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DETERMINATION OF KINETIC CHARACTERISTICS OF DISSOCIATION OF COMPLEXES OF META-TETRA(HYDROXYPHENYL)CHLORIN AND DEXTRAN-POLY-*N*-ISOPROPYLACRYLAMIDE COPOLYMER BY FLUORESCENCE SPECTROSCOPY

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The ability of the thermosensitive copolymer dextran-poly-N-isopropylacrylamide (D-PNIPAM) to bind and release the photosensitizer (PS) meta-tetra(hydroxyphenyl)chlorin (mTHPC) was investigated using fluorescence spectroscopy techniques. It was shown that the efficiency of the copolymer to absorb mTHPC molecules depended on its phase state: mTHPC was efficiently adsorbed by D-PNIPAM (copolymer in globular conformation) at temperatures above 34–35°C, but the PS was practically not adsorbed on D-PNIPAM (copolymer in coil conformation) at temperatures below 34–35°C. The presence of additional structural rearrangements in the globule of D-PNIPAM under the action of high temperatures (>45°C) was shown using dynamic light scattering. The mTHPC dissociation rates from complexes with D-PNIPAM formed at 37–60°C were compared. The mTHPC release rate constants from the polymer globule were calculated. It was shown that complexation of mTHPC with D-PNIPAM at high temperatures (45–60°C) almost doubled the release rate of PS molecules from the copolymer globule at physiological temperatures as compared to similar complexes formed at 37–40°C. The time required for thermally induced structural rearrangements in D-PNIPAM was estimated. The globule-coil transition in the D-PNIPAM molecule caused by a temperature decrease below 34–35°C took less than a minute, while the reversibility of conformational changes in the copolymer globule when the medium temperature rose above 45°C required ~150 min. The results suggested that thermally dependent conformational rearrangements in the D-PNIPAM copolymer could be used for efficient regulation of the PS release rate in cellular and tissue systems.

Keywords: *meta-tetra(hydroxyphenyl)chlorin, thermosensitive copolymer, dissociation rate, phase transition.*

Introduction. Photodynamic therapy (PDT) is a relatively new method for treating malignant neoplasms and other diseases (ophthalmological, dermatological, etc.) that is based on the use of nontoxic compounds, i.e., photosensitizers (PSs), that are activated by visible light to destroy pathological cells and tissues [1–3]. The outcome of PDT depends on the photophysical and pharmacokinetic properties of the PS [4, 5]. The PS *meta*-tetra(hydroxyphenyl)chlorin (mTHPC) is one PS that is widely used in clinical practice [5, 6]. The limited solubility of mTHPC in aqueous media prevents delivery of it to target cells and tissues. An approach based on the use of specialized pharmacological forms for administration of PSs can solve this problem. Liposomes, protein nanoparticles, polymer systems, dendrimers, etc. have been examined as such forms [7–9].

Stimulus-sensitive polymers characterized by a coil–globule reverse phase transition influenced by an external stimulus, e.g., temperature, are considered a promising type of PS nanocarriers [10, 11]. For example, the thermosensitive star-like copolymer dextran-poly-*N*-isopropylacrylamide (D-PNIPAM) was shown to be capable of encapsulating nonpolar chlorin e_6 derivatives and releasing them as a function of medium temperature [12]. It has also been shown that D-PNIPAM can bind mTHPC [13].

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