CHAPTER I

INTRODUCTION

The Rational for the Study

Alpha hydroxy acids (AHAs) have emerged as a category of substances that are exceedingly important to cosmetic active ingredient. AHAs range from simple aliphatic compounds to complex molecules. Many of these substances can be derived from natural sources and are often referred to as fruit acids. AHAs act as a solvent for the intercorneocyte matrix reducing excessive epidermal keratinization. This soft feeling leads to thinning of stratum corneum useful in the renewal of epidermis, and to visible reduction of facial line. In addition, AHAs have more effects such as reversing photo-damage and reducing brown spot (Ditre C.M., 1996).

The debate on natural versus synthetic AHAs has ranged for several years. It has been found that the therapeutic index of the natural AHAs surpasses that of the synthetic AHAs. It is likely that the natural AHAs contain natural soothing agents which can reduce the irritation potential, and do not interfere with stimulatory activity of AHAs (Smith W.P., 1994).

For centuries, extract from natural products have been used to treat a variety of skin conditions. Fruit pulp of tamarind has been used for scrubbing to provide smooth and light skin appearance. The fruit pulp of tamarind contains naturally occurring AHAs including tartaric acid (8-23%), lactic acid (2%), citric acid and malic acid (Dassanayake M.D., 1991). As we know, lactic acid is a highly effective moisturizer. Citric acid, when topically applied, stimulates collagen synthesis. Tartaric acid and malic acid boost skin elasticity (Greave M.W., 1990). The actions of these compounds to skin, therefore, result in the improvement of skin properties. Unfortunately, high AHAs concentrations are combined to high potential for skin irritation as well as burning (Perugini et al., 2000). Moreover, its hydrophilic property causes the difficulty to penetrate to skin by lipophilic

pathway. The controlled system loading AHAs may provide advantage by lowering side effects and increasing penetration of AHAs to skin.

Liposomes have been shown great potential as delivery system (Weiner, 1989). Liposomes are lipid bilayer vesicles enclosing an aqueous compartment. Since Bangham's and Horne's preparation in 1964, liposomes are the most widespread model for biological membranes. These aggregates are useful in biological, biomedical and biotechnical applications as delivery systems due to their extraordinary capacity to load both hydrophilic and lipophilic molecules. Phospholipids are main composition of the liposomes that cause the selective permeability of the phospholipidic membrane in human skin. The mechanism of liposome action on transferring active agent through the skin is probably due to the composition of the vesicle bilayer similar to that of skin lipid thus leading to fusion of vesicles in the intercellular space of the skin (Lopez O. et al., 2002). As a matter of fact liposomes can induce the possibility of active agents penetration into skin and preserve them from environmental condition.

The major problem in liposome formulations is its unstability during the storage, leading to the leakage of the entrapped agent and consequently undesirable effect. An increase in rigidity of liposome's shell by interacting with polymer may minimize this problem. Additionally, the controlled delivery, together with the enhancing skin permeation of the encapsulated agent may obtain from the rigid liposome.

Among available polymers today, chitosan meets the requirements of being natural, bioadhesive, biocompatible and biodegradable polymer. Chitosan are polysaccharide polymer obtained from chitin by deacetylation process. The cationic property of chitosan can improve skin compatibility with cosmetic formulations and enhance penetration of bioactive cosmetic ingredient (Guo J. et al., 2003). Additionally, some study has reported the potential of using the association of chitosan coated liposome to improve liposome stability and control delivery of hydrophilic compound (Perugini et al, 2000). Regarding this reason, we had been interested in developing chitosan coated liposome system to control the deliver of natural AHAs extracted from the tamarind's fruit pulp. In addition, the developed system would study for effects on the

keratinocyte proliferation in keratinocyte cell and melanogenesis inhibitory effect in melanocyte cell, compared to the unentrapped extract in the solution.

Objectives of the study

The objectives of this thesis are as follows:

1. To develop chitosan coated liposome system for controlling the release of the natural AHAs extracted from the tamarind's fruit pulp.

2. To investigate in vitro release of the developed system containing the extract through the dialysis membrane.

3. To investigate the effects of the developed system containing the extract on melanogenesis inhibitory and keratinocyte proliferation.

Expected output of the study

This study aimed to develop chitosan coated liposome system which has ability to control the release, improve the permeability of the loaded natural AHAs through the skin and increase the efficiency in melanogenesis inhibition of the loaded natural AHAs.