ALBUMIN/THIACALIX[4]ARENE NANOPARTICLES AND THEIR SELF-ASSEMBLY WITH CIPROFLOXACIN

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Sulfobetaine derivatives are widely used in biomedicine due to their unique properties. Such interest in sulfobetaine surfactants is due to the fact that they are generally not hazardous to skin and eyes, exhibit low toxicity, have good water solubility and foaming properties. Their macrocyclic analogs, *p-tret*-butylthiacalix[4]arene derivatives tetrasubstituted at the lower rim with sulfobetaine fragments, exhibit similar properties to non-macrocyclic surfactants. Interest in these macrocycles is due to the presence of several binding sites: macrocyclic cavity, amide and betaine fragments, while remaining electroneutral in the physiological environment.

The formation of drug complexes with proteins is one of the important factors in the effectiveness and targeted action of the drug on the body for many years. It is also known that drug distribution, metabolism and drug efficacy depend on the degree of drug binding to serum albumin. As an albumin was taken widely characterized transport protein bovine serum albumin, and as a drug – ciprofloxacin, one of the most effective antibiotics of a wide spectrum of action, which finds its application in clinical practice. In this connection, there is an interest to consider the interaction of ciprofloxacin with calixarenes and protein, and to study the influence of the obtained macrocycles on the binding of the antibiotic to BSA.

The aim of this work was to obtain new polyfunctionalized derivatives of *p-tret*-butylthiacalix[4]arene functionalized at the lower rim with ester, amino- and alkylsulfonate fragments, and to study their aggregation ability with respect to a model protein and a drug, namely bovine serum albumin and ciprofloxacin.

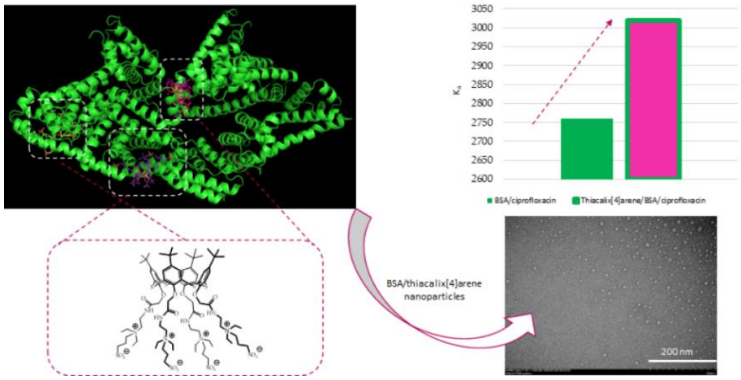

Fig. 1. Graphical abstract binding of thiacalix[4]arene/BSA and ciprofloxacin

In the course of this work, derivatives of *p-tret*-butylthiacalix[4]arene, tetrasubstituted at the lower rim with sulfobetaine fragments differing by propylidene and butylidene linkers in a *cone* configuration, were synthesized. Supramolecular self-assembly under different conditions, namely two- and three-component systems, was studied. By investigating the aggregation abilities of the calixarene/BSA system, it was found that both calixarenes formed monodisperse systems with protein at different molar ratios of the components: 1:1 for calixarene with propylidene tail and 1:10 for calixarene with butylidene tail. It was found by fluorescence method that such stable monodisperse calixarene/protein systems were more effective in binding ciprofloxacin than each component separately, which was confirmed by binding constants.

These results open new opportunities for the development of new targeted delivery systems in biomedicine.

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