Silane Modulation of Protein Conformation and Self-assembly | Biological Engineering

08/04/2017

Abul Bashar Mohammad Giasuddin
Doctoral Candidate Dissertation Defense
Department of Biological Engineering

Advisor - David Britt, 435-797-2158
david.britt@usu.edu

Downloadable PDF

Full Abstract

Proteins may self-assemble and form insoluble amyloid type fibrils, which are responsible for diseases like Parkinson’s, Huntington’s, Mad Cow Disease, Cataracts, Spongiform Encephalopathy, and Alzheimer’s. Amyloid fibrils comprised of highly ordered #-sheet stabilized by an extensive network of intermolecular hydrogen bonds, hydrophobic surfaces, and favorable packing of side chains. Due to these highly-organized structures, amyloid fibrils are resistant to degradation and depolymerization. This research investigated the use of hydrophobic silane based polymeric nanoparticles to inhibit fibrillation of a model globular protein, #-Lactoglobulin (BLG). After a comprehensive hydrolysis and condensation study of two hydrophobic silanes, 3,3,3,-trifluoropropyl methoxy silane (3F) and n-propyltrimethoxy silane (nPM), nanoparticulate forms of these silanes were assessed for antifibrillation activity. Fluorinated hydrophobic polymeric nanoparticles successfully inhibited amyloid fibrillation through modulation of the secondary structures of BLG, resulting in the formation of nanocomposite particles rather than self-assembling into fibrils. In contrast, the non-fluorinated nanoparticles failed to inhibit fibrillation. The success of the inhibition of the amyloid fibrillation by the fluorinated silane-based polymeric nanoparticles led to further investigation on their use as: 1) carriers for small hydrophobic drug molecules, and 2) enhancing the structural and chemical properties of spider silk protein assemblies. An array of analytical tools, including optical density, dynamic light scattering, atomic force microscopy, scanning electron microscopy, infrared spectroscopy, fluorescence spectroscopy, and molecular modeling were employed in these studies. From this research, the hydrolysis and condensation pathways of trifunctional hydrophobic silane monomers were characterized and optimized, and a new facile one-step and environmentally friendly method for synthesizing superhydrophobic silica nanoparticles developed. Applications of the resulting nanoparticles in modulating protein secondary structure, inhibiting protein self-assembly, and as carriers for hydrophobic drugs were demonstrated from this research.