



## Influence of Liposomes and Niosomes on the *In Vitro* Permeation and Skin Retention of Finasteride

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### Abstract

In this work we sought to determine whether vesicles (liposomes/niosomes) were able to enhance finasteride concentration in the dermis layer, including the pilosebaceous units (PSU). Such enhancement could be beneficial in the treatment of some androgen-related skin disorders. Hamster flank skin was used to study <sup>3</sup>H-finasteride permeation via vesicles and a hydroalcoholic solution (HA). The drug-containing vesicles were composed of dimyristoyl phosphatidylcholine (DMPC) or egg lecithin: cholesterol: dicetyl phosphate (liposomes) and polyoxyethylene alkyl ethers (Brij<sup>®</sup> series) or sorbitan monopalmitate (Span 40): cholesterol: dicetyl phosphate (niosomes) and were prepared by the film hydration technique. Determination of finasteride content by HPLC showed 80-97% drug entrapment efficiency in the vesicles. The amount of <sup>3</sup>H-finasteride penetrated into and permeated through hamster skin 24 h after topical application of vesicles ranged from 5.5 to 13% of the initial dose, compared to 24%, observed with HA ( $p < 0.05$ ). The amount of finasteride deposited within the different skin strata via gel-state Span 40 and lecithin vesicles was lower, when compared with liquid-state Brij97, Brij 76: Brij 97 and DMPC vesicles. The fraction of finasteride found in the dermis layer was greatest where DMPC liposomes were used (7.8%). The vesicles significantly reduced drug permeation as indicated by the flux of finasteride from vesicles (0.025-0.058  $\mu\text{g}/\text{cm}^2\cdot\text{h}$ ), where compared with the HA (0.13  $\mu\text{g}/\text{cm}^2\cdot\text{h}$ ), ( $p < 0.01$ ). This study demonstrated the potentials of liquid-state vesicles in reducing the percutaneous absorption of finasteride and increasing its concentration and retention in the dermis layer.

**Keywords:** Deposition; DSC; Finasteride; Liposome; Niosome; Permeation.

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### 1. Introduction

Skin disorders such as acne, seborrhea, hirsutism and androgenic alopecia are

secondary to excess local activity of androgens, especially dihydrotestosterone (DHT), in the pilosebaceous units (PSU). DHT is formed from testosterone via the pivotal enzyme, 5 $\alpha$ -reductase. The possibility to enhance the concentration of 5 $\alpha$ -reductase inhibitors at the PSU, to alleviate the disease

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states associated with or originating from, has been implicated in a number of studies [1-4].

Finasteride is a known  $5\alpha$ -reductase inhibitor [2, 5-7] expected to be pharmacologically active at the PSU. There have been several clinical studies on the efficacy of oral finasteride for the treatment of seborrhoea [7], female hirsutism [8-10] and androgenetic alopecia [7, 11-15]. Finasteride has also been used topically to treat androgenetic alopecia [16]. Finasteride topical formulations, if provide sufficient drug concentrations at the PSU, would be advantageous over oral tablets, because of their reduced systemic side effects.

In recent years, many attempts have been made to enhance drug deposition in the hair follicle and PSU using delivery systems such as nanoemulsions [17, 18], low-molecular weight dextrans [19], microspheres [20, 21], iontophoresis [22-24] and niosomes or liposomes [1, 17, 25-33]. Niosomes are shown to have some advantages over liposomes with respect to chemical stability, lower costs and the large number of surfactant classes to design these vesicles on demand [34-37]. Formulation factors like lipid composition and charge may affect skin distribution of drugs [28, 38-42]. The therapeutic efficacy of vesicular formulations can be affected by the physical state of vesicles [34, 43]; bilayers in the liquid state are not closely packed as in the gel state and penetrate more easily across the skin strata.

