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Dicationic surfactants with glycine counterions for oligonucleotides transportation

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Dicationic gemini surfactants (consisting of two hydrophobic tails and two cationic head groups linked by a spacer group and two counteranions) are potentially good candidates to bind, protect and deliver nucleic acids [1–3]. Hereby, the aspect of amino acid, namely glycine as counterions of gemini surfactants was explored for application in gene therapy. This study was conducted on small, double-stranded DNA and RNA oligomers and two quaternary bisimidazolium salts, having 2,5-dioxahexane and 2,8-dioxanonane spacer groups.

Surfactants toxicity level has been assessed by conducting MTT assay and their ability to bind nucleic acid has been tested by electrophoretic tests. Nucleic acid conformation and its changes upon the addition of surfactants were established by circular dichroism and Fourier transform infrared spectroscopies. The structures of formed complexes were characterised by small angle scattering of X–ray synchrotron radiation.

A series of SAXS data sets were collected at EMBL, at BioSAXS beamline P12 of the Petra III synchrotron (Hamburg, Germany) [4]. All SAXS measurements were conducted on an automated system consisting of a BioSAXS sampler robot, thermostated capillary (diameter 1 mm) and a Pilatus 2M detector. In a typical measurement, the data were collected over a period of 60 s as twenty independent images (3 seconds each), which were subsequently combined and averaged.

Both tested surfactants appear to be extremely promising components for delivery systems for small nucleic acids [5]. These surfactants are able to form stable complexes with both DNA and RNA oligonucleotides at low, not harmful concentrations, causing condensation of the nucleic acids but also ensuring the maintenance of their native conformation. Furthermore, a variety of structures is formed in the studied systems which is a feature connected to a high transfection efficiency.

The surfactant with the 2,5-dioxahexane spacer was proven to be less effective at binding DNA and RNA oligonucleotides and has a higher CMC value compared with the 2,8-dioxanonane surfactant, nevertheless it is characterized by lower toxicity. The DNA duplex maintains the B-form and the RNA oligomer maintains the A-form upon addition of the surfactants. The studied surfactants form a micellar phase in solution and micelles were present in all studied lipoplexes; however in the system whit short spacer surfactant and DNA a hexagonal phase is also formed; and the 2,8-dioxanonane surfactant-based systems have a tendency to form a cubic phase both with RNA and DNA.

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