Open Access Maced J Med Sci **electronic publication ahead of print,**
published on August 30, 2019 as https://doi.org/10.3889/oamjms.2019.414

ID Design Press, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences.
https://doi.org/10.3889/oamjms.2019.414
eISSN: 1857-9655
Global Dermatology

Treatment of Psoriasis: Novel Approaches to Topical Delivery

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Citation: Wollina U, Tirant M, Vojvodic A, Lotti T. Treatment of Psoriasis: Novel Approaches to Topical Delivery. Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2019.414

Keywords: Topical drug therapy; Psoriasis; Nanoparticles; Laser-assisted drug delivery; Foams; Niosomes; Ethosomes

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Received: 12-Jul-2019; **Revised:** 04-Jul-2019; **Accepted:** 15-Jul-2019; **Online first:** 30-Aug-2019

Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

Abstract

Topical treatment is the cornerstone for the management of mild to moderate psoriasis. Despite efforts in drug development, patient's satisfaction with the available topical treatments is limited. A strategy to improve safety, efficacy and comfort of topical treatment provides the development of new drug delivery and drug carrier systems. This review provides an overview of recent advances in this field with a focus on psoriasis. Laser-assisted drug delivery, foam formulations, nanoparticles, ethosomes, and niomes are considered. Hopefully, these new developments will improve topical drug therapy and patient satisfaction.

Introduction

Easy accessibility of skin is a major factor for topical treatment. Topical drug delivery is depended on skin barrier properties, physicochemical properties of drug and vehicle, and interaction between drug and its vehicle with the skin layers. Penetration into intact skin is usually limited to hydrophilic substances smaller than 500 Da. This explains why highly hydrophilic or highly lipophilic compounds or such compounds with a higher molecular weight are much less suitable for conventional topical drug therapy [1].

Psoriasis is a chronic inflammatory skin disease affecting about 2% of the world population that harms various dimensions of quality of life of patients [2]. Topical drug therapy is the cornerstone in the treatment of mild to moderate psoriasis. It offers a direct targeting of affected skin by avoiding systemic adverse events. However, patient satisfaction with available treatments remains modest [3].

There are three major pathways by which drug release into the skin and into the systemic circulation by topical application have to be considered: (a) percutaneous absorption - the passage of topically applied materials into the skin, (b) percutaneous penetration - the passage of material from the stratum corneum surface through the skin to the systemic circulation, and (c) permeation – the passage of material through a skin by diffusion or by pores.

Percutaneous penetration is measured by in vitro skin models such as skin disks, human or animal tissue samples in special skin chambers. Percutaneous penetration measurements are performed in vivo in animal models or humans since they are dependent on blood circulation. Drug concentrations are usually measured by high-performance liquid chromatography (HPLC) or mass spectrometry [4]. Proton nuclear magnetic resonance

(^{1}H NMR) spectroscopy allows the characterisation of the most represented proton-containing low-molecular-mass compounds in a biological sample and their representation in a spectrum [5].

In recent years, several technologies have been developed to enhance the efficacy and safety of topical drug therapy. Furthermore, new drug carriers offer the opportunity to introduce new molecules into topical psoriasis therapy. For these purposes, vesicular drug delivery systems including niosomes, proniosomes, liposomes and transferosomes, nonvesicular drug delivery systems such as foams, gels, and nanoparticles have been developed [6]. Hopefully, by using these new technologies, better patient satisfaction with topical treatment could be achieved.

Ablative Fractional Lasers

Fractional ablative lasers can enhance the permeation of topical drugs into the skin through microscopic ablation zones (MAZs) of precise dimensions. At this moment, the skin barrier can be negotiated, and drug delivery markedly improved [7].

Several studies investigated topical methotrexate. Methotrexate is a folic acid analogue. The mechanism of action is the inhibition of 5-aminoimidazole-4-carboxamide ribonucleotide transformylase, thus increasing intracellular and extracellular adenosine which has anti-inflammatory activity. Methotrexate has been used for a long time in the systemic treatment of both psoriasis and psoriasis arthritis. In contrast to its use in oncology, methotrexate is used just once a week in low dosages (usually 7.5-25 mg) orally, subcutaneously or intravenously in both indications [8]. Systemic treatment, however, is limited by possible methotrexate toxicities [9].

A systematic in vitro study with a low-power 2,940 nm ablative fractional erbium YAG laser investigated the correlation between laser parameters and tissue. Deeper MAZ depth increased the concentration of methotrexate in the deeper tissue layer. The biodistribution of the drug was surprisingly not compromised by coagulation zones of various thickness around MAZ. The ratio of skin deposition versus transdermal permeation was constant, not depending on the MAZ depth. Methotrexate distributed radially from the MAZ. Saturation of the skin occurred after 7 hours at a ten-fold concentration compared to intact skin [10].

The same technique can be applied to the treatment of nail psoriasis [11].

In a clinical trial using nanoparticulated methotrexate in jojoba oil-based microemulsion, fractional erbium YAG laser resulted in a faster clinical response compared to intact skin, i.e. 3 weeks vs 8 weeks [12].

Foams

Foams are colloids composed of two or three distinct phases: hydrophilic liquid continuous phase with a foaming agent, throughout which a gaseous dispersion phase is distributed, and sometimes a third hydrophobic dispersed phase. Pharmaceutical aerosol foams commonly exhibit three transition states: liquid in the can, propellant/aerosol as it leaves the can and foam on the skin of the patient [13].

A fixed combination of calipotriol and betametasone dipropionate is on the market and found to superior to betamethasone ointment [14]. Betamethasone dipropionate in micronised particles can be easily suspended homogeneously. Calcipotriol, on the other hand, is a greater challenge and needs to be dissolved in a carefully selected vehicle component to ensure even distribution. The product contains an emollient vehicle base, with calcipotriol and betamethasone dissolved in a mixture of volatile propellants, butane and dimethyl ether. Dimethyl ether also acts as a solvent that enhances the solubility of the active ingredients allowing them to dissolve completely. It has been demonstrated that this anti-psoriatic foam formulation is more effective at week 12 than systemic methotrexate or acitretin, and it is more effective at week 16 as systemic apremilast measured by the PASI75 response [15].

Nanofibres

Curcumin is a herbal substance with anti-inflammatory activities, that is of interest also in topical psoriasis therapy [16]. Cellulose nanofiber (CNF) is a biocompatible biomaterial with film-forming properties and excellent mechanical properties. Fibres of a diameter of approximately 500 nm were embedded in a composition containing shea butter and Capmul MCM EP and loaded with curcumin (liquid@CNF). They employed a variety of analytical methods including scanning and transmission electron microscopy, Fourier transform infrared spectroscopy, also known as FTIR analysis. The FTIR analysis method uses infrared light to scan test samples and observe chemical properties. X-ray photoelectron spectroscopy was used to analyse the surface chemistry of the curcumin preparation. Besides, atomic force microscopy was used to measure the local properties of curcumin-CSF. In a mouse model

with imiquimod-induced psoriasis-like dermatitis, deposition of curcumin was increased 2-fold compared with films missing the lipid component. Curcumin-CNF improved dermatitis in vivo including a reduction of pro-inflammatory cytokines in a range close to commercially available topical corticosteroids. Furthermore, the films had a skin hydration effect [17].

Nanoparticles and Nano Emulsions

Another option to overcome skin barrier is the use of nanoparticles, especially for hydrophilic compounds. The most commonly used nanoparticles for topical drug delivery are polymeric nanoparticles, nano-emulsions, liposomes and solid lipid nanoparticles, metal nanoparticles, and dendrimers. Nanoparticles are used to enhance the solubility of highly hydrophobic drugs. They provide a sustained and controlled release of drugs while increasing their stability. Nanoparticles are capable of delivering higher concentrations of drugs to target areas. Nanoparticles can accumulate in hair follicles and thereby overcome the skin barrier [18].

Curcumin-loaded nanoparticles (NPs) made of poly (lactic-co-glycolic acid) with a mean particle size of 50 nm and 150 nm. In vitro, these NPs exerted a stronger anti-proliferative activity of human HaCaT keratinocytes than curcumin alone. Psoriatic skin samples were used for in vitro penetration studies. Curcumin-loaded NPs delivered more curcumin into the skin than curcumin hydrogel. Curcumin-loaded NPs was investigated in vivo in the imiquimod-induced mouse model versus tacrolimus cream. Clinical symptoms, histology and inflammatory cytokines improved most with curcumin-loaded NPs with 50 nm NPs reaching the most pronounced effects [19].

