Chapter 1: The section A of this chapter describes novel conformationally ordered $\alpha/\beta$-hybrid peptides derived from repeating L-proline and anthranilic acid building blocks. These oligomers adopt a compact, right-handed helical architecture and have ability to display an unusual periodic pseudo $\beta$-turn network of 9-membered hydrogen-bonded rings formed in forward direction of sequence by 1$\rightarrow$2 amino acid interactions, both in the solid and in the solution-state. These oligomers involving only two amino acid residues in the turn formation, is in stark contrast to the native $\beta$-turns that involve four residues to form H-bonded network featuring backward 1$\leftarrow$4 amino acid interactions.

Fig. 1: Molecular structures of oligomers with repeating sequence of proline (Pro) and anthranilic acid (Ant) residues.

The section B of this chapter describes the structural modulation of Ant-Pro oligomers by chirality alteration of the proline residues. The results suggest that the chirality altered oligomers show well-defined helical conformation featuring 9-membered hydrogen bonding interactions. The homochiral oligomers display right-handed helical architectures. On the contrary, the heterochiral oligomers display left-handed helical architectures.

**Fig. 2:** Molecular structures of Ant-Pro oligomers with chirality modulation of proline (Pro) residues.

This section also describes hydrogelation property of a hetero foldamer (7) featuring alternating anthranilic acid-proline residues on the backbone. Substitution modulation of the aromatic rings unequivocally suggests that the iodine atoms on the Ant ring and chloride counter anion plays pivotal role in the hydrogelation process. Rheological and morphological studies suggest that the foldamer 7 forms distorted spherical particles connected by a bridge or loop and leading in a networked structure with enhanced viscosity and elasticity.
Fig. 3: Molecular structure of foldamers showing different substitutions on the aryl ring.

[Iodine-specific hydrogel formation of Ant-Pro hetero foldamers.
Kale, S. S.; Kotmale, A. S.; Dutta, A. K.; Sudha, J. D.; Rajamohanan, P. R.; Ajayaghosh, A.; Sanjayan, G. J. (Manuscript to be communicated)]

The section C of this chapter describes the design and synthesis of Ant-Pro oligomer-xanthine conjugates as potential adenosine receptor antagonist.

Fig. 4: Molecular structures of Ant-Pro oligomer-xanthine conjugates.

Chapter 2: This chapter deals with the influence of orthanilic acid (2-aminobenzenesulfonic acid, $^8$Ant) on the conformational preferences of hybrid oligomers.

The first part of this chapter describes the influence of sulfonamide on the conformational preferences of (Pro-$^8$Ant-Aib)$_n$ hybrid oligomers and comparison of carboxamide vs sulfonamide in peptide folding. (Pro-$^8$Ant-Aib)$_n$ oligomers containing sulfonamide displays 11-membered hydrogen bonded right-handed helical conformation. On the contrary, the corresponding carboxamide (Pro-Ant-
Aib)_n oligomers show 6-membered H-bonded left-handed helical conformation in both solid and solution-state.

![Chemical structures and molecular models](image)

**Fig. 5:** Molecular structures of (Pro-S-Ant-Aib)_n oligomers. Crystal structures of tripeptide (14) and hexapeptide (15) displaying 11-membered hydrogen bonding.

[Carboxamide vs Sulfonamide in peptide backbone folding: A Case Study with a Synthetic oligomer.

This section also describes the conformational effect on 11-membered hydrogen bonding by modulation of (i+1) and (i+3) residue of (Pro-S-Ant-Aib) tripeptide building block. The solid-state and solution-state conformational investigations suggest that 11-membered hydrogen bonding is robust and sustain substantial conformational modulations.

![Chemical structures and molecular models](image)

**Fig. 6:** Molecular and PyMOL-rendered crystal structures of 16 and 17 showing robust C11 membered pseudo β-turn.

[Orthanilic acid-Promoted Reverse-Turn Formation in Peptides:
The second part of this chapter describes the conformational preferences of (Aib-$^5$Ant-Aib)$_n$ and (Aib-$^5$Ant-Pro)$_n$ hybrid oligomers. As part of this work, we also undertook efforts to understand the conformational effects of altering the amino acid sequences in the oligomer backbone. In case of (Aib-$^5$Ant-Aib)$_n$ oligomers, crystal structure of hexapeptide 19 displays 7 and 11-membered mixed hydrogen-bonding and in case of (Aib-$^5$Ant-Pro)$_n$, hexapeptide 22 displays six-membered hydrogen-bonding.

Fig. 7: (a) Molecular structures of (Aib-$^5$Ant-Aib)$_n$ oligomers and PyMOL rendered crystal structure of 19. (b) Molecular structures of (Aib-$^5$Ant-Pro)$_n$ oligomers and PyMOL-rendered crystal structure of 22.

[Effect of β-aminobenzenesulfonic acid on the conformational features of heterofoldamers.
Kale, S. S.; Kunjir, S. M.; Gawade, R. L.; Puranik, V. G.; Rajamohanan, P. R.; Sanjayan, G. J. (Manuscript under preparation)]

Chapter 3: This chapter deals with the design, synthesis and biological evaluation of novel hybrid analogues of nocodazole as potential tubulin binding agents. Nocodazole is an anti-neoplastic agent which interferes with the polymerization of microtubules. We have designed a series of hybrid analogues of nocodazole (24-27) as potential tubulin binding agents.

Hybrid nocodazole analogues (24-27) have been evaluated with combretastatin A4 under standard condition. The analogues (24, 25 and 27) show comparable IC$_{50}$ value for inhibition of tubulin assembly. This study shows that further modification of these analogues will be useful in the development of potent anticancer agents.

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Chapter 4: This chapter deals with a general synthetic route to bicyclic amino acid-carbohydrate-conjugates, which would be useful as conformationally restricted hydroxyethylamine (HEA) transition-state isosteres. The prominent features of this system are the bicyclic rigid core displaying $\alpha$-amino acid side chain and hydroxyethylamine moiety, both of which would be potentially important for receptor interactions, leading to various biomedical application.

Fig. 9: Designed strategy for amino acid-carbohydrate conjugates as potential conformationally restricted hydroxyethylamine (HEA) transition-state isosteres.

[Bicyclic amino acid-carbohydrate-conjugates as conformationally restricted hydroxyethylamine (HEA) transition-state isosteres: