

Review

Novel topical drug carriers as a tool for treatment of psoriasis: Progress and advances

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Psoriasis is a chronic inflammatory skin disease portrayed by erythematous, papulosquamous lesions. It is characterized by excessive growth and aberrant differentiation of keratinocytes. The conventional topical treatments that have been used in the past, such as coal tar and dithranol, have low efficacy, poor aesthetic and cosmetic appeal, leading to poor patient compliance while systemic therapies such as methotrexate, cyclosporine and acitretin produce significant side effects. In recent years, several novel carriers like liposomes, nanostructured lipid carriers (NLC), etc. have been used in psoriasis, with promising results. Small and relatively narrow size distribution with novel carriers permits site specific delivery to the skin, with improved drug solubilization of hydrophobic drugs and bioavailability. This review highlights the recent advancements in the field of novel carriers for topical applications of antipsoriatic active moieties and bioactives.

Key words: Novel carriers, topical, antipsoriatic drugs, psoriasis, skin.

INTRODUCTION

Psoriasis is a psychosocially, and at times medically, debilitating disorder that affect 1 to 3% of the population world wide (Afifi et al., 2005). Psoriasis has a serious impact on health related quality of life, including physical and emotional well-being (Golant and Guttman-Yassky, 2011). It basically involves excessive growth and deviant differentiation of keratinocytes (Lowe et al., 2007). Psoriasis pathogenesis is closely associated with disease-including T helper 1 (Th1) and T helper 17 (Th17) cells (Heidenreich et al., 2009). About 80% of patients with psoriasis vulgaris are treated topically (Peeters et al., 2005). The conventional topical medications in the management of psoriasis are fraught with several limitations, which the novel carriers are reported to circumvent with safe and long term use (Witman, 2001; Prohić et al., 2007). Novel carriers such as liposome, niosome, microemulsion, nanoemulsion, nanostructured lipid carrier and ethosomes have indeed brought us closer to the goal of safe and efficacious

treatment of the disease (Katara et al., 2010).

Pathophysiology of psoriasis

Psoriasis is an immunologically mediated disease caused by activation of T lymphocytes in dermis (primarily CD4+ cells) and epidermis (predominantly CD8+ cells) (Nickoloff, 1999). The activation of T-cells is dependent upon its binding with the antigen presenting cells (APCs). This process is mediated through surface molecules used for adhesions, including leukocyte function associated antigen (LFA)-1 and CD2 on the T cells and intercellular adhesion molecule (ICAM)-1, and LFA-3 on the APCs (Lowe et al., 2004).

The T-cell receptor (TCR) for the specific T-cell recognizes an antigen presented on the major histocompatibility complex (MHC I or II) by the APC. Activated T cells proliferate and enter the circulation via trafficking through the interaction between LFA-1 and ICAM-1, and extravasate via diapedesis through the endothelium at site of inflammation in the skin. At this point, the T-cells propagate the immunologic process through the secretion of pro-inflammatory (type 1 or Th1) cytokines, which include interleukin (IL)-1, tumor necrosis

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Table 1. Classification of types of psoriasis and their features (Naldi and Gambini, 2007).

S/N	Type	Features
1	Plaque	Scalp lesions are well-margined, scaly plaques. At times severe hyperkeratosis can accumulate, tightly bound down by hair. Permanent hair loss is seldom seen, but may occur when excessive traction is applied to the hair to scale.
2	Pustular	Primarily seen in adults. It may be localized to certain areas of the body, e.g. hands and feet. Can be generalized, covering most of the body. It tends to go in a cycle as reddening of the skin followed by formation of pustules and scaling.
3	Guttate	Appears as small, red, separate spots on the skin. Lesions usually appear on the trunk and limbs and commonly number in the hundreds. Sometimes lesions form on the scalp, face and ears. They are not usually as thick as the lesions that characterize plaque psoriasis. This form can precede or co-exist with other forms of psoriasis, such as plaque.
4	Flexural	Differs from lesions elsewhere in that, although it is erythematous, it is not usually scaly. Exudation may be prominent.
5	Erythrodermic	It is the least common type of psoriasis and may occur once or more during a lifetime in 1 to 2 percent of people who develop psoriasis. It generally appears on people who have unstable plaque psoriasis. This means the lesions are not clearly defined. Widespread, fiery redness and exfoliation of the skin characterize this form. Severe itching and pain often accompanies it.

