CHAPTER V

CONCLUSIONS

The stable lipid emulsion corresponding to the unchanged physicochemical properties after sterilization and through the storage time after addition of drugs is the purpose in formulating lipid emulsion. The use of lipid emulsion via intravenous route, the droplet size should be in the range of 0.2 to 0.5 μm and no particle size greater than 1 μm presenting in the emulsion. Lipid emulsion produced by natural phospholipids either from soy or egg sources usually give unstable emulsion. The purity and/or the fatty acid composition contained in the lecithins are considered as the important part in emulsifying properties of lecithins, which also influence in the stability of emulsion. This study was emphasized on formulation of lipid emulsion which exhibited stable physiochemical characteristics to be used in incorporating of oil-soluble vitamins.

Many parameters were investigated in this study. The results from investigation revealed that sterilization using autoclaving decreased the stability of emulsion. pH of emulsion reduced after autoclaving as results from the hydrolysis of lecithins which led to the free fatty acid formation. The reduction in pH affected the zeta potential of emulsion. At low pH, the ionization of some phospholipids was reduced resulting in a diminution of the negative zeta potential value. It is known that the zeta potential or surface charge of oil droplets prevents the close contact or coalescence of oil droplets by electrostatic repulsive force (Lawrence, 2000). A decrease in surface charge promotes close approach of oil droplets resulting in physical instability.

Increasing recycle time of homogenization in emulsion preparation up to 10 recycle times provided the size reduction and improved size distribution of oil droplets. However, small droplet size achieved using mechanical force was not considered as the good method in producing stable emulsion. The emulsifier was considered as the more critical parameter in promoting long term stability of emulsion (Weiner, 2000a).

The properties of oil used in emulsion formulation also influenced the characteristics of formulated emulsion. It was found that emulsions formulated using blended oil exhibited less stability than those formulated using soybean oil when the same emulsifiers were employed. It can be explained that MCT oil was more sensitive to hydrolysis than soybean oil. In addition, the use of 10% oil produced more stable emulsion than using 20% oil.

The combination of emulsifiers enhanced the emulsifying properties of emulsifiers in reducing surface tension and forming strong interfacial film barrier to prevent coalescence. The use of co-emulsifiers, stearylamine and Tween 80, in combination of main emulsifier, phospholipids, showed the effective stabilizing property in that there was no any physical instability observed in emulsions. The coalescence was prevented by synergistic effect by either stearic stabilization resulting from the use of Tween 80 or electrostatic repulsive force produced by stearylamine.

The emulsion composition obtained from the previous study was used as a guideline for based emulsion incorporating oil-soluble vitamins. The based emulsion consisted of 10% soybean oil emulsified using 1.2% egg lecithin in combination with 0.9% Tween 80 and 0.3% stearylamine or 0.06% phoaphatidylglycerol. The amount of oil-soluble vitamins added was follow as recommended for daily uptake, vitamin A 3300 I.U., vitamin D 200 I.U., vitamin E 10 I.U. and vitamin K 0.15 mg.

The physicochemical characteristics of formulated lipid emulsion after sterilization and storage was similar. The sterilization method, either autoclaving or filtration did not affect the physicochemical properties of emulsion. Moreover, the whole physicochemical properties seemed to improve by the addition of vitamins. The higher in surface charge and neutral in pH were noted while the particle sizes of emulsions containing vitamins were approximately equal to those obtained from the emulsions formulated without the addition of vitamins.

The results of osmolality measurement of filtrated formulated emulsion containing oil-soluble vitamins showed the suitability to be used for parenteral administration. The maximum osmolality found in formulated emulsion was 363 mOsmol/kg in formulation using egg lecithin, Tween 80 and stearylamine as emulsifiers.

The vitamin contents found in emulsions after sterilization by autoclaving were analyzed within 2 days after preparation. The results showed that all vitamins lost approximately 20% after autoclaving and being kept for 2 days in refrigerator.

Another group of formulated lipid emulsions containing oil-soluble vitamins using different sterilization methods, autoclaving or filtration which were kept for 2 months in refrigerator were analyzed. The statistic analysis indicated that the sterilization method did not significantly affect the vitamin content in emulsion formulated using egg lecithin, Tween 80 and stearylamine and egg lecithin, Tween 80 and phosphatidylglycerol ($P \leqslant 0.05$). The analysis showed that the amount of vitamins lost after storage for 2 months was approximately 40-50% for vitamin A palmitate, almost 80% for vitamin D_3 and less than 35% for vitamin K_1. Conversely, there was no loss of vitamin E acetate found in same formulations.