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Hydrophilic block copolymers for doxorubicin incapsulation

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Application of the micelle-type polymeric nanocontainers are considered as one of the most perspective ways to realize the targeted delivery of toxic and water-insoluble drugs into certain cells of living organisms. As it was shown earlier, the asymmetric triblock copolymers (TBCs) contained chemically complementary polyacrylamide and poly(ethylene oxide) (PAAm-*b*-PEO-*b*-PAAm) or its monomethyl ether (MOPEO-*b*-PAAm) form micellar structures in aqueous solutions [1,2]. The influence of the anticancer agent doxorubicin (DOX) on the micellization process due to the interaction between DOX and copolymer micelles was established. This opened new prospects for using such copolymers as nanocontainers for DOX and other toxic and poorly soluble drugs.

The present work is focused on the anionic derivatives of asymmetric TBC sample (M_{nPEO}=6 kDa), which were obtained by alkaline hydrolysis reaction and tested by potentiometric titration. Their molecular parameters, the system of hydrogen bonds, micellization and DOX encapsulation in aqueous solutions as compared to initial TBC sample were investigated using NMR, FTIR, UV-Vis spectroscopy, and static light scattering. It was shown that the reaction rate and the limit hydrolysis degree in TBC macromolecules were essentially higher than those in the case of high-molecular-weight polyacrylamide. The formation of H-bonds such as “the mixed dimmers” with participation of carboxylic and amide groups was established in the partially hydrolyzed TBCs. Micelles of the modified TBC with small hydrolysis degree demonstrated practically the same stability in aqueous medium as those of the initial TBC sample that was confirmed by close CMC and -$\Delta G°$ values. At the same time, their encapsulation ability with respect to DOX was essentially higher than that of the micelles of non-modified TBC. The enhanced biological activity of the DOX-loaded micelles as compared to DOX is discussed.

1. *Kunitskaya, L. et al.* The Self-Assembly of Diblock Copolymers MePEG-b-PAAm Into Miccelar Structures and Their Interaction with Doxorubicin // Mol. Cryst. Liq. Cryst.-2011.**-536.-**P. 398-404.
2. *Zheltonozhskaya, T. et al.* Micelles of PAAm-b-PEO-b-PAAm TriblockCopolymers and Their Binding with Prednisolon // Mol. Cryst. Liq. Cryst.-2011.**-536**.-P. 380-391.