Although finasteride is being used orally in the treatment of alopecia, and it has been used as a hydroalcoholic topical solution in a clinical study [16], its skin permeation and biological effects on PSU has not yet been reported in the literature. In this study, we sought to examine deposition of liposomes- and niosomes-encapsulated  $^3\text{H}$ -finasteride into the different strata of the Golden hamster flank skin. We also wanted to compare the skin permeation of finasteride via vesicles with hydroalcoholic solution. Therefore, we undertook some studies to determine the

extent to which liposomes/niosomes containing finasteride promote permeation through or deposition into skin and the possible mechanisms involved.

## 2. Materials and methods

### 2.1. Materials

Non-ionic surfactants: Brij 72 (polyoxyethylene 2 stearyl ether), Brij 76 (polyoxyethylene 10 stearyl ether), Brij 97 (polyoxyethylene 10 oleyl ether), Span 40 (sorbitan monopalmitate) and cholesterol (chol) were purchased from Fluka (Switzerland). Dicapryl phosphate (DCP) was obtained from sigma. Dimyristoyl phosphatidylcholine (DMPC) was from Nippon Fine Chemicals (Japan).  $^3\text{H}$ -finasteride, having the specific activity of 25 Ci/mmol, was purchased from American Radiochemicals (ARC, USA) and finasteride was from CIPLA Inc. (India). Clobazam was kindly provided by Hakim Pharmaceuticals (Tehran, Iran). Hyamine hydroxide (ICN Biochemical) was used as a tissue solubilizer. Ready Value<sup>®</sup>, Ready Organic<sup>®</sup> and Ready Protein<sup>+</sup><sup>®</sup> scintillation cocktail were obtained from Beckman (USA). Sephadex G-25 coarse was bought from Pharmacia LKB (Uppsala, Sweden). Egg lecithin, acetonitrile LC grade and methanol LC grade were obtained from Merck (Germany). All other chemicals and solvents were of analytical grade. HPLC-grade deionised water was produced using Direct-Q<sup>™</sup> (Millipore, France).

### 2.2. Animals

Male adult Golden Syrian hamsters (weighing 80-110 g), 10-12 weeks of age, were purchased from Pasteur Institute (Tehran, Iran). The animals were housed one per cage in plastic boxes on sawdust with tap water. The animals were housed at a photoperiod of about 14 h-light and 10 h-darkness and ambient temperature, for at least 2 weeks prior to the experiments. The skin overlying

the flank organs was closely shaved with an electric hair clipper. The experiments using animals were approved by the university's ethics committee.

### 2.3. Vesicle preparation

Multilamellar vesicles (MLVs) were prepared by the film hydration method as reported by Baillie et al. [44] with some modifications. Lipid components of niosomes comprising one surfactant or two surfactants: chol: DCP (7:3:1, m.r.) or liposomes consisting egg lecithin or DMPC: chol: DCP (8:2:1, m.r.) were dissolved in chloroform: methanol (2:1, v/v). The total lipid concentration was 30 mM. Finasteride solution in the same solvent (0.53 mM) was spiked with  $^3\text{H}$ -finasteride at 8  $\mu\text{Ci}/\text{ml}$  and added to the lipid solution in a round bottom flask. The solvents were removed using a rotary evaporator at a reduced pressure. The dried thin film was hydrated with PBS (pH 7.4) for 30 min at 10 °C above the phase transition temperature ( $T_c$ ) of the amphiphiles while shaking. The dispersion was left for 4 hours at room temperature (RT) to complete hydration and then stored at 4 °C overnight before use.

### 2.4. Determination of finasteride entrapment efficiency (EE%)

Finasteride-containing MLVs were separated from untrapped drug by size exclusion chromatography (SEC) using Sephadex G-25 coarse gel and PBS (pH 7.4) as eluting solvent. Empty liposomes/niosomes, extruded through 400 nm polycarbonate membrane (Nucleopore, Canada) were used to presaturate the column. Typically, a 100  $\mu\text{l}$  sample of finasteride-niosomes was loaded on the column, and then PBS (pH 7.4) was used as the eluting solvent at a flowing rate of 1 ml/min. The turbid fraction containing vesicles was collected and dissolved in methanol:PBS (1:1,

