CHAPTER V

CONCLUSION

This present study is an attempt to develop the mucoadhesive microspheres using propranolol hydrochloride as model drug for sustained release nasal delivery by spray drying technique. Spray dried propanolol hydrochloride microspheres with various polymer were produced. At certain conditions, the product from spray dryer could not be collected. The addition of some ingredients such as maltodextrin, Aerosil® and propylene glycol could improve the yield percentage and the morphology of product. Hence, the suitable spray dried microspheres were composed of drug, hydrophilic polymer and some specific ingredients as described above. Furthermore, the various processing factors were investigated. Inlet air temperature, pump feed rate and atomizing air flow rate played an important role on the spray dried microsphere characteristics.

Three mucoadhesive polymers such as carbopol 934P, chitosan, and HPMC representing as anionic, cationic, and non-ionic, respectively were used. The chemical interaction between drug and the investigated polymers were determined by using several techniques such as FTIR spectrophotometry, thermal analysis (DSC) and powder X-ray diffraction. The IR spectra of all microsphere formulations were unchanged as comparing with the pure drug indicating that no electrostatic interaction was occured. Moreover, the hydrogen bonding between functional groups, carbonyl group of carbopol 934P and the hydroxyl group of HPMC was not remarked. This revealed that there was no interaction between these two components during mixing and spray drying process. In addition, DSC thermogram and powder X-ray diffraction pattern were also shown that the drug was changed from crystalline form to amorphous form except chitosan microspheres.

The physical properties of mucoadhesive microspheres such as morphology, particle size and size distribution, powder characterization (angle of repose and bulked density), % yield, % moisture content, % loading efficiency, mucoadhesive and swelling properties were determined. In addition, the release study of all preparations was performed. Spray-dried products of spherical shape and smooth

surface could be obtained. Particle size distribution of all formulations was narrow according to the low span value. All formulations gave the appropriate particle size in the range of 10-50 μm which was suitable for nasal drug delivery system. Carbopol 934P and combined polymer (carbopol/HPMC with high carbopol ratio) microspheres provided appropriate physical properties. Despite of the moderate mucoadhesive property, carbopol 934P microspheres gave both the highest swelling property and viscosity resulting in the prolonged release of drug. In the case of chitosan microspheres, the highest mucoadhesive property provided, however, the percentage of drug release was lower than that of carbopol 934 P microspheres. Although, total swelling properties of chitosan was similar to carbopol 934P, the viscosity of chitosan was lower giving faster drug release. HPMC microspheres exhibited wide particle size distribution, bulky microspheres, and the lowest swelling property. Furthermore, they exhibited the lowest mucoadhesive property and low viscosity resulting in faster drug release.

In order to study the permeation of propranolol hydrochloride passthrough the cell culture, the nasal cell culture (RPMI 2650) was employed as a barrier model. The nasal cell line could be grown on the polyester filter membrane as monolayer with specific condition. The condition of permeation study was performed at 37 °C for 5 hours. The permeation of drug from HPMC microspheres was similar to chitosan microspheres whereas drug permeation from carbopol 934P microspheres exhibited the lowest. In addition, the combination of hydrophilic polymers (HPMC and carbopol 934P) as mucoadhesive polymer provided drug permeation profile between those of HPMC or carbopol 934P alone. The result from permeation study was closely related to in vitro drug release study.

According to the stability studies, the physical properties and drug release profiles of selected formulations of each polymers were determined. All formualtions showed good stability in both physical properties and release characteristics. All properties of microspheres expressed nearly identical to those of freshly prepared products. Thus, at specific storage conditions, the interested microspheres from each polymers could offer the potential for appropriate nasal mucoadhesive microspheres.

In order to obtain more informations about the drug penetration passthrough nasal membrane, The effect of these three polymers on the opening of tight junction should be further investigated.