An amphiphilic polymer, RRR-α-tocopheryl succinate-grafted-ε-polylysine conjugate (VES-g-ε-PLL), was synthesised and self-assembled into skin penetrating polymeric NPs with a hydrodynamic diameter of only 24.4 nm. In these NPs curcumin could effectively be encapsulated with a drug loading capacity of 3.49% and an encapsulating efficiency of 78.45%. Silk fibroin was used as a hydrogel-based matrix to enhance further topical delivery of curcumin-NPs, which resulted in a slower release. In vivo studies on imiquimod-induced psoriasis-like dermatitis in mice, curcumin-NPs-silk fibroin gel demonstrated a high skin-permeating capability and a stronger anti-inflammatory activity. This was investigated by inhibitory effects on the expression of pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNFa), nuclear factor-κB and interleukin-6) [20].

Bacterial cellulose (BC) represents an interesting biocompatible nanomaterial. BC can be easily manipulated to improve its properties and/or functionalities resulting in several BC-based nanocomposites such as BC/collagen, BC/gelatin, BC/fibroin, BC/chitosan. Bacterial cellulose/carboxymethylcellulose (BC / CMC) biocomposite nanofibers can also serve as drug carriers. This was investigated using methotrexate, a conventional systemic antipsoriatic drug with anti-folate activity. Biocomposites loaded with methotrexate may be used as an alternative for the topical treatment of psoriasis. There was a decrease in the elastic modulus as the degree of substitution of CMC increased. Intermediate substitute CMC grade led to a slightly decreased MTX release rate, suggesting that the degree of substitution of CMC is a key factor to modulate the biocomposite properties [21].

Spherical methotrexate-loaded chitin nanogel (MCNG) with a particle size of 196 nm was formulated for topical use in psoriasis. Exposure of HaCaT keratinocytes and THP-1 cells to MCNG showed a significant level of cellular toxicity. MCNGs inhibited COX-2 and LOX-5 enzymes expressed in THP-1 cells. Skin permeation studies revealed an increased transdermal flux of methotrexate from MCNG in comparison with methotrexate solution treated samples. Furthermore, it could be shown that MCNG exerted anti-psoriatic efficacy on an imiquimod-induced mouse model of psoriasis. No dermal and systemic toxicities were reported [22].

Pentoxifylline (PTX) is an anti-inflammatory activity compound and exerts inhibitory activity against TNFa, one of the major proinflammatory cytokines involved in psoriasis. Therefore, it is of potential interest in topical psoriasis therapy — colloidal nanostructured lipid carriers (NLCs) with a size of less than 200 nm. PTX was loaded and encapsulated to the extent of 10% and 90% in the NLCs. In vitro studies suggested high retention of PTX in the skin (84%). In vivo, imiquimod-induced psoriasis in the mouse model was employed. PTX-loaded NCLs demonstrated a significant improvement of histological changes in the affected epidermis [23].

In contrast to PTX, topical corticosteroids are established drugs in psoriasis therapy. They are the cornerstone of topical outpatient treatment worldwide. Mometasone furoate-loaded NLCs with a droplet size of approximately 160 nm, a zeta potential-0.086 mV and entrapment efficiency of 60.0 % were transformed into a hydrogel using Carbopol 940 to optimise viscosity for topical use. Drug permeation studies showed prolonged drug release as compared to commercial mometasone formulation. The mometasone skin concentration was 2.5-fold higher than commercial corticosteroids. In vivo studies in imiquimod induced skin inflammation in Wistar rats demonstrated the absence of parakeratosis in mometasone-loaded NLC treated lesions [24].

Nanogels are water-soluble cross-linked

polymer networks with nanometer-size dimensions. They can be designed to incorporate different types of anti-psoriatic compounds and are promising carrier systems for topical drug delivery. Gels produced with macromolecules and fibres can be classified as polymers with molecules attached to the fibres throughout the gel resulting in a polymer (chemical gel) or supramolecular gels (physical gels), in which smaller molecules are attached van der Waals interactions, hydrogen bonds or coulombic forces [25]. While chemical gels are robust materials, physical gels are more suitable for drug delivery. These gels are also softer. While most physical gels are made by polymeric subunits, low-molecular-weight gelators (LMWGs) are smaller molecules that self-assemble to form fibres. Such gels have qualities that made them interesting for drug delivery, such as thermoreversibility and degradability [26].

