INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	ASHIM PAUL
Roll Number	:	10612244
Programme of Study	:	Ph.D.

Thesis Title: Development of New Strategies for Peptide Based Drug Design against Alzheimer's Disease.

Name of Thesis Supervisor(s)	:	Dr. Bhubaneswar Mandal
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SHORT ABSTRACT

The thesis entitled, "Development of New Strategies for Peptide Based Drug Design against Alzheimer's Disease", is divided into six main chapters along with the experimental section and future directions. The thesis mainly focused on the development of peptide based molecules to modulate the aggregation of Amyloid-β peptide which is the main culprit peptide for Alzheimer's disease. The *in-vivo* aggregation of Amyloid β peptide (Aβ, a 39-42 residue polypeptide) to form cytotoxic oligomers and amyloid fibrils that causes in cell damage in brain and the pathogenesis of Alzheimer's disease. In this thesis, we have described the importance of aromatic amino acids for amyloid formation and showed that the aromatic side chain of peptide sequence interacted prior to the conformational transition or backbone interaction. We have developed anthranilic acid containing β-sheet breaker α/β-hybrid peptide (BSBHp) as a potent inhibitor against Aβ peptide aggregation, also showed its efficacy to disrupt the preformed fibrillar aggregates of Aβ into non-toxic species. We also developed a pro-drug peptide (PDp) which can aligned with the Aβ aggregates and generated kink *in situ* that disrupts the Aβ aggregates into non-toxic species. Finally, we have developed a synthetic zipper peptide which selectively arrested Aβ peptide and the presence of N-methylation in its construct stopped the self-aggregation of Aβ peptide and disaggregates the Aβ amyloid into non-toxic species. All the developed peptide based molecules have shown significant efficacy on the disruption of Aβ aggregates present in the human-cerebrospinal fluid. These peptide based molecules have shown significant anti-Alzheimer's activity *in vitro* and can be used as lead molecules against other amyloid associated diseases.