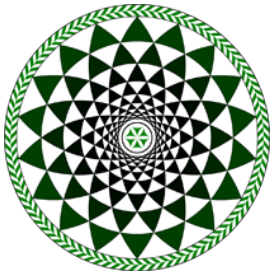

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pH induced structural polymorphism in DNA-phospholipid-additive complexes

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The pH profile of pathological tissues, such as upon acquisition of inflammation, infection, and cancer, is significantly different from that of the normal tissue. Also cellular components such as the cytoplasm, endosomes, lysosomes, endoplasmic reticulum, etc. are known to maintain their own characteristic pH values. For example, the pathway of the gene-vector complex is accompanied with the drop in pH from physiological (pH 7.4) to the acidic in lysosome (pH 4.5). Hence, pH-responsive drug carriers are aimed at increasing the intracellular drug bioavailability by rapidly releasing their payload in the endosomes after cellular uptake, and/or facilitating the drug transit to the cytoplasm.
DNA polyanion interacts with a dispersion of cationic liposomes forming colloidal particles with organized microstructure, called lipoplexes. They attract attention as delivery vectors for genetic material. Despite the fact that cationic liposomes have been used for transfection, and commercial lipid formulations are available, their efficiency needs to be improved.
We will discuss structural polymorphism of two groups of lipoplexes prepared from neutral phospholipids with positive charges created by two groups of pH responsive additives, either by N-alkyl-N,N-dimethylamine-N-oxides or fatty acids and divalent cations. The microstructure of formed complexes was examined using a small angle synchrotron X-ray diffraction (SAXD). We identified a large variety in structures, from one dimensional lamellar phase up to three dimensional cubic phases depending on the complexes composition, pH and temperature. The binding capacity of complexes for DNA differs in the range 30-95 % as we derived from spectrophotometry. In the field of pharmacy, non-lamellar phases such as hexagonal or bicontinuous cubic phases attract attention as promising group of carriers for a large spectrum of drugs, genetic material (DNA, siRNA), small proteins or peptides including.

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