Chapter 7

Concluding remarks

In this study several cyclic peptides and peptidomimetic compounds have been studied. Conformational and mechanistic aspects have been studied in detail. This understanding has led to incorporation of certain drug like features in these compounds. Prospective usage of cyclic peptides and peptidomimetic compounds as drug carriers and drug delivery systems has been discussed in detail. Delivery of an antibiotic at target using peptide nanotubes has been simulated. Advantages associated with such delivery are discussed. Main outcome of entire study may be summarized as follows:

1. Conformational aspects and mode of action of known transport antibiotics nactins have been studied. Several low energy conformations are possible with hydrophobic groups disposed outwards.

2. Cyclic transport antibiotics carry ions across bacterial cell membranes to be emptied inside cell. Their selectivity for large cations has been explained based on high influx of small cations leading to overall repulsive interactions.

3. Potency of cyclic compounds to act as transport antibiotic depends on conformational reorganization required to carry the ion. If ion is too strongly held by electrostatic interactions then compound’s capability to deliver ion inside bacterial cell is reduced leading to reduction in potency observed.

4. A series of cyclic peptidomimetic compounds were designed and evaluated for their use as preventive drugs in Alzheimer’s disease.
5. A lead compound with CH₂NH peptidomimetic backbone in a 2,4,2,4 cyclic system with gly, ala, and ethyl type substituents has been suggested as optimum choice with a balance of low conformational reorganization coupled with moderate electrostatic stabilization of zinc.

6. Molecular weight of suggested lead compound is appropriate with hydrophobic groups disposed outwards for facile diffusion through cell membrane and BBB.

7. Suggested lead compound is expected to remove zinc from human brain and body.

8. Cyclic peptides and peptidomimetic compounds have also been investigated as possible carriers of L-Dopa. A small cyclic compound with CH₂NH has been suggested as possible carrier of L-Dopa. This compound is expected to undergo passive diffusion through BBB to enhance drug’s bioavailability inside brain.

9. Drug is delivered from carrier at target by enzymatic or non enzymatic means. No premature explosion of drug from carrier is expected.

10. Some self aggregating cyclic peptide and peptidomimetic systems were studied to understand characteristics required for self assembly. The type of backbone and size of backbone determine the diameter of pore formed.

11. Flat cyclic systems with small substituents show better self assemblage. Highly hydrophobic backbone is not suited for self aggregation.

12. Nanotube formation of length up to 76Å was observed in (ala)₁₂ system with an optimum distance of 2.6 - 3.1Å between two adjacent systems.
13. Gentamicin delivery was studied utilizing a peptide cyclic system in trimer form to enhance its bioavailability and subsequently its therapeutic value.

This study has thus highlighted several interesting applications of cyclic systems in medicinal chemistry. Experimental progress along these lines may prove to be beneficial in medicine.