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RECENT ADVANCES IN TOPICAL NIOSOMAL DELIVERY FOR THE TREATMENT OF PSORIASIS

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ABSTRACT

Psoriasis is renowned as a complex, chronic skin ailment that can have a significant impact on physical and mental health. It commonly causes red, scaly patches on the skin, even if some patients have no dermatological symptoms. Various drugs have been included in the treatment regimen of psoriasis which can be given orally as well as topically. However, the topical route for drug administration has advantages over the oral route as it avoids hepatic first pass effect, provides continuous drug delivery and improves patient compliance. In spite of many advantages, the lack of effective delivery of drug from existing topical systems has always been considered as the major limitation as low stratum corneum permeability limits the usefulness of topical drug delivery. This possibility of overcoming this barrier leads to emerging technology for development of drug-vesicular systems. The objective of vesicular system is to deliver the drug molecule to specific site without afflicting normal tissue. In comparison to conventional systems, these novel systems differ in their composition. The difference in composition influence the nature of self-assembled supra structure in terms of their shape, size, and surface properties. This leads to different class of carriers, viz. liposomes, niosomes, and transferosomes. Niosomes are formed from the self-assembly of non-ionic amphiphiles in combination with other lipid surfactants in aqueous medium. Niosomes have attracted a great deal of attention in the delivery of dermal drugs because of many advantages over the other vesicular systems, as they are biodegradable, non-toxic, amphiphilic in nature, penetration enhancers and effective in the modulation of drug release properties. The review focuses on available topical systems for the treatment of psoriasis and the effectiveness of niosomal topical delivery for the treatment of psoriasis.

KEYWORDS: Niosomes, topical drug delivery, psoriasis, polymers, drug-vesicular systems.

INTRODUCTION

Psoriasis is a skin disease affecting millions of persons worldwide. It is clinically characterized by erythematous, sharply demarcated papules and rounded plaques, epidermal hyper proliferation overlying immune-mediated inflammation, leading to profound adverse effects on patient's physical, social and mental wellbeing. Various pro inflammatory cytokines, such as interleukins (ILs), tumor necrosis factor (TNF), and interferon-γ (IFN-γ), has been identified. Complex cellular interactions among epidermal keratinocytes, mononuclear leukocytes, neutrophils, dendritic cells, and activated T cells, together with growth factors, chemokines and cytokines are involved in the development of psoriasis. Psoriasis is a chronic, autoimmune disease that appears on the skin. It occurs when the immune system sends out faulty signals that speed up the growth cycle of skin cells. Psoriasis is not contagious. It commonly causes red, scaly patches to appear on the skin, although some patients have no dermatological symptoms. The scaly patches commonly caused by psoriasis, called psoriatic plaques, are areas of inflammation and excessive skin production.[1]

The cause of psoriasis is not fully understood, there are two main hypotheses about the process that occur in the development of disease.

1. The first considers psoriasis as primarily a disorder of excessive growth and reproduction of skin cells, the problem is simply seen as a fault of the epidermis and its keratinocytes.
2. The second hypothesis sees the disease as being an immune-mediated disorder in which the excessive reproduction of skin cells is secondary to factors produced by the immune system. T cells (which normally help protect the body against infection) become active, migrate to the dermis and trigger the release of cytokines (tumor necrosis factor-alpha TNFα, in particular) which cause inflammation and the rapid production of skin cells. It is not known what initiates the activation of the T cells.

