CHAPTER V

CONCLUSIONS

This study was designed to investigate the stability of chloramphenicol by forming complexation with 2-HP-β-CD and the application of this complex in eye drops formulation. The study involved the stability of chloramphenicol itself and in complexation with 2-HP-β-CD. The conclusions of the studies were as follows :

1. Phase solubility diagram was obtained for the chloramphenicol : 2-HP-β-CD system in water. The solubility of chloramphenicol increased on addition of 2-HP-β-CD, displaying a A-type phase diagram. A stability constant was 118 M^{-1}. The soluble complex had a stoichiometry of 1 : 2 (chloramphenicol : 2-HP-β-CD).

2. Solid inclusion compounds have been prepared by freeze-drying. The freeze-dried products were evaluated by IR spectroscopy, differential thermal analysis and X-ray diffractometry. It was found that the freeze-drying technique could be used to prepare the amorphous state of drug inclusion complex.

3. It is important to adjust viscosity, pH and tonicity of aqueous ophthalmic preparation to minimize the discomfort upon instillation in the eye. When they were kept at room temperature and 45°C/75% RH for 4 months, the pH of all preparation were around 7.6 that similar to the pH of natural tear, the tonicity of preparation containing HP-β-CD were slightly increased and the viscosity were rather low, thus viscosity-increasing agent is necessary.

4. The degradation kinetics of reconstituted powder (Formula I and II) for eye drops after reconstitution with their vehicle, chloramphenicol complex solution and chloramphenicol eye drops BPC 1973 were investigated at 65°, 55°, 45°, 37°C and at room temperature (25°C). In the case of solid state (Formula I and II) were investigated at 45°C and 75%RH and room temperature for 4 months. The degradation of chloramphenicol in all preparations were found to be the first order kinetics. The extrapolated degradation rates

at 25°C were obtained from Arrhenius plot. The heat of activations which calculated from the slope of Arrhenius equation was between 18-25 kcal/ mol.

The reconstituted powder (Formula II) for eye drops containing 2-HP-β-CD was most stable. The shelf-life was four times longer than the chloramphenicol eye drops BPC 1973. The extrapolated shelf-life at 25°C according to the 90-100 % LA was 7.74 months (6.48-9.25 months), according to BP 1993 was 14.74 months (12.34-17.62 months). The extrapolated shelf-life at 8°C was more than that at 25°C. In addition, if it was kepted in solid state, the shelf-life of reconstituted powder for eye drops would be longer.

5. From antimicrobial activity test, the formation of the complex did not change the antimicrobial activity of free chloramphenicol base.

6.The test of eye irritation in rabbit, the preparation of chloramphenicol eye drops containing 2-HP-β-CD did not cause corneal cloudiness, did not produce conjunctivitis, did not cause swelling, congestion, hemorrhage of the iris and did not altre pupillary light reflex. Although 2-HP-β-CD did not produce eye irritation in rabbit. Further studied for irritability and other topical adverse effect in human is required.