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Studies of dsDNA and siRNA oligomers in complexes with tricationic surfactants using biophysical methods

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Among the most intensively studied areas of the science today we can find gene therapy – the innovative and probably the most promising method for treatment of all types of diseases so far incurable. The aim of gene therapy is the induction of changes in the gene machinery of diseased cells that cause blockage or destruction of abnormal genes or contribute to the production of factors acting antagonistically. This could be done by introducing a short RNA molecules (transgenes) which are able to act in this way. Unfortunately, in practice, it creates a lot of problems, mostly in the introduction of these nucleic acid to the cell without inducing immunological response. The solution is to find a suitable carriers, which could solve these problems[1-4].

Our research indicates that this potential have spatial structures formed by self-organized quaternary ammonium salts – surfactants [5]. In the range of new amphiphilies, tricationic surfactants, featuring three hydrophobic chains (hydrophobic moieties) and three polar head groups linked by a spacer, seems to be quite promising. Their physicochemical properties making them able to create a stable, biocompatible complexes with dsDNA and siRNA.

In this work we present results of small angle X-ray scattering (SH-SAXS), circular dichroism (CD), gel electrophoresis studies and cellular tests of the complexes formed between two tricationic surfactants: 1,2,3-propantriol [oxomethyl-3-(1-dodecylimidazolium)] chloride and 1,2,3-propantriol [(oxomethyl) dimethyldodecylammonium] chloride with short 21 bp double stranded nucleic acid oligomers dsDNA and siRNA [6-7].

First of all we conducted complexation process, than characterized main structural parameters of the obtained structures (like size, shape, spatial structure, resultant charge, morphology), described conformational changes of nucleic acids bound in them and finally we prepared probable models of these complexes. Moreover we performed also toxicity tests on HeLa and human fibroblasts cell cultures using our systems to find out their influence on these lines. All these results proved to be very interesting.

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