MECHANISM OF PSORIASIS

Psoriasis occurs more likely in dry skin than oily or well-moisturized skin, and specifically after an external skin injury such as a scratch or cut (Koebner phenomenon). Psoriasis has a large hereditary component, and many genes are associated with it, but it is not clear how those genes work together. Most of them involve the immune system, particularly the major histocompatibility complex (MHC) and T cells. Certain variations (mutations) of those genes are commonly found in psoriasis.[2,3]

In psoriasis, immune cells move from the dermis to the epidermis, where they stimulate skin cells (keratinocytes) to proliferate. Psoriasis does not seem to be a true autoimmune disease. In an autoimmune disease, the immune system confuses an outside antigen with a normal body component, and attacks them both. But in psoriasis, the inflammation doesn't seem to be caused by outside antigens (although DNA does have an immunostimulatory effect).Immune cells such as dendritic cells and T cells move from the dermis to the epidermis, secreting chemical signals, such as tumor necrosis factor-α, interleukin-1β, and interleukin-6, which cause inflammation, and interleukin-22, which causes keratinocytes to proliferate.[3] It is a complex interaction between altered keratinocytic proliferation & differentiation, inflammation & immune dysregulation. The *earliest changes* are vascular. There is swelling & intercellular widening of endothelial cells followed by deregulation of mast cells around post-capillary venules. Hours later activated macrophages appear in the lower epidermis where there is loss of desmosome tonofilament complexes. Finally lymphocytes & neutrophils appear. Tonofilaments are decreased in number and diameter and lack normal aggregation. Keratohyaline granules are decreased in size and number. The cornified cells retain organelles and nucleus as parakeratotic cells. The basal keratinocytes show cytoplasmic processes protruding into dermis through gaps in the basal lamina and they correlate with disease activity. The intercellular spaces between all epidermal cells are widened because of deficiency in the glycoprotein rich cell surface coat. The spongiform pustule of Kogoj, one of the most characteristic features of psoriasis is located in the uppermost portion of spinous and granular layers. Here neutrophils lie intercellular in a multilocular pustule in which sponge like network is composed of degenerated and flattened keratinocytes. The capillary loops in dermal papillae in psoriasis show wider lumen, bridged fenestrations & gaps between endothelial cells, extravasation of RBCs and inflammatory cells & thickened basement membrane. They may be due to deposition of amorphous substances & accumulation of collagen fibrils in the BMZ.

EPIDERMAL CELL KINETICS

The rate of epidermal cell replication is markedly increased as suggested by the higher number of basal and suprabasal mitotic figures. The mitotic activity varies in different lesions & even within the same lesion. It correlates with degree of parakeratosis. Early investigations suggested that the transit time of cells from basal cell layer to uppermost row is shortened to 7 days in psoriasis from 53 days in normal epidermis. Further investigations showed the germinative cell cycle shortened from 311 to 36 hrs i.e. 8 fold faster proliferation in psoriasis,

doubling of proliferative cell proliferation in psoriasis from 27000 to 52000 cells/sq mm of epidermal surface area, 100% of germinative cells of epidermis enter growth fraction instead of only 60% for normal subjects. However another study showed that the germinative cell cycle time in normal epidermis is 200 hrs while in psoriasis it is only 2 fold faster i.e. 100 hrs. The source of cycling cells in suprabasal layers is not yet well defined. It could be expanded population of basal keratinocytes or could be recruited from transit amplifying cells (TAC) which are suprabasal keratinocytes committed to terminal differentiation that undergo rounds of amplifying divisions above basal layer. Keratin studies suggest TAC since they express K1/K10 & K6/K16 keratins and not K5/k14 as basal keratinocytes do.

KERATINOCYTE DIFFERENTIATION

Keratinocytes undergo a process of differentiation as they migrate upward through the epidermis from basal layer to cornified layer when several structural proteins are synthesized. One such protein family is keratins, which are intermediate filaments, found in the cytoplasm of all epithelial cells. Studies show that in normal epidermis K5/K14 are expressed in basal keratinocytes and K1/K10 are expressed in suprabasal keratinocytes. Involucrin, one of the major precursor proteins of cornified cell envelope are detected higher in granular & cornified layers. In psoriatic skin basal keratinocytes continue to expressK5/K14. However keratins K1/K10 are replaced by so called hyper proliferation associated keratins K5/K16.Also involucrin expressed prematurely in lower suprabasal layers. K17 also found in upper suprabasal keratinocytes while normally they are found in deep outer root sheath of hair follicle.

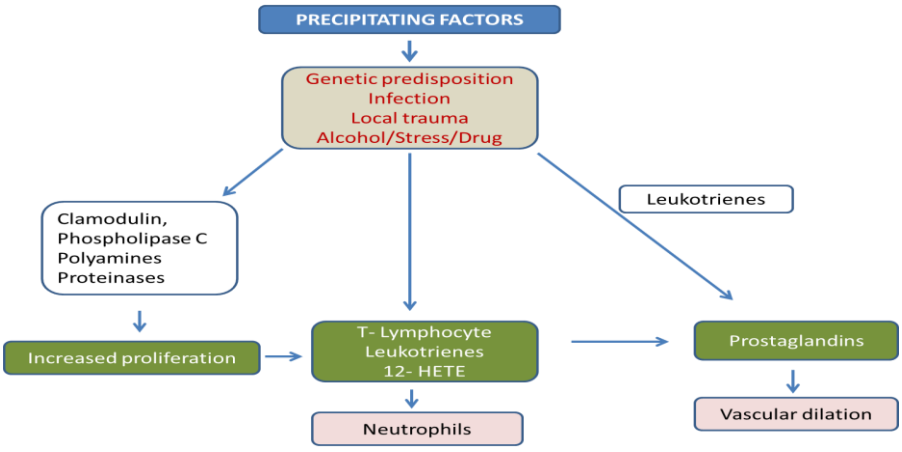


Fig. (1). Pathogenesis of psoriasis

CONDITION AGGRAVATING PSORIASIS

Conditions that have been reported as accompanying a worsening of the disease include infections, stress, and changes in season and climate. Certain medicines, including lithium salt, beta blockers and the Antimalarial drug chloroquininine have been reported to trigger or aggravate the disease. Excessive alcohol consumption, smoking and obesity may exacerbate psoriasis (Behnam *et al.*, 2005). Individuals suffering from the advanced effects of the Human immunodeficiency virus, or HIV, often exhibit psoriasis (Montazeri *et al.*, 1999).

SEVERITY

The degree of severity is generally based on the following factors: the proportion of body surface area affected; disease activity (degree of plaque redness, thickness and scaling); response to previous therapies; and the impact of the disease on the person. mild (affecting less than 3% of the body), moderate (affecting 3-10% of the body) or severe.[37]

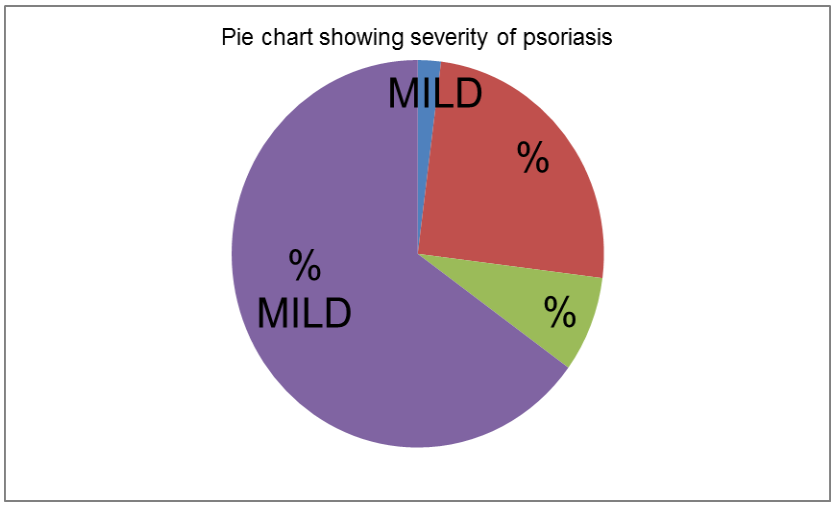


Fig. (2). Pie chart showing severity of psoriasis

TREATMENT OF PSORIASIS

There are a number of different treatment options for psoriasis. It include topical, oral, systemic, Psoriasis treatment aimed to.

- Interrupt the cycle that causes an increased production of skin cells, thereby reducing inflammation and plaque formation.
- Remove scale and smooth the skin, which is particularly true of topical treatments that you apply to your skin.

