, negatively affects the affinity of DNA for porphyrins. The reasons for this are that the intercalation complex of DNA with porphyrins is largely stabilized by electrostatic interaction between the positively charged nitrogen atoms of the pyridyl rings and the negatively charged oxygen atoms of the phosphate group of DNA. These electrostatic interactions draw the porphyrin into the duplex, compensating for the unfavorable steric effects arising from intercalation. In the case of monohetaryl-substituted porphyrins, one of these electrostatic contacts is absent, while the steric effect from the presence of a bulky hetaryl substituent, on the contrary, increases. It is interesting to note that subsequences (1) and (2) coincide, except for the position of triMPyP3O. Probably, the complex of DNA with triMPyP3O has some additional stabilization. It is likely that this stabilization is due to the formation of H-bonds between the oxygen atom of the porphyrin and one of the DNA helices, which is distorted. The rest of the hetaryl-substituted porphyrins do not exhibit such stabilization (subsequence (1), Table 1), since the electron-donating ability of sulfur in triMPyP3S is much lower than that of the oxygen atom. In the case of triMPyP3N, the reason for the absence of additional stabilization is the tertiary nitrogen atom, the methyl group of which hinders the participation of the nitrogen atom in H interactions.

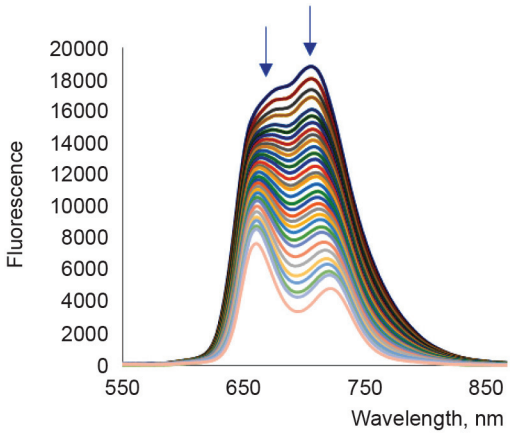

Figure 3. Fluorescence spectra of titration of TMPyP4 ($1.2 \cdot 10^{-5}$ M) with DNA (0–$4.5 \cdot 10^{-5}$ M) in Tris-HCl buffer at 25 °C, λ_{ex} = 425 nm.

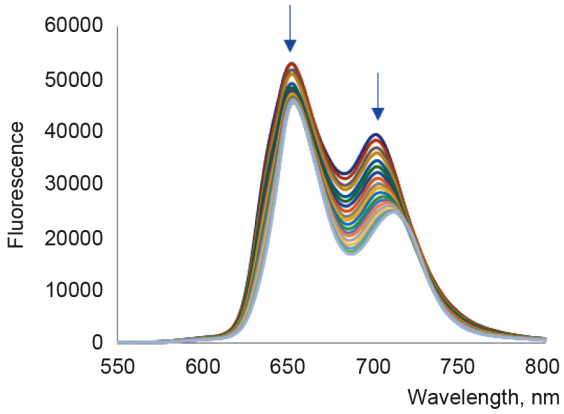

Figure 4. Fluorescence spectra of titration of triMPyP3N ($4.2 \cdot 10^{-6}$ M) with DNA (0–$1 \cdot 10^{-5}$ M) in Tris-HCl buffer at 25 °C, λ_{ex} = 425 nm.

When analyzing the fluorescence spectra of the studied porphyrins during their intercalation into DNA, a feature was found – the nature of the quenching of porphyrin fluorescence during intercalation into DNA depends on the position of the *N*-methyl group. In the case of the para-isomer, intercalation of porphyrin into DNA causes quenching of porphyrin fluorescence (Figure 3), while maintaining the position of fluorescence maxima, but band inversion is recorded. These spectral changes are caused by quenching of the excited state of porphyrin due to π-π binding to nitrogenous bases of the DNA duplex, and the inversion of fluorescence bands, according to the literature, is explained by a change in the state of pyrrole protons of the porphyrin reaction center (shift of tautomeric equilibrium).[19] The fluorescence quenching of porphyrins with meta-isomeric peripheral substituents manifests itself differently. First, the position of the fluorescence maximum

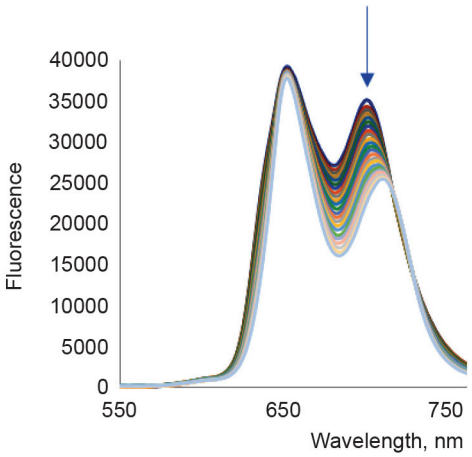

Figure 5. Fluorescence spectra of titration of triMPyP3O ($4.2 \cdot 10^{-6}$ M) with DNA ($0–1 \cdot 10^{-5}$ M) in Tris-HCl buffer at 25 °C, λ_{ex}=425 nm.

in the far-wavelength part of the spectrum changes, it shifts from 702 nm to 713 nm, while the position of the fluorescence maximum in the region of 647 nm is retained. Secondly, fluorescence is quenched much more strongly in the long-wavelength part of the spectrum (Figures 4, 5). It is difficult to unambiguously interpret these changes, but they do not contradict the considered model of binding "semi-intercalation".