Bis-imidazolium (1·2 Br) salts are cationic surfactants that could form micelles and deliver anionic drugs. The electrostatic attraction between the positively charged surfactant and the negatively charged drug is responsible for a slow but sustained release of the drug [27]. Triamcinolone acetonide and betamethasone 17-valerate are commonly used topical corticosteroid for inflammatory skin disorders such as psoriasis. The 1·2 Br carrier material permitted a high level of drug release and did not limit permeation of the drug into human skin as measured by Franz cells. Gels derived from 1·2 Br released up to three times more triamcinolone or betamethasone than two commercial products, which served as controls. Also, the speed of drug release was ten times faster if they were incorporated in gel 1·2 Br. Permeation studies using Franz cells show that gel 1·2 Br promotes the entry of the drug through the skin four times more rapidly than the commercial formulations. The gel also promotes retention of the drug in the skin two times (betamethasone) and 20-fold (triamcinolone) more than the commercial formulations. In conclusion, 1·2 Br carrier material ensures a faster action and higher bioavailability to the pharmacological target [28].

Further investigations demonstrated that several other possible compounds for topical psoriasis therapy could also be included and stabilised in nanostructures supramolecular gels such as methotrexate or tacrolimus [29].

PUVA-therapy – 8-methoxy psoralen (8MOP) plus ultraviolet A irradiation – is an established treatment for psoriasis, vitiligo and cutaneous T-cell lymphoma amongst other dermatoses [30].

8MOP has been incorporated into a nanoemulsion (NE) that showed a mean droplet diameter of 24.98 ± 0.49 nm, polydispersity index of 0.091 ± 0.23, pH values of 6.54 ± 0.06, the refractive index of 1.3525 ± 0.0001, and apparent viscosity of 51.15 ± 3.66 mPa at 20°C. The formulation was characterised by ex vivo permeation study using porcine skin with fluorescence HPLC and transmission electron microscopy, to determine the amount of drug retained in stratum corneum, viable epidermis, and dermis. Ex vivo permeation revealed that 8.5% of the applied 8MOP dose permeated through the biological membranes, with a flux of 1.35 μg cm^{-2} h^{-1}. The drug retention in viable epidermis and dermis was twice as high as normal cream with 10.15 ± 1.36 μg cm^{-2} compared to stratum corneum with 1.95 ± 0.71 μg cm^{-2}, respectively [31].

Since NE may have a relatively low viscosity, hydrogel-thickened NEs using chitosan have been prepared to improve topical applicability. The size of chitosan molecules influences drug release [32].

Cignolin (syn. dithranol or anthralin) is the most potent topical drug in psoriasis therapy with the longest remission times [33]. However, skin irritation and staining hamper its broader use. Microspongues as delivery systems for cignolin may overcome these problems. In one study, microsponges were composed of poly (amido) amine dendrimers, ethylcellulose, polyvinyl alcohol, dichloromethane, sodium metabisulphate, and distilled water. In vitro studies demonstrated that such a formulation could prevent autooxidation of cignolin. Microsponge gel of dithranol may provide further advantages of reduced side effects, increased elegance, enhanced formulation flexibility, and modified drug release [34].

Cignolin has also been used with NLCs for better application and efficacy. Cignolin-loaded NLCs were prepared by hot-melt homogenization with particle size < 300 nm, polydispersity index (PDI) < 0.3 and percentage entrapment efficiency of ~100%. The NLCs were loaded into a gel and evaluated for drug release, spreadability, rheological behaviour, and staining. Anti-psoriatic efficacy was evaluated in the imiquimod-induced psoriatic plaque model in comparison with conventional 1.15% w/w cignolin ointment. Topical application of cignolin-loaded NLC gel reduced the PASI score. There was a significant reduction in IL-17, 22, 23 and TNFa as measured by enzyme-linked immunosorbent assays [35].

Cyclosporine A (CsA) is a calcineurin inhibitor which acts on T-cells and is an effective systemic treatment for psoriasis. However, systemic administration of CsA can cause dose-dependent toxic effects, which may be circumvented by topical drug delivery. Topical use, however, is hindered by its high molecular weight of 1,202 Da [36].

Recently a topical liposomal gel containing CsA loaded cationic liposomal nanocarriers has been developed. Optimised liposomal carriers prepared by the ethanol injection method were loaded with CsA and applied in a gel formulation on imiquimod-induced plaque model. Thereby, clinical symptoms could be improved, and key pro-inflammatory cytokines for psoriasis such as tumour necrosis factor-α, IL-17, and IL-22 were reduced [37].

A CsA-loaded microemulsions using oleic acid as oil phase, either Tween®80 or a soluble derivative of vitamin E (TPGS) as surfactants and either Transcutol®, propylene glycol or 1,3 propanediol as co-surfactants. Several Tween®80-based and 4 TPGS-based formulations were tested ex vivo, loaded with 6 mg/g CsA and applied ex-vivo on porcine skin for 22 h. A 3- or 6-fold higher cutaneous accumulation compared with CsA in propylene glycol could be obtained by a low-viscosity Tween®80-based microemulsion (9.78 ± 3.86 µg cm^{-2}) and with a high viscosity TPGS-based microemulsion (18.3 ± 5.69 µg cm^{-2}), respectively. The uptake of CsA by porcine skin was noted as early as two hours after application [38].

