INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study	:	**Ph.D.**

Thesis Title: **Study of sequence dependent in-situ peptide cyclization and its applications as biomolecules**

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The peptides are gaining escalating recognition due to its progress in the area of biotechnology and bioengineering. The work presented in the thesis mainly centred on the design and synthesize of side chain modified peptides which can form cyclic peptide *in situ* at the physiological condition without the need for any external reagents *in-vitro*. Further, the cyclization concept has been applied to release bioactive molecules and also to inhibit the protein aggregation. Peptides are early leading for the realistic design to deliver bioactive molecules as they can provide target specificity, potency, resistance towards chemical or enzymatic hydrolysis and longer resident times for more effective duration of action to improve biological efficacy and minimize side effects. In the second chapter, a quick conversion of a smartly designed linear tri-peptide (RXE, X= P/ A/ G) into the cyclic one has been demonstrated to release the bioactive molecules in a controlled manner *in-vitro*. This method may be a new direction to design peptide-drug conjugates where no external stimuli will be needed to release the drug. On the other hand, an increasing number of human diseases seem to be associated with protein aggregation, which directly contributes to or modulates the associated pathology. Amyloids are insoluble protein aggregates with highly ordered β-sheet conformations that differ from its native states conformation. Misfolding and aggregation of the amyloid β (Aβ) peptide into fibrillar aggregates is a cause of Alzheimer's disease (AD) which is a progressive neurodegenerative disorder and the most common form of dementia. Various strategies are being developed for the treatment of Alzheimer's disease though there is no cure available till date. In the third and fourth chapters, *in situ* side chain peptide cyclization has been introduced as a β-sheet breaker strategy, and this is a promising therapeutic approach against AD and related disorders. In the fifth chapter, inspiring from the concept of aspartimide formation; N→N and **O→N** acyl migration have been applied to release the bioactive molecules *in-vitro*.