v/v). The finasteride content of the vesicles was then determined by HPLC using  $\text{C}_{18}$   $\mu\text{Bondapak}$  Waters column ( $4.6 \times 250$  mm, 10  $\mu\text{m}$ ) at 210 nm (UV detector, Waters, USA); the mobile phase consisted of 40:60 (v/v) acetonitrile:15 mM  $\text{KH}_2\text{PO}_4$  (pH 4.5) and was pumped at a rate of 1.4 ml/min at room temperature. Clobazam was used as internal standard. Finasteride entrapment efficiency is expressed as percent of initial amount of drug which was entrapped within the vesicles.

[EE% = (drug amount in turbid fraction/total drug amount initially used)  $\times$  100]

### 2.5. Vesicle characterization

The freshly prepared MLVs was first examined under light microscope (Leitz, Germany) and polarized light microscope (Olympus Optical Co., Japan) for the absence of any finasteride or cholesterol crystals or surfactant aggregates. The vesicle size distribution was determined by a Single Particle Optical Sensing (SPOS) method using Klotz<sup>®</sup> particle sizer (Germany).

### 2.6. Differential scanning calorimetry (DSC)

A Mettler TA 4000 (Germany) equipped with a DSC-30 measuring cell, was used for calorimetric analysis. The temperature and energy was calibrated by indium as standard. The niosomal suspensions were concentrated by ultracentrifugation (Beckman L5-50, 16,000  $\times$  g, for 30 min at 4 °C). Fifteen  $\mu\text{l}$  samples containing approximately 1.5  $\mu\text{mole}$  lipid were placed in a small aluminum pan and sealed. An equal amount of PBS was placed in the reference pan. The niosomal samples were scanned at a rate of 5 °C/min, in the 0-80 °C range. Transition temperature was defined as trace moves off the baseline in the thermogram, i.e. the onset of the transition ( $T_c$ ) [34, 35, 45-48].

### 2.7. Hydroalcoholic solution of finasteride

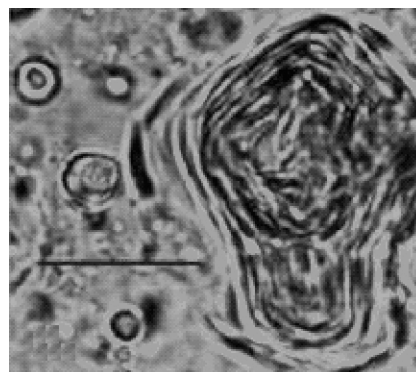
Finasteride and  $^3\text{H}$ -finasteride were dissolved in ethanol: propylene glycol: PBS pH 7.4 (56: 24: 20, v/v) in order to obtain a final drug concentration of 0.53 mM (and 8  $\mu\text{Ci/ml}$  activity).

### 2.8. In vitro deposition and permeation studies

Full thickness of flank skin was excised from freshly sacrificed hamster with ether and its subcutaneous fat was carefully removed using scalpel and scissor. The skin was mounted on the vertical Franz diffusion cells (Ashk-e-Shishe, Tehran, Iran), with the epidermal side facing up (skin area of 0.502  $\text{cm}^2$ , receiver volume of 8.5 ml). The receiver chamber was filled with PBS (pH 7.4) solution and the temperature was maintained at 37  $^{\circ}\text{C}$ .

Forty  $\mu\text{l}$   $^3\text{H}$ -finasteride liposomes or niosomes was applied on the hamster skin ( $n=3$ ) and massaged for 2 min with a small glass spatula. All experiments were carried out under non-occluded conditions. Samples of 0.5 ml were withdrawn from the receiver chamber periodically and replaced with the same amount of PBS. The samples were mixed well with 5 ml Ready Value<sup>®</sup> liquid scintillation cocktail to produce a stable clear-phase gel.

