Impact of metal and metal oxide nanoparticle functionalization by low-molar mass polyphenols on their activity in protein fibrillation processes

The ageing population is a process that began to develop dynamically at the beginning of the 20th century. In the last few years, the intensity of the ageing population increased significantly, which with a simultaneous decrease in the birth rate makes that the percentage of old people in society is growing rapidly. Increasing number of elderly people causes that the number of people suffering on dementia and neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, also growth up significantly. Neurodegenerative diseases are related to progressive damage of cells of nervous system, which in most cases do not have ability to regeneration and proliferation. Therefore, the brain damage resulting from neurodegenerative diseases lead to mental impairment and irreversible problems with physical motion.

Neurodegenerative diseases are incurable. Therefore, they are in the center of interest of scientists who are looking for the methods to prevent them. Pathogenesis and etiology of neurodegenerative diseases have not been fully understood and described in the literature. Nevertheless, it was established that in the case of hereditary neurodegenerative diseases as well as in the case of these which were acquired, formation of pathological protein structures that accumulate in nervous cells and damage neurons is a major factor responsible for the degeneration of nerve system. Many literature evidences proved that undesired aggregation of the proteins to fibrils is related to etiology of neurodegenerative diseases. Moreover, it was proved that the formation of toxic fibrils can be induced by chemical substances exhibiting pro-fibrilliar properties. On the other hand, it was established that some chemicals and nanostructures are able to reduce and prevent the uncontrolled fibrillation of proteins. It was proved, that some metal and metal oxide nanoparticles, which are nanometric structures of sizes smaller than 100 nm, exhibit anti-fibrillar properties. It is worth mentioning that methods of preparation of diverse types of nanoparticles of controlled size, shape and surface properties are well-developed and described in the literature. Nevertheless, it is still not known how to design and synthesize nanoparticles with the desired anti-fibrillar properties which will be inhibit formation of toxic structures of proteins which are responsible for the induction of neurodegenerative diseases.

Our hypothesis is that the activity of metal and metal oxide nanoparticles mainly depends on their surface properties which are tuned by stabilizing agents. It seems plausible that electrostatic interactions occurring between colloidal nanoparticles and monomers of proteins or peptides are crucial for induction of fibrillation. Because these issues have not been undertaken in the literature previously, they will be investigated within the scope of proposed project.

The aim of this project is the development of methods of functionalization of selected metal (silver and platinum nanoparticles) and metal oxide (magnetite, titanium oxide, zinc oxide) nanoparticles with polyphenols of well-documented activity in the protein fibrillation processes. Gallic acid and rosmarinic acid belong to the low-molar mass of polyphenols of well-documented activity in the fibrillation processes. Moreover, both selected polyphenols are antioxidants of antibacterial and antivirial properties. Some literatures reports have shown that these polyphenols also are able to inhibit cancer development.

We assume that the functionalization of metal and metal nanoparticle surfaces by these polyphenols of anti-fibrillar properties will inhibit fibrillation processes more strongly than free polyphenols and nanoparticles. It is planned to prepare polyphenol-functionalized nanoparticles using three independent approaches: 1) a ligand exchange reaction on metal nanoparticles surfaces, 2) electrostatically-driven adsorption of polyphenols on metal and metal oxide nanoparticle surfaces and 3) during the chemical reaction (esterification) between polyphenols and hydroxyl groups of metal oxide nanoparticle surfaces. Hen-egg-white lysozyme (HEWL) (model protein used in the fibrillation processes), amyloid-β-peptide ($A\beta_{1-42}$) (component associated with AD) and α-synuclein (α-syn) (component associated with PD) were selected for the research on fibrillation processes. The research will compare the rate of formation of toxic fibrils and their morphology in physiological conditions in the presence and absence of functionalized nanoparticles.

The research results obtained during the project implementation are expected to help verify the main hypothesis of synergistic effects of nanoparticles and polyphenols in protein fibrillation processes. Finally, it is believed that the knowledge gained during the realization of the proposed project will help to develop new pathways in prevention of neurodegenerative diseases based on the inhibition of the processes of uncontrolled aggregation of proteins and the formation of toxic fibrillar structures.