TOPICAL DRUG DELIVERY IN PSORIASIS

Skin membrane allow penetration of all material to some extent via stratum corneum through intercellular lipids.[39] The state of hydration of stratum corneum is one of the most important factor in determining the rate of percutaneous absorption. In psoriasis there is rigidization of skin increased the level of cholesterol and fall in level of ceramide. Several topical therapeutic agents are available for the treatment of psoriasis, none of them can be regarded as an ideal drug molecule. This may be due to inherent side effect or their improper incorporation in conventional vehicle. Due to variation in physiochemical characteristics of carrier and active component used, degree of drug absorbtion through skin vary. Formulation like cream, ointment, and lotion are frequently used for topical delivery of antipsoriatic agents.

CHALLENGES FOR TOPICAL DRUG DELIVERY

- Variability in percutaneous absorbtion.
- Reservoir capacity of skin.
- Irritation & other toxicity due to drug.
- Heterogeneity and inducibility of the skin in turn – over and metabolism.
- Inadequate definition of bioequivalence criteria.
- Incomplete understanding of technologies to facilitate or reduce percutaneous absorption.

Table 1. List of drugs encapsulated in topical carrier system & their advantages over conventional system

Drugs used for treating psoriasis	Novel drug delivery system	Advantages over conventional drug delivery system
Terpenoids triptolide)	Solid-lipid nanoparticles	Improved penetration
Methotrexate	Ethosomes[41], niosomes[42], iposomes[43]	Improved therapeutic index, improved healing properties
Cyclosporine	Solid-lipid nanoparticles[40]	Enhanced site specificity
Corticosteroid	Skin-lipid liposomes[44]	Improved skin delivery
Retenoids	Liposomes[45]	Improved penetration
Tacrolimus	Nanoparticles[46] Liposomes[47]	Improved skin transport effect
Temoporfin	Liposomes[53-54]	Improved topical delivery
Dithranol	Liposomes[23] Niosomes	Devoid of irritation & staining
Coal tar	Lecithinized coal tar formation, lipid coated microparticles[49-50]	Better antipsoriatic activity, meet skin irritation challenges.
5- aminolevulinic acid	Ethosomes[51]	Enhanced penetration
Dyphylline	Liposomes[52]	Improved penetration properties
Psoralen	Solid-lipid nanoparticles[53]	Increased skin penetration as well provide controlled release of drug
Tamoxifen	Liposomes[54-55]	Enhanced skin retention of drug molecule as well skin permeation

NIOSOMES AS A DRUG DELIVERY SYSTEM

Niosomes is a novel drug delivery system, in which the medication is encapsulated in a vesicle.The vesicle is composed of a bilayer of non-ionic surface active agents and hence the name niosomes. The niosomes are very small, and microscopic in size. Their size lies in the nanometric scale. Although structurally similar to liposomes, they offer several advantages over them. Niosomes have recently been shown to greatly increase transdermal drug delivery and also can be used in targeted drug delivery, and thus increased study in these structures can provide new methods for drug delivery.

TOPICAL DELIVERY OF NIOSOMES IN PSORIASIS

Niosomes, non-ionic surfactant vesicles, are widely studied as an alternative to liposomes. These vesicles appear to be similar to liposomes in terms of their physical properties. They are also prepared in the same way and, under a variety of conditions, form unilamellar or multilamellar structures. Niosomes alleviate the disadvantages associated with liposomes, such as chemical instability,(Vora *et al.*,1998). They have the potential for controlled and targeted drug delivery.(Namdeo *et al.*, 1996). Niosomes enhanced the penetration of chemicals and drugs through the SC.(Ciotti *et al.*,2002). Niosomes to enhance permeability is their ability to modify SC structure; the intercellular lipid barrier in the SC may become looser and more permeable by niosome treatment.(Fang *et al.*,2001). Another reason is altering adsorption and fusion of niosomes with the skin's surface, which leads to a high thermodynamic activity gradient of drug at the interface. In niosome formulation, non-ionic surfactant itself, acts as a permeation enhancer, which might partly contribute to the enhanced niosomal drug permeation.

