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Capsaicin delivery into the skin with lipidic nanoparticles for the treatment of psoriasis

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Abstract

The study aims to explore the potential of solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) in improving the topical delivery of capsaicin (CAP) by in vitro and in vivo studies. The lipidic nanoparticles were prepared by solvent diffusion method and were characterized for average particle size, zeta potential and entrapment efficiency. TEM photomicrographs revealed that the particles were nanometric in size. Higher amount of CAP can be encapsulated in the NLCs (87.4 ± 3.28) as compared with SLNs (79.7 ± 2.93%). The cumulative amounts of CAP permeated through the skin and retained in the SC were higher in the case of NLCs as compared with plain drug solution and SLNs. SLNs and NLCs exhibited minimum to no irritation. All the results concluded that NLCs and SLNs have shown a good ability to increase drug accumulation in the various skin layers but NLCs may be a more potential carrier for topical delivery of CAP for an effective therapy of psoriasis.

Keywords: CAP, lipidic nanoparticle, skin, topical delivery

Abbreviations: CAP: Capsaicin; CA, Compritol 888 ATO; HIF-1α, Hypoxia-inducible factor-1α; NLCs, Nanostructured lipid carriers; OA, Oleic acid; PC, L-α Egg phosphatidylcholine; PF68, Pluronic F-68; PII, Primary irritation index; SC, Stratum corneum; SLNs, Solid lipid nanoparticles; TEM, Transmission electron microscope

Introduction

Psoriasis is a polygenetic autoimmune multifactorial disease that manifests prominent alterations in the cutaneous microvasculature (Agarwal et al. 2001). It is characterized by hyperplastic regenerative, excessive growth and differentiation of keratinocytes. Various topical therapies are available for its treatment as first treatment option. Capsaicin (CAP) is found to adjust the translation of hypoxia-inducible factor-1α (HIF-1α) through transient receptor potential vanilloid receptor subtype 1 receptor, thereby inducing normal differentiation by inhibiting the hyperproliferation of psoriatic epidermis (Yu 2011). Treatment of psoriatic skin requires high drug levels at specific site of the skin with less systemic absorption. Topical therapy is the primary option and treatment of choice for mild to moderate psoriasis; however stratum corneum (SC) imposes a stern barrier for localized skin delivery. Use of nanocarriers has been advanced as a promising method to increase the drug transport across the skin (Agrawal et al. 2012).

Therapeutic potential of topically applied CAP (trans-8-methyl-N-vanillyl-6-nonenamide) is attributed to the inhibition of cutaneous vasodilatation and blockade of the axon reflex vasodilatation produced by a variety of erythematogenic chemicals. Moreover, topical CAP is a potent substance P depletory which serves as an important factor in the pathophysiology of psoriasis (Chhabra et al. 2012). However, topical administration of CAP to human skin is limited due to the induction of erythema accompanied by sting, burning and pain sensations (Lowes et al. 2007).

Another difficult aspect of the topical delivery of CAP is the barrier nature of the SC and its complexity in controlling and not determining the exact amount of drug that reaches to different skin layers. Differential drug distribution in the various skin layers also depends on the physicochemical characteristics of the vehicle. Several new drug carrier systems are used to eliminate the adverse effects and control the release of the drug at the intended target without reducing the efficacy (Desai et al. 2013, Teichmann et al. 2007). Nanocarriers made up of biocompatible lipids are gaining increasing attention for the topical delivery of poorly soluble drugs for both pharmaceuticals and cosmetics (Pardeike et al. 2009). Among them solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) have emerged as an alternative carrier system than traditional carriers, such as polymeric nanoparticles, emulsion and liposomes. They have demonstrated to their application in case of several drugs evaluated for topical therapy of skin diseases (Fang et al. 2008).

