CHAPTER-5

SUMMARY
Synthesis of peptide analogues of somatostatin on a newly developed polymeric support is the main objective of the work. Due to the optimum hydrophilic-hydrophobic balance of the 1,6 HDODA-PS resin, compatibility of the growing peptide chain and the insoluble crosslinked polymeric support is much better than that of the standard Merrifield resin. The peptides were synthesised on a 2% HDODA-PS support.

Chapter 2 is review on peptidomimetics. It gives the methods for preparation of peptidomimetics giving examples. The review also describes imitation of secondary structures, scaffold peptidomimetics, non peptide mimetics and peptoids. A brief note on peptidomimetics of somatostatin is also included.

Chapter 3, which is the experimental section deals with the synthesis and functionalisation of polymer, synthesis of side chain protected amino acids, solid phase synthesis of peptides and their cyclisation via disulfide bond formation.

Results and discussion part is dealing with the characterization of the resin and side chain protected amino acids using IR spectroscopy characterization of peptides using HPLC and NMR. Purification of the linear and cyclic peptides are also given.

Somatostatin analogue peptides synthesised are
1. **Octreotide**

\[ \text{D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr} \]

2. **Tyr^3-Octreotide**

\[ \text{D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr} \]

3. **RC 160**

\[ \text{D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp} \]

The peptides were synthesised on 2% chloromethylated 1,6-HDODA-PS resin and 2% PS-DVB resin using Boc/benzyl ester strategy. In both cases final cleavage was done by TFA, containing 1,2-ethane dithiol, thioanisol and m-cresol. DCC/HOBt method was used for coupling. NMP was used as the solvent. After cleaving the peptides from the resin, they were purified and characterized by HPLC and NMR. The peptide was obtained in >90% yield on the PS-HDODA resin. But on the PS-DVB resin the peptides were obtained in about 60-70% yield. Purity was also better with PS-HDODA resin. Thus it is evident that the PS-HDODA resin is more suitable for peptide synthesis than is the Merrifield resin.

The linear peptide was hydrogenated to remove the side chain protecting groups and cyclised using iodine in methanol under nitrogen.
Since radiolabelled somatostatin analogues are used for the detection and treatment of carcinoid tumors there has always been a challenge for the large scale synthesis of these peptides in high purity. Synthesis of these peptides on the new resin, 1,6-HDODA-PS proves that the resin is highly suitable for the synthesis of biologically active peptides.