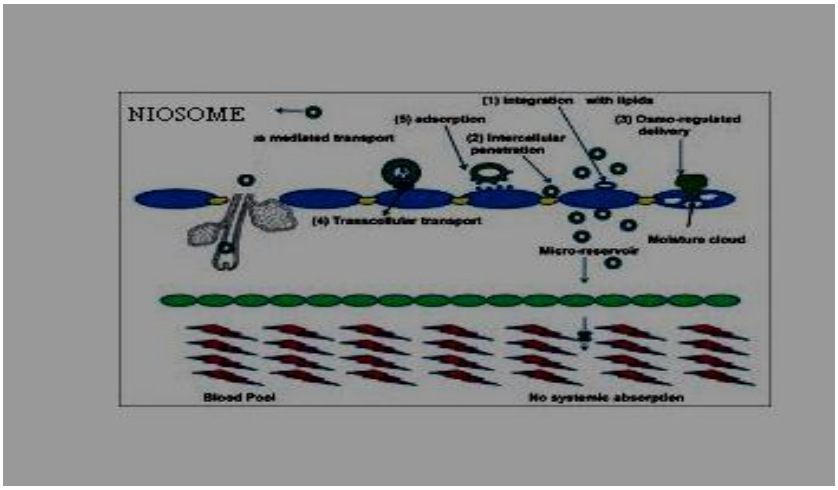


Figure 5: Transport of niosomes across the skin

Table 2: Effect of nature of drug on formation of noisome.

Nature of the drug	Leakage from the vesicle	Stability	Other properties
Hydrophobic drug	Decreased	Increased	Improved trans-dermal delivery
Hydrophilic drug	Increased	Decreased	–
Amphiphilic drug	Decreased	–	Increased encapsulation, altered electrophoretic mobility
Macromolecule	Decreased	Increased	–

VESICULAR INTERACTION WITH SKIN

Vesicle–skin interactions were visualized with isolated human SC incubated for 48 h and vesicles prepared from CHOL and polyoxyethylene alkyl ether surfactants. (Hofland *et al*.,1994) reported that, after this incubation time, liquid as well as gel-state vesicles fused at the superfi cial layer of the SC, but that only liquid-state vesicles induced perturbations in lipid organization and formation of water pools within the SC. (Abraham and Downing .,1990) showed fusion and adsorption of vesicles onto the SC surface, forming stacks of lamellae and irregular structures on top of the skin depending on vesicle composition. Hence, vesicle–skin interactions are strongly dependent on the physiological properties of the vesicular systems.

Tretinoin (TRE) is a widely used drug in the topical treatment of acne.(Pariser *et al.*, 2010).Tretinoin-loaded niosomes were prepared from polyoxyethylene lauryl ether, sorbitan esters and a commercial mixture of octyl/decyl polyglucosides, in the presence of cholesterol and dicetyl phosphate. Results showed that in the presence of cholesterol all the amphiphiles used were able to form stable vesicle dispersions with or without tretinoin.(Manconi *et al*,2002).Tretinoin (TRA) is effective in the topical treatment of different skin diseases such as acne vulgaris, icthyosis and psoriasis (Peck, 1984; Peinni and Vigolti, 1991; Layton and Cunlife, 1992). Topical administration of tretinoin provides effective treatment of dermatologic disorders while decreasing systemic exposure and toxicity (Kligman et al., 1969; Layton and Cunlife, 1992). However, its topical application is limited by several drawbacks, such as skin irritation, very low water solubility and photolability (Elbaum, 1988; Lehman *et al*., 1988).

