CHAPTER I

INTRODUCTION

Nowadays, surfactants are widely used in development of new drug delivery systems for enhancing the effectiveness of poorly soluble drugs. Microemulsions, one of surfactant systems consisting of oil, surfactant, cosurfactant and water, have attracted considerable attention in recent years.

They possess interesting physicochemical properties, namely transparency, low viscosity, thermodynamic stability, high solubilization power, and low interfacial tensions. Because of these specific properties, microemulsions can be useful as new pharmaceutical dosage forms for overcoming solubility problem (Solans, Pons and Kunieda, 1997).

Microemulsions have three main types; namely oil-in-water, water-in-oil and bicontinuous microemulsions, depending on their compositions. All of them have been employed as possible therapeutic systems to allow sustained or controlled drug release for topical, transdermal, oral, rectal, and parenteral administration (Swarbrick and Boylan, 1994). The use of microemulsion as drug delivery system offers more predictable and more extensive drug absorption than the emulsion.

Oil-in-water microemulsions have been used to solubilize steroidal drugs such as prednisolone, hydrocortisone, betamethasone, testosterone and its ester and progesterone. Interestingly, it has been noted that hydrophobic drugs need to have a significant solubility in the dispersed oil phase for the oil-in-water microemulsion system to offer a marked benefit over the micellar system alone (Lawrence and Rees, 2000).

Perhaps the most significant problem associated with microemulsion formulations is the difficulty associated with excipient acceptability, especially for parenteral adminitration. Polyoxyethylene sorbitan monooleate (Tween® 80), polyoxyethylene sorbitan monolaurate (Tween® 20), block copolymers of polyoxyethylene polyoxypropylene (poloxamer series), polyoxyethylene castor oil derivatives (Cremophor® EL) and polyoxyethylene-660-(12)-hydroxystearate (Solutol® HS15) have been reported to have minimal toxicity and appear acceptable for oral and parenteral uses (Klang and Benita, 1998 and Lawrence and Rees, 2000).

In many cases, the formations of microemulsion require the cosurfactant for reducing the interfacial tension between oil and water phase. The cosurfactants are attempted to use in pharmaceutical formulation such as short chain alcohol, glycerin, ethylene glycol and propylene glycol, polyhydroxy compound (Lawrence, 1996). However, when microemulsion is diluted, some of cosurfactants partition more

strongly to the aqueous phase. It is the effect of depleting the cosurfactant concentration at the oil/ water interface, thereby destabilising the microemulsion droplet. In case of o/w microemulsion, the microemulsion droplet structure is often retained on dilution by a biological aqueous phase, thereby permitting oral and parenteral administration. In contrast, the use of w/o microemulsion for oral and parenteral drug delivery is complicated by the fact that they are destabilised to a much greater extent when diluted by an aqueous phase (Lawrence and Rees, 2000).

Unfortunately, microemulsion formulations normally compose of high percent of surfactants and cosurfactants, which have been reported to have a high degree of toxicity to erythrocytes. In order to make these systems dramatically useful, it is necessary to explore the toxicity of formulating microemulsion formed using commercially available and pharmaceutically acceptable components.

In this study, the formulation of microemulsions using pharmaceutical ingredients to prepare oil-in-water microemulsions will be investigated. The systems will be characterized to assure the suitability for use as drug delivery vehicle for parenteral route. The toxicity on human erythrocytes will be measured in order to determine whether the systems are appropriate for any drug parenteral administration.

The objectives of the study

The aims of this study were as follows:

1. To investigate the effect of different nonionic surfactants and cosurfactants on the formulation of oil-in-water microemulsions.
2. To investigate the physicochemical properties of the microemulsion.
3. To determine the toxicity of the microemulsions on erythrocyte hemolysis.