After 24 h, the donor compartment was carefully rinsed with 300  $\mu\text{l}$  buffer ( $\times 5$ ). The excised skin was removed from diffusion cell and fixed on a board using pins, with the epidermal side up. The flank skin was processed into its respective strata as follows. Eighteen pieces of adhesive tape, 1.9 cm wide and about 6 cm long, were used to complete stripping the stratum corneum (SC); 3 strips to remove the surface SC, 7 strips to remove intermediate SC and 8 strips for inner SC. The amount of drug remaining in the deeper skin strata was determined in the residual of the full



**Figure 1.** Optical micrographs of finasteride-containing Brij 72:cholesterol:dicetyl phosphate (7:3:1, m.r.) niosomes prepared by film hydration method (Bar = 10  $\mu\text{m}$ ).

thickness skin.

The tape strips were immersed in 5 ml Ready Protein<sup>+</sup><sup>®</sup> scintillation cocktail for 72 hours at 37  $^{\circ}\text{C}$  to dissolve the stratum corneum. To solubilize the tissue specimens, they were placed in Hyamine hydroxide (tissue solubilizer, ICN) for 48-72 hours at 37  $^{\circ}\text{C}$ . The solution was mixed with 1 ml hydrogen peroxide (30% v/v), which was added drop-wise, incubated for 24 h at RT, then mixed with Ready Value<sup>®</sup> scintillation cocktail containing 0.7% glacial acetic acid, and again incubated at RT for 2 days before counting. The  $^3\text{H}$ -finasteride was determined using a liquid scintillation counter (Beckman LS 6500 scintillation counter, USA).

### 2.9. Data analysis and statistics

The data is expressed as mean $\pm$ SD. Statistical analysis was performed by the student "t" test or analysis of variance (ANOVA) followed by Tukey post Hoc test using SPSS 11.5 for Windows. The level of significance was taken at  $p$ -values  $<0.05$ .

## 3. Results and discussion

### 3.1. Vesicle preparation and characterization

All of the vesicles exhibited X-cross images under polarized light microscope, indicating the lamellar structure of the bilayer membrane. The mean area-number diameters

**Table 1.** Physical characteristics of vesicles and *in vitro* study of <sup>3</sup>H-finasteride deposition in and permeation through the hamster flank skin, 24 hours following the topical application of drug-containing negatively-charged liposomal/niosomal formulations and hydroalcoholic drug solution, using Franz diffusion cells.