Work has been carried out on tretinoin niosomal formulations(Wang et al., 1995; Manconi *et al*., 1999).The incorporation of TRA in niosomes could give the same benefits reported above

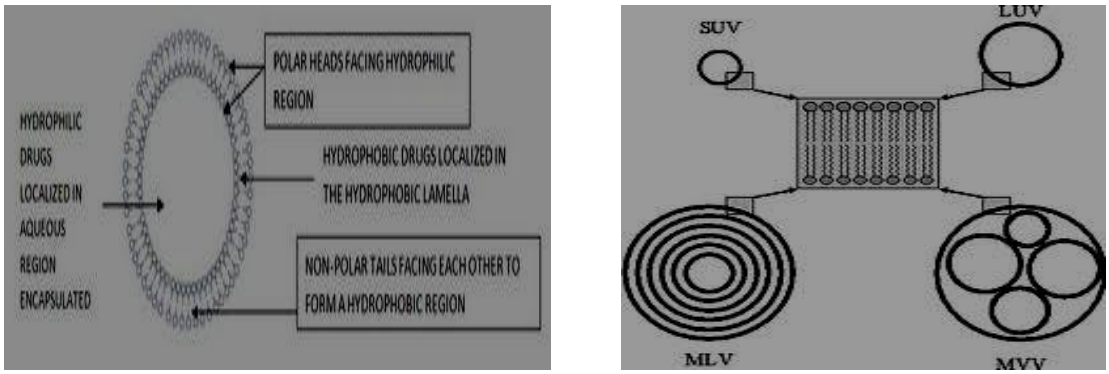
for liposomes. More precisely the presence of non-ionic surfactants could improve its skin penetration and increase its accumulation in the superficial skin strata. This paper present relationship between the method of preparation, the nature of the bilayer components, and size distribution, entrapment efficiency and vesicular structure. Consequently, several vesicle formulations with different techniques (i.e. the film method, sonication and extrusion) and using different types of surfactants. Surfactant used are non-ionic surfactants with estereal (Sorbitan esters) or ethereal linkage such as polyoxyethylene lauryl ether (Brij30) to form stable tretinoin niosomal formulations. In addition to non-ionic surfactant monomers already used in pharmaceutical niosomal formulations (i.e. Span 40 and 60, Brij30). The size of the TRA-incorporated sorbitan ester vesicles were smaller than those of for hydrosoluble molecules (Yoshioka *et al*., 1994; Uchegbu, 1994). These results confirm the strong influence of the nature of the drug incorporated in the niosomes on vesicle sizes. Dithranol, with a long history of use spanning over more than 100 years, is one of the most effective topical therapies in psoriasis. But in the existing form of products, it has not been fully accepted, mostly because of its irritation and staining properties. This made a long-standing demand on the researchers world wide to search for the modified molecule or formulation. Dithranol (1,8-dihydroxy-9-anthrone), first synthesized in 1916 have since been in clinical use in the treatment of psoriasis. The target organelle for dithranol is mitochondria as therapeutic interaction occurs with the electron transport chain on the inner mitochondrial membrane resulting in a reduction of ATP synthesis (Mehrle et al., 1994). Vesicular systems of dithranol with and without salicylic acid. The formulations, when tested on more than 12 patients for 4 weeks, proved to be effective and devoid of irritation and staining.(Gidwani *et al.,2003).* It shows dithranol in greatly reduced doses (0.5%) in niosomes could clear the psoriasis plaques to match that of 1.15% commercially available dithranol ointment.(Agarwal *et al.*,2007) The advantages of liposomal dithranol in terms of efficacy and compliance (nonirritancy and nonstaining) . Methotrexate (MTX) is the gold standard drug used systemically in psoriasis, though there are not many products available for its topical application. Methotrexate is indicated in the symptomatic control of severe, recalcitrant, and disabling psoriasis. The oral or parenteral route of administration causes systemic toxicity. The topical route of delivery, though, reduces systemic toxicity and has limited applicability due to restricted permeability. Liposomal and niosomal MTX topical formulations have also been investigated with limited success to achieve drug localization in the skin. it provide absorption promoting effect probably by improved adhesion between formulation & tissue due to chitosen. Niosomal

systems in chitosan gel (0.25%) resulted in a better efficacy, tolerance, and patient compliance, when compared to a marketed formulation.(Lakshami P.K. *et al.*, 2007).

