# ABSTRACT

## X-RAY CRYSTALLOGRAPHIC STUDIES ON SOME NON-CODED AMINO ACID-BASED PEPTIDES

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Non-coded amino acid-based synthetic peptides have gained significant interest due to their potential applications in various fields, such as therapeutics, nanotechnology, antibacterial activity, vaccine development research, etc. Because of their huge importance in various fields, designing new peptides based on non-coded amino acids in different structures is always challenging, as is synthesizing other peptides for applications.

**Chapter 1** includes a brief introduction and background study of non-coded amino acid-based peptides ($\alpha$, $\beta$, and $\gamma$ hybrid peptides) and their potential uses in various fields were discussed through X-ray crystallographic studies.

**Chapter 2** contains methodology studies, including peptide crystallization and stepwise single crystal crystal XRD studies of non-coded amino acid-based peptides.

**Chapter 3** contains a study that elucidates the conformational characteristics of the achiral α/β hybrid peptide Boc-[Gly-tBuβ3,3Ac6c]4-OMe(P1) through a single crystal XRD study. Mixed intra-molecular $C_{12}$, $C_{22}$, and $C_{26}$ type H-bonds and solvent molecules (water) mediated H-bonds stabilize the overall structure of the octapeptide **P1**. Adding bulky groups like tBu$\beta^{3,3}$Ac$_6$c in $\beta$-residues leads to specific preferences for the ($\phi$, $\theta$, $\psi$) torsion angles of the β-peptide, which leads to overall conformational preferences in the $\alpha/\beta$ hybrid peptide. We have discovered a unique paper clamp-like fold, observed in **P1**, which has not been reported in natural or any synthetic non-coded amino acid-based peptides

**Chapter 4** deals with a study that elucidates the conformational characteristics of chiral α-L-amino acid and $\beta$3,3Ac$_6$c dimeric repeats in $\alpha/\beta$ hybrid peptide, Boc-[Leu-$\beta^{3,3}$Ac$_6$c]$_4$-OMe(**P2**) through a single XRD study. Four molecules are present in the triclinic space group due to solvent-mediated symmetry breaking. The self-assembly of peptide **P2** forms channels filled with solvent molecules (dioxane and ethanol) that present interesting patterns in the crystal packing. This comparison with the previously published similar structures of tetrapeptides and pentapeptides containing $\alpha/\beta$ hybrid peptides confirms that there are specific preferences for the ($\phi$, $\theta$, $\psi$) torsion angles for $\beta^{3,3}$Ac$_6$c peptides and such $\alpha/\beta$ hybrid dimeric repeats can indeed lead to helical folds stabilized by $C_{11}/C_9$ H-bond even in much longer peptides.

**Chapter 5** contains a study that elucidates the conformational and supramolecular interaction studies of α/γ hybrid tripeptides, Boc-X-$\gamma^{4L}$Phe-$^{L}$Val-OMe (**P3-P7**) where X is an *L/D* amino acid ($^{D}$F/$^{L}$F/$^{D}$A/$^{D}$L, and $^{L}$P) through a single crystal XRD study. We have discovered a tri-peptide-based β-hairpin fold that is stable without any intramolecular H-bonded interactions, which is normally observed in such β-hairpin fold. This fold remains stable even with changes in the sequence of the tri-peptide by varying the first amino acid with the L/D configuration in the sequence.

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