CHAPTER-4
(RESULT & DISCUSSION)

RESULTS AND DISCUSSION

In the present study Tizanidine HCl microspheres were prepared by emulsification followed by cross linking technique and were studied for their shape, size, drug incorporation efficiencies, drug release rates and surface characteristics. Chitosan was selected as a polymer for the preparation of mucoadhesive microspheres due to its biodegradable and mucoadhesive properties. The effect of formulation variables such as polymer concentration, drug concentration, amount of cross linking agent, stirring rate, type of external phase was studied.

Surface morphology and particle size

Shape of the microspheres were studied with the help of optical micrographs. The microspheres were spherical with smooth surface, glossy in nature and were not aggregated.

- The mean particle diameter of the prepared microspheres varied from 55.3 to 89.5µm.
- As the concentration of chitosan was increased, the size of microspheres also increased proportionally. The increase in mean particle diameter may be due to increase in viscosity with increasing polymer concentration. This viscosity affect the droplet formation during the emulsification process.
- Average particle size increases with increasing drug concentration and particles were more widely distributed.
- Particle size was further increased with increasing amount of cross linking agent. This results in formation of more cross linked structure which further increases the viscosity of the formulation medium thereby leading to formation of larger microspheres.
- The microspheres were prepared under the stirring condition of 2000, 1700, 1400rpm, on decreasing the rpm particle size increased. It may be due to the increased mechanical shear force, which resulted in the decrease in droplet size during the emulsification process.

In general it was observed that the size of spherical matrix could be easily controlled by varying the agitation speed and the concentration of the polymer.

Swelling ability

The swelling ability of microspheres in phosphate buffer pH6.6 were determined.

- The swelling of microspheres increases the particle size and dissolution of microspheres.
- Chitosan microspheres swell quickly within 30mins.
- Maximum swelling was observed with the microspheres with less cross linking agent and swellability decreases with increase in cross linking density and amount of polymer. This could be due to increasing cross linking of hydroxyl group of the polymer with the cross linking agent.

Drug Incorporation efficiency

- The Drug Incorporation efficiency were found to be good with all batches and was minimum in batch A3EP3 and maximum in batch A3.
- The results show that an increase in concentration of polymer caused slight increase in the Drug Incorporation efficiency. This is evident by the comparison of batch P1, P2, P3. This slight increase in Drug Incorporation efficiency may be due to formation of larger microspheres with increasing polymer concentration, entrapping greater amount of drug.
- The Drug Incorporation efficiency were increased by increasing drug: polymer ratio from 1:4 to 1:3 and 1:3 to 1:2, but DIE were increased more by increasing drug: polymer ratio from 1:4 to 1:2.

Release studies

- Batch no. A3(,drug :polymer ratio 1:3,2000 rpm,Glu 1ml,DOSS 0.1%) show the highest release rate and Batch no.A3D0SS2(drug :polymer ratio 1:3,2000 rpm,Glu 1ml,DOSS 0.3%) show the lowest release rate.
- It was observed that drug polymer ratio has marked influence on drug release profile.. An increase in drug polymer ratio from 1:4 to 1:3 and 1:3 to 1:2, increased the drug release rate, therefore $t_{50\%}$ (time taken for 50% drug release) decreased significantly.
- The release rate of drug is also affected by stirring rate during preparation of microspheres. The microspheres prepared at 2000 rpm have faster release rates than microspheres prepared at 1700 and 1400 rpm. The comparison of the batch

sets A3,A3R1 and A3R2 for 2000,1700 and 1400 rpm show the difference in $t_{50\%}$ value(Fig. 2.9, 2.14, 2.15).This may be due to increase in mechanical shear force which resulted in increased surface area. The release rate of drug from microspheres is directly proportional to surface area.