Abstract

Self-association of proteins into higher order structures such as amyloids and collagen-assemblies is a fundamental process in biology. In nature, the self-assembly process of triple-helical collagen molecules is known to generate higher order structures which are vital to both structural and functional properties of extra cellular matrix. However, the process of amyloid formation of proteins is mostly linked to many health complications including a series of neurodegenerative diseases. Until now, ~40 different proteins including huntingtin, α-synuclein and lysozyme are known to form disease-linked amyloids. To understand the mechanism of diseases linked to amyloid formation and excess collagen accumulation, it is critical to unravel the underlying principles of such process of self-assembly of soluble proteins/peptides into insoluble higher-order structures.

This work has explored the effect of selected proteins, natural compounds and surface-functionalized nanoparticles on the aggregation of both collagen and amyloidogenic proteins. Different biophysical techniques were used to understand the effect of these compounds on the conformation, activity and aggregation properties of selected proteins. Further, *in silico* studies were performed to identify crucial biomolecular interactions. Important findings are: (a) type I collagen prevents amyloid formation of lysozyme; (b) evidence of rapid coaggregation among proteins during amyloid formation; (c) capsaicin inhibits collagen fibril formation and increases the stability of collagen fibers; (d) eugenol prevents amyloid formation of globular proteins; (e) strategically designed surface-functionalized nanoparticles show anti-amyloid activity. These findings improve our mechanistic understanding of protein aggregation process which may possibly facilitate the development of therapeutics against pathologies related to protein aggregation.

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