CHAPTER V

CONCLUSION

The stable lipid emulsion corresponds to the unchanged physiochemical properties after sterilization and through the storage time. The lipid emulsion giving particle size in the range of 0.2 to 0.5 μm and no particle size greater than 1 μm was considered for the purposes of parenteral. The stability of emulsion was mainly dependent on the type and amount of emulsifier. In most cases, the cosurfactants were required to act as auxiliary emulsifier which could improve the stability, especially at high concentration of oil phase. This study was focused on a combination of cosurfactant and egg phospholipids to stabilize the lipid emulsion. Furthermore, the preparation conditions such as the speed of homogenizer, the pressure and the number of cycle through the high pressure homogenizer should be considered. The influence of different model of high pressure homogenizer on the emulsion properties was also additionally observed.

According to the results, the mean diameter of 10% lipid emulsion decreased either with increasing cycle number or the pressure of homogenizer. Although the stable fine emulsion could be produced by either Emulsiflex C5 or Emulsiflex C50, the emulsions produced by the latter had slightly smaller size. For the processed parameter, the number of only 5 homogenization cycles together with a pressure of 15,000 psi were needed to produce homogeneously fine lipid emulsion with the particle size of less than 0.5 μm.

For the effect of heat sterilization, the reduction in pH of emulsion was observed as resulted from the hydrolysis of phospholipids leading to the free fatty acid formation. The reduction in pH could affect the zeta potential surface charge around an oil droplet of emulsion which prevents the close contact or coalescence of oil droplets by electrostatic repulsive force. A decrease in surface charge promotes close approach of oil droplets resulting in physical instability.

Using only egg phospholipid even increasing its concentration, neither one cannot be obtained the stable lipid emulsion. It was possibly due to a single emulsifier was not enough to reduce interfacial tension and form strong film barrier to prevent coalescence. In contrast, a combination of surfactants has been reported to have a synergistic effect on enhanced stability of emulsion and has been attributed to produce strong mixed surfactant film.

From the experiments, using a combination of egg phospholipids and cosurfactant (namely, Tween® 80 and Vitamin E-TPGS), 10% and 20% soybean oil, the prepared emulsion was stable after autoclaving and storage after 4 weeks either at room temperature or in accelerate conditions (4°C and 40°C). The results indicated that the emulsifying property of egg phospholipid was improved with an addition of a suitable type and amount of cosurfactant. The mean particle size of emulsions can markedly be decreased by an addition of Tween®80 and Vitamin E-TPGS. In contrast, when sodium oleate was used as a cosurfactant the emulsion was not stable after autoclaving and during storage. The findings indicated that the synergistic effect of nonionic cosurfactant by steric stabilization emerging from the polymeric surfactant layer. In addition, the particle size of 20% soybean oil emulsion was bigger than 10% soybean oil emulsion, possibly due to an increase in the internal oil phase.

Furthermore, the amount of cosurfactant and the total concentration of a surfactant mixture were studied. The most suitable formulation obtained contained 10% soybean oil emulsified with egg phospholipid and Vitamin E-TPGS at a weight ratio of 2:1 and at a total emulsifier concentration of 1.5% w/w. The physicochemical properties determined after autoclaving and storage for 24 hours at room temperature were: particle size of 0.199 μm, zeta potential of -41.77 mV, pH of 6.97 and osmolality of 324 mOsm/kg which were in agreement with pharmacopial requirements for intravenous use. However, the formulation containing egg phospholipids and Tween®80 at a weight ratio of 2:1 at total emulsifier concentration of 1.5% w/w was also promising, even though its particle size was slightly larger than the emulsion containing Vitamin E-TPGS. The pH of the emulsion was slightly decreased during storage either at room temperature or in accelerate condition while the zeta potential was increased as a function of time in all conditions. Finally, the Vitamin E-TPGS emulsions were passed the criteria of the sterility test according to USP27 (2004) for sterile product. Moreover, the emulsion illustrated the same degree of hemolysis as commercial emulsion which was considered to be suitable for intravenous use.

Suggestion for further study

The further studies are needed to investigate the stability testing complied with FDA requirements. *In vivo* study should be done to ensure the safety before clinically use. The scale-up of production should be developed for industrial manufacturing in the country as an alternative product to the imported emulsion. Also, for emulsion containing vitamin E, the assay of vitamin should be monitored if it will be claimed for supplement of vitamin E deficiency.