The lipidic nanoparticles offer a great potential for the administration of active molecules and simultaneously for

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their improved therapeutic efficacy. They are beneficial in many aspects with great feasibility of incorporation of lipophilic drugs, enhanced physical stability, increased bioavailability, prevention of degradation, low cost and enhanced penetration through skin by being nano-sized and rich in lipid content (Gupta and Vyas 2012). Accumulation of the nanometer-sized particles is favored due to the close contact with superficial junctions of corneocyte clusters and pores between corneocyte. Moreover, their lipid core aids in epidermal targeting, controlled release and the drug penetration through the SC due to the formation of an intact film on the skin surface upon drying (Gupta et al. 2011).

SLNs are prepared using solid lipids which lead to some problems like limited drug loading, risk of gelation, drug expulsion and leakage during storage caused due to lipid polymorphism (Gupta et al. 2012, Almeida and Souto 2007). NLCs, the new generation alternative of lipidic nanoparticles, consist of a blend of spatially different lipid molecules, that is, solid lipid (s) with liquid lipid (s) (Joshi and Patravale 2008) where the amount of liquid lipid can be varied to attain controlled release of the drug (Hu et al. 2005). This blend generates a typical crystalline structure with many imperfections providing more space for drug loading. Their potential for dermatological applications has also been established for topical treatment module of many drugs (Pardeike et al. 2009). The beneficial features of SLNs and NLCs for topical route of application are widely reported in the literature. Drug in the superficial/surface layers of nanoparticles can burst release, whereas drug–lipid interactions and drug localization in the core of the particles could produce slow and prolonged release. Indeed, these carriers have been explored as suitable systems to modify the penetration/permeation of drugs through the skin. The previous studies established that SLNs and NLCs dispersion of calcipotriol, methotrexate (Lin et al. 2010) and acetretin (Agrawal et al. 2010) (antipsoriatic drugs) is appreciably useful for skin targeting through topical application and offers localized effect (of the drugs).

In view of the available literature, exploring the potential of SLNs and NLCs in improved or modified topical drug delivery of CAP seems promising possibility. The main purpose of our investigation was to develop and evaluate the most effective system for successful topical delivery of CAP. Furthermore, the present study aimed at fabricating SLNs and NLCs and investigated their relative in vitro skin permeation, drug localization in the different skin layers and retention resulting in altered efficacy and toxicity. Moreover, in order to mimic the clinical situation hyperproliferative skin was used as a skin barrier for delivery of CAP.

Materials and methods

Materials

CAP, L-α Egg phosphatidylcholine (PC), pluronic F-68 (PF68) and sephadex G-50 were purchased from Sigma Chemicals Co. St. Louis, Missouri (USA). Compritol 888 ATO (CA) used as solid lipid material was generously provided by Colorcon Asia Ltd. Oleic acid (OA) was used as liquid lipid material, obtained from Fluka. All other reagents and solvents were either of analytical or high-performance liquid chromatography (HPLC) grades.

Preparation of drug-loaded SLNs and NLCs dispersion

SLNs and NLCs with or without CAP were prepared by solvent diffusion method in an aqueous system as reported earlier with slight modification (Hu et al. 2005). Briefly, 100 mg of selected lipid (CA/CA and OA) and drug was dissolved completely in a 10 ml 1:1v/v mixture of acetone and ethanol in a water bath at 70°C. This lipid solution was dispersed into 100 ml of an acidic aqueous phase containing 2:1 ratio of PC and PF68 under continuous mechanical agitation (Remi Instruments, Mumbai, India) at 4000 rpm at room temperature for 5 min. Aggregates of lipidic nanoparticles were prepared by adjusting the pH value to 1.20 by addition of 0.1 M hydrochloric acid. The aggregate of nanoparticle dispersion was then centrifuged (25,000 rpm for 30 min, Hitachi CPMax-100, Japan); the pellet obtained was then re-suspended in distilled water. In the formulations of SLNs and NLCs, compritol 888 ATO was used as a core material. Oleic acid was used with compritol 888 ATO as a core material in case of NLCs' formulations.

