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Functionalized Titanium Dioxide Nanoparticles for Targeting and Disrupting Amyloid Fibrils

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Abstract : Amyloidoses are a family of diseases characterized by abnormal protein folding that leads to aggregation. They accumulate to form fibrillar plaques which are implicated in the pathogenesis of Alzheimer, prion, diabetes type II and other diseases. To the best of our knowledge, despite extensive research efforts devoted to plaque aggregates inhibition, there is yet no cure for this phenomenon. Titanium and its alloys are found in growing interest for biomedical applications. Variety of surface modifications enable porous, adhesive, bioactive coatings for its surface. Titanium oxides (titania) are also being developed for photothermal and photodynamic treatments. Inspired by this, we set to explore the effect of functionalized titania nanoparticles in combination with external stimuli, as potential photothermal ablating agents against amyloids. Titania nanoparticles were coated with bi-functional catechol derivatives (dihydroxy-phenylalanine propanoic acid, noted DPA) to gain targeting properties. In conjunction with UV-radiation, these nanoparticles may selectively destroy the vicinity of their target. Titania modified 5 nm nanoparticles coated with DPA were further conjugated to the amyloid-targeting Congo Red (CR). These Titania-DPA-CR nanoparticles were found to target mature amyloid fibril of both amyloid-β (Aβ 1-42 a.a). Moreover, irradiation of the peptides in presence of the modified nanoparticles decreased the aggregate content and oligomer fraction. This work provides insights into the use of modified titania nanoparticles for amyloid plaque targeting and photothermal destruction. It may shed light on future modifications and functionalization of titania nanoparticles for different applications.

Keywords : titanium dioxide, amyloids, photothermal treatment, catechol, Congo-red
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