factor (TNF)- α , and interferon (IFN)- γ . These cytokines secretion results in the production of Th2 cytokine including IL-4, IL-10 and IL-11. Each cytokine down regulates the other's responses (Adorini and Trembleau, 1997). The final outcome of this bio-event is the formation of the psoriasis plaque through keratinocyte proliferation, an increase of activity and migration of other inflammatory cells and vascular changes (Hern et al., 2001).

Psoriasis has been considered basically as a disease of the keratinocyte, owing to its major clinical features of abnormal scaling and epidermal thickening. Clinically, the vascular nature of psoriasis is manifested by the erythematous plaques which exhibit pinprick bleeding on removal of scale (Auspitz sign), and is seen histologically with dilated tortuous capillaries, a prominent early feature of plaques. Histological studies have shown a fourfold increase in surface area of the superficial vascular plexus in psoriasis, and an increase in endothelial cell proliferation (Creamer, 1997). Angiogenic factors over-expressed by lesional keratinocytes include vascular endothelial growth factor (VEGF), IFN- γ , and IL-8 (IL8).

VEGF in particular, appears to play a central role in angiogenesis in psoriasis. This cytokine is also a potent mediator of inflammation and increases vascular permeability. Its synthesis by keratinocytes, activated T cells and endothelial cells, is induced by cytokines such as tumor growth factor- α (TGF- α), IFN- γ , and TNF- α . VEGF is over-expressed in psoriatic epidermis, and its receptors (KDR and Flt-1) are over-expressed on papillary microvessels. Transgenic mice over expressing VEGF in the epidermis were reported to develop a

psoriasis-like condition (Xia et al., 2003). Serum concentrations of VEGF are increased in erythrodermic psoriasis (Creamer et al., 1996), and a correlation between plaques VEGF, psoriasis area and severity index (PASI) and serum VEGF values was also reported (Creamer et al., 2002). The hyperpermeability induced by VEGF has been proposed as the cause of microalbuminuria and pulmonary edema in patients with severe psoriasis.

The main factors responsible for psoriasis therefore include the angiogenic factors, over-expression of VEGF in the psoriatic epidermis, transfer in bone marrow transplants from affected individuals, reduced TNF concentrations and increased concentrations of natural killer (NK T) cells.

Psoriasis has been classified into several types as presented in Table 1. Table 2 lists the various drugs that have been used for psoriasis.

Need for novel carriers

Presently, it has become increasingly apparent that the development of new drug alone is not sufficient to ensure progress and success in drug therapy, since the main reasons for the failure of therapy remain poor drug solubility, insufficient drug concentration due to poor absorption, rapid metabolism and elimination, drug distribution to other tissues combined with high drug toxicity, and high fluctuation of plasma level due to unpredictable bioavailability after per oral administration, including the influence of food on plasma levels (Mehnert and Mader, 2012). A promising strategy to overcome

Table 2. Various drugs for psoriasis with their mechanism of action and side effects.