Size and zeta potential

Transmission electron microscope (TEM) of SLNs and NLCs was performed to characterize them in terms of size. It was performed after drying on 3 mM formalin (0.5% plastic powder in amyl acetate)-coated copper grid (300 mesh) at 60 kV (Philips Morgagni 268, Eindhoven, The Netherlands) after staining negatively using uranyl acetate (4%), and photomicrographs were taken at suitable magnifications (Philips Morgagni 268, Eindhoven, The Netherlands). The average particle size and zeta potential of the CAP-free and CAP-loaded nanoparticulate dispersion were determined by photon correlation spectroscopy, using the Zetasizer nano ZS90 (Malvern Instruments, Ltd., Malvern, UK).

Entrapment efficiency

The entrapment efficiency (EE %) of CAP-loaded SLNs and NLCs was determined by measuring the concentration of unentrapped CAP in the lipidic dispersion as reported elsewhere (Vobalaboina and Kopparam 2004, Das et al. 2012). Briefly, dispersion of nanoparticles was subjected to centrifugation for 20 min at 25,000 rpm (Hitachi CPMax-100, Japan). The amount of CAP in filtrate was determined by HPLC method. All analyses were performed in triplicate. The mobile phase used was a mixture of methanol and water (3:2 v/v); it was used at a flow rate of 0.6 ml/min. The detection was done at a wavelength of 280 nm (Agarwal et al. 2001).

In vitro skin permeation and retention studies

Experiments were performed by using locally fabricated Franz diffusion cell with the diffusion area of 3.14 cm^2. Hair of the dorsal skin of the albino rat was carefully removed and the excised skin was washed with physiological saline solution after removing the subcutaneous fat and connective tissue. Subsequently, skin was examined for intactness and then preserved in a refrigerator at 4°C for subsequent use (Magnusson and Koskinen 2000). The skin was secured

between the donor and receptor compartments of the diffusion cell with the SC facing donor compartment. One milliliter of a formulation was placed on the donor compartment. The diffusion medium in the receptor compartment was a 10 ml mixture of PBS pH 7.4:ethanol solution (1:1v/v) (Agarwal et al. 2001), which was maintained at 37 ± 1°C and continuously stirred using a small magnetic bar at 100 rpm throughout the experiment.

At pre-determined time intervals up to 24 h, 200 µl of the fluid was withdrawn and replaced with an equal volume of fresh fluid (blank receptor medium) to maintain a constant volume of receiver compartment. The experiments were repeated in triplicate. The samples were analyzed using HPLC, as mentioned in the above section. Excess formulation was removed after 24 h by wiping the test area with the help of cotton swab, washed 3 times with PBS:ethanol mixture (1:1v/v), and then dried using a filter paper.

To determine the drug concentration in the SC, 20 tapes (Transpore™, VWR International, Herlev, Denmark) were applied with constant pressure for 2 min and carefully removed gradually with constant force applied at a 45° angle to the skin, using clean forceps (Raza et al. 2012). The first two strips were discarded due to potential amount of drug remaining on the skin surface and strips 3–20 were collected. The tapes were pooled in a tube containing PBS (pH 7.4):ethanol mixture (1:1 v/v). Then, the tubes were vortexed for 20 min, sonicated for 30 min and vortexed again for 1 h to extract CAP from the tapes. To determine the drug amount in the viable skin (epidermis and dermis), the remaining skin was cut into small pieces and homogenized (York, Mumbai, India) in PBS (pH 7.4):ethanol (1:1 v/v) mixture after vortexing for 20 min. The resulting solution was sonicated for 30 min, vortexed again for 30 min and centrifuged at 10,000 × g (Hitachi CPMax-100, Japan) for 30 min. The amount of CAP extracted from tapes and remaining in the skin samples was determined by using HPLC.

In vivo studies

All the study protocols were approved by the Animal Ethical Committee of Dr. H.S. Gour University (Sagar, India). Studies were performed according to the guidelines compiled by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA, Ministry of Culture, Government of India). All the experimental rats were housed in cages, with access to food and water *ad libitum* until use.

