National Institute of Technology Rourkela

Synopsis Seminar

Seminar Title	: Optimization of metal oxide nanoparticle-induced conformational dynamics and associated flocculation of α-Synuclein and RNA for biological applications
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Venue	: LS office
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Abstract	: The advent of nanotechnology has been immense in recent times in biomedical research, especially for using metal nanoparticle due to its tunable size and surface physicochemical properties. The prominence of metal nanoparticles in physiological environment needs to be assessed thoroughly to understand the subsequent changes after its exposure to a multifaceted biological system. The biomolecules as per their affinity and concentrations in the biological system, interacts with the nanoparticle interface, resulting in a continuous process of adsorption and desorption. This leads to formation of dynamic nano-corona that decides dispersivity and cytotocompatibility of the nanoparticle. Thus, the interactions of protein or RNA biomolecules (relatively dynamic biomolecules of cytosol) with metal nanoparticle surfaces provides valuable insights about its interfacial behaviour in biological milieu. Moreover, the effect of such interactions help in understanding the associated conformational changes in biomolecules that can either be beneficial or detrimental. The current work explores the influence of metal oxide nanoparticle on conformational dynamics and associated biomolecule-nanoparticle complex formation, i.e., flocs formation. The work initially focused on the interactions of bare and surface functionalised zinc oxide nanoparticles (ZnONPs) with intrinsically disordered protein (IDP), likeα-synuclein (αS), which upon misfolding leads to onset/progression of Parkinson&rsquos disease. The findings provide insights on ZnONP-mediated mitigation of protein fibrillation propensity and aggregation-mediated cytotoxicity. It was observed that the ZnONP interfaces, with moderated physicochemical properties, efficiently trap αS monomers into nano-corona forming the non-amyloidogenic and non-cytotoxic flocs. Furthermore, the oxidative stress, serves as a critical molecular mediator of different irreversible changes in biomolecules, like glycation, which is anticipated as another pathophysiological mechanism underlying the neurodegenerative disease. The glycation of protein occurs when an aldehyde or ketone group of sugar reacts with the amino group of protein in a non-enzymatic process and the subsequent formation of reactive oxygen species further leads to advanced glycation end-products formation. Therfore, the second objective of the thesis focused on understanding the effect of ZnONP interfaces on moderating αS glycation and consequential formation of toxic intermediates associated with aggregation of the glycated protein. It was observed that αS adsorption onto ZnONP surfaces reduces the extent of glycation by sterically inhibiting the initial interaction between the oxidation-prone amino acid side chains and glycating agents. This occurs by preferentially sequestering αS monomers into nano-corona, forming flocs. The nanoparticle-based moderation of the protein amyloidosis and glycation were predominantly dependent on the biomolecule-induced flocculation by entropically trapping the molecule in flocs. Therefore, to validate this observation we selected another dynamic biomolecule i.e., RNA whose structure and stability is dependent on entropically driven processes, like base stacking, water release into surroundings. Hence, the third object of the thesis explored the interfacial interaction of RNA with iron oxide nanoparticle (FeONP) and the resulting complexes&rsquo stability in presence of RNase A nuclease. Like the IDP, the adsorption of RNA onto FeONP surface entropically traps the biomolecule into flocs and exhibited conformational stability against RNase A mediated degradation due to steric hindrance. Thus, the overall work indicated that the optimized interfacial interaction, via moderating physicochemical properties of the nanoparticle, with biomolecules, like αS and RNA leads to flocs formation. Therefore, it can be used in nanoparticle-based approaches for biological applications to likely delay the onset/progression of PD or to enhance the shelf-life of RNA-based therapeutic formulations.