CHAPTER 5
CONCLUSION

Liposomes with the entrapped tranexamic acid (TA) were prepared by the chloroform-film method with sonication. Liposome compositions were hydrogenated soya phosphatidylcholine / cholesterol / charged lipid in the molar ratio of 7:2:1. The obtained liposome was demonstrated as multilamellar vesicles (MLVs) by TEM. Positively charged liposomes with and without the entrapped drug and negatively charged liposome without the entrapped drug had larger particle size than negatively charged liposomes with the entrapped drug investigated by light scattering particle analyzer. The pH values of all liposome formulations was 7 to 8, except for the negatively charged liposome without the entrapped drug which gave the pH of 3.4. The quantitative analysis technique used for TA determination was a spectrophotometric method. The UV detection at wavelength of 415 nm of TA after derivertized with 2,4,6 trinitrobenzosulfonic acid was used. The percentages range of the entrapped TA in all liposome formulations were 13 to 15 %. The amount of the loading of TA in liposome formulation was increased with increasing initial drug concentration.

The physical notation of the deterioration of the liposome formulation can be observed by showing the increase turbidity when compared with the freshly prepared formulation. The thermogravimetric analyzer was also used to study for the determination of the temperature range before decomposition of the lipids and the drug. All lipid compositions in liposome formulations were degraded at temperature approximately higher than 200 °C, except for stearylamine which decomposed at lower than 200 °C. The thermogram determination by a differential scanning calorimeter of all liposome formulations indicated that cholesterol can increase the stability of liposomal membranes by showing the increased transition temperature. Both positive and negative liposome formulations with the entrapped drug gave the enthalpy of transition value lower than their blank liposomes. TA may interfere with the lipid bilayer formation thereby reducing the enthalpy of transition of the

liposome formulations. The higher the entrapped TA concentration, the more effect of this interferance can be observed.

An amount of TA remaining entrapped in all liposome formulations at 4, 30 and 45 °C for 90 days was best fitted to the first order kinetics. The leakage rate of the positively charged liposome was higher than the negatively charged liposome and increased with increasing temperatures. The negative liposome formulation[7:2:1 (10%TA,-)] was the best stable formulation because it gave the longest shelf life of 65.13 days at 4 °C, 45.59 days at 30 °C and 35.07 days at 45 °C. In chemical stability study, TA entrapped in all liposomes showed high stability of about more than 90% of the drug remaining at 4, 30 and 45 °C for 90 days. This result agreed with the previous stability study of TA in aqueous solution.

In the *in vitro* release study, TA entrapped in liposome formulations showed the sustained release effect comparing to the drug in solution. There was no significant difference in the release rate of the positively and negatively charged liposome formulations. All showed the release rate of about 6 to 8 % per $hr^{\frac{1}{2}}$. TA entrapped in all liposome formulations gave the slower release rate of about 3 times than from the solution.

The best formulation was concluded to be the negatively charged liposome formulation [7:2:1 (10%TA,-)]. This formulation showed the highest physical and chemical stability with suitable sustained release profile. The result from this study suggests the challenge and interesting of the future development of TA entrapped in liposomes for parenteral and topical application. The developed topical product of TA can be served not only as a depot system but also a product of TA with low irritation as well.