Another study investigated CsA-loaded polymeric micelles using the biodegradable and biocompatible MPEG-dihexPLA diblock copolymer. These polymeric micelles deliver CsA without penetrating the skin. They increased the aqueous solubility of CsA by 518-fold. Supra-therapeutic amounts of CsA were delivered to human skin (1.4 ± 0.6 µg cm^{-2}) after application of the formulation with 1.67 mg/ml CsA and 5 mg/ml copolymer for the only 1h without transdermal permeation. The micelles were preferentially deposited between corneocytes and in between the clusters of corneocytes [39].

Tacrolimus is a specific calcineurin inhibitor approved or atopic dermatitis and with moderate antipsoriatic activity for intertriginous psoriasis [40]. It suffers from poor cutaneous bioavailability when administered topically as protopic ointment. Therefore, polymeric micelles using methoxy-poly (ethylene glycol)-dihexyl substituted polylactide (MPEG-dihexPLA) diblock copolymer loaded with 0.1% tacrolimus was investigated in vitro. Delivery experiments using human skin resulted in significantly greater tacrolimus deposition compared to protopic 0.1% ointment, i.e. 1.50 ± 0.59 versus 0.47 ± 0.20 µg cm^{-2}). The increase in cutaneous drug concentrations was due to improved drug load of stratum corneum, viable epidermis, and upper dermis, while the copolymer was unable to penetrate the stratum corneum. Preferential deposition of tacrolimus-loaded micelles into the hair follicle was also documented [41].

Another study investigated a hybrid system based on nicotinamide (NIC) and nanoparticles (NPs) encapsulating tacrolimus to improve percutaneous drug delivery. NIC increased both the solubility and permeability of tacrolimus. NIC demonstrated self-assembly with amphiphilic hyaluronic acid-cholesterol conjugates. Thee NPs showed a higher encapsulation efficiency of 79.2% ± 4.2%, and the combination of NPs with NIC exhibited a significant synergistic effect on tacrolimus absorption within the skin (2.39 ± 0.53 µg cm^{-2}) and penetration through the skin (13.38 ± 2.26 µg cm^{-2}) as measured by confocal laser scanning microscopy. The cellular uptake of tacrolimus in HaCaT cells was also improved by NPs [42].

One trial investigated the applicability of NIC-based hybrid systems with chitosan instead of hyaluronic acid on tacrolimus efficacy in an animal model of atopic dermatitis (AD). AD-like skin lesions were induced by 1-chloro-2, 4-dinitrobenzene (DNCB) in BALB/c mice. In vitro and in vivo skin permeation studies demonstrated that this NIC-chitosan-NPs system significantly enhanced tacrolimus cutaneous permeation and penetration compared to commercial tacrolimus ointment. The treatment efficacy on clinical symptoms, histological analysis, and molecular biology of the AD-mice demonstrated that NIC-chitosan-NPs were more potent than the commercial ointment while using only one-third of their dosage [43]. The anti-TNFa fusion protein etanercept (molecular weight 150 kDa) is an effective drug in the systemic treatment of moderate to severe psoriasis. Due to the high molecular weight, the compound cannot penetrate human skin [44].

Recently, etanercept was successfully and stable encapsulated in thermoresponsive nanogels (tNG). Topical application of etanercept-loaded tNGs to human skin equivalents, prepared from primary human keratinocytes and fibroblasts and treated with TNFa, or tape striped human skin resulted in inefficient drug delivery throughout the stratum corneum and into the viable epidermis. Effective etanercept delivery was depended on temperature triggered release following topical application. Anti-inflammatory activity on TNFa, intercellular adhesion molecule 1, and thymic stromal lymphopoietin was measured by immunochemistry, enzyme-linked immunoassays, and Western blots. It was shown that the formulation was non-toxic for monocyte-derived Langerhans cells [45].

