CHAPTER 5: SUMMARY AND CONCLUSION

5.1. SUMMARY AND CONCLUSION:

Major challenge to controlled/sustained release drug delivery system is to uphold the drug delivery system at exacting site for extensive time period for local and systemic bioavailability of drug also these system has disadvantage of less gastric retention time, which is a physiological limitation that leads to lower bioavailability of drug.

Mostly, for a conventional dosage form the dosing intervals of the drug are much less than the drug half life leads to numerous limitations.

The remedy for above problems is the development of controlled and targeted drug delivery system of existing drugs which are effective and safe. Therefore bioadhesive dosage form has been selected which remained intact at an exacting site for extensive time period to provide a longer residence time and prolonged release of drug.

Objective of present work was to design and develop various bioadhesive drug delivery systems by using different polymeric systems which got place in the drug delivery research in order of prolonging time of contact in a variety of drug administration routes of mucosal origin, so that the drug delivery system can be maintained at an exacting position for prolong duration for local disease treatment and systemic drug bioavailability. Also, to fabricate such controlled bioadhesive drug delivery systems which can offer the advantages of better therapeutic efficacy and is easier to comply with than the conventional regimens requiring more frequent dosing and minimize side effects.

In present study among various bioadhesive polymers such as Carbopol, hydroxypropylmethyl cellulose (HPMC K4M, HPMC K15M, HPMC K100CR), sodium carboxymethyl cellulose, ethyl cellulose or surelease, gaur gum are studied along with their different combinations and compositions, also the effect of their different concentrations on development of various better different bioadhesive drug delivery systems.
Bioadhesive buccal drug delivery system was developed in the form of bioadhesive buccal tablet using different bioadhesive polymers i.e. for the carvedilol controlled drug release from tablet in the buccal cavity, to increase the bioavailability of carvedilol and reducing the dose dependant side effects. By direct compression method the carvedilol bioadhesive buccal tablets were prepared with the use of polymers for instance Methocel K15M, Methocel K4M, Sodium carboxy methylcellulose, which are hydrophilic polymers and Carbopol 974P was used as the base polymer which is hydrophobic polymer but show good bioadhesion. Various formulations C1 to C23 of bioadhesive buccal tablets of carvedilol were prepared using various polymers in different proportions and combinations. The prepared different formulations were characterized for various parameters like weight variation, content uniformity, friability, surface pH, hardness, in-vitro release, swelling index, bioadhesive strength and stability study. The formulation C3 containing bioadhesive polymer concentration of 35% the Methocel K4M given promising results with the water insoluble drug carvedilol with adequate swelling, bioadhesive strength, good residence time, ex-vivo drug permeation and allows sustained drug. To the Korsmeyer and Peppas diffusion model the dissolution data was subjected. To interpret the release rate of carvedilol from batch C-3 tablets different kinetics were applied. The release of C-3 was best fitted to Square Root t kinetics.

Bioadhesive multiparticulate drug delivery system was developed which adheres to the gastric mucosa ensuring sustained drug release from this site and therapeutic effect of drug involved would be effective. For enhancing the gastric residence time of Cinnarizine drug the bioadhesive microsphere by emulsification/solvent evaporation method were prepared by using various polymers viz, Ethyl cellulose in combination with Carbopol 934 P or HPMC K4M in different proportions and combinations. By performing micromeritic studies, % drug entrapment, bioadhesion study, drug release study and stability studies the microspheres were evaluated. The microspheres of batch A2 had considerable drug entrapment, considerable bioadhesion and in vitro drug release. The microspheres of A2 batch followed the Non-Fickenian release profile via both diffusion and chain relaxation
mechanism from Carbopol. An optimized batch A2 of microspheres was selected and evaluated for stability study, spectroscopic IR studies, SEM studies and DSC studies. The microspheres were then formulated in Capsule dosage form. As per the results obtained, it was concluded that bioadhesive microspheres of A2 batch comprising 63.5mg Ethyl cellulose, 0.65mg Carbopol 934P and 50mg Cinnarizine found to be acceptable in requisites of % drug entrapment, drug release and bioadhesiveness.

Bioadhesive gastro retentive oral sustained release tablets of Baclofen were developed by using bioadhesive polymers viz, Carbopol 934 P, HPMC K 100 CR and Guar Gum in different proportions and combinations by direct compression technique. The prepared different formulations were evaluated for content uniformity, friability, hardness, weight variation, in-vitro release, swelling index, bioadhesive strength and stability studies. All the formulations complied with the official compendia’s for physical characterization and shown good results for in-vitro bioadhesion, swelling index and drug release in-vitro. Formulation B10 which contain Carbopol 934P & HPMC 100CR was the most promising formulation as the degree of in-vitro release was high as compare to other formulations for once a day medication of Baclofen. Also, formulation B10 had significant bioadhesion strength and desirable swelling index. The dissolution data was subjected to the Korsmeyer and Peppas diffusion model. To interpret the release rate of Baclofen from bioadhesive oral tablet of formulation B10 various kinetics were applied. Results indicated that release of B10 best fitted Higuchi square root t matrix model. Tablets of Batch B10 were optimized batch selected and stability study, IR spectroscopy was carried out. Stability study conducted under stress conditions for two months. After two month, for in vitro drug release, bioadhesive properties the tablet was evaluated. Any considerable changes were not found, hence this formulation was stable. Tablet of Batch B10 did not show any change in the IR pattern peaks of pure drug and formulation indicates there was not any incompatibility in between drug Baclofen and polymer used. Thus, the prolonged gastric retention of drug is achieved by bioadhesive polymers which controls the drug delivery system localized in the stomach, where it delivers the drug properly for prolonged duration.
Thus, conclusion can be drawn that, by using bioadhesive polymers such as carbopol, hydroxypropylmethyl cellulose (HPMC K4M, HPMC K15M, HPMC K100CR), sodium carboxymethyl cellulose, ethyl cellulose or surelease, gaur gum various bioadhesive drug delivery systems were developed successfully, which have achieved the goal of prolonging time of contact in a variety of drug administration mucosal routes, to maintain a delivery system at an exacting position for prolong period for local disease treatment and systemic drug bioavailability, and to enhance the gastric retention for prolonged and predictable time. Hence, the objective to develop such bioadhesive controlled drug delivery systems which can offer the advantages of better therapeutic efficacy than the conventional regimens requiring more frequent dosing and minimize side effects, has been achieved. Thus, the fluctuations in plasma concentration due to frequent administration of conventional immediate release (IR) formulations can be overcome by these controlled release Bioadhesive drug delivery systems.