CHAPTER V

CONCLUSIONS

PTU is a promising agent to be developed into a topical formulation for psoriatic therapy. A niosomal preparation may be an appropriate delivery system for such purpose. This study focused on the development of PTU niosomes and formulation factors affecting drug permeation including the possible mechanism of action of niosomes. In the development of PTU niosomes, the feasibility of formation of PTU niosomes, characteritics of resultant preparations such as entrapment efficiency, size and size distribution, phase transition, release profile and stability were studied. Conclusions can be drawn from the study as follows:

1. It was feasible to prepare PTU niosomes from some commonly available nonionic surfactants by a method that was devoid the use of organic solvent. These nonionic surfactants were Span® (20, 40 and 60), Brij® (52 and 76), GDS and L-595.

2. Cholesterol (CHO) was required in all cases for niosome formation from Span® and Brij®. The appropriate ratio of surfactant to CHO varied with surfactants. The most appropriate compositions for Span® (20, 40 and 60) and Brij® (52 and 76) were at surfactant:CHO by weight ratios of 60:40, 70:30, 60:40, 70:30, and 50:50, respectively. For GDS system, the weight ratio of GDS:CHO:Brij® 76 was 45:15:40 w/w. The weight ratios of L-595:PEG-8-L in water and phosphate buffer, pH 7.4 were at 50:50 and 70:30, respectively.

3. The two commonly used stabilizers for niosomes, dicetylphosphate (DCP) and Solulan® C24, affected vesicle formation and properties. DCP interfere with feasibility of noisome formation from Span® and Brij® but Solulan® C24 did not.

4. Entrapment efficiency, size and size distribution, and phase transition of niosomes depended on type of nonionic surfactants, presence of a stabilizer, and aqueous phase.

5. All formulations of PTU niosomes were physical stable within 2 months of storage at ambient temperature.

6. The release of PTU from the four selected formulation: Span® 20:CHO:Solulan® C24 57.5:37.5:5 w/w, Span® 40:CHO:Solulan® C24 67.5:27.5:5 w/w and L-595:PEG-8-L 50:50 w/w in water, and GDS:CHO:Brij® 76 45:15:40 w/w in phosphate buffer, pH 7.4, based on the thermodynamic state, size, and entrapment efficiency, was retarded and followed the first-order kinetics. The release rate constants depended on entrapment efficiency and the physical state of the bilayer.

7. The formulation factors affecting PTU permeation across newborn pig skin were thermodynamic state of the bilayers, type of nonionic surfactant, and vesicular structure though physical state and vesicular structure did not clearly affect some formulations.

8. The liquid crystalline state vesicles (Span® 20:CHO:Solulan® C24 57.5:37.5:5 w/w in water) gave the highest PTU permeation among the three formulas tested in this study while the elastic vesicles (L-595:PEG-8-L 50:50 w/w in water) gave the lowest permeation. However, most permeation parameters were not statistically different except for Q_{24} and EF of Q_{24} in the liquid crystalline state and gel state vesicles (Span® 40:CHO:Solulan® C24 67.5:27.5:5 w/w in water). No significant difference was found between the gel state and elastic vesicles.

9. The effect of the existence of vesicular structure on PTU permeation was clearly important in Span® 20:CHO:Solulan® C24 and Span® 40:CHO:Solulan® C24 formulas while in GDS:CHO:Brij® 76 45:15:40 w/w and L-595:PEG-8-L 50:50 w/w the role of vesicular structure was not remarkable.

10. Entrapment efficiency and the free drug release mechanism were not likely to be the mechanism of action of all PTU niosomal formulations tested in this study.

11. The dominating mechanism of action of PTU niosomes depended on the formulations. For Span® 20:CHO:Solulan® C24, Span® 40:CHO: Solulan® C24, and GDS:CHO:Brij® 76 the dominating mechanism might be the penetration enhancing properties of the vesicle components and the mechanism involving vesicle-skin transfer. The dominating mechanism of action of L-595:PEG-8-L might be a vesicle-skin transfer using transepidermal osmotic gradient.

The results of this present study show that it was possible to formulate the lyophobic drug, PTU, into niosomes. The bilayer composition and the aqueous medium played an important role in physicochemical properties of resultants niosomes since the drug was partly soluble in the bilayer and partly soluble in the aqueous phase. Modification of bilayer composition affected the release profile and skin delivery of the drug from niosomal vesicles. PTU niosomes enhance PTU permeation across the skin as compared to aqueous solution. Therefore, PTU niosomes might be used as a topical preparation for psoriatic therapy. However, data information from this study was not enough to conclude that PTU niosomes should be better than available products such as PTU lotions. Further studies such as in vitro comparison between permeation of PTU niosomes and available products and clinical study in psoriatic patients should be performed. These information should also be used as basic knowledge for pharmaceutical scientists who wish to formulate a noisome delivery system for other drugs with similar properties to PTU.