Liposome/niosome composition	Physical characteristics		Skin compartments					
			(Percent mean of applied dose $\pm$ SD, n=3)					
	<sup>a</sup> d <sub>AN</sub> $\pm$ SD ( $\mu$ m)	<sup>b</sup> EE% $\pm$ SD	Surface SC <sup>c</sup>	Strips 4-10	Strips 11-18	Flank remain	Percutaneous permeated <sup>d</sup>	Mass balance <sup>e</sup>
Ethanol:PG:PBS (56:20:24 v/v %)			72.3 $\pm$ 3.1	8.2 $\pm$ 0.8	5.1 $\pm$ 2.0	6.6 $\pm$ 0.8	4.1 $\pm$ 0.4	96.4 $\pm$ 4.8
Lecithin:chol:DCP (8:2:1, m.r.)	1.97 $\pm$ 0.07	82 $\pm$ 3.3	84.3 $\pm$ 8.3	1.5 $\pm$ 0.7	0.7 $\pm$ 0.1	1.7 $\pm$ 0.4	1.7 $\pm$ 0.3	89.9 $\pm$ 9.0
DMPC:chol:DCP (8:2:1, m.r.)	2.16 $\pm$ 0.13	89 $\pm$ 8.5	75.3 $\pm$ 8.0	2.3 $\pm$ 0.2	1.7 $\pm$ 0.6	7.8 $\pm$ 1.8	1.8 $\pm$ 0.47	88.9 $\pm$ 8.6
Span 40:chol:DCP (7:3:1, m.r.)	4.44 $\pm$ 0.15	94 $\pm$ 5.2	81.0 $\pm$ 7.9	2.5 $\pm$ 0.8	1.1 $\pm$ 0.1	1.5 $\pm$ 0.4	1.4 $\pm$ 0.1	87.6 $\pm$ 8.6
Brij 72:chol:DCP (7:3:1, m.r.)	3.88 $\pm$ 0.23	97 $\pm$ 1.6	82.9 $\pm$ 9.1	1.4 $\pm$ 0.4	1.1 $\pm$ 0.1	2.2 $\pm$ 0.6	1.8 $\pm$ 0.3	89.2 $\pm$ 8.0
Brij 76:chol:DCP (7:3:1, m.r.)	2.96 $\pm$ 0.14	80 $\pm$ 7.1	81.5 $\pm$ 6.1	1.8 $\pm$ 0.5	1.1 $\pm$ 0.2	2.8 $\pm$ 0.9	2.5 $\pm$ 0.5	90.1 $\pm$ 6.6
Brij 97:chol:DCP (7:3:1, m.r.)	1.98 $\pm$ 0.06	93 $\pm$ 3.9	84.9 $\pm$ 4.1	2.1 $\pm$ 0.2	1.5 $\pm$ 0.4	4.9 $\pm$ 0.6	2.6 $\pm$ 0.7	96.0 $\pm$ 3.4
Brij 76:Brij 97: chol:DCP (3.5:3.5:3:1, m.r.)	2.38 $\pm$ 0.08	93 $\pm$ 1.1	81.3 $\pm$ 10.4	2.9 $\pm$ 0.7	1.8 $\pm$ 0.3	4.3 $\pm$ 0.8	2.9 $\pm$ 0.7	92.5 $\pm$ 0.9

<sup>a</sup>Mean area-number diameter (n=3); <sup>b</sup>Finasteride entrapment efficiency in the vesicles (n=3); <sup>c</sup>SC=Stratum corneum; <sup>d</sup>Determined in the receiver chamber of Franz diffusion cell; <sup>e</sup>Percent of applied dose determined in all skin compartments and the receiver chamber of Franz cell.

(d<sub>An</sub>) of MLVs ranged from 2 to 4.4  $\mu$ m (Table 1). Brij 76 formed discomes (large disk-shape vesicles) or MLVs where 20 or 40 mole% of cholesterol was included, respectively. Brij 72 formed polyhedral MLVs in a viscous gel medium (Figure 1). The entrapment efficiency (EE %) of finasteride in the recovered MLVs ranged from 80 to 97% (Table 1).

### 3.2. Differential scanning calorimetry

Niosomes prepared from saturated alkyl chains surfactants (e.g. Brij 76, Figure 2a) had a significantly higher T<sub>c</sub> than the vesicles prepared from unsaturated alkyl chain surfactants of the same length (Brij 97), (35.4 °C vs. 21 °C). The DSC of niosomes composed of the mixture of 1:1 mole ratio of saturated and unsaturated surfactants (i.e.,

Brij 76:Brij 97) showed an endothermic transition at 21 °C and a trace change in the base line (Figure 2b). Brij 72 niosomes had an endothermic transition at 55.4 °C. Inclusion of cholesterol at higher concentrations (> 30 mole%) abolished the gel-liquid transition of span 40 and Brij 72 niosomes.

