

# A natural heptameric peptide exhibits multifaceted inhibitory role in the fibrillation pathway of amyloid-beta

Rajanya Bhattacharyya<sup>1</sup>, Sayan Bhattacharjee<sup>1</sup>, Bani Pathak<sup>1</sup>, and JAYATI SENGUPTA<sup>1</sup>

<sup>1</sup>Indian Institute of Chemical Biology CSIR

May 5, 2020

## Abstract

**Background and Purpose** Alzheimer's disease (AD) pathogenesis involves amyloid- $\beta$  (A $\beta$ ) aggregation where the intermediate oligomers are considered the prime toxic species. Here, we aimed to identify an effective peptide sequence from a medicinal plant-derived enzyme having anti-amyloidogenic properties against A $\beta$ . **Experimental Approach** LC-MS/MS followed by computational analysis identified the active peptide (termed here as Pactive). Visualization techniques along with biophysical and biochemical approaches were used to determine the anti-amyloidogenic potency of the purified enzyme and peptides identified from the enzyme. Cytotoxicity was measured on SHSY-5Y cell lines. Interaction studies were done with bio-layer interferometry (BLI) and bio-stability of the peptide was assessed by NMR. Pactive induced conformational alterations of A $\beta$  monomer and oligomers was determined with DSC and NMR. **Key Results** A small heptameric peptide (Pactive) identified from a medicinal plant-derived fibrinolytic enzyme proved to be a multifunctional inhibitor against A $\beta$  aggregation. The results suggested that Pactive arrests A $\beta$  molecules in non-toxic off-pathway oligomers that can no longer participate in the cytotoxic fibrillation pathway. Mechanistically, Pactive binding induces conformational alterations in the A $\beta$  molecule, thus modulating its hydrophobicity, one of the key players in inducing aggregation. **Conclusions and Implications** The study identified a natural peptide Pactive (GFLHQQK) that displays potential anti-amyloidogenic properties against A $\beta$  aggregation. The bio-stability of Pactive in human blood serum as well as its non-toxic nature makes it a promising therapeutic candidate against Alzheimer's, for which no disease-modifying treatments are available till date.

## Hosted file

Bhattacharyyaetal\_BJP\_Final18March2020.pdf available at <https://authorea.com/users/304978/articles/435557-a-natural-heptameric-peptide-exhibits-multifaceted-inhibitory-role-in-the-fibrillation-pathway-of-amyloid-beta>

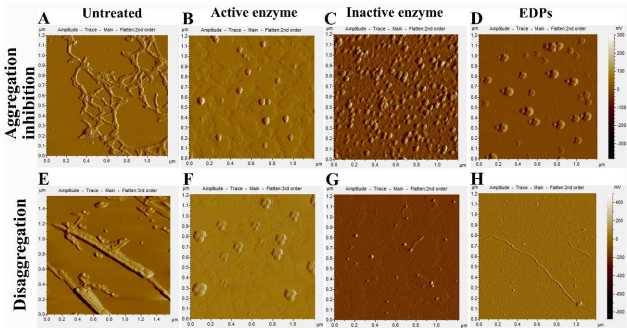


Figure 1