CHAPTER V

CONCLUSIONS

This study elucidated that MEG and LC could be prepared by using commercially available and pharmaceutically acceptable excipients. Suitable type and ratio of oil, surfactant and cosurfactant provided spontaneous formation by gently mixing without external energy. Thermodynamically stable lamellar and hexagonal phase of liquid crystal including phase transformation upon contacted with excess water could be obtained. Interestingly, unique physicochemical property of this structure made an alternative sustained delivery for intrapocket administration of local antibiotic drugs. The overall possibility of MEG and LC to be a potential route of periodontal drug delivery using this phase structure and the results were as followed:

1. Type and ratio of oil, surfactant and cosurfactant influenced the formability and existing region of MEG including the structure and physical appearance of the obtained MEG and LC. Their concentrations are in acceptable range, they were also non-irritant and non-toxic MEG forming component. Furthermore, B, C, B_{72} and G as cosurfactant could not form MEG at any ratio. The areas of MEG in pseudo-ternary phase diagrams were mostly increased with the decreasing oil to surfactant ratio.

2. The oil with low molecular weight could be solubilized to a greater extent than that with the higher molecular weight as shown that the maximum amount of oil solubilization of IPM was more than those of SBO and CO which were ranked from low to high molecular weight (IPM<SBO<CO).

3. Most of the non-ionic forming MEG were o/w type and had birefringent property. Under cross-polarizer, the lamellar, hexagonal phase and cubic phase could be obtained from these investigated MEG.

4. All ingredients used also had effects on viscosity and appearance including the color of final product. Increasing the amount of surfactant would increase the viscosity of the system.

5. Surfactant and cosurfactant type had major effect on the physicochemical properties of MEG and LC system particularly on the dye solubility,dilution, conductivity, syringeability, viscosity, pH, birefringent property, particle size, drug released and stability of the system.

6. The TEM photomicrographs showed spherical shape of particle which droplet diameter was in nanosize range between 25-85 nm. Surfactant and cosurfactant ratio had influence on the mean particle diameter of MEG. The droplets size decreased with increasing the surfactant to cosurfactant ratio. After freeze-thawing, the particle shape of MEG remained spherical and the mean droplet diameter was statistically increased ($P<0.05$).

7. The inclusion of metronidazole molecule into the structure of MEG and LC did not affect their structure and maximum loading was 1.5% w/w. Furthermore, the appearance of drug loaded MEG and LC was similar to drug free system both before stability testing and after stability study.

8. The viscosity of MEG and LC system was high especially in cremophor RH40, Brij 35 and Lutrol F-68 as cosurfactant system and most formulations exhibited non-Newtonian behavior. Moreover, viscosity of MEG was increased after drug incorporation and no precipitation was observed after freeze-thawing and FDA stability testing except the increasing in viscosity of both MEG and drug-loaded MEG.

9. Eventhough high viscosity of most MEG and LC system, the non- newtonian and shear thinning behaviors could be obtained. These brought about the good syringeability and injectability of the MEG and LC systems.

10. The characterization of their rheology including syringeability, flowability, injectability demonstrated that this system possessed appropriate properties as intrapocket delivery system for periodontal therapy. Surprisingly, it could transform lamellar phase to stiff viscous gel when contacted with excess of water providing sustained released of drug.

11. *In vitro* drug diffusion from MEG and LC system was sustained more than 24 hours and their release kinetics primarily followed first order kinetic and Higuchi model. Furthermore, less viscous formulation resulted in higher and faster drug diffusion whereas lamellar or hexagonal phase structure that could induce more viscous and stiffing system resulted more sustained release than other formulations.

12. Antimicrobial activity of representative formulation before stability testing, after freeze-thawing and after FDA stability study showed no statistical difference of inhibition zone diameter ($P>0.05$). Furthermore, MEG also showed inhibition zone against *P. gingivalis* similar to MEG containing metronidazole.

13. This study clearly showed antimicrobial activity and efficacy of 1.5% w/w of metronidazole MEG against *P. gingivalis* which was a representative of anaerobic bacteria in periodontal diseases. Surprisingly, this study found that oil, surfactant and cosurfactant used in formulation of MEG base also showed antimicrobial activity similar with drug load MEG and LC but lower inhibition zone diameter than MEG base and drug-loaded MEG was obtained.

14. Both freeze- thawing and FDA stability testing showed the excellent physicochemical stability of MEG base and MEG containing metronidazole. Most of selected formulations were physicochemically stable after accelerated condition and FDA stability testing.

15. The ability of MEG and LC phase to incorporate and control release of drug, , to enhance chemical and physical stability of incorporated drug, their phase behavior, ease of application by syringes including antimicrobial activity made these phase structure an excellent candidate for use as periodontal delivery.

16. According to stability study, most of representative formulations were stable, remained good appearance, good physicochemical property and still exhibited inhibition zone against *P. gingivalis* upon after accelerated condition.

This study could be employ as useful basic knowledge for further development of novel periodontal and intra-pocket drug delivery systems. The further investigation should be performed *in vivo* and clinical study toward the patient with peridontal disease under dentist controlling. Moreover, the suggestion for pilot study of liquid crystal and MEG could be applied for loading other cosmetics ingredient due to the membrane mimetic property of lipid bilayers including adsorption enhancer, non-irritant of this drug delivery sytem. According to this study, metronidazole MEG gel had potential to be a method of choice and exellent dosage form for peridontal disease treatment. Consequently, the potential to prepare in advance industrial scale should be further investigate together with evaluate the possibility to use and exploit the domestic excipient from natural instead of expensive oils and surfactants.