Vesicle Preparation & vesicle characterization

Multilamellar vesicles (MLVs) were prepared according to the film hydration method as previously reported .The phospholipids or surfactants, cholesterol, DCP and tretinoin (4 mg/ml) were dissolved in chloroform. The organic solvent was vacuum evaporated and the resulting lipid film was dried under a nitrogen stream for 30 min. The obtained lipid film was then hydrated under mechanical stirring with distilled water (pH 5). The final pH of the prepared formulations ranged between 5.3 and 5.8. Large unilamellar vesicles (LUVs) were prepared by the extrusion technique. Niosomes made of Span 80, vesicular dispersions showed a very low stability and a high TRA leakage (Manconi *et al.*, 2002). Dithranol niosomes were prepared by thin film hydration method(Agarwal *et al*., 2001).

Vesicle were characterised by transmission electron microscopy (TEM) for vesicle formation and morphology; dynamic laser light scattering for mean size and polidispersivity index; HPLC for incorporation efficiency; and in vitro drug release through a synthetic membrane both to check stability and as a prerequisite to the investigation of the topical application. The method of vesicle purification used in this study was gel chromatography, which is faster than dialysis, and therefore, may prevent the destabilisation of our vesicles, as previously suggested for C12 sorbitan monoester vesicles (Uchegbu, 1994; Yoshioka *et al*., 1994). However, as reported in the experimental section, the purification of these vesicle dispersions was also performed by dialysis. Triton CG 110 vesicles were not found to have less stability but their incorporation efficiency was almost 100%.



I. **II**

Figure 5: Structure of different type of vesicles

I* ► Structure of noisome II* ► Type of niosomes (MLV- Multilamillar vesicle, SUV- Small unilamillar vesicle, LUV- Large unilamillar vesicle, MVV- Multivesicular vesicle).

Transmission electron microscopy (TEM)

The vesicle formulations were examined by transmission electron microscopy to characterize the microstructure. A drop of vesicle dispersion was applied to a carbon film-covered copper grid.

Most of the dispersion was blotted from the grid with filter paper to form a thin film specimen, which was stained with 1% phosphotungstic acid. The sample was then examined and photographed with a Zeiss EM 109 transmission electron microscope at an accelerating voltage of 80 kV.

Incorporation efficiency (E%)

Sorbitan monostearate (C18) vesicles always showed an increased entrapment efficiency with respect to sorbitane monopalmitate (C16) niosomes. These results are similar to those reported for unsonicated sorbitan monoester niosomes loaded with doxorubicin, confirming the hypothesis that *E*% may be correlated to the hydrophobicity of the alkyl chain of the sorbitan esters (Uchegbu and Florence, 1995). Niosomes obtained from surfactant monomers with an ethereal linkage (Brij 30 and Triton CG 110) always presented a high *E*% which did not seem to be affected by the preparation method of vesicles, the size of which was very similar whatever the method used. Although (Kiwada et al. 1985) suggested that alkyl glycosides shorter than C14 could not form vesicle structures and might be removed by dialysis, we observed a high *E*% and good stability for octyl/decyl polyglucoside vesicles. Tretinoin, in this case, together with cholesterol may improve the ability of octyl/decyl polyglucoside to form stable vesicular aggregates because of its high hydrophobicity (log *K*O/W=6.3) and its amphipatic structure. In fact, its molecule contains a C9 alkyl chain which can modify the Critical Packing Parameter (CPP) and, therefore, the molecular geometry (Israelachvili, 1985) leading to very stable dispersions. All studied formulations were checked for their stability for 2 months without finding any differences in size or drug retention. (Manconi,2002). Saturation of lipid domains with reference to drug where low PC content provides limited entrapment capacity (Patel and Mishra, 1999). The increase in the entrapment efficiency is attributed to the ability of CHOL to cement the leaking space in the bilayer membranes, which in turn allow enhanced drug level in liposomes (Plessis et al.,1996). Tretinoin, in this case, together with cholesterol may improve the ability of

