CHAPTER I
INTRODUCTION

The liquid crystalline state, also called mesophase or mesomorph, is the intermediate state of matter between crystalline solid and isotropic liquid (Brown, 1972; Vyas, Jaitely, and Kanaujia, 1997). The structure of liquid crystal may be prepared by heating a crystalline solid, causing a change in molecular arrangement. The resulting liquid crystal is called thermotropic liquid crystal. Liquid crystalline systems can also be prepared by adding the proper amount of a polar solvent, commonly water, to the crystalline soild, and the resulting liquid crystal is thus called lyotropic liquid crystal. Many amphiphilic compounds such as surfactants and phospholipids have a tendency to form lyotropic liquid crystals upon addition of water. Molecules of amphiphiles in water form a variety of structural patterns. Most lyotropic liquid crystals found are of the lamellar phase and the hexagonal phase. In the lamellar phase, molecules are arranged in bilayer separated by water layer. Lipophilic substances are retained in the bilayer whereas hydrophilic substances are dissolved in the water layer while amphiphilic substances are retained in both layers (Eccleston, 1990). In the hexagonal phase, amphiphiles are arranged in two cylindrical patterns depending upon the molecular structure of a particular amphiphile. In one pattern, the polar groups of the molecules are turned outward interacting with water, and the lipophilic substances are contained inside. In the other pattern, the polar groups of the molecules are pointed inward, and the hydrophilic substances are retained inside (Brown, 1972; Vyas et al., 1997). Liquid crystals are not only formed simply by mixing surfactants or phospholipids with water; other components such as oils or long chain alcohols also

participate in building up the structures (Mueller-Goymann and Frank, 1986; Rong and Friberg, 1988). Furthermore, several studies reported that the presence of additional substances, such as sucrose or sodium chloride, can influence the structure of liquid crystals. Sucrose was reported to decrease both the distance and the amount of water between the bilayer of the liquid crystal as a result of the osmotic effect, which is directly proportional to the concentration of sucrose (Tenchov et al., 1996). Sodium chloride was reported to exert some effects on the formation rate of liquid crystals, and in some systems the formation of liquid crystals are completely inhibited (Powell et al., 1994). X-ray diffraction and differential scanning calorimetry are useful for the examination and study of liquid crystal structure alteration while polarized light microscopy is a simple and rapid technique to detect the formation of liquid crystal and the patterns of liquid crystal structure (Rosevear, 1954).

Liquid crystals have been studied for both pharmaceutical and cosmetic applications. Wahlgren, Lindstrom, and Friberg (1984) reported that the liquid crystal system formed from lecithin increases water solubility of hydrocortisone from 1:3,500 to 1:20 when dissolved in a lamellar liquid crystal structure and that the hydrocortisone molecules may be trapped between lecithin molecules. Geraghty et al. (1996) studied the release of propantheline bromide and oxybutynin hydrochloride from the liquid crystal prepared from glyceryl monooleate and water and found that the drugs were released in the sustained release pattern. There are also a number of studies on the potential of liquid crystalline structure to increase drug solubility, drug entrapment, and drug release (Mueller-Goymann and Frank, 1986; Rong. Friberg, and Brin, 1995). Moreover, the liquid crystal system is capable of increasing stability of some substances. Swarbrick and Carless (1964) found that the rate of oxidation of benzaldehyde in lyotropic liquid crystal encountered in ternary systems consisting of

betaine-benzaldehyde-water were significantly lower in the mesophase than in isotropic systems. Liquid crystals are also useful in cosmetics. Suzuki et al. (1992) found that cleansing cream in the form of liquid crystals could remove cosmetics better and could be more easily rinsed off than the common cleansing creams which were not in the liquid crystalline phase.

From these studies, it is clear that the liquid crystalline system has a strong potential for developing into delivery systems where increased solubility of low solubility active compounds as well as controlled delivery are needed. Liquid crystalline systems can exist in many phases, such as lamellar phase and hexagonal phase, and can be prepared from a variety of substances including surfactants and phospholipids. Though phospholipids are beneficial in terms of safety because of their known biocompatibility, surfactants have some advantages over phospholipids due to their lower cost and better stability. This study was intended to concentrate upon comparison between liquid crystals formed from surfactants and those formed from phospholipids, using lecithin as a model. The comparison was made in terms of formation and structures of liquid crystals. The effects of additional substances on the formation and structures of liquid crystals were also investigated. Assessment on the possibility of using the liquid crystalline system as a drug delivery system for topical purpose was attempted by investigating the ability of the system to solubilize drugs with low aqueous solubilities and the potential of the system to control drug release. In addition, the stability of the system upon storage was also examined. Two model drugs were used. Propylthiouracil (PTU) was selected as a representative of molecules that are slightly soluble in both water and lipid phases, and triamcinolone acetonide was chosen to represent molecules that are lipophilic. The results of this study may be used to gain further insights into the formation and modification of liquid crystalline

structures for future development of these systems in delivering active compounds for pharmaceutical and cosmetic purposes.

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Objectives

The purposes of this study were as follows:

1. To study the formation and structures of liquid crystals from surfactants and lecithin

2. To study the effects of additives (trehalose, urea, sodium chloride and α-tocopherol) on the formation and structures of liquid crystals

3. To assess the possibility of using liquid crystals as a drug delivery system by evaluating the potential of the system to increase drug sclubility, to control drug release, and to modify rate of water evaporation, and by examining the stability of the system upon storage.