### 3.3. *In vitro* skin distribution and permeation

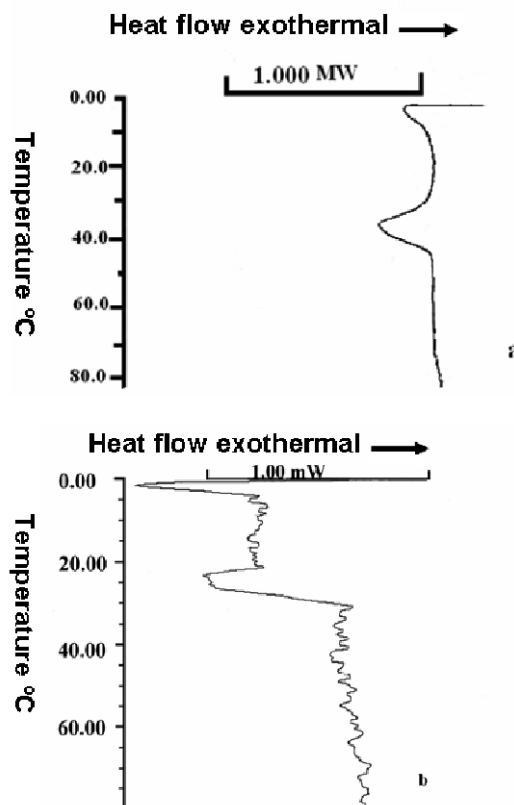
Mean percentage of <sup>3</sup>H-finasteride determined in isolated hamster flank skin following *in vitro* permeation studies are presented in Table 1. The total amount of finasteride penetrated into and permeated through hamster skin 24 h after topical application of liposomes and niosomes ranged from 5.5 to 13% of the initial dose, compared to 24%, observed with hydroalcoholic solution

( $p < 0.05$ ). The lower extent of drug permeation via MLVs may indicate that the lipid bilayers of niosomes/liposomes were rate limiting in drug permeation. Other reasons could be the size of vesicles and/or their  $T_c$  which may further contribute to impeding drug permeation. Similarly, Bernard et al. [38] suggested that liposomes clearly delayed the drug permeation compared with solution but better localized the drug in the sebaceous structure (targeting effect of liposome). Deposition of finasteride into the stratum corneum (strips 4-18) was significantly higher via hydroalcoholic solution compared to MLVs ( $p < 0.05$ ). This could be due to quick fixation of finasteride to the stratum corneum following solvent evaporation. Moreover, ethanol is a very effective skin penetration enhancer [49].

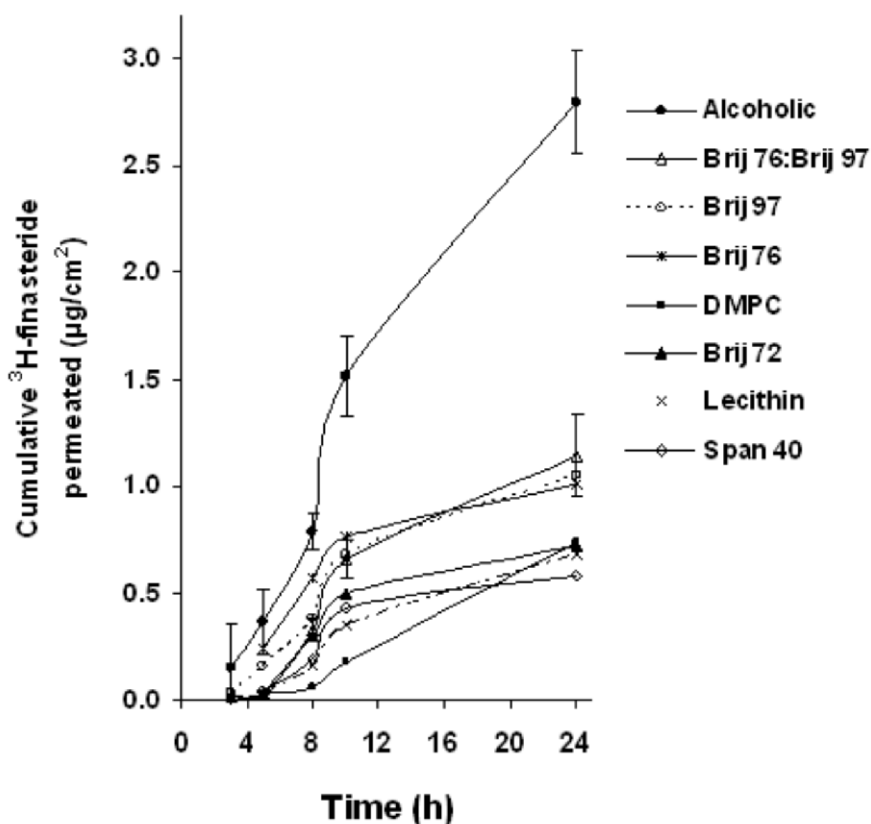
The topically applied formulation undergoes dehydration at the temperature of the skin, i.e.  $\sim 32^\circ\text{C}$ . At this temperature, niosomes made of Brij 52, Brij 72, Brij 76 (Figure 2a) and span 40 remain in the gel-state, whereas vesicles comprising amphiphiles of liquid-state nature, i.e. having the  $T_c < 32^\circ\text{C}$ , begin to melt (Figure 2b), resulting in the bilayer fluidization, and partial release of the amphiphiles from the bilayers. The amount of finasteride deposited within the different skin strata was lower from gel-state Brij 72 and Span 40 niosomes and lecithin liposome, compared to liquid-state Brij 97, Brij 76:Brij 97 and DMPC MLVs and also gel-state Brij 76 niosomes,  $p < 0.05$  (Table 1). An explanation is that non-ionic surfactants of higher hydrophilicity (i.e. Brij 76 and Brij 97) appear to increase leakage of drug from the vesicles [43], which as a result improves delivery of lipophilic molecules. The fraction of finasteride found in the dermis layer, following application of different formulations, was greatest when DMPC liposomes were used. Low transition temperature and penetration enhancing effect of DMPC may account for this high drug

