National Institute of Technology Rourkela

Registration Seminar

Seminar Title	: Glycosylation Effects on the Stability and Aggregation of Peptides and Proteins: A Computer Simulation Study
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Venue	: Seminar Room, Chemistry Department
Date and Time	: 30 Apr 2025 (4 PM)
Abstract	: The applications of protein-based therapeutics in diseases have led to a substantial growth in the field of molecular pharmacology in recent decades. A series of physical and chemical instability problems occur during the production, purification, storage, and delivery, impacting therapeutic efficacy. Aggregation or self-assembly is a common but unwanted process that alters the pharmacokinetic properties of peptides and proteins. On the other hand, the stability of proteins is an essential parameter for therapeutic development. Aggregation generally happens due to the non-covalent association of polypeptide chains. Such a phenomenon reduces the physical stability of peptides and proteins, creating toxicity and immunogenicity. Therefore, preventive measures need to be taken to inhibit such processes. Glycosylation, a post-translational modification involving the attachment of sugar moieties to proteins, has been shown to enhance protein stability and prevent aggregation. However, controversy exists on its effects on proteins. Insulin aggregation presents a significant challenge in diabetes management, as it affects insulin's bioavailability and therapeutic efficacy. This study focuses on the effects of glycosylation of a peptide fragment of insulin, a sequence known for its amyloid-like fibril formation. The peptide at the asparagine (N) residue was glycosylated with single mannose and di-mannose, and their aggregation propensity was investigated using atomistic molecular dynamics (MD) simulations. Additionally, we attempted to explore the effects of glycosylation on insulin monomers by attaching mannose at multiple sites in different combinations and performing MD simulations at both physiological (300K) and elevated (400K) temperatures. We believe our findings will provide insights into the stabilizing and aggregation inhibition due to glycosylation and its potential role in preventing insulin fibrillation, contributing to the development of improved insulin formulations for diabetes treatment.