CHAPTER I

INTRODUCTION

Lactic acid is a hygroscopic alpha-hydroxy acid derived from natural food. It is used topically for increasing of moisture content and plasticity of the stratum corneum for the treatment of xerosis and ichthysis vulgaris (Mccallion and Li Wan Po, 1993 ;Hardman et al., 1996). Lactic acid is also a keratolytic agent that promotes exfoliation and renewal of skin cells in the treatment of hyperkeratotic skin disorders and verrucae (Rieger, 1992; Hardman et al., 1996). In cosmetics, lactic acid is also used as an anti-wrinkle by the hypothesis that it interferes with ionic bonding of cells of the stratum corneum (Van Scott and Yu, 1984). In addition, it may turn on the biosynthesis of dermal glycoaminoglycans and other intercellular ground substances that can be responsible for eradication of fine wrinkles (Sargisson, 1994). In pharmaceutics, because of its keratolytic action, lactic acid reduces thickness of the stratum corneum which is an important barrier in dermal drug delivery, so it may be useful in increasing drug absorption into the skin (Wurster and Kramer, 1961; Knutson et al., 1985).

Topical application of lactic acid causes skin irritation due to its acidity. Many clinical studies have found that the ability of lactic acid to stimulate cell renewal decreases as the pH increases. At pH 3 lactic acid shows some degree of irritation and significant stimulation of cell renewal. At pH 7 little or no irritation is observed, and very little stimulation is observed (Smith, 1994). Besides skin irritation, its high solubility in water makes it easily washed off when applied to the skin.

Liposomes are well recognized as potential drug carriers. They have been proposed to penetrate into the skin (dermis) through the "lipid channels" of the

1990). Liposomes increase the permeability of skin for various entrapped drugs and, at the same time, diminish the side effects of these drugs (Lasch and Wholrab, 1986; Wholrab et al., 1989). Hence, one approach to sustain the action and decrease irritation of lactic acid is to entrap it within liposomes.

Liposomes are formed when certain phospholipids are dispersed in excess water (Bangham et al., 1965). The lipid molecules arrange themselves in bilayers that, above the main transition temperature (T_m) of the phospholipids, spontaneously vesiculate and enclose an aqueous core (Fromherz and Ruppel, 1985). Drug molecules can either be entrapped in the aqueous compartment or intercalated into the lipid bilayer depending upon their physicochemical characteristics and the composition of the lipids.

Since the liposomal structure allows slow osmotic diffusion of water or water soluble agent through the lipid membrane onto the skin (Idson, 1995), liposomal formulation of lactic acid should retain skin moisture and decrease skin irritation. Lipid components of liposomes which are arranged in bilayers can also prevent water evaporation from the skin (Idson, 1985, 1988, 1992). However, because of the high solubility of lactic acid in water, encapsulation of lactic acid in liposomes is rather low which may limit the use of liposomes as a delivery system for the drug (Talsma and Crommelin, 1992). Therefore, this study was aimed at investigating some factors that may affect encapsulation of lactic acid in liposomes such as the concentration of lipid and lactic acid, charge on bilayers, pH, ionic-strength of medium, and addition of cholesterol in lipid composition in order to improve lactic acid entrapment. The release of lactic acid and the stability of liposomes were also studied .

Objectives

The purposes of this study were as follows:

1. To prepare lactic acid liposomes by reverse phase evaporation method and investigate some factors which may affect lactic acid entrapment in liposomes.
2. To characterize prepared lactic acid liposomes in terms of encapsulation efficiency.
3. To determine release rate of lactic acid from liposomes with different compositions.
4. To study factors affecting stability of lactic acid liposomes.