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A designed small molecule as a potent inhibitor of insulin amyloid formation

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Amyloidogenesis is a well-known phenomenon observed in various diseases like Alzheimer's, Parkinson's, Diabetes Mellitus type-II etc.¹ Recent research associated with amyloidosis mainly focuses on the understanding of the process itself and finding of potential fibrillation inhibitors. With the increase in the number of diabetic patients, many cases of insulin amyloidosis have been reported all over the world. Injection amyloidosis is a medical condition in which extracellular mass of amyloid fibrils is observed at repeated insulin injection site in type II diabetic patients.²

In the present study, the inhibitory effect of an oligo-pyridyl based small organic molecule on insulin fibrillation was studied using Thioflavin T fluorescence assay (ThT assay), Circular Dichroism (CD) and Transmission Electron Microscopy (TEM). The fibre formation was less in case of molecule treated insulin and was confirmed by ThT assay. The secondary structural transition from α -helix (in native insulin) to β -sheet (fibrillated insulin) was also found to be reduced which correlates with the less fibrillation. Short and thin fibrils observed in TEM imaging gives a morphological insight of the fibril assembly formed in the presence of the molecule. Structure Activity Relationship (SAR) studies gives an insight into the important interactions of different segments of the molecule with the protein to inhibit the fibrillation process. Further studies are in progress to see the cytotoxic effect of insulin aggregates and its inhibition in presence of the molecule. This study will show the importance of various hydrophobic and hydrophilic interactions to inhibit insulin fibrillation.

References and Notes:

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