Compound	Mechanism of action	Side effect	Reference
Coal tar	DNA suppression	Messiness, staining, odor, irritant, allergic, phototoxic responses and folliculitis	Walter et al. (1978)
Psoralens	Suppresses DNA synthesis by cross-linking DNA strands	Long term risks include skin cancer and premature ageing of skin	Greaves et al. (1978)
5-Aminolevulinic acid	Antiproliferative effect	Photosensitivity and irritation	Ibbotson (2002)
Anthralin	Antiproliferative effect	Irritation and staining of the skin, nails and clothing	Fuchs et al. (1990)
Tazarotene	Antiproliferative and anti-inflammatory activities	Pruritis, erythema, burning and desquamation	Weinstein et al. (2003)
Vitamin D analogues	Keratinocyte proliferation, enhance cellular differentiation	Irritation and hypercalcemia	Takahashi et al. (2003)
Acitretin	Normalizes keratinocytes proliferation and differentiation	Mucocutaneous reactions, pruritus and hypertriglyceridemia	Rossi and Pellegrino (2009)
Corticosteroids	Anti-inflammatory and immunosuppressant	Burning, skin atrophy, photosensitivity and irritation	Lebwohl et al. (2005)
Methotrexate	Anti-inflammatory and immunosuppressant	Myelosuppression, hepatic fibrosis and pulmonary fibrosis	Leon et al. (2007)
Cyclosporine	Immunosuppressant	The risk of infection, with long term use and non-melanoma skin cancer	Heydendael et al. (2003)
Tacrolimus	Immunosuppressant	Burning, itching, skin cancer and lymphoma	Scheinfeld (2004)
Pimecrolimus	Immunosuppressant	Burning, itching, skin cancer and lymphoma	Scheinfeld (2004)

these problems includes development of suitable drug carrier system to achieve controlled and localized delivery of the active drug according to the specific need of the therapy. The size of the carriers designed depends on the desired route of administration, and ranges from few nanometers (colloidal carriers) to the micrometer range (microparticles), and to several millimeters (implants). Implants and microparticles are too large for drug targeting and intravenous administration (Nanjwade and Patel, 2011). Therefore, colloidal carriers have attracted increasing attention during the recent years. Investigated systems include nanoparticles, nanoemulsions, microemulsions, liposomes, ethosomes, nanosuspensions, micelles and soluble polymer-drug conjugates.

Topical drug carriers and challenges in dermal delivery

During the last decades, inorganic and colloidal

particles such as nanocapsules, nanospheres, nanostructured lipid carrier, etc. have been explored for dermal/transdermal drug delivery. The successful implementation of these systems for drug delivery completely depends on their ability to penetrate through several anatomical barriers, sustained release of their content and their stability in the nanometer size. Different colloidal drug delivery systems (including liposomes, dendrimers and polymeric nanoparticles, in addition to solid lipid nanoparticles), were developed to overcome physicochemical limitations of potential therapeutic compounds such as poor solubility, low permeability, short half-life, high molecular weight, side effects and systemic toxicity (Almeida and Souto, 2007).

Stratum corneum is the main barrier in the percutaneous absorption of topically applied drugs. Small and relatively narrow size distribution with novel carrier permit site specific delivery to the skin with improved drug solubilization of

hydrophobic drugs and better bioavailability. The problem of lipid imbalance can be resolved by delivering the unsaturated fatty acids like linoleic acid to restore the normal skin conditions by lipid carriers (Morganti et al., 2001). This provides lipid enriched hydrating conditions to help retain the drug molecules within the dermal layers at or near to the site of action.

NOVEL CARRIERS USED IN PSORIASIS

In recent years, attempts have been made for successful delivery of antipsoriatic agents by employing novel carriers (Table 3).

Liposome

Liposomes are microscopic structures consisting of one or more concentric spheres of lipid bilayers enclosing aqueous compartments. As drug carrier

systems for topical treatment, liposomes are reported to be superior over conventional topical preparations. Phospholipids, being the major component of liposomal systems, are easily integrated with the skin lipids and maintain the desired hydration conditions to improve drug penetration and localization in the skin layers (Moghimi and Patel, 1993; Cevc et al., 1996; Schmid and Korting, 1996).

The use of liposomes as drug carriers seems to be promising, exhibiting therapeutic prospects with a reduction of side effects. Liposomal encapsulation of retinoids, for example vitamin A acid or tretinoin reduced the local irritation (Trapasso et al., 2009). Reports suggest that liposomal encapsulation of tacrolimus in topical formulation enhanced its penetration through skin. These characteristics may allow liposomal tacrolimus to be effective against psoriasis without the need of occlusive dressings. If liposomal tacrolimus penetrate into the blood stream, reports with other models suggest that it will be less toxic than free tacrolimus. This will be more important to patients who require higher concentrations of ointment to large areas of skin (Patel et al., 2010). Bhatia et al. (2004) developed and characterized tamoxifen loaded liposome for topical therapy and reported improved skin permeation of Tamoxifen (TAM) and retention in the skin.