deposition. Similar findings by Ganesan et al. [50] indicate that although liposomes clearly do not pass through the skin, they do induce remarkably different permeation behaviors of solute entrapped within them.

In order to administer finasteride via the topical route, a preparation is desirable which improves penetration into the skin, especially in sebaceous gland-containing zone, while reducing systemic absorption. MLV-mediated effect on finasteride permeation through flank skin is compared to hydroalcoholic solution in Figure 3. The cumulative amount-time profiles of finasteride permeation followed the zero-order kinetics ( $R^2 > 0.84$ ). The MLVs had a significantly greater retaining effect on finasteride compared to hydroalcoholic solution (ANOVA,  $p < 0.01$ ). These results agree well with those of Weiner and co-workers [50] who reported that skin



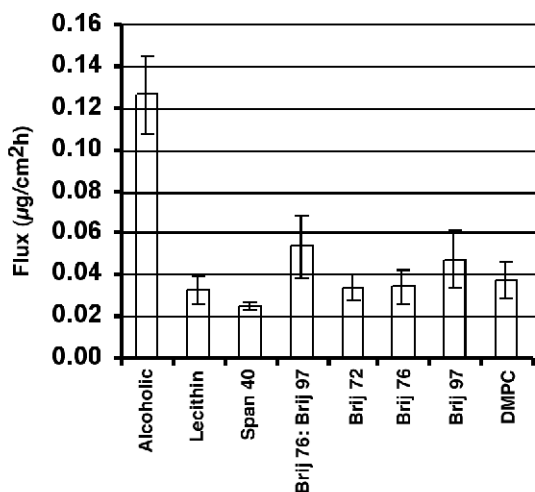
**Figure 2.** Differential scanning calorimetric thermograms of finasteride-containing niosomes comprising: a) Brij 76:chol:DCP (7:3:1, m.r.) and b) Brij 76:Brij 97:chol:DCP (3.5:3.5:3:1, m.r.).



