DESCRIPTION FOR THE GENERAL PUBLIC

The aim of the project is the characterization of influence of gemini surfactants on the conformation (the three-dimensional shape or form of a polypeptide chain) and structure of selected amyloidogenic proteins and peptides. Prions are the proteins which can adopt different conformations due to inherent conformational flexibility. They bind to the cell membranes and play important role in cell-cell adhesion (attachment of substance to the surface of another substance) and intracellular signaling. In a normal functioning cell, proteins with impaired conformation are degraded by lysosomal proteinase. Pathological form of a prion protein PrP_{Sc} ("scrapie" form) has a different conformation, resistant to enzymatic and physicochemical factors and partially to protease. Moreover, as a result of the aggregation, pathological prion protein accumulates in the form of aggregates or amyloid fibrils in the central nervous system. A similar situation is observed in the case of the human cystatin C, which is able to forming oligomer or neurotoxic amyloid plaques for a mutant (L68Q) and co-precipitation with the β amyloid plaques.. As a result of the deposition of these proteins in patients with various neurodegenerative diseases - for example, prionoses (infectious spongiform encephalopathies - in humans this is Creutzfeldt-Jakob disease, Gerstmann-Straussler-Scheinkear syndrome (GSS), fatal familial insomnia (FFI), kuru disease) amyloidosis of Icelandic type or Alzheimer's disease - occure permanent damages, leading to death. In recent years, it is estimated that at least 27 different proteins are amyloidogenicznymi agents of various diseases conformational. It is believed that the gemini surfactants prevent the aggregation of amyloidogenic protein, with the result that will form micelles.

In planned studies gemini surfactants will be used, because - as compared to conventional surfactants - they are characterized by a lower critical micelle concentration (CMC), which facilitates the use of small quantities of material. Cationic gemini surfactants, to be used in the project, will be derivatives of bis-imidazole connector with variable width and a differ length of alkyl side chains.

Structural information on complexes surfactant - protein will be obtained using advanced spectroscopic methods, ie: small-angle scattering of synchrotron radiation (SAXS), circular dichroism (CD), transmission electron microscopy (TEM), diffusionmetry NMR and infrared spectroscopy with Fourier transformata (FTIR).

SAXS is a technique that enables the analysis of the structure and interactions of biological molecules in solution. SAXS studies provide information on the structure and a global conformation of the tested molecule (s). Therefore, by using SAXS systems can be tested mixed systems surfactant - protein or surfactant - peptide. In turn, the CD study will be essential in determining conformational changes in the secondary structure of proteins and peptides induced by gemini surfactants. Infrared spectroscopy allows the study of molecular vibrations and gives precise information about the components of secondary structure proteins. Whereas, the FTIR studies complement the independent results from measurements of the CD. DOSY method allows measurement of the translational diffusion of molecules in solution. The planned study provides an estimate of the diffusion coefficient (and the hydrodynamic radii) of the mixed systems surfactant - a protein (or peptide). Transmission Electron Microscopy (TEM) as one of the methods of analysis of the microstructure of materials is often used to provide information on the shape and size distribution of biological particles. The project provides an analysis of emerging aggregates and amyloid using classical microscopy TEM (with negative contrast).

The obtained during the studies structural information on resulting surfactant-protein complexes will be important in understanding the molecular basis of braking of neurodegenerative diseases, and the gained knowledge will be used in the design of therapeutic drugs.