CHAPTER I

INTRODUCTION

Concerted efforts during the last few decades to improve drug effectivness in therapeutic and preventive medicine have been greatly assisted by parallel developments in molecular and cell biology. Such developments have given a new impetus to the concept, first articulated, early this century, of conferring selectivity on drugs through targeted delivery. The concept entails the use of carriers which can bring drugs to, or facilitate their release where they are needed. Carriers can do so either through an ability, inherent or acquired to interact selectively with biological targets or because they are instructed to release drugs near or at the target in ways that are conducive to optimal pharmacological action. Examples of such carriers include albumin conjugates, antibodies, lectins, glycoprotiens, DNA, dextrans,erythrocytes,lymphoid cells, polymers, polypeptides, polysaccharides, nanoparticles and **liposomes** (1).

Liposomes are microscopic vesicles composed of membrane-like lipid layers surrounding aqueous compartments. The aqueous compartment which is trapped in the lipid vesicle can contain many types of polar compounds ranging from inorganic ions to macromolecules(2) while the non-polar drugs can bind to the liposome membranes(3). By altering the lipid composition, liposomes can be produced which differ in trapping ability, permeability and surface charge. These characteristics equip the liposomes with potential carrier ability for chemotherapeutic agents(4).

While liposomes have been investigated for many years as parenteral drug carrier systems, particularly for the selective delivery of anticancer, antibiotic and antifungal agents(5), they have only for approximately one decade, been considered for topical drug delivery including opthalmic(6,7) pulmonary(8-11) and dermal/transdermal(12-14) delivery. For liposomes to be a viable alternative to topical/local administration of free drug, they should not only control the rate of drug release but also be retained, at the site of application.

The most frequently prescribed topical preparations contain corticosteroids which are highly effective in treating skin disorders. However, due to percutaneous absorption in chronic and extensive treatment, unwanted systemic effects may be produced(15). Results of several studies indicate that liposomes, depending on their lipid composition, size, surface charge and other ingredients present in the liposomal product can act as drug localizers for this class of drugs(16-18).

The aim of the present investigation was to optimize liposomal formulations of triamcinolone acetonide (TRMA), flucinolone acetonide (FLU) and clobetasol propionate (CLO) with respect to Drug : Egg Phosphatidyl Choline (PC) : Cholesterol (CHOL) ratio and gel base by using in vitro and in vivo techniques followed by clinical trials. For this purpose, the research envisaged was as follows :-

(1) To prepare liposomes of TRMA, FLU and CLO using different ratios of PC and CHOL.

(2) To characterize the prepared liposomes.

(3) To prepare liposomal gels of TRMA, FLU and CLO liposomes using HPMC K4M gel base.

(4) To conduct in vitro permeation studies for all the liposomal gels prepared and compare the various permeation parameters for all the gels amongst themselves and those for the free drug gel.

(5) To prepare liposomal gels of TRMA using the liposomal composition, found most suitable following in vitro studies and stability studies, in different gel bases viz. HPMC E4M gel base, Carbopol 941 gel base and poly vinyl alcohol gel base and study the in vitro permeation behaviours thereof.

(6) To conduct skin blanching assays, on healthy human volunteers, for liposomal formulations found promising following in vitro studies.

(7) To conduct clinical trials in patients with dry bilateral eczema using one liposomal formulation per drug, found promising following in vivo studies.

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