Nanocomposites and nanomaterials

Fluorescent trimethine cyanine dyes for detection of protein amyloid aggregates

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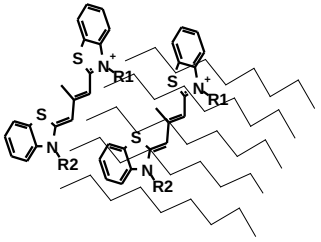
Nanosized unsoluble protein aggregates - amyloid fibrils possessing a cross-β structure have been found in many neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, etc. The wide use of recombinant proteins medicine required their tight quality control, particularly over the protein fibrillization products. Besides, the study of the fibrillization mechanism could provide a new insight into the pathogenesis of amyloid diseases and finally lead to developing of the agents preventing protein aggregation.

Here we report fluorescent trimethine cyanine dyes containing different N,N'-substituents (R1 and R2, see Fig.) as probes for sensitive detection of amyloid fibrils (insulin and lysozyme were used as model proteins) and monitoring of the fibrils formation.



The studied dyes are slightly fluorescent in free state and in the presence of monomeric proteins; but their emission intensity increases in dozens of times upon formation of fibril seeds and their next growth. It was shown that the nature of N,N'- substituents could determine the affinity of the dye molecule to the fibrillar formation of certain protein. The dyes containing alkyl groups, hydroxy groups and phenyl groups as N,N'-substituents are more sensitive to fibrils formed by lysozyme; at the same time, cyanines with quaternary amino group give more pronounced fluorescent response in the presence of insulin fibrils. The presence of N,N'-alkyl sulfo group in the molecule results in the same sensitivity of dye molecule to both fibrillar proteins.

Fluorescent response of cyanine molecule is associated with its fixation in the β-pleat (groove) of amyloid fibril. The specificity of dyes to different fibrillar proteins could be explained by interaction between the N,N'-substituents of dye with side residues of amino acid chains.