**Figure 3.** Permeation profiles of <sup>3</sup>H-finasteride through hamster flank skin after topical application of drug-containing negatively-charged niosomal/liposomal formulations and hydroalcoholic drug solution using Franz diffusion cells. Each point represents the mean  $\pm$  SD (n=3).

permeation of lipophilic active compounds was lower via liposomes than via solutions. The flux of finasteride from Brij 76, Brij 97 ( $t=3.3$ ,  $p=0.028$ ) and Brij 97 ( $t=2.1$ ,  $p<0.01$ ) niosomes and DMPC liposome ( $t=2.2$ ,  $p=0.08$ ) was higher, where each compared with the flux of drug from gel-state Span 40 niosome using Student t-test. On the other hand, permeation rates of finasteride from gel-state Span 40, Brij 76, Brij 72 niosomes and lecithin liposomes were not significantly different ( $p>0.05$ ) (Figure 4). Differences in effect on drug transport between the liquid-state MLVs and the gel-state vesicles may be explained by differences in skin-formulation interactions, i.e. either due to the extent of interaction between vesicles and the stratum corneum [50]. The surfactant molecules of liquid-state nature are thought to permeate into the intercellular lipid bilayers,

thereby reducing the crystallinity of the intercellular lipid bilayers and thus increase the permeability of these bilayers [51]. In contrast, surfactant molecules forming rigid gel-state bilayers can not penetrate into the stratum corneum, and thus they are not able to induce a penetration enhancing effect [52]. On the other hand, the packing nature of unsaturated fatty acids (i.e. Brij 97) can change the fluidity of SC lipid structure and facilitate the skin permeation of drugs [53, 54]. Thus, transfer of drug from the lipid bilayers of vesicles into skin can occur as long as the bilayers are in a liquid-crystalline state. There is a relationship between the penetration-enhancing ability of niosomes and their effect on the ultrastructure of SC. Hofland et al. [52] using freeze fracture electron microscopy confirmed that adsorption of niosomes on the outermost layer of the SC by forming



**Figure 4.** The flux of 3H-finasteride across hamster flank skin from various negatively-charged niosomes/liposomes compared to hydroalcoholic solution (as control). Each vertical bar and its error bar represent mean  $\pm$  SD (n=3).

stacks of bilayers on top of the SC. On the other hand, lipid bilayer structure of the stratum corneum can be disrupted by the niosome and liposome formulations.

Niosomes appear to have potential as a novel drug carrier system for both dermal and transdermal delivery of drugs [52]. One important question is whether intact vesicles are able to penetrate into the stratum corneum or even into the deeper layers of the skin. Although it is generally believed that intact liposomes do not penetrate compact layers of the stratum corneum [55], the specific mechanisms of liposome action in the skin strata remain to be enlightened. The mechanisms behind the vesicle-skin interaction are still unclear. Vesicle disintegration in the sebum-filled hair follicles seems to be likely; however, intact MLVs may also enter and traverse the follicle duct. On the other hand, maintenance of drug-liposomal bilayers interaction in the hair follicle may also be possible [26]. It is generally believed that the intercellular route may dominate during steady state penetration of compounds; however, it has been argued that the skin appendages (hair follicles, pilosebaceous and eccrine glands) may offer an alternative pathway for a diffusing

molecule [49]. Lauer et al. [25] proposed a theory that upon dehydration, the liposomal bilayers may yield a fluid liquid-crystalline state in which bilayers containing drug can partition and pack into the follicular ducts that contain lipids.

#### 4. Conclusion

The MLVs had a significantly greater retaining effect on finasteride permeation compared to the hydroalcoholic solution (ANOVA,  $p < 0.01$ ). Negatively-charged DMPC, Brij 97 MLVs and Brij 76: Brij 97 MLVs, all being in the liquid-state, facilitated the deposition of finasteride into dermis layer, when compared with hydroalcoholic solution. In contrast, vesicles composed of surfactants of gel-state nature did not enhance delivery of the drug to the dermis layer, possibly due to lower interaction with and lack of penetration into the skin dense layers. Therefore, phase transition temperature of amphiphiles used to prepare vesicles from may play an important role in permeation of drug through skin. More comprehensive studies are required to demonstrate the potentiality of this route of drug delivery. However, in order to truly ascertain the significance of follicular delivery, appropriate models and quantitative methods must still be developed. Greater understanding of the control mechanisms, which govern this complex structure, may accelerate rational design of hair follicle-specific drug delivery systems.

#### Acknowledgements

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