**MVTS SAS-MOST Project**

**Dynamical study of formation/destruction of protein amyloid aggregates targeted by magnetic zeolite nanocomposites**

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**Abstract.** Both natural and synthetic nanoparticles have practical applications in a variety of areas, ranging from environmental remediation to an emerging multidisciplinary field that combines chemistry, engineering, physics, biology, and medicine. Proteins are important biological macromolecules that are fundamental to the proper functioning of cells and organisms; therefore, the impact of nanoparticles in living organisms at the protein level is a critical issue that is attracting increasing attention from researchers.

Nanoparticles are being explored for their role in diagnosing, preventing, treating or even causing amyloid diseases. Amyloid-related diseases are characterized by unusual protein-protein interactions of normally soluble proteins that have undergone structural transitions and result in the formation of intracellular and extracellular amyloid aggregates. The pathogenesis of these and other neurodegenerative diseases remains unclear, and effective treatments are currently lacking. It was demonstrated that nanoparticles can significantly influence the process of protein amyloid fibrillization. Additionally, over the last decades, there has been increased interest in the studies of *in vitro* and *in vivo* applications of NPs in radiation, photodynamic and thermal therapies. In turn, natural zeolite nanoparticles, especially clinoptilolite (CZ) is a promising material for biomedicine and pharmaceutics due to its non-toxicity, thermal stability, expanded surface area, and exceptional ability to adsorb various atoms, organic molecules, photodynamic agents, and nanoparticles into micro- and mesopores.

In addition to amyloid pathology, our aim was to study the physical properties of the bio-nano-composites, particularly those, which contain within themselves magnetic (Fe3O4-based) nanoparticles, including zeolite. The results demonstrated that magnetic component of magnetic fluids was important for their anti-amyloid activity, however, the physico-chemical properties of NPs such as type of coating layer, charge, concentration, etc. determined the extent of inhibition/depolymerization activity.

Our results suggest that inhibiting activity of nanoparticles can be explained by protein binding with nanoparticles resulting in decreasing of concentration of the free protein molecules in bulk and diminish the nucleation process, which represents the initial step in fibrillogenesis. Moreover, the NPs can bind to active sites of protein (central protein hydrophobic motif important for fibrillization) and thus block the formation of the amyloid aggregates. On the other hand, the ability of the NPs to destroy the amyloid fibrils could by caused by interaction between nanoparticles and hydrophobic residues of the fibrils and therefore interrupts the interface between two neighboring beta-sheets.

The nonlinear optical properties of clinoptilolite type of natural zeolite allowed using the multiphoton microscopy in imaging of CZ nano/micro-particles and visualizing of dye adsorption /desorption processes. CZ magnetic nano/micro-particles can be considered as safe and effective multimodal probes for MRI and optical imaging, thermo- and phototherapy as well as effective containers for controlled drug delivery.

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