Calcipotriol, a vitamin D analogue was successfully delivered in lipopolymer poly(ethylene glycol)-distearoylphosphoethanolamine (PEG-DSPE) liposomes with a significant increase in drug deposition into the stratum corneum (Knudsen et al., 2012). The size of the liposomes affected the penetration of calcipotriol into the stratum corneum, as smaller unilamellar vesicles enhanced drug penetration as compared to large multilamellar vesicles. This also indicated that the liposomes to some extent migrate as intact vesicles into the stratum corneum. Srisuk et al. (2012) compared the physicochemical characteristics and *in vitro* permeability of methotrexate entrapped deformable liposomes prepared from phosphatidylcholine (PC) and oleic acid, with conventional liposomes prepared from PC and cholesterol (CH). The deformable liposomes displayed enhanced permeability and this was attributed to the elastic characteristics of the oleic acid containing liposomes, as well as skin penetration enhancer effect of oleic acid.

Nagle et al. (2011) investigated the potential benefits of combining menthol with methotrexate in a vesicular gel base for improving the drug penetration, its dermal availability and patient acceptability. Antipsoriatic efficacy of the formulations tested *in vivo*, using the rat tail model, indicated that the vesicular gel containing menthol led to maximum drug retention in the skin. The *in vivo* studies also ascertained the effectiveness of the formulation in inducing a normal pattern of differentiation in the rat tail skin that initially showed parakeratosis, which is also characteristic of psoriatic epidermis.

Li et al. (2010) reported an ultra deformable cationic liposome for transdermally delivering plasmid DNA to mouse skin. The antipsoriatic efficacy in the K14-VEGF transgenic mouse model by transdermal delivery of murine IL-4 was observed. Plasmid DNA was transdermally delivered to vicinal sites of epidermis and hair follicles. Plasmid DNA expression was detected in ear skin.

Niosome

The low cost, greater stability and ease of storage of non-ionic surfactants led to the exploitation of these compounds as alternative to phospholipids, the main constituent of liposomes (Uchegbu and Vyas, 1998). Niosomes are microscopic lamellar structures formed on admixture of a non ionic surfactant, cholesterol and a charge inducing agent, with subsequent hydration in aqueous media (Uchegbu and Florence, 1995; D'Souza et al., 1997). Niosomes comprises of an architecture consisting of both hydrophobic and hydrophilic moieties, and as a result can accommodate drug molecules of varying solubilities (Namdeo and Jain, 1996). Niosomes have been evaluated in many pharmaceutical applications and were reported to reduce systemic toxicity by drug encapsulation and minimize clearance of such agents from the body by slow drug release. Agarwal et al. (2001) developed dithranol entrapped in liposomal and niosomal vesicles (0.5%), and found both of them superior to conventional formulation, while liposomes showed better results than niosomes employing mice skin. Marianecchi et al. (2012) investigated the niosomes made up of surfactants (Tween 85 and Span 20) and cholesterol for the delivery of ammonium glycyrrhizinate (AG), useful for the treatment of various inflammatory based diseases. The *in vitro/vivo* efficacy of the ammonium glycyrrhizinate/niosomes was studied in murine and human models of inflammation. The AG-loaded non-ionic surfactant vesicles showed no toxicity, good skin tolerability and were able to improve the drug anti-inflammatory activity in mice. Furthermore, an improvement of the anti-inflammatory activity of the niosome delivered drug was observed on chemically induced skin erythema in humans.