octyl/decyl polyglucoside to form stable vesicular aggregates because of its high hydrophobicity (log *K*O/W=6.3) and its amphipatic structure. In fact, its molecule contains a C9 alkyl chain which can modify the Critical Packing Parameter (CPP) and, therefore, the molecular geometry (Israelachvili, 1985) leading to very stable dispersions. All studied formulations were checked for their stability for 2 months without finding any differences in size or drug retention. (DNS5 and DNS6) resulted in loss of entrapment efficiency. Further, increasing the CHOL level increases the entrapment of drug from 1.54 mg/174 mg (DNS3) to 1.97 mg/210 mg (DNS4) but with a further increase in this level of CHOL the entrapment is reduced. This deciphers that the CHOL level beyond a certain level starts disrupting the bilayered structure leading to loss of drug entrapment levels (Redziniak and Perrier, 1996).

RELEASE STUDY

In vitro diffusion studies of TRA in different vesicle formulations were performed through a silicone membrane using vertical Franz diffusion cells (Rofarma, Milan). The receiver compartment had a volume of 7 cm3 and an effective diffusion area of 0.636 cm2. The receptor compartment was filled with a hydroalcoholic solution (ethanol:water 50:50) which was constantly stirred with a small magnetic bar and thermostated at 37 °C throughout the experiments. About 1 ml of each vesicle suspension with or without (control) TRA incorporated was placed on the silicone membrane surface and then the diffusion cells were covered with aluminium foil to prevent light exposure. A methanolic solution of TRA was also studied as a reference. Samples of the receiving solution were extracted after elapsed times of 2, 4, 6, 8 and 24 h and replaced with an equivalent volume of hydroalcholic solution to ensure sink conditions. The samples were mixed with the appropriate amount of I.S. and analysed by HPLC. At the end of the experiments, samples of the donor phase were analysed and checked for TRA content and vesicle stability. TRA recovery from the donor and receptor compartment was always more than 95–96% of the applied dose.(Manconi, 2002).

CONCLUSION

Vesicular systems have been realized as extremely useful carrier systems in various scientific domains. Over the years, vesicular systems have been investigated as a major drug delivery system, due to their flexibility to be tailored for the treatment of psoriasis. Orally administered drugs used in treatment of psoriasis has a limited use in glaucoma due to the systemic side effects associated with its use. Topical therapy is the mainstay of treatment for mild to moderate psoriasis and serves as a useful adjunct support to systemic therapy in

severe disease. However, efficacy and compliance to topical therapy in psoriasis have been a major concern. (Bhupinder Singh,2010). Several topical therapeutic agents are available for the treatment of psoriasis. Nevertheless, none of them can be regarded as an ideal drug molecule. This may either be due to their inherent side effects or their improper incorporation in the conventional vehicles. Niosomal formulation enhance permeability & increases bioavailability of drug.(Deepika aggarwal,2004).Niosomes basically possess an infrastructure consisting of hydrophilic, amphiphilic and lipophilic moieties together and as a result can accommodate drug molecules with a wide range of solubilities. there are 3 major types of niosomes -multilamellar vesicles (MLV, size >0.05 µm), small unilamellar vesicles (SUV, size -0.025-0.05 µm), large unilamellar vesicles (LUV, size >0.10 µm). MLVs vesicles exhibit increased-trapped volume and equilibrium solute distribution. Niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase to regulate the delivery rate of drug and administer normal vesicle in external non-aqueous phase. Niosomes are alternative to liposomes, as liposomes has certain disadvantages such as –they are expensive, their ingredients like phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special storage and handling and purity of natural phospholipids is variable. Like liposomes, aqueous suspension of niosomes may exhibit aggregation, fusion, leaching or hydrolysis of entrapped drugs, thus limiting the shelf- life of niosomes dispersion. Niosome preparation is time-consuming, requires specialized equipment, and is inefficient, particularly if smaller quantities are required for particular application or dose.

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