Abstract

Self-assembly process of proteins into defined higher order structures is a fundamental process which influences both structural and functional properties of many tissues in human body. Formation of amyloid fibrils due to protein aggregation is known to cause several medical complications such as the onset of various neurodegenerative diseases, complications during DNA-recombinant synthesis and formation of aggregates during storage of protein therapeutic agents. Because the process of protein aggregation has lethal impacts, it is necessary to find effective strategies to target such aggregation process. One of the straight forward strategies for targeting protein-aggregation linked diseases is to find potential inhibitors against such aggregation process.

This work has focused on making of stable and effective nanoparticles coated with inhibitor molecules to target the amyloid aggregation of selected globular proteins, considering them as convenient model amyloidogenic proteins. This work has also explored the effect of selected surface-functionalized nanoparticles on collagen fibril formation. First section of this thesis covers a fundamental investigation of amyloid aggregation of a single metabolite phenylalanine and its effect on amyloid formation of globular proteins, exploring the critical role of hydrophobic and aromatic side-chains during protein aggregation. Next sections of this work have explored the inhibition effect of piperine-coated gold nanoparticles and capsaicin-coated silver nanoparticles against aggregation of insulin and serum albumin respectively. Finally, the inhibition effect of nanoparticles coated with aromatic residues has also been tested on collagen fibril formation under *in vitro* conditions. The results signify a unique approach to target protein aggregation through nanoparticle based inhibitors.

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