CHAPTER I

INTRODUCTION

Vitamin A has been used to denote specific chemical compounds such as retinol or its ester. Retinoid exhibit the biological properties of retinol. It refers to the chemical entity retinol or other closely related naturally occurring derivatives. Retinols also include structually related synthetic analogues that do not need to have retinol-like (vitamin A) activity.

Euler and Moore (1929) demonstrated that carotene is a potent source of vitamin A. β-carotene is the most active carotenoid found in plants. Retinoids are presented in tissue of animals. Synthetic retinol is the all-trans isomer. The structural modifications of retinol are possible without loss of its activitiy. Retinoic acid is very potent in promoting growth and controlling differentiations and maintenance of epithelial tissue.

Vitamin A plays an important role in visual function, growth and differentiation of epithelial tissue and reproduction. For dermatological aspect, retinol controls epithelial differentiation in mucus secreting or keratinizing tissue. Basal epithelial cells are stimulated to produce mucus. It is also known that retinol can alter

or modulate total collagen synthesis (Counts, 1988). The ability of retinol in differentiation of epidermis, controlling or modulating the collagen synthesis tends to oppose changes that occur with aging. The sign of aging is wrinkles. Wrinkles arise from the loss of tension and elasticity through interaction between reduced water content of stratum corneum, thickening of stratum corneum, atopy of the epidermis, change in amount and quality of dermal collagen and elastic fibers, change in the three dimensional structure of the dermis and other changes resulting from external and internal factors (Mitsui, 1998). It is suggested that the skin aging process involved the cutaneous changes. The processes lead to the decreasing of blood supply to the dermis. The number of sebaceous ducts and the secretion from them also decrease. The epidermis is thinned as well as the collagen and elastin decrease (Schmitt, 1996).

However, there are some problems in its instability. Retinol is easily oxidized by heat and light (Ji, 1999). So retinyl ester has been employed in cosmetic formulations. The most popular and stable retinyl ester is retinyl palmitate (Boehnlein, 1994). It is used in a number of skin products intent to alliviate the symtoms of dry skin (Guenin, 1995). It increases elasticity of skin and prevent the roughness of skin (Ji, 1999). However, the anti-aging effect on human skin with retinol acid treatment is convincingly documented in a number of studies (Song, 1999).

Figure 1 shows metabolism of vitamin A and its derivatives. It is well established that all-trans retinol is converted to all-trans retinoic acid in two-step oxidative process, it is first converted to retinaldehyde then to retinoic acid (Charles, 1998). Connor and Smit reported that a small quantity of retinoic acid was formed in hairless mouse skin after topical application of retinol (Boehnlein, 1994). In addition, Boehnlein, Sakr, Lichtin and Bronaugh (1994) demonstrated that retinol is formed in hairless guinea pig and human skin after topical application of retinyl palmitate (Boehnlein, 1994). However, the action of retinyl palmitate in skin may depend on its conversion to retinoic acid in order to promote growth of epithelial tissue (Boehnlein, 1994).

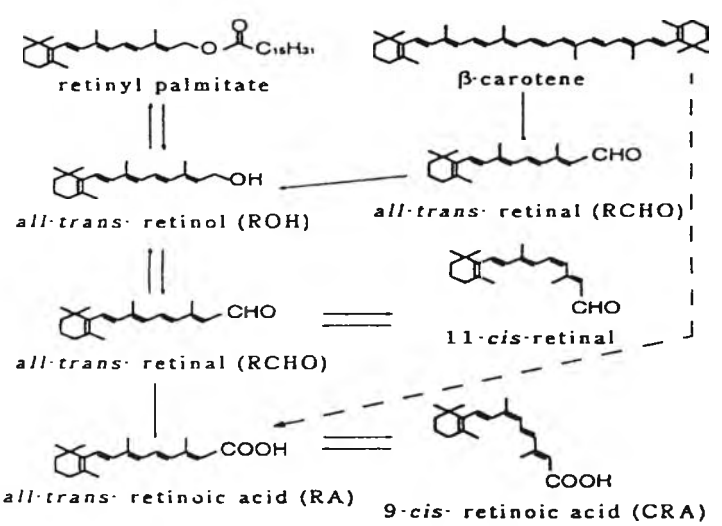

Figure 1. Metabolism of vitamin A and its derivatives.(Ji,1999)

Although Retinyl palmitate is used instead of retinol because retinyl palmitate is more stable than retinol. Retinyl palmitate is also lipophilic that it is difficult to

penetrate the skin (Song, 1999). In addition, the effects of retinyl palmitate on skin are the increasing of both the collagen synthesis and the epidermal thickness in hairless mouse skin model. So these effects of retinyl palmitate indicated that the topical application of retinyl palmitate can alter the composition and morphology of hairless mouse skin (Counts, 1988). Therefore, the high amount of retinyl palmitate is decidedly feasible in thee aspect of anti-aging agent.

As a result, the drug carrier concept had been potentially considered to improve this characteristic. Some nonionic surfactants has been used as penetration enchancers for lipophilic compound. Niosomes, nonionic surfactant vesicles act as colloidal drug carriers which can entrap both hydrophilic and hydrophobic solutes (Yoshioka, 1994). Hopefully, niosomes could carry highly lipophilic drug to the deeper skin leading to more desirable effects. It was important for the technical viewpoint as it possessed greater stability and avoided some disadvantages associated with liposomes, vesicles formed from natural phospholipids, such as variable purity of phospholipid (Vora, 1998). Niosomes appear to be similar to liposomes in terms of their physical properties, being prepared in the same ways and, under a variety of conditions, form unilamellar or multilamellar structures.

In the process of niosome preparation, the optimization of drug loading is a crucial factor in the formulation of drug delivery systems (Uchegbu, 1998). In addition, cholesterol usually added in niosome formulation as a membrane additive.

Naturally, this kind of retinyl ester was so lipophilic that it was difficult to penetrate the skin (Song, 1999). It had very low permeation rate into the deeper skin. As a result, the drug carrier concept had been potentially considered to improve this characteristic.

In order to optimize the drug loading in vesicular formulation. The level of cholesterol was examined whether it has an influence on retinyl palmitate entrapment in vesicles. Each retinyl palmitate niosome formulation will be chosen to investigate the trend in retinyl palmitate niosomes coming from Span40, Span60 and Span85 as a drug carrier in feasible anti-aging formulation because the effective retinyl palmitate should remain in viable epidermis and the dermis. So the permeation of retinyl palmitate niosomes was investigated in shed snake skin. Many researchers used shed snake skin in penetration studies.

The purposes of this study were as follows:

1.To prepare retinyl palmitate niosomes.

2.To characterize prepared retinyl palmitate niosomes

3.To study entrapment efficiency of retinyl palmitate niosomes prepared by the series of nonionic surfactants.

4.To study the skin permeation of retinyl palmitate using niosomes as carriers.