Niosomal methotrexate in chitosan gel was tested for irritation and sensitization on healthy human volunteers, followed by its assessment through double-blind placebo-controlled study on psoriasis patients (Lakshmi et al., 2007). The human repeated insult patch test did not produce any significant irritation or sensitization on healthy human volunteers. The placebo and marketed gels were compared with niosomal methotrexate gel. At week 12, with niosomal methotrexate gel, there was reduction in total score from 6.2378 ± 1.4857 to 2.0023 ± 0.1371 . These results suggested better efficacy of niosomal methotrexate gel as compared to placebo and marketed methotrexate gel.

Table 3. Previous work on novel carriers for psoriasis.

Drug	Limitations of conventional form	Novel carrier	Effect observed	Reference
Tacrolimus	Normal skin transport	Liposome	Facilitated entry into the tough barrier consisting of stratum corneum. Better solubility of drug	Patel et al. (2010)
		Nanolipid carrier	Provide good occlusion property and solubility	Pople and Singh (2011)
Coal Tar	Skin irritation and staining	Phospholipid lipid carrier	Reduce irritation and better solubility	Bhatia et al. (2008)
Anthralin	Irritation and staining	Liposome	Increase the stability of drug. Increases the penetration of drug through skin	Saraswat et al. (2007)
		Niosome	Enhance stability of drug	Agrawal et al. (2001)
		Liposome	Increases drug uptake and target deeper skin layer	Mahrle et al. (1991)
Vitamin D analogues	Local irritation	Nanostructured lipid carrier	Enhanced skin permeation and negligible skin irritation	Lin et al. (2010)
Corticosteroids	Skin irritation	Nanocapsule suspension	Greater stability of drug	Fontana et al. (2010)
		PEG-NLCs	High entrapment efficiency and improved drug stability	Doktorovova et al. (2010)
5-aminolevulinic acid	Poor skin penetration	Liposome	Enhance drug uptake	Casas and Battle (2006)
		Liposome	Compatible with skin lipid	Venosa et al. (2008)
		Ethosome	Better skin permeation and targeting deeper skin layer	Fang et al. (2009)
		Nanoemulsion	optimize topical drug permeation negligible skin disruption and acceptable safety	Zhang et al. (2011)
		Liposome	Higher rate of drug transfer across skin	Dragicevic-Curic et al. (2009a)
Temoporfin	Low aq. solubility	Invasome	Enhanced drug uptake	Dragicevic-Curic et al. (2009b)
Psoralens	Low penetration	Microemulsion	Enhanced drug uptake and provide photostability	Baroli et al. (2000)
		Liposome hydrogel	Enhance drug uptake	Ali et al. (2008)
		Deformable liposome	Better skin permeation and targeting deeper skin layer	Trotta et al. (2004)
Methotrexate	Low penetration	Niosome	Enhance stability of drug	Lakshmi et al. (2007)
		Microemulsion	Enhanced drug uptake and provide photostability	Zhi and Jin (2011)
		Nanogel	Greater stability of drug	Ali et al. (2008)
		Microemulsion	Increase the stability of drug	Umezawa and Ozawa (2007)
Cyclosporine	Limited cutaneous permeation	PLGA-nanoparticle	Rapid dissolution of drug and good stability	Jain et al. (2011)
Acitretin	Scaling, erythema, burning, stinging	Nanostructured lipid carrier	No major systemic side effects, the main topical side effect was irritation	Agrawal et al. (2010)

Microemulsion

Microemulsions are thermodynamically stable isotropic systems in which two immiscible liquids (water and oil) are mixed to form a single phase by means of an appropriate surfactant or its mixture. The short to medium chain alcohols are

generally considered as co-surfactants in the microemulsion system. The presence of surfactant and co-surfactant in the system makes the interfacial tension very low. Therefore, microemulsions form spontaneously, with an average droplet diameter of 10 to 140 nm. Microemulsions have the ability to deliver larger

amounts of water and topically applied agents into the skin than water alone or other traditional vehicles such as lotions or creams because they act as a better reservoir for a poorly soluble drug through their solubilization capacity. Although microemulsion can be used to deliver drugs via several routes, the system has been extensively

studied as a vehicle for topical and transdermal administration (Peltola