In another study, two different tNGs were synthesized, i.e. tNG_dPG_tPG-a combination of dendritic polyglycerol with poly (glycidyl methyl ether-co-ethyl glycidyl ether) (p(GME-co-EGE)) and tNG_dPG_pNIPAM with poly(N-isopropylacrylamide). These tNGs were capable of incorporating high amounts of the corticosteroid dexamethasone and tacrolimus. Cellular uptake and intracellular localisation were investigated in cell cultures of normal human keratinocytes and HaCaT cells. Neither cytotoxic nor genotoxic effects were noted. There was no induction of reactive oxygen species in keratinocytes. tNGs with a thermally triggered release at 35°C seem to be optimal for topical application on human skin [46].

Ethosomes

Ethosomes are flexible nanovesicles composed of multiple, concentric layers of flexible phospholipid bylayers, with 20 to 45% of ethanol, glycol and water. They are used for dermal and

transdermal delivery of molecules since they can penetrate the stratum corneum [47].

However, percutaneous absorption and penetration of lipophilic 8MOP in intact skin are poor. After the development of microemulsions about 20 years ago, more recently nanocarriers were investigated for improved drug supply of 8MOP. In vitro skin permeation demonstrated a permeability of psoralen-loaded ethosomes superior to that of liposomes. With psoralen-loaded ethosomes, transdermal flux and skin deposition could be increased 3.50 and 2.15 times compared to psoralen-loaded liposomes [48].

One trial used spherical and multilamellar ethosomes incorporated into Carbopol® 934 gel. They were characterized for drug content, rheological behaviour, texture profile, in vitro release, ex vivo skin permeation and retention, skin photosensitization and histopathological examination. Ethosomal formulations showed significant skin permeation and accumulation in the epidermal and dermal layers as demonstrated by fluorescence microscopy study using ^{123}rhodamine while phototoxicity was not enhanced [49].

Niosomes

Niosomes represent non-ionic surfactant-based vesicles formed mostly by non-ionic surfactant and cholesterol. They can entrap lipophilic drugs into vesicular bilayer membranes and hydrophilic drugs. Niosomes are osmotically active [50].

Acitretin is a vitamin-A analogue with antipsoriatic and anti-inflammatory activities. Systemic acitretin therapy warrants a close laboratory monitoring to prevent severe adverse events. Niosomes of approximately 370 nm were loaded with acitretin. Acitretin nanosized niosomal gel offered an enhanced ex vivo permeation profile drug deposition in the viable skin layers compared with acitretin gel. Acitretin-loaded nano-niosomes demonstrated an increased antiproliferative activity in HaCaT cell culture. Topical application of acitretin nano-niosomal gel to a mouse tail model achieved a significantly higher amount of orthokeratosis, drug activity, and reduction in epidermal thickness compared with controls. The formulation was characterised by improved tolerability and much less skin irritation [51].

Niosome technology has also been investigated for PUVA therapy with 8MOP. 8MOP niosomes were prepared by the thin-film hydration method along with cholesterol demonstrated a high entrapment efficiency (83-90%) with vesicle diameters between 111.1 and 198.8 nm. Physical stability over 6 months at different temperatures was good. Niosome formulations were incorporated in 5% sodium carboxy methylcellulose-hydrogel matrix which showed a more retarded 8MOP release compared to niosomal vesicles. The skin penetration of the niosomes was studies in vivo by confocal laser scanning microscopy using ^{123}rhodamine-loaded niosomal hydrogels compared to plain ^{123}rhodamine hydrogel. In vitro drug permeation and deposition studies with rat skin demonstrated improved penetration and accumulation of 8MOP after 8h [52].

Proniosomes are liquid crystalline compact niosome hybrids which upon hydration form niosomes. They support physical stability such as leaking, fusion, aggregation and provide convenience in dosing, distribution, transportation and storage. Therefore, proniosomes seem to be superior to conventional niosomes [53].

A non-ionic surfactant based proniosomal gel (PNG) was developed to improve topical delivery of tazarotene – a retinoid for psoriasis. The PNG was had a vesicle size of 3.26 µm. Different formulations were investigated for drug release through cellulose membrane and rat skin, which showed a prolonged release of entrapped tazarotene. The formulations varied in drug permeation and retention in vitro. The male Albino NMRI mice tail model was used for in vivo studies. Span 60 based PNG formulations were able to increase drug accumulation in skin and reduce parakeratosis in the horny layer [54].

Conclusions

Topical drug delivery is a field of recent research with great clinical implications. In contrast to the development of targeted systemic treatments and biologics, improved topical drug delivery is focused on the great majority of psoriasis patients with mild to moderate disease. Various anti-inflammatory drugs and herbal compounds are under investigation. Hopefully, a number these topical treatments become available for the dermatologic practice.

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