Drug localization in the different skin layers by in vivo tape stripping

The dorsal skin of albino rat was washed with physiological saline solution after the removal of hair. Drug localization in different skin layers was determined by the method reported by Song and Kim (2006) (Knudsen et al. 2012), with slight modification. Animals were anesthetized with an intraperitoneal injection of ketamine hydrochloride (100 mg/kg). CAP-NLCs and CAP-SLNs (1%) were applied topically onto the well-marked test area (2 × 3 cm) on the dorsal skin with an approximate CAP amount (Magnusson and Koskinen 2000). After 24 h, the rats were sacrificed by cervical dislocation and the skin was stripped as mentioned in the above section. Excess formulation was wiped off with a cotton swab, washed 3 times with PBS 7.4:ethanol mixture (1:1 v/v) and then dried with the help of a filter paper. To determine the drug concentration in the SC and other layers of viable skin, a similar procedure was followed or adopted as described in the previous section.

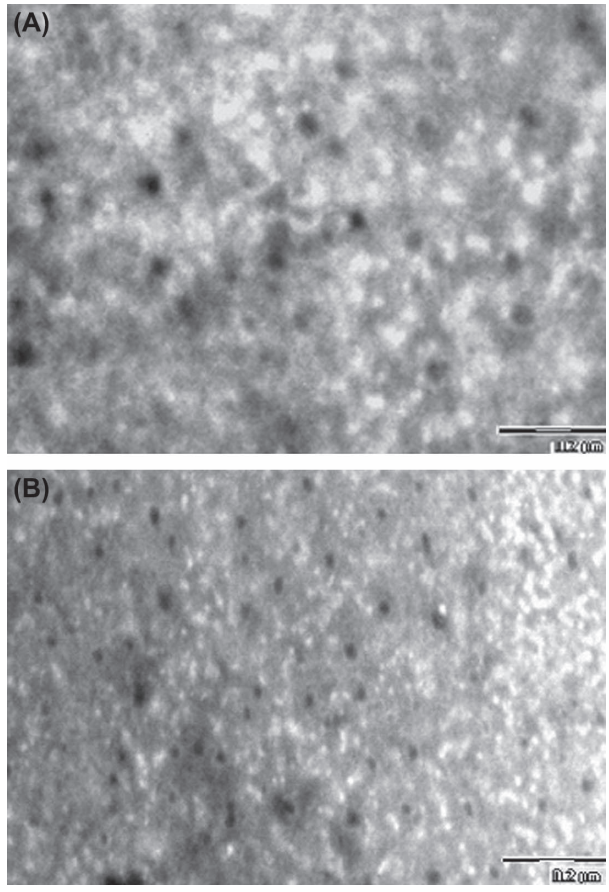

Figure 1. TEM photomicrographs of CAP-loaded SLNs formulation (A) and NLCs formulation (B).

Skin-irritation test

The Draize patch test was carried out on rabbits to determine the degree of irritation of CAP formulations (Song and Kim 2006). The back of the animals was made hair free with the help of a razor 24 h prior to the application of formulations. A 0.5 ml formulation was applied on shaved skin with uniform spreading over the area of 4 cm^2. The skin was observed for any visual change, such as erythema

Table I. The different physicochemical parameters of the formulations.

Formulation	Lipid phase	Emulsifiers	Size (nm)	Zeta potential (mV)	PDI	EE%
CAP-SLNs	CA	PC	182.5 ± 4.8	− 35 ± 1.7	0.189 ± 0.02	79.7 ± 2.93
CAP-NLCs	CA + OA	PC + PF68	145.3 ± 3.2	− 39 ± 2.1	0.156 ± 0.09	87.4 ± 3.28

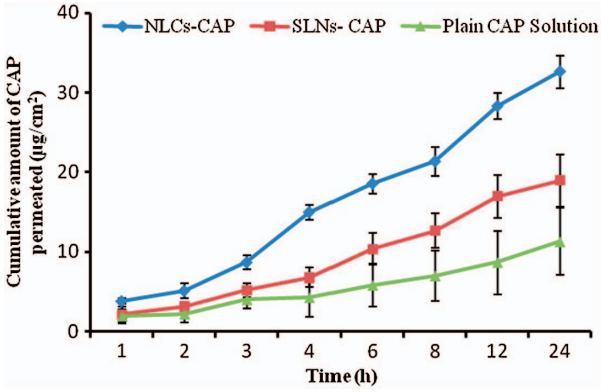

Figure 2. In vitro skin permeation of CAP for SLNs, NLCs and plain drug solution. Values are expressed as mean ± standard deviation ($n = 3$).

at 24, 48 and 72 h after the application of formulations. The mean erythemal scores were recorded (ranging from 0 to 4), depending on the degree of erythema, as follows: no erythema = 0; slight erythema (barely perceptible-light pink) = 1; moderate erythema (dark pink) = 2; moderate to severe erythema (light red) = 3; and severe erythema (extreme redness) = 4 grade.

