CHAPTER V

CONCLUSIONS

In this study, experimental fractional factorial design was initially built to investigate the influence of five factors on production yield and moisture content of spray-dried products. These factors concerned both the spray solution parameters (%solid content, %additive and polymer/extract ratio) and the spray drying parameters (inlet temperature, feed rate). Then, the optimal operating conditions were estimated by response surface methodology. Central rotational composite design was used to locate the experimental range containing the optimum for both maximize production yield and minimizing moisture content.

1. First screening experiments consisting of fractional factorial designs revealed that the most significant factors were inlet temperature and %solid content ($P<0.01$). Then, the optimum operating conditions were estimated by response surface quadratic model for %yield and linear model for %moisture content ($P<0.05$), respectively.

2. The optimum region by overlay plot was carried out using the optimal formulation (flow rate 5 ml/min, polymer/extract ratio 1:1, additive 0.5%, inlet temperature 160°C and solid content 3.4 %) to evaluate the repeatability of the spray-drying technique. The observed means of the responses obtained for %yield and %moisture content were in range of the prediction intervals at 95% confidence level. The results clearly showed that the model fitted the experimental data well and described the region studied well.

3. All formulations of microspheres varied from fractional factorial design and optimal formulation had high percentage of loading of above 80%. The characterization of microspheres revealed that centella extract was molecularly dispersed inside the microspheres or/and existed in an amorphous state as the form of a solid dispersion. The release profiles of asiaticoside and madecassoside from these microspheres showed a fast release.

4. The optimal microsphere formulation had small particle size (5.19±0.02 μm). It showed the positive zeta potential of 32.87±1.39 mV and had ability to adhere with mucus on pig rectum more than 240 minutes.

5. The poloxamer solution composed of 18/4% w/w of P407/P188 mixtures was the optimal system which had the gelation temperature (33.6±0.15°C), gel strength (46.8±1.30 seconds) and setting time (30 seconds). It was suitable for liquid suppository base.

6. The conventional oleaginous base suppository (Suppocire®AM) containing pure centella extract showed the slowest release rate, whereas those containing centella microspheres gave the fastest release rate. This might be explained on the basis of the Suppocire® AM was lipophilic and spray-dried centella extract with chitosan was greater soluble than pure centella extract. So, they provided a general summary of the relationship of drug release which the water soluble drug with oily base showed rapid release.

7. The conventional water-soluble base suppository (PEGs) gave higher dissolution rates than poloxamer-based liquid suppository. The result suggested that PEG was soluble in the dissolution medium, while poloxamer was not soluble but gelled. Gel structure was more closely packed and act as a resistant barrier for drug release. Furthermore, PEGs base in this study contained high fraction of low molecular weight PEGs that dissolved rapidly.

8. The release rate from Suppocire®AM base containing both pure centella extract and spray-dried with chitosan were fitted with first order model (R^2 = 0.9890-0.9980). Similarly the release rate from PEGs base containing pure centella extract and spray dried were fitted with first order model (R^2 = 0.9473-0.9859). The release rate from poloxamer containing both pure centella extract and spray-dried with chitosan were fitted with Higuchi model (R^2 = 0.9977-0.9990).

9. The results of this investigation fulfilled the purposed of the study. The *in situ* gelling suppository containing *Centella asiatica* extract spray-dried with chitosan

could be prepared. However, the further studies regarding *in vivo* release and clinical trial should be performed.