Chapter 5

Summary and Conclusions

Drug delivery research is advancing rapidly. By controlling the precise level and/or location of a drug in the body, side effects have been reduced. Lower doses have been developed and new therapies were made possible. In the present study, an attempt was made to develop gastro retentive hydrogel tablets and liposomes for Cefditoren pivoxil, with the objective to reduce dosing frequency by maintaining a continuous therapeutic blood level of the drug which in turn improves the patient compliance and acceptability.

Two novel drug delivery systems for Cefditoren pivoxil were designed and developed using different polymers and evaluated for both *In vitro* and *In vivo*. The hydrogel tablets were prepared by direct compression method and liposomes were prepared by thin film hydration technique. The prepared hydrogel tablets were evaluated for thickness, hardness, content uniformity, swelling behaviour, stability and *In vitro* dissolution and pharmacokinetic parameters. The prepared liposomes were evaluated for entrapment efficacy, particle size distribution, morphology, drug leakage studies, zeta potential, *In vitro* drug diffusion and pharmacokinetic parameters. *In vivo* studies were carried out for both liposomes and hydrogel tablets in New Zealand white rabbits. Pharmacokinetic parameters, namely, the peak height concentration ($C_{\text{max}}$), time of the peak concentration ($t_{\text{max}}$), elimination half-life ($t_{\frac{1}{2}}$) and elimination rate constant ($k_e$) were determined. The areas under the plasma concentration time curves (AUC) were also calculated.

Chapter 1 deals with an introduction to acute bacterial exacerbations of chronic bronchitis and respiratory tract infections, its prevalence, types, stages and causes. It also briefly explains gastro retentive drug delivery systems and liposomal drug delivery systems along with a literature survey on these systems. Scope and objective of the present study along with the different stages of proposed work were also included.
Chapter 2 deals with preformulation studies like calibration curve, solubility, method development and compatibility studies. Compatibility studies were carried out on the drug, polymers and their mixtures by using FT-IR spectroscopy and DSC thermograms. Quantification of Cefditoren from Cefditoren pivoxil tablets were carried out by using FTIR spectroscopy (TQ analyst software).

Chapter 3 deals with the formulation and evaluation of gastro retentive oral hydrogel tablets. It includes selection and optimization of the formulation and physical, *In vitro* and *In vivo* evaluations.

Chapter 4 deals with the formulation and evaluation of liposomes. It includes selection and optimization of the formulation and physical, *In vitro* and *In vivo* evaluations.

The following are some of the important conclusions made from the present study;

- The method developed for determination of Cefditoren pivoxil in tablets using FTIR spectroscopy was found to be simple, rapid and eco-friendly technique. The high percentage recoveries of Cefditoren pivoxil from pharmaceutical formulations show the feasibility of the model. This results show that FTIR spectroscopy can be a potential analytical technique for qualitative and quantitative analysis of Cefditoren pivoxil in pharmaceutical formulations.

- The data on the physical parameters generated are such as bulk density, thickness, hardness, moisture content, content uniformity, swelling behaviour, entrapment efficacy, particle size distribution and zeta-potential are found to be favourable for the development of oral hydrogel tablets and liposomes.

- The swelling index studies of hydrogel tablets were carried out for 24 h. The results showed that the rate of swelling index was fast due to the presence of amino groups in the Na CMC. No destruction of the tablet was seen even though there was a faster swelling. This further confirms the prepared hydrogel tablets had the capability to withstand in the gastrointestinal environment.
In case of hydrogel tablets, the *In vitro* drug dissolution behaviour clearly indicates that the formulations containing, Carbopol as gelling agent and Sodium-carboxy methyl cellulose as stabilizer and sodium bicarbonate as gas generating agent has shown improved *In-vitro* drug release.

*In vivo* studies reveal that the developed hydrogel tablets (CHT7) show an increased half-life and have high bioavailability when compared to the marketed tablet.

The surface studies by SEM on liposomes before and after addition of cryoprotectants during lyophilization reveal that drug is dispersed uniformly in the formulations and the texture of the liposomes remain uniform spherical vesicles without any drug leakage.

The particle size measurements and zeta potential for freshly prepared multilamellar liposomal formulations CPLVIA and CPLVIB were studied. It was observed that the mean particle diameter of multi lamellar vesicles of CPLVI and CPLVIB was found to be in between 417.3(nm) and 571.2 and Zeta potential was -4.64 and -4.88 respectively. From the results it was clear that both the formulations CPLVI and CPLVIB showed low electrolytic reactions which in turns improve the stability of liposomal formulations.

*In vivo* studies reveal that the developed liposomes (CPLVIB) show an increased half-life and have high bioavailability when compared to the marketed tablet.

All the formulations are found to be stable for three months, since no significant changes in drug release, content uniformity and other physical properties are observed.

The present findings, taken together, suggest that hydrogel tablets and liposomes of Cefditoren pivoxil can give better therapeutic effect in the management of ABECB, uncomplicated skin and skin structure diseases, *Haemophilus influenza*, *Klebsiella pneumonia* and community-acquired pneumonia, as indicated by the pharmacokinetic parameters evaluated in rabbits.