ANALYSIS OF RELEASE PROCESSES OF TEMOPORFIN (mTHPC) FROM DEXTRAN70-POLY (N-ISOPROPYLACRYLAMIDE) COPOLYMER IN BLOOD SERUM

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One of the ways to solve the problem of low drug watersolubility is to use special delivery systems based on nanostructured materials. An important factor in the development of such technologies is the monitoring of drug release from the nanocarriers.

In this work we carried out the monitoring of 5,10,15,20-tetra(m-hydroxyphenyl)chlorin (mTHPC) release from dextran70-poly(N-isopropylacrylamide) copolymers (D70-PNIPAM) using the spectral approach. mTHPC is one of the most promising clinically approved second generation photosensitizers [1]. The main limitation of its application in photodynamic therapy is a low watersolubility. To prevent mTHPC aggregation and facilitate its administration several special formulations, such as liposomes,bioconjugates, copolymers have been proposed [2].

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. mTHPC could be simply encapsulated into the D70-PNIPAM copolymers at the temperature above critical one. It was demonstrated, that the addition copolymers to the aqueous mTHPC solution is accompanied with complete monomerization of photosensitizer. Indeed, photosensitizer molecules penetrate into a rigid polymer matrix resulting in the increase of mTHPC fluorescence polarization degree up to 0,33. When cooling to below critical temperatures, mTHPC molecules release from the complexes forming molecules aggregates in the aqueous surrounding. Meanwhile in the serum solutions, the release process is accompanied with the binding of mTHPC to the plasma proteins (mainly to high density lipoproteins and low density lipoproteins).

Spectral data analysis has shown that the shape of mTHPC excitation spectrum in serum and complexes with D70-PNIPAM significantly differs (Fig.1) allowing us monitor temperature-induced redistribution of mTHPC from copolymers to serum proteins (Fig.2).

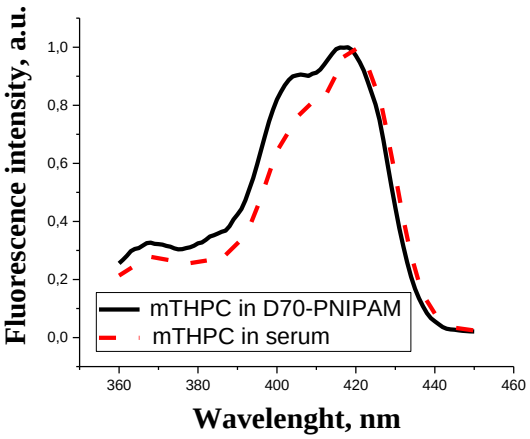

Fig. 1. Normalized fluorescence excitation spectra of mTHPC in D70-PNIPAM and serum.

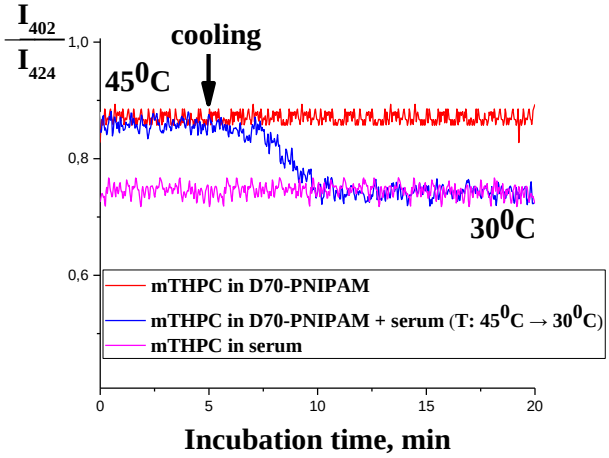

Fig. 2. Temperature-induced redistribution of mTHPC from D70-PNIPAM to serum. λem = 652 nm.

Based on the measurements of the ratio of intensities of fluorescence excited at 402 nm and 424 nm, the redistribution rate of mTHPC between D70-PNIPAM and serum can be estimated.

Acknowledgements: The work was carried out with the financial support of the Belarusian Republican Foundation for Fundamental Research (BRFFR) [grant number M19UKRG-002]; the Ministry of the Education and Science of Ukraine: joint Ukrainian-Belarusian research and development projects № M110-2019.

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