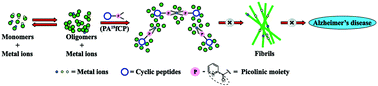
**Cyclic peptidomimetic with copper chelating ligand inhibits fibrillogenesis of Amyloid-β**

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**Abstract**

Amyloid-beta peptide (Aβ) misfolding and formation of toxic oligomer followed by fibril formation is one of the major causes of Alzheimer’s disease. On the other hand, excessive deposition of copper, zinc and iron also promotes amyloid aggregation. In recent times, several cyclic peptides modified in various ways have been used as potential amyloid inhibitors. Head-to-tail cyclic peptides with alternating D, L amino acids inhibits amyloid formation significantly. Herein, we report our designed head-to-tail cyclic peptidomimetics with only one D-amino acid in the sequence that shows significant inhibition of amyloid aggregation when used in 2-fold molar excess to that of Aβ. In one of our designed peptidomimetics we have attached a copper chelating ligand and investigated its efficacy towards amyloid aggregation inhibition and confirmed by various bio-physicals tools such as thioflavin T (ThT) fluorescence assay, dynamic light scattering (DLS), transmission electron microscopy (TEM), and Congo-red stained birefringence studies. The non-toxicity of our designed cyclic peptidomimetics was confirmed by the MTT assay on the mouse neuronal cell line. Such peptidomimetics works synergistically, firstly by restraining the conformational change in Aβ-peptide and also restores metal ion homeostasis. Such peptidomimetics can be of great help in understanding the mechanism of Aβ-aggregation and can prove to be a novel therapeutic approach.1



**Figure 1.** Graphical representation of working mode of the cyclic peptidomimetics inhibiting Aβ-aggregation.

**Keywords:** Alzheimer’s disease, Amyloid fibrils, Metal chelation.

**References:**

[1] Kalita, S.; Kalita, S.; Kawa, A.H.; Shill, S.; Gupta, A.; Kumar, S.; Mandal, B. *RSC Medicinal Chemistry*, **2022**,*13*, 761.