Summary
10. SUMMARY OF THESIS

Ideally, controlled drug delivery systems aim to deliver drug at a rate dictated by the needs of the body over the period of treatment and therefore the active agent should be transported solely to the site of action or as per the need of the disease. CDDSs are particularly designed to exert control on drug release to further enhance drug’s efficacy, safety and compliance. For therapeutic advantages for certain forms of pain management, psychiatric and sleep disorders, biphasic delivery systems where an initial rapidly releasing loading dose is followed by a more gradual controlled dose are increasing in popularity.

Thus, development of oral controlled release systems has been a challenge to formulation scientists because of the difficulty in localizing the system in target areas of the gastrointestinal tract. In practical terms, an oral controlled release system shall allow a reduction in dosing frequency as compared to when the same drug is presented as a traditional dosage form. Controlled release preparations using alternate routes have also been formulated but oral route still remains preferable.

This thesis presents an extension of applicability of the oral controlled drug delivery system for drugs with different solubility with different polymeric substances. The aim of this study was to formulate hydrophilic matrix tablets of different drugs as Metoprolol Succinate, Ambroxol HCl, Zolpidem Tartrate and Cinnarizine with a controlled drug release over a specific time period. For this purpose, HPMC K4M, K100M, K200M, Xanthan gum, Guar gum and different grades of Carbopol as Carbopol 934P, 974P, 971P, 71G and Polycarbophil were chosen as the matrix forming polymeric materials. The influence of polymer type and concentration on the physical properties and dissolution of the tablets were investigated. The release mechanisms of all the matrix formulations were examined.

- In general, designing monolithic controlled release drug delivery systems for providing 24 h release, especially for highly water-soluble agent, as Metoprolol Succinate is quite challenging. Thus present investigation was undertaken to fabricate controlled release monolithic matrix tablets and three layer matrix tablets of Metoprolol Succinate using different individual and combination of hydrophilic polymers as matrixing agent. The drug and the swellable polymer
were mixed together and compressed into monolithic and three layer matrix tablets which were capable for controlling the release of highly water soluble Metoprolol Succinate.

The objectives of the present study was to formulate Ambroxol HCl CR matrix tablets by direct compression using different hydrophilic swellable polymers and by melt granulation using different hydrophobic binders and investigate the influence of different polymer concentrations on drug release in matrices. Granules prepared by melt granulation exhibited better physical strength and have smoother surfaces than those obtained by wet granulation. Various waxes as Bees wax, Paraffin wax, stearic acid, Lubritab and Polymeg with HPMC K4M were used for melt granulation and investigated their different concentrations on drug release profile by $3^2$ full factorial design.

Rapid initial release of Zolpidem Tartrate enables rapid initial absorption, rapid onset of action and sleep induction and due to controlled release properties of the formulation, the prolonged action and consequently sleep maintenance can be achieved with the designed biphasic release Zolpidem Tartrate single layer monolithic matrix tablets, bilayer and compression coated tablets.

Floating drug delivery systems (FDDS) are among the several approaches that have been developed in order to increase the gastric residence time and controlled drug delivery of pH dependent Cinnarizine and was done by matrix formulation with different polymers and also $3^2$ optimization method was used using Carbopol 71G and sodium bicarbonate.

Thus, different approaches of controlled drug delivery system have been achieved with matrix formulation of drugs by suitable method using different polymers.

- The viscosity and proportion of polymers were major factors affecting the drug release.
- The difference between higher viscosity grades of the HPMC polymers as HPMC K100M and K200M does not seem to be effective on the drug release profiles of highly water soluble drug as Metoprolol Succinate. Carbopol 71G with less proportion 1:0.5 only was found to be sufficient to control the drug release as per the USP specifications. Gums and HPMC
K4M were more effective in combination with Carbopol 71G rather than alone. Xanthan gum alone was not effective but in the form of three layer matrix tablets was more effective as rate controlling agent.

- The effect of higher viscosity grade of HPMC as HPMC K200M was more effective to control the drug release of Ambroxol HCl and also with combination of CCS, gave biphasic release of Zolpidem tartrate as per USP requirement.

- $3^2$ full factorial design was successfully used for Melt granulation process and can be applied to a variety of drugs and the desired dissolution properties of the final dosage form can be obtained by the appropriate selection of the wax content, type of wax or granule size. The controlled release of Ambroxol HCl depends on the leaching of the drug through the granule matrix and diffusion through swellable layer.

- The Carbopol 71G was more effective for the formulation of floating drug delivery system with less floating lag time and controlled release of Cinnarizine.

- The optimized formulations for each drug for each method were found to be stable in accelerated conditions at $40^\circ C/75\%$RH for 3 months with respect to % cumulative drug release and drug content.

Thus, the development of the formulation in the present study was mainly based on the type of polymer, different ranges of concentration of polymers and the drug. Various polymers in different combinations were used so as to get tablet with quality parameters, which match with marketed product’s properties. So, in the present study attempts were made to minimize the concentration of polymer and other excipients as well as to get quality (good physical and analytical release profile parameters) of the matrix tablets of drugs.

The conclusions arrived in this thesis indicated that the controlled release formulations of Metoprolol Succinate, Ambroxol HCl and Zolpidem tartrate developed in this investigation was found to be equivalent to commercial market products, based on in vitro release studies. Thus the objectives envisaged in this thesis were arrived.