In vitro skin permeation through hyper-proliferative skin

Tape-stripping technique was used to produce hyper-proliferative skin that mimics psoriasis-affected skin (Shah et al. 2007). The hair-free dorsal skin was stripped using a Transpore™ tape (VWR International, Herlev, Denmark) twice daily for 5 days and the stripping was repeated 10 times for each process. Hyper-proliferation of the skin was verified by histological observation. Each specimen was dehydrated using ethanol, embedded in paraffin wax and stained with hematoxylin and eosin. For each skin sample, three different sites were examined and evaluated under light microscopy (Eclipse 4000, Nikon, Tokyo, Japan). The permeation studies were performed for plain CAP solution, CAP-SLNs and CAP-NLCs as reported in the previous section.

Statistical analysis

All the results are expressed as mean ± standard deviation. The treated groups were compared with control by employing the Student t-test and analysis of variance (ANOVA) test using the Graph Pad INSTAT software, version 3.00 (Graph Pad Software, San Diego, CA). A value of $p < 0.05$ was considered statistically significant.

Table II. Results of in vitro permeation and skin retention study from lipidic nanoparticulate and plain solution: amount permeated through the skin at 24 h, percentage of CAP accumulated into the skin at the end of the permeation experiments (24 h).

Formulation code	CAP permeated through the skin at 24 h (µg/cm²)	Flux (µg/cm²/h)	Total CAP accumulated in to skin (%)
CAP-NLCs	32.62 ± 2.34	27.45 ± 2.27	30.07
CAP-SLNs	18.97 ± 2.15	16.78 ± 1.14	21.91
Plain CAP solution	11.28 ± 1.92	10.80 ± 1.59	10.11

The data were expressed as percentage of dose applied per unit area. Each point represents the mean ± S.D. ($n = 3$).

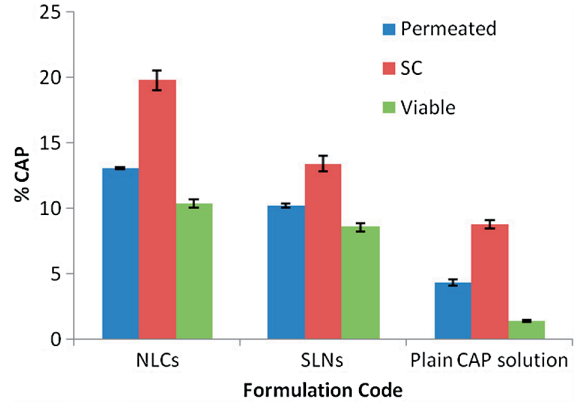

Figure 3. Percentage of CAP for SLNs, NLCs and plain drug solution for in vitro permeation and skin-retention studies. Values are expressed as mean ± standard deviation ($n = 3$).

Results and discussion

Preparation and characterization of carrier system

The SLNs and NLCs systems, for topical/localized delivery of CAP, were developed for greater skin retention of drugs. Delivery, penetration and localization of the drug in the different skin layers are greatly affected by the composition of the nanocarrier system (Fang et al. 2008). TEM photomicrographs (Figure 1) show that CAP-loaded SLNs and NLCs are nano-metric in size. The properties such as particle size, zeta potential and the polydispersity indices of the resultant SLNs and NLCs are listed in Table I. The average size of CAP-loaded particles was found to be slightly larger than that of drug-free particles, which may be due to the incorporation of CAP in the SLNs and NLCs matrix. Smaller size of the NLCs may be attributed to the amorphous core (due to the presence of liquid lipid content), while the crystalline lipid core of the SLNs may be responsible for their larger size (Demerjian et al. 2006, Liu et al. 2007). The chemical nature of the lipid matrix and surfactants imparts a high negative residual charge on the nanocarrier system. No significant difference was recorded between the zeta potentials for NLCs and SLNs. Negative zeta potential maintains the small size

