CHAPTER V

CONCLUSIONS

In this study, doxycycline hyclate loaded chitosan microspheres were prepared using emulsification and ionic gelation technique. The chitosan microsperes were incorporated into glyceryl monooleate-based drug delivery systems. The effect of drug concentrations, chitosan concentrations and tripolyphosphate concentrations on percentage yield, encapsulation efficiency, release mechanisms and antimicrobial activity were investigated. The results of this study can be concluded as follows:

1. The chitosan microspheres were found to be spherical, some aggregated particles were observed. The sizes of microspheres were in the range 17.41-130.97 μm, the yield percentage were in the range 27.72-91.27% and the percentage encapsulation efficiency were in the range 1.40-105.11%

2. From the Box-Behnken experimental design and the optimization by the contour plot the optimal formulation was predicted. The other two formulations (formulation 11 and 15) which showed from the experimental results with high percentage encapsulation efficiency and optimal percentage yield were also included in the further studies.

3. The high encapsulation efficiency may result from the high concentration of drug load and STPP. This would be due to the strong wall was formed and the drug may not leak from the microspheres in the process of washing.

4. The chitosan microspheres could sustain the release of doxycycline hyclate over a period of 12 hrs. The release kinetics followed Higuchi's equation which indicated that the release of doxycycline hyclate from these microspheres was diffusion controlled.

5. From the accelerated stability study, at 40, 50, 60 and 70 °C the degradation followed the first order kinetic. The Arrhenius plot permitted the calculation of the extrapolated shelf lifes at 30 °C of doxycycline hyclate loaded chitosan microspheres optimal formulation, formulation 11 and 15 as 47.04 days, 22208.38 days and 245.65 days, respectively.

6. The ternary phase diagram of glyceryl monooleate-sesame oil-water were constructed. Regarding the formation of reverse hexagonal liquid crystalline form and shortest *in situ* gel forming time, the glyceryl monooleate-based drug delivery system was selected from the ternary system in the ratio of 6:15:79 (triglyceride: monoglyceride: water). The glyceryl monooleate-based drug delivery systems were incorporated with doxycycline hyclate equivalent to 10 % of the system.

7. The doxycycline hyclate loaded chitosan microspheres in glyceryl monooleate-based drug delivery system gave the prolonged release of doxycycline hyclate over a period of 48 hr. The release kinetics followed Higuchi's equation indicating that the release of doxycycline hyclate from these system was diffusion controlled.

8. Doxycycline hyclate loaded chitosan microspheres in glyceryl monooleate-based drug delivery system and in PBS pH 6.8 exhibited antimicrobial activities against *Stapphylococcus aureus* ATCC 6538P *in vitro* within 24 hrs.

9. The injectability through the syringe needle guage no. 23 of the glyceryl monooleate based drug delivery system could be improved by increasing the sesame oil from 6% to 12%.

The results from this investigation have exhibited that the glyceryl monooleate-based drug delivery system containing doxycycline hyclate loaded chitosan microspheres is potential for clinical application use for periodontitis. Nevertheless, the clinical study of the product must be performed in the further investigation.