A NOVEL PHOSPHONIUM DYE FOR AMYLOID FIBRIL DETECTION

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Protein misfolding coupled with the formation of insoluble aggregates, amyloid fibrils, is currently associated with a number of human diseases [1]. One of the main approaches to detection and characterization of amyloid fibrils is based on monitoring the fluorescence changes of Thioflavin T (ThT) and a range of novel markers [2]. Despite being widespread, ThT suffers from the two main drawbacks: i) it may affect the stability of fibrillar intermediates; ii) the spectral properties of ThT are dependent on pH and fibril morphology. In view of this, a variety of new fluorescent probes are continuously evaluated for their ability to serve as the markers of amyloid fibrils. In the present study a novel phosphonium dye TDV1 has been tested for its sensitivity to the amyloid fibrils of cationic protein lysozyme and anionic protein albumin prepared *in vitro* by incubation of the protein solutions (glycine buffer, pH 2) at 60 ºC for 14 days. TDV1 displays a weak fluorescence in polar solvents, excellent chemical and photophysical stability [3]. Furthermore, this dye has been employed *in vivo* as DNA minor-groove binder and as a marker of the mitochondrial potential due to its low toxicity and highly efficient cellular uptake. The analysis of TDV1 fluorescence spectra showed high specificity of the probe to amyloid fibrils, along with a more pronounced fluorescence response compared to ThT. Furthermore, TDV1 displayed the ability to sense the difference in the morphology of lysozyme and albumin amyloid fibrils in terms of the shift of the dye emission maximum and the change in its quantum yield. A novel technique for differentiating between amyloid fibril polymorphs through measuring the 3D fluorescence spectra of TDV1 has been developed. The potential sites of TDV1-fibril binding have been identified using the molecular docking approach.

References

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