Preliminary Studies for the Preparation of Casein-loaded Liposomes to Inhibit $A\beta_{1\text{-}40}$ Fibrillogenesis

G. Di Prima[1], S. Raccosta[1], M.R. Mangione[1], F. Librizzi[1] and R. Carrotta[1].

1. Consiglio Nazionale delle Ricerche – Istituto di Biofisica, Palermo, Italy.

giulia.diprima@pa.ibf.cnr.it

Keywords: Liposomes, α_{s1}-casein, Drug Delivery.

α_{s1}-Casein is a natural protein which constitutes the most prevalent form of casein in bovine milk. α_{s1}-Casein is amphiphilic, almost unfolded, and consist of two highly hydrophobic zones separated by an hydrophilic region. Previous studies have demonstrated the ability of α_{s1}-Casein to inhibit *in vitro* the nucleation phase of amyloid β-peptide (Aβ) fibrillogenesis by sequestering Aβ species on its surface. One of the main hallmark for Alzheimer Disease (AD) is the extracellular deposition in brain tissues of proteinaceous plaques, rich of well-ordered Aβ peptide amyloid aggregates. Although such an evidence, oligomeric intermediates in the fibrillogenesis have been discovered to be the most toxic species able to interfere with membranes and disturbing the cell functioning. In this context, a challenging therapeutic approach could target such early toxic oligomeric species. In order to exploit the inhibiting action of α_{s1}-Casein as a possible AD treatment, it is crucial to define a controlled method to efficiently load, protect and deliver the protein to the brain. Liposomes are spherical phospholipids-based vesicles characterized by excellent biocompatibility and biodegradability, low toxicity, ability to incorporate and protect both hydrophilic and hydrophobic drugs as well as to cross the Blood Brain Barrier in order to access the Central Nervous System. Based on all these considerations, novel proteoliposomes composed by phospholipids, cholesterol and α_{s1}-Casein were prepared and characterized. The proteoliposome preparation protocol was optimized in order to obtain the best results. Nanosystems were characterized by different biophysics techniques, such as light scattering, zeta-potential, laurdan fluorescence, chromatography and AFM imaging.