Chapter I

Introduction

Psoriasis is a prevalent chronic skin disease which affects between 0.5 and 3% of general population (Barker, 1991). It is characterized by epidermal hyperplasia and a greatly accelerated rate of epidermal turnover (Weinstein and Krueger, 1993; Gennaro, 1995). People with psoriasis may suffer discomfort, restricted motion of joints, and emotional distress (National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), 1997). The cause of psoriasis is unknown, although it appears to be an autoimmune disease with a likelihood for genetic predisposition. Conventional topical treatments (such as emollients, coal tar, and dithranol) have been messy, cosmetically unacceptable, and of low efficacy, while systemic therapies such as methotrexate, cyclosporine, and acitretin have suffered from significant side effects (Mier and Kerkhof, 1986; Weller, 1996; NIAMS, 1997). Thus, new therapies of psoriasis are currently in development.

Propylthiouracil (PTU), an old antithyroid drug with a new application, has been shown to be useful both orally (Elias, 1993) and topically (Elias, 1994) for some patients with psoriasis. In addition, the lack of cumulative toxicity and its low cost (Werner et al., 1989; Elias, Goodman and Rohan, 1993a; Elias, Goodman and Rohan, 1993b) may make PTU a viable therapeutic option in the treatment of patients with psoriasis. Although topical 5% lotion of PTU in propylene glycol and hydrophilic petrolatum produced significant resolution in patients with psoriasis, there is no study investigating the effect of other dosage forms that may be more suitable for the treatment of psoriasis.

Liposomes, compared to more conventional systems (such as ointments, creams, and lotions) may improve the ability of drugs to pass through the skin. Also, liposomes could increase the duration of action while reducing systemic effects (Betageri, Jenkins and Parsons, 1993). Supawadee (1998) found that the solubility of PTU in liposomes composed of soy-lecithin is higher than that in purified water or in non-ionic cream base.

The release study also showed that PTU liposomes tend to yield sustained release. Many studies (Idson, 1985; Idson, 1988) have indicated that liposomes allow slow osmotic diffusion of water or water-soluble agents out of the lipid membrane onto the skin. Liposomes provide, in one structure, a combination of skin moisturizing effect of a humectant for water absorption and lipid components for skin occlusion that can prevent water evaporation from the skin. Therefore, encapsulation of PTU in liposomes may have some potential in the treatment of dry and scaly psoriatic skin with a decrease in the natural moisturizing factor (NMF) content (Barry, 1983). However, systematic research of formulation factors on PTU liposomes or even other lyophobic agents has been scarce.

The purpose of this study was to investigate some formulation factors that may affect encapsulation of PTU in liposomes: lipid concentration, inclusion of charged lipid, pH, and cholesterol. The release of PTU, water evaporation from liposomal formulations, in vitro biological activity of PTU liposomes, and short-term physical stability of liposomes were also studied to assess the feasibility of using liposomes as a delivery system for PTU in psoriasis. This study may provide useful information in development of topical PTU liposomes for the treatment of psoriasis.

Objectives

The specific objectives of this study were as follows:

1. To study the effect of liposomal composition (lipid concentration, pH, charge, and cholesterol) on PTU entrapment
2. To determine water evaporation profile and release profile of PTU from liposomes with different compositions
3. To evaluate in vitro biological activity of PTU liposomes in comparison with PTU solution
4. To study short-term (8 weeks) physical stability of PTU liposomes.