INFLUENCE OF SERUM CONCENTRATION ON THE PHOTOSENSITIZERS EXIT FROM THEIR COMPLEXES WITH TEMPERATURE-SENSITIVE DEXTRAN-POLY (N-ISOPROPYLACRYLAMIDE) COPOLYMER

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One of the ways to solve the problem of low watersolubility of drug compounds is to use special delivery systems based on nanostructured materials [1]. An important factor in the development of such technologies is the control of the release of drug products from the composition of nanocarriers.

In this work we consider the spectral method of analysis of 5,10,15,20-tetra(m-hydroxyphenyl)chlorin (mTHPC) and its porphyrin analogue 5,10,15,20-tetra(m-hydroxyphenyl)porphyrin (mTHPP) yield from dextran-70-poly(N-isopropylacrylamide) copolymers (D70-PNIPAM). mTHPC is one of the most promising clinically approved second generation photosensitizers [2]. After introduction of mTHPC and mTHPP into blood their molecules form large aggregates affecting distribution processes. To prevent an aggregation of mTHPC and mTHPP in blood, several special formulations, such as liposomes, bioconjugates, copolymers were developed. In our work we synthetized a star-like copolymer with Dextran core and grafted PNIPAM arms. D70-PNIPAM copolymers are in the condensed state at temperatures above the critical point. At temperatures between 34-35 °C, there is a phase transition, which leads to significant changes in the structure of the polymer molecule. D70-PNIPAM properties modulated by this phase transition include the hydrophobicity, particle size, porosity, colloidal stability and rheology.

The addition of mTHPC to the polymer solution at temperatures above critical is accompanied by its binding. It is observed full monomerization of mTHPC aggregates, sensitizer molecules penetrate into a rigid polymer matrix, resulting in increasing mTHPC fluorescence polarization degree up to 0,33. When cooling to below critical temperatures, mTHPC molecules dissociate from the complexes and their subsequent aggregation in the aquatic environment is observed. In serum solutions, the dissociation process is accompanied by the binding of mTHPC to plasma proteins (mainly to high and low density lipoproteins). mTHPP exhibits similar behavior in the copolymer solution at different temperatures.

Spectral data analysis has shown that fluorescence characteristics of mTHPC and mTHPP in serum and complexes with D70-PNIPAM differ significantly.

The differences in excitation and emission spectra of fluorescence for mTHPC and mTHPP complexes with a copolymer and in serum solutions can be used to measure the rate of photosensitizers output. Using this approach, the stability of complexes in solutions with different serum contents was evaluated.

Bibliographic references

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