Block Copolymers as Bile Salt Sequestrants: Complex Formation and Thermoresponsive Behavior

Karin Schillén

Division of Physical Chemistry, Department of Chemistry, Lund University, Lund, Sweden

To study the formation and characterize the structure of mixed complexes of oppositely charged block copolymers and surfactants are of great significance for practical applications. In this context, biocompatible block copolymers and biosurfactants (like bile salts) are particularly interesting.

Poly(*N*-isopropyl acryl amide) (PNIPAM) diblock copolymers with a positively charged block of poly(3-acrylamidopropyl)-trimethylammonium chloride (PAMPTMA(+)) interact strongly with oppositely charged bile salt surfactants to form mixed complexes in water. The mixed system presented here contains the bile salt sodium deoxycholate (NaDC). It was explored at a constant copolymer concentration and at a range of molar negative charge fractions and temperatures. The cryogenic transmission electron microscopy (cryo-TEM) experiments at room temperature revealed two types of co-assembled complexes of radically different morphology and inner structure that co-exist at equimolar charge condition. One of them has an intriguing tape-like supramolecular morphology that is striped, which has never been observed before in oppositely charged polymer-surfactant systems. Both complexes are formed mainly as a result of the electrostatic attraction between the positively charged copolymer blocks and bile salt anions but the effect of the polymer on the bile salt self-assembly is critical. In addition to cryo-TEM, static light scattering, small angle X-ray scattering, and electrophoretic mobility measurements were performed. The thermoresponsivity of the mixed system was found to be highly dependent on the PNIPAM phase behavior as revealed by differential scanning calorimetry, where a temperature-induced aggregation process was monitored over the whole composition range.

This study highlights the potential of using linear amphiphilic block copolymers as bile salt sequestrants in the treatment of bile-acid related diseases, which are caused by bile acids in the large intestine, and hypercholesterolemia, where lowering the level of cholesterol in the body is necessary. There is yet room for improvement of the currently used sequestrants since they have poor patient compliance.