Mod Chem Appl 2018, Volume 6
DOI: 10.4172/2329-6798-C2-012

Dual monitoring and inhibition of amyloid aggregation using luminescent rhenium complexes of bis(benzothiazole)-based tetraarylethylenes

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Dual monitoring and inhibition of amyloid aggregation using luminescent rhenium complexes of bis(benzothiazole)-based tetraarylethylenes: The deposition of amyloid beta (Aβ) peptides in the human brain is the main pathological hallmark of Alzheimer's disease (AD). Luminescent probes targeting Aβ aggregates are promising tools for advancing early diagnosis and therapy of AD. In this work, luminescent tricarbonyl rhenium complexes of tetraarylethylene (TAE) ligands are developed for monitoring amyloid aggregation. The photophysical properties of the complexes, as well as their binding affinities to amyloid aggregates, are tuned by variation of the number of thiophenes in the TAE ligands. These complexes display selective turn-on response with large Stokes shift upon binding to amyloid fibrils and can be extended for *in vitro* diagnostic applications. Compared to thioflavin T, these probes are more sensitive in the detection of early-stage amyloid fibrillation and possess submicromolar binding affinities towards Aβ42 fibrils. Additionally, the general and modular design approach implemented in this study should facilitate the development of second-generation TAE-based diagnostic tools for studying protein aggregation in an AD. Theranostics that integrate therapeutic and diagnostic functionalities have emerged as promising tools to overcome the weakness of the current approaches in AD therapy. Polyphenols, such as curcumin and epigallocatechin 3-gallate (EGCG), have shown *in vitro* and *in vivo* ability to suppress amyloid fibril formation. Structurally modified rhenium complexes of bis(benzothiazole)-based tetraarylethylenes that possess polyphenolic groups found in small molecules that are known to impede fibril oligomerization were developed. The polyphenolic-containing complexes function as theranostic tools for monitoring as well as inhibiting amyloid aggregation. The luminescence profiles of these complexes displayed increased emission (in a sigmoidal manner) in response to the three phases of amyloid fibril formation: lag phase, exponential growth phase and finally stationary phase. Luminescence studies and atomic force microscopy (AFM) revealed inhibition of Aβ42 aggregation by these complexes *in vitro*. A neuroprotective effect of the polyphenolic-containing complexes against Aβ42-induced cytotoxicity in neuronal cells was also demonstrated. This work would open up new avenues in the development of theranostic tools for neurodegenerative diseases.

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