Abstract

In the twenty-first century, one of the most calamitous consequences of misfolded proteins is protein aggregation inside the biological system to produce toxic amyloids, which impair normal functioning of cells and trigger symptoms of various life-threatening disorders, commonly known as amyloidosis. Surprisingly, no particular medications are available for clinical therapy to prevent amyloidosis. Hence, extensive research in that area is very much necessary to overcome amyloidosis-related diseases.

The present thesis is focused on possible ways to prevent amyloidosis or removal of fibrils. Firstly, a novel nanocomposite biomaterial has been established by making use of graphene quantum dots (GQDs) based series of nanocomposites and a modified GQDs that exhibited super disintegrating properties for amyloids (reversal of monomers from amyloids). In the next work, some small organic molecules have been well-thought-out to assess whether these molecules can modulate the fibrillation process or not to prevent the forward process toward matured fibrils.

The detailed experimental results highlight that our as-synthesized nitrogen-doped-GQD-decorated cobalt hydroxide (Co-NGQD) showed a very high degree of alienation of insulin amyloids (AIns), which gets reflected in the diminution of thioflavin T fluorescence (arising out of amyloid fibrils) more than 85% even at 10 μg/mL dose. Besides, AIns get reverted exclusively into soluble monomeric insulin forms. Importantly, cytotoxicity of the end products after administration of Co-NGQD to AIns has been found to be drastically diminished in the presence of Co-NGQD. We expect that our findings provide a valuable synergy toward eradicating amyloidogenic diseases by simple application in the form of nanomedicine.

In the next study, we have introduced two small organic molecules, folic acid (FA) and methotrexate (MTX), to prevent serum albumin fibrillation. In the presence of FA, the thermal fibrillation of bovine serum albumin (BSA) is considerably suppressed, and that with human serum albumin (HSA) is almost fully suppressed. On the other hand, MTX completely prevents both BSA and HSA fibrillations. These discoveries are also expected to provide clinical potential therapeutic values for possible medications with structural similar small organic molecules.