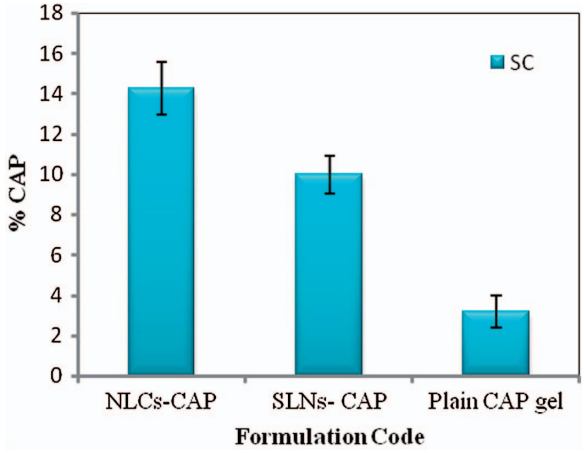

Figure 4. Percentage of CAP for SLNs, NLCs and plain drug solution in the SC for in vivo studies. Values are expressed as mean ± standard deviation ($n = 3$).

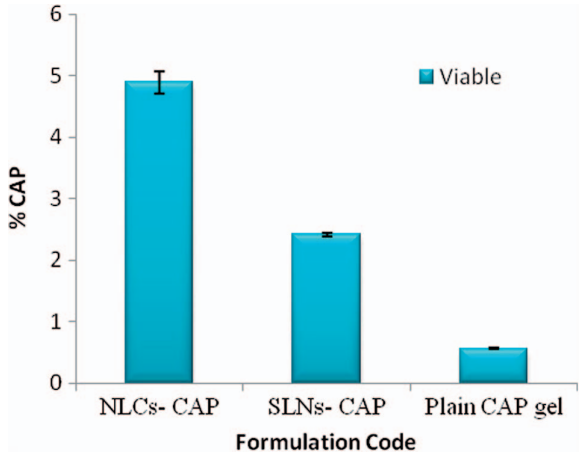

Figure 5. Percentage of CAP for SLNs, NLCs and plain drug solution in viable skin for in vivo studies. Values are expressed as mean ± standard deviation ($n = 3$).

and suspension stability of these systems provided by the electrostatic repulsion.

Entrapment efficiency

The entrapment efficiency of the developed SLNs and NLCs is recorded in Table I. It can be seen that the encapsulation of CAP in the NLCs (87.4 ± 3.28%) is higher than that in the SLN (79.7 ± 2.93%)-based formulations. Massive disturbance in crystal order occurs on inclusion of liquid lipids with solid lipids in the case of NLCs resulting in greater imperfections in the crystal lattice. These imperfections may provide more space to encapsulate drug moiety, thus leading to enhanced drug entrapment efficiency (Weyenberg et al. 2007).

In vitro skinpermeation and retention studies

In order to assess the skin targeting capability of the SLNs and NLCs, the permeation ability of CAP through the hairless rat skin was examined by conducting in vitro skin permeation and retention studies.

In this study, permeation data obtained from CAP-SLNs and CAP-NLCs were compared with plain CAP solution (0.6 mg/ml). Lipid-based formulations (NLCs > SLNs) showed higher amount of CAP permeation as compared with plain CAP solution (Figure 2). Higher drug permeation may be the attributed to structural composition of lipid nanoparticles. The cumulative amounts of CAP permeated from plain CAP solution, SLNs and NLCs at 24 h after dosing were 11.28 ± 1.92 µg/cm^2, 18.97 ± 2.15 µg/cm^2 and 32.62 ± 2.34 µg/cm^2, respectively. The steady-state permeation rates of CAP from plain CAP solution, SLNs and NLCs were 10.80 ± 1.59 µg/cm^2/h, 16.78 ± 1.14 and 27.45 ± 2.27 µg/cm^2/h, respectively. The plain CAP solution showed 2.5 and 1.5 times low flux as compared with NLCs and SLNs, respectively. Results indicate higher CAP permeation through the albino rat's skin in the case of CAP-NLCs.

