Abstract No.128

Gold Nanoparticle as a Drug Delivery System for Thiol-Containing Purine Antimetabolites

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Over expression of different efflux membrane transporter proteins such as p-glycoprotein (P-gp), multidrug resistance protein 1 (MRP1) and breast cancer resistance protein (BCRP) is associated with high levels of resistance to a variety of anticancer agents. In spite of many synthetic purine derivatives being tested so far, as anticancer drugs, 6-Mercaptopurine (6MP) and 6-Thioguanine (6TG) are the only purine antimetabolites that are currently in use for cancer treatment. The thiol group of these drugs may increase their elimination through conjugation with thiol-containing molecules. Gold nanoparticles (GNPs), on the other hand exhibit strong binding affinity towards thiols, and therefore above mentioned purine antimetabolites can be easily loaded on their surface. In the current research, GNPs were synthesized and characterized for their shape, size and percent entrapment efficiency using transmission electron microscopy (TEM), UV/vis spectroscopy and thermal gravimetric analysis (TGA). To estimate the improvement of drug delivery of GNPs, MCF-7 breast cancer cell line was treated by both 6TG and 6TG-functionalized GNPs (6TG-GNPs). The results of this and previous studies revealed that GNPs significantly enhance the anti-cancer activity of 6TG and 6MP, suggesting enhanced intracellular uptake of the drugs by endocytic mechanism. Therefore, the improved anti-proliferation activity of these purine antimetabolites by GNP carriers could make possible the reduction of the overall concentration of the drug, renal clearance and its side effects during cancer treatment.

Keywords: Anticancer Activity, Gold Nanoparticles, Purine Antimetabolites.

Abstract No.129

Investigation on Elasticity of Intact and Diabetic RBC Membrane Using Optical Tweezers

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As a useful nondestructive nano-tool for manipulating isolated biological cells and individual molecules, optical tweezers (OT) have been used widely in many research areas such as biology, medicine and physics. The nanometer positioning ability along with sub-picoNewton force resolution have turned OT into a valuable tool in biology and physical sciences.The elastic nature of a red blood cell (RBC) plays an important role in blood flow in themicrocirculatory system in which a typical RBC passes through blood vessels of diameter less than its diameter by deforming itself to a large extent. The mechanical properties of RBC membrane can provide valuable biological information.We measured the elasticity of the RBC membrane using OT. OT was used to apply calibrated forces to human erythrocytes via streptavidin coated polystyrene beads with a diameter of 3.28μm bound to their membrane. By applying enough stretching force, a tether could be formed from the membrane. The force at which the tether formed, and the force required to keep the tether while separating the trapped bead and RBC, could be used as parameters that could be used to calculate the rigidity of the membrane. The maximum force exerted by optical tweezers on the normal cell was~a few tens pN. In the next phase we're going to study the elastic properties of diabetic RBC membrane.

Keywords: Optical Tweezers, Red Blood Cell, Microcirculatory System, Streptavidin Coated Polystyrene Beads, Tether, Stretching Force.

Abstract No.130

Effect of Silica Nanoparticle Supported Imidazolium Ionic Liquid on Thermal Reversibility of Human Carbonic Anhydrase II

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Irreversibility caused misfolding and aggregation for proteins which are a common phenomenon both in the cell, in-vitro protein refolding and

the corresponding biotechnological applications. Most importantly, it is involved in a wide range of diseases, including some of the most prevalent neurodegenerative disorders. Denaturation of human carbonic anhydrase II (HCA II) (EC 4.2.1.1) is irreversible, therefore any efforts in order to induce reversibility can be important. In this report, we show the chaperone ability of silica nanoparticle supported imidazolium ionic liquid (SNImIL) on HCA II at pH 7.75. The mechanism for chaperone activity of SNImIL as a nano chaperon on aggregation and percentage of reversibility of HCA II was investigated by various techniques such as UV–Vis, fluorescence spectroscopy and differential scanning calorimetry (DSC). The results shown the percentage of reversibility of HCA II is increased up to %42 in the presence of SNImIL after 24 hours incubation and also decreased the aggregation rate.

Keywords: Human Carbonic Anhydrase II, Silica Nanoparticle Supported Imidazolium Ionic Liquid, Reversibility, Differential Scanning Calorimetry, Aggregation Rate.

Abstract No.131

A Comparative Study of Non-Hydrolytic Activities of Acetyl and Butyrylcholinesterase Enzymes and Their Impact on The Formation of Beta-Amyloid Aggregation

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Alzheimer disease (AD) is one of the most common neurodegenerative dementias, caused by silent plaques that are created by fibril formation of beta amyloid (Aβ) peptide. Aβ, is a portion of transmembrane receptor-like amyloid precursor protein (APP) in neuron cells. Recent investigations have shown that acetylcholinesterase (AChE) plays a crucial role in the promotion of Aβ aggregation beside its role in the rapid hydrolysis of the neurotransmitter acetylcholine (ACh). Butyrylcholinesterase (BChE), because of similar structure and function to AChE may also have role in thia phenomena. Both AChE and BChE have a peripheral anionic site, beside their active site, and it is proposed that it is involved in the promotion of amyloid fibrillation presumably through interactions with Aβ. In this study we have investigated about this promotive effect of AChE and BChE on amyloid aggregation in vitro. Our preliminary results showed that both enzymes could significantly increase Aβ42 thioflavine T (ThT) fluorescence intensity, considered as a quantitive index of amyloid aggregation, when they were incubated with Aβ. In the continuation of these studies we will examine the synergistic effects of these two enzymes (if any) and the effects of their inhibitors of Aβ aggregation, with the use of techniques such as circular dichroism (CD) and atomic force microscopy (AFM) in addition to thioflavine T fluorescence spectroscopy.

Keywords: Beta Amyloid (Aβ), Fibril Formation, Acetylcholinesterase (AChE), Butyrylcholinesterase (BChE).

Abstract No.132

Effects of Ionic Strength and Chaotropic Agents on Lysozyme Aggregation

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Protein aggregation is an important topic in biological research, and investigations on the mechanisms of amyloid aggregation in brain and other tissues is of prime importance. Human lysozyme (HuL) is an amyloidogenic protein that its mutant variants cause hereditary systemic amyloidosis. Since hen egg white lysozyme (HEWL) and HuL have a high degree of structural and sequential homology, it has been used as a model protein in this study to investigate the mechanism of amyloid formation of proteins. In this study we examined different concentrations of sodium chloride (0.1, 0.3, 0.5, 1, 1.5, 50, 100 and 500 mM NaCl) to see at which concentration of NaCl the lysozyme aggregation could be affected significantly. Our investigation showed that at all of the above concentrations, aggregation of lysozyme still occurred. Our results showed that only 500 mM concentration of sodium chloride could decrease aggregation of lysozyme molecules significantly. We obtained our data through Thioflavin T (ThT) fluorescence, circular dichroism (CD) spectroscopy and atomic force microscopy (AFM). In the continuation of present study we will also examine different concentration of chaotropic agents such as urea, guanidine hydrochloride (GuHCl) and guanidinium thiocyanate (GITC) on lysozyme aggregation. In vitro experiments not only help to decipher the complex molecular mechanisms of amyloid fibrillation, but also would help to design therapeutic agents against devastating pathological conditions such as neurodegenerative diseases and systemic amyloidosis.

Keywords: Aggregation, Hen lysozyme, Ionic strength, Chaotropic agent, Amiloid fibrils.