Conclusions

A spectral study of the processes of interaction of water-soluble cationic porphyrins with DNA was carried out. It was found that all studied porphyrins form intercalation complexes with DNA when a certain molar ratio of DNA base pairs to porphyrins is reached. DNA shows high affinity for porphyrins containing para-isomers in peripheral substituents. Intercalation complexes of DNA with porphyrins with meta-isomers in peripheral substituents are characterized by spectral features, such as: a smaller bathochromic shift of the Soret band (up to 10 nm), the emission spectrum of intercalated porphyrins is observed without inversion of the intensity of the emission bands. The intercalation interaction of monohetaryl-substituted porphyrins with the DNA duplex probably proceeds by the mechanism of semi-intercalation. In a comparative analysis of the affinity of DNA for monohetaryl-substituted porphyrins, an assumption was made about additional stabilization of intercalation complexes of DNA with triMPyP3O due to the binding of the oxygen atom of the hetaryl fragment of porphyrin to the lateral surface of the distorted DNA helix. This assumption needs additional verification when analyzing the structure of DNA in complexes with the studied porphyrins. The results obtained can be used for the development of a scientific direction associated with the search for drugs – cytostatics, capable of causing a conformational change in the duplex by binding to DNA, and hindering DNA recognition by receptor proteins.

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References

1. Trannoy L.L., Lagerberg J.W., Dubbelman T.M., Schuitmaker H.J., Brand A. *Transfusion* **2004**, *44*, 1186.
2. Otvagin V.F., Nyuchev A.V., Kuzmina N.S., Grishin I.D., Gavryushin A.E., Romanenko Y.V., Koifman O.I., Belykh D.V., Peskova N.N., Shilyagina N.Y. *Eur. J. Med. Chem.* **2018**, *144*, 740.
3. Fiel R.J. *J. Biomol. Struct. Dyn.* **1989**, *6*, 1259.
4. Fiel R., Munson B. *Nucleic Acids Res.* **1980**, *8*, 2835.
5. Marzilli L., Banville D., Zon G., Wilson W. *J. Am. Chem. Soc.* **1986**, *108*, 4188.
6. Lipscomb L.A., Zhou F.X., Presnell S.R., Woo R.J., Peek M.E., Plaskon R.R., Williams L.D. *Biochemistry* **1996**, *35*, 2818.
7. Pratviel G., Pitié M., Bernadou J., Meunier B. *Angew. Chem. Int. Ed.* **1991**, *30*, 702.
8. Kumar S., Cheng X., Klimasauskas S., Mi S., Posfai J., Roberts R.J., Wilson G.G. *Nucleic Acids Res.* **1994**, *22*, 1.
9. Savva R., Pearl L.H. *Nat. Struct. Biol.* **1995**, *2*, 752.
10. Lebedeva N.S., Yurina E.S., Gubarev Y.A., Syrbu S.A. *Spectrochim. Acta A* **2018**, *199*, 235.
11. Gubarev Y.A., Lebedeva N.S., Yurina E.S., Syrbu S.A., Kiselev A.N., Lebedev M.A. *J. Pharmaceut. Analysis* **2021**, *11*, 691–698.
12. Peacocke A., Skerrett J.H. *Trans. Faraday Soc.* **1956**, *52*, 261.
13. Walker G.T., Stone M.P., Krugh T.R. *Biochemistry* **1985**, *24*, 7462.
14. Nafisi S., Saboury A.A., Keramat N., Neault J.-F., Tajmir-Riahi H.-A. *J. Mol. Struct.* **2007**, *827*, 35.
15. Dharanivasan G., Jesse D.M.I., Chandirasekar S., Rajendiran N., Kathiravan K. *J. Fluoresc.* **2014**, *24*, 1397.
16. Pasternack R.F., Caccam M., Keogh B., Stephenson T.A., Williams A.P., Gibbs E.J. *J. Am. Chem. Soc.* **1991**, *113*, 6835.
17. Kang J., Wu H., Lu X., Wang Y., Zhou L. *Spectrochim. Acta A* **2005**, *61*, 2041.
18. Pratviel G. *Coord. Chem. Rev.* **2016**, *308*, 460.
19. Lebedeva N.S., Malkova E., Popova T., Kutyrev A., Syrbu S., Parfenyuk E., Vyugin A. *Spectrochim. Acta A* **2014**, *118*, 395.

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