CHAPTER V
CONCLUSIONS

Over the years, several strategies were used to solve some limitations of suppositories especially in storage condition. One of the resolutions is the dosage form called 'rectal capsule'. In the ordinary, rectal capsule means of soft shell capsule, however, liquid filled in hard gelatin capsule is recognized as better in terms of rapid disintegration, enhancement of drug dissolution and thermostable process. However, liquid leakage from capsule is the most important factor to concerned.

In this experiment, Licaps® was the best type of hard gelatin capsule to prevent liquid leakage due to their specific design for liquid filling into hard capsule. Mineral oil was the suitable vehicle for filling into Licaps® because its characteristic of no moisture absorption, high viscosity, high surface tensions and prolonging leakage time. Additionally, it was the material that has been commonly used in suppository. Colloidal silicon dioxide hydrophilic grade (Aerosil200) was the appropriate substance used as thickener in mineral oil. They became gel-like networks in mineral oil and induced higher viscosity with thixotropic behavior. However, the thickener could retard dimenhydrinate release from liquid base depending on the concentration of thickener. In the potential application of the drug delivery system, non-ionic surfactant are the useful compound that have the ability of to solubilize the drug compound completely in the formulation. Tween 80 or Cremophor® RH40 was the most appropriate surfactants for improving drug release. It was apparent that the increasing of release depended on HLB of surfactant. The use of drug dragger was another way to improve the drug. The combination of surfactant and drug dragger could improve the release profile comparable to the marketed dimenhydrinate suppository.

The appropriate formulation exhibited thixotropic rheogram, viscosity of 300 mPa.s at 25 ^{o}C that was found in the range of recommended viscosity which should be between 300-600 mPa.s. The surface tension of liquid formulation was 45 dyne/cm^{2}

following to the limitation that should be preferable not less than 30 dyne/cm^2. The formulation could prolong leakage time more than 30 days.

The selected formula was filled into Licaps® using liquid filling machine connecting to semiautomatic capsule filling machine. It was convenient, fast and no complicated process that could gave weight variation in the range of ± 5% whereas the drug content was 101% in the range of USP label claimed. The investigation demonstrated the feasibility of capsule coating with cellulose and polyarylate group by perforated pan coater and fluid-bed coater. The coating process provided good film distribution around the capsule shell especially the junction between cap and body. However, fluid-bed coater was better than perforated pan coater for capsule coating. Nevertheless, other properties of coated capsule produce using two coaters such as gliding effect, brittleness, disintegration time and dissolution profiles were not different. SEM of HPMC coating film revealed the homogeneous and continuous surface without porous or cracking. The addition of plasticizer had no effect on the morphology, In contrast, Eudragit® L film apparent to exhibit a rough and porous, however, the incorporation of plasticizer into Eudragit® L films such as PEG 6000 and TEC could produce smooth and continuous film. The addition of plasticizer almost had no effect on roughness of HPMC film whereas the smoothness of Eudragit® L film was observed when adding plasticizers. Cellulose film produced good sliding effect of capsule when contacted with water but it might be sticky when storing for a long time. Eudragit film had no gliding effect whereas PEG coating improved the gliding effect without sticky effect. The addition of plasticizer could reduce water vapor permeation of HPMC film as follow; DEP>TEC>PEG 6000 when compared with unplasticized film. The dissolution of liquid filled of dimenhydrinate capsule in phosphate buffer was rapid and complete within 30 minutes. Nevertheless, the dissolution time of coated rectal capsule was longer than of Gravol® suppository but the release of coated capsule might be improved by reducing the amount of HPMC coating polymer.

The stability study indicated that the selected formula, prepared using the pilot manufacturing procedure, were stable for at least 4 months. The coated capsule

displayed no cracking or wrinkling of film whereas the liquid system were not separated or not leaked but the color became darken when storing for a long time. However, the formula exhibited little moisture sorption but storage in closed container could reduce this problem. For drug content, it was in the range of 90-100%, however the tendency in drug content decreased at 45^{o}C.