Table III. Mean erythemal scores and PII observed for various CAP formulations obtained at the end of 24, 48 and 72 h ($n = 3$).

	Erythemal scores			
Formulation code	24 h	48 h	72 h	PII
NLCs	0	0	0	0
SLNs	0	0	0	0
Plain CAP solution	3	2	2	2.33
Control (Formulation)	0	0	0	0

The drug accumulated in the skin is recorded in Table II. The percentage of CAP permeated through the skin and accumulated into the SC as well as viable skin for all formulations at the end of the experiments has been compiled in Figure 3. A significantly higher SC retention of drug was obtained for NLCs (4.5 times) and SLNs (3.13 times) as compared with plain CAP solution. The drug retention for all the formulations was maximal in SC. Moreover, NLCs produced a significant higher drug accumulation in viable skin, compared with SLNs or plain solution (Figure 3, Table II).). Compared with the plain solution, NLCs showed 7.5-fold, while SLNs showed 6.2-fold higher accumulation of drug in viable skin.

The possible reasons for higher amount of CAP penetration and accumulation into the skin layers following SLNs and NLCs applications are lipidic composition, small size, penetration enhancer effect of surfactants and also the interaction between SLNs and NLCs with the SC lipids, providing a deposit effect of drug in the skin. Lipidic compositions of SLNs and NLCs are more similar to SC lipids, in contrast to plain solution which may promote the accumulation of the encapsulated CAP moiety into the upper skin layers, thus creating a reservoir which may prolong the skin residence time. Moreover, Oleic acid present in the NLCs may be responsible for the higher drug retention and penetration effect which may also integrate as well as mix with skin lipids to loosen their structure by disturbing the lamellar arrangement of the lipids (Souto et al. 2004, El Maghraby et al. 2008, Qingzhi et al. 2009, Zakir et al. 2010).

In vivo drug localization in the skin layers

Figures 4 and 5 show the amount of CAP accumulated in the various strata of skin, after 24-h post application period from different formulations. The absorption of CAP following the application of different formulations through SC (Figure 4) decreased in the following sequence: NLCs > SLNs > plain drug solution. The data showed 4.48-fold and 3.13-fold higher SC retention in the case of NLCs and SLNs systems, as compared with plain solution. On the other hand, the amount of drug recovered from viable skin following application of formulation followed the same order as recorded in the case of SC; however, the extent of amount accumulated was significantly low, as compared with SC. The data presented in Figure 5 showed that the amount of drug in the viable skin from NLCs was 2.9 times less than the amount measured in the SC. Apart from this, it was also observed that the drug extracted following SLNs and drug solution from viable layers of skin was 4.1 and 5.6 times less than that recovered from SC. Compared with the plain solution, NLCs showed 8.7-fold, while SLNs showed 4.32-fold higher accumulation of drug in viable skin. These results were in accordance with the earlier reports (Fang et al. 2008). Thus, the developed CAP-loaded NLCs formulations have the potential to deliver the effective amount of drug in a sustained

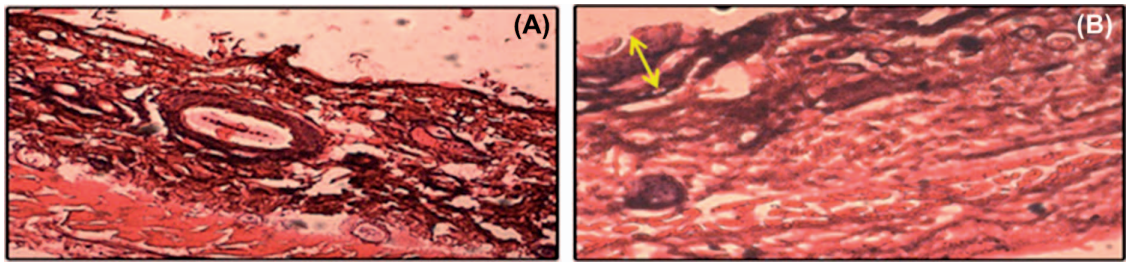

Figure 6. Histologic examination of hairless albino rat skin in (A) the non-treated control group and (B) the group subjected to a tape-stripping technique. *Arrows* indicate the thickness of the epidermis.

and controlled fashion. This enables the maintenance of localized depot and, therefore, prolonged residence time of CAP in viable skin for the effective and improved treatment of skin diseases.

Skin-irritation test

Application of CAP is associated with skin irritation, which limits its applicability and acceptability by the patients. It is necessary to study the irritation caused by NLCs, SLNs and plain CAP solution to ensure that the topical preparations are safe and innocuous. The skin-irritation studies indicated that SLNs and NLCs exhibited minimum to no irritation, as compared with plain solution, even after 72 h of application (Table III). The primary irritation index (PII) was found to be 0.00 for SLNs and NLCs, showing no irritation. Therefore, the developed lipid nanoparticles formulations resulted in no erythema and were safe, as compared with the plain solution.

Skin permeation of CAP across hyper-proliferative skin

Figure 6 depicts representative examples of light microscopic images of vertical skin sections of normal and hyper-proliferative skin. As shown in the figure, tape-stripping technique increased the epidermal thickness that confirms the predominant changes of the psoriasis-like skin. Figure 7 compares CAP fluxes across normal and hyper-proliferative skin. Drug permeation through the hyper-proliferative skin was comparatively lower than the normal skin with all the formulations. Fluxes obtained from CAP- NLCs, CAP- SLNs and plain CAP solution were found to be 22.56 ± 1.56 μg/cm^2/h, 13.98 ± 1.74 μg/cm^2/h and 4.45 ± 1.12 μg/cm^2/h, respectively.

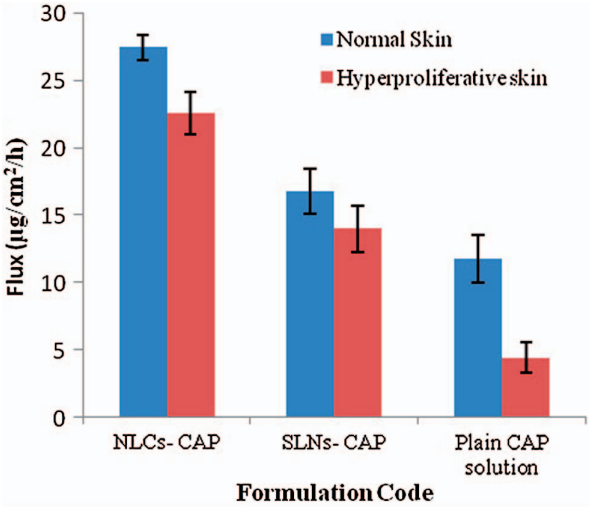

Figure 7. Comparison of the CAP fluxes from an aqueous suspension and nanoparticulate systems across normal and hyperproliferative skin. Each value represents the mean ± SD ($n = 3$).

Conclusion

This study concludes that both SLNs and NLCs are efficient carrier systems for topical delivery of CAP. NLCs have proven to be suitable carriers for the delivery of active pharmaceuticals through the topical route as indicated by zeta potential value (good physical stability) and a high entrapment efficiency value. A solvent diffusion method in aqueous system was used to prepare the CAP-NLCs and CAP-SLNs with better drug encapsulation. Although both SLNs and NLCs can be used as effective carriers of lipophilic drugs depending on the desired drug permeation profile, NLCs might be a better option compared with SLNs for the skin conditions like psoriasis as it has demonstrated better skin permeation through the hyper-proliferative skin. Moreover, improved deposition at the target site, that is skin, would be highly beneficial and more effective with better patient compliance. The results indicate that the NLCs exhibited lower size with higher drug entrapment efficiency, higher skin permeation and greater skin retention with no skin irritation and thus could potentially be explored as a carrier for topical delivery of drugs.

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Declaration of interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

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