Chapter 7

Summary & Conclusion
CONCLUSION

Carvedilol is a BCS class II drug. These category of drugs have low solubility and high permeability and hence less bioavailability. The enhancement of oral bioavailability of BCS class II drug especially poorly water soluble drugs remains one of the most challenging aspects of drug development. This can be overcome by developing modified pharmaceutical dosage forms.

In the present study three different modifications namely solid dispersions, solvent deposition and inclusion complexes were utilized to improve the solubility of carvedilol. In each methods polymer concentrations and amount of solvent were taken as variable.

- The Preformulation studies (compatibility study-FTIR) revealed that there was no significant interaction between drug and excipients.
- The best polymers were selected for solid dispersions, solvent deposition and inclusion complexes, based upon the percentage yield, drug content and percentage drug release which were found to be satisfactory when compared to other polymers.
- Optimization of carvedilol- SD, Sol. D, IC were done. Process variables such as polymer concentrations and amount of solvent were optimized. Optimized formulation of SD, Sol. D and IC were chosen for evaluation.
- Saturation solubility studies indicate that the solubility of the drug was increased and XRD, DSC showed that the crystalline nature of drug was lost or decreased significantly in the optimized formulation of SD, Sol. D and IC, indicating the drug was present in a solubilised form in the formulations.
- The size and surface morphology of optimized formulations were studied by Scanning Electron Microscopy analysis.
- In-vitro dissolution studies of optimized carvedilol - SD, Sol. D and IC showed enhancement in the dissolution properties of carvedilol, indicating that SD, Sol. D and IC could improve dissolution of carvedilol.
Pre-compression studies showed that all the optimized formulations possess acceptable flowability and compressibility.

Optimized carvedilol - SD, Sol. D and IC could be formulated into tablets by direct compression method.

Post compression evaluation indicates that the physical parameters of entire formulated tablets were within the acceptable limit.

The optimized formulation of carvedilol - SD, Sol. D and IC tablets showed increase in dissolution rate than tablet prepared with pure drug.

The optimized carvedilol - SD, Sol. D and IC tablets were compared with the available marketed tablet of carvedilol for different tests.

The kinetics studies of tablet showed that the drug release from the system predominately followed Higuchi’s square root of time kinetics. The slope of Korsmeyer Peppas plot indicated that the tablets followed super case II transport mechanism.

In vivo pharmacokinetic study of optimized carvedilol - SD, Sol. D and IC tablets in the rabbit model showed excellent improvement in bioavailability and peak plasma concentration in comparison to pure drug tablet.

Stability studies of prepared tablets confirm that no significant change was observed throughout the period of study as per ICH guidelines and the dosage form was stable throughout the period of study.

This study contributes to our understanding of the effect of various solid dispersions, solvent deposition and inclusion complexes techniques on the oral bioavailability of carvedilol. From the experimental findings, the prepared solid dispersions, solvent deposition and inclusion complexes are capable of surmounting the shortcomings of oral administration of carvedilol, such as high dosing frequency, low bioavailability and patient incompliance. Conclusively, the studies can be judiciously explored to develop suitable platform technologies for preparing effectual and cost-effectual solid dispersions, solvent deposition and inclusion systems demonstrating improved bioavailability potential of other BCS.
class II drugs. The current investigations, therefore, report the successful development of systematically optimized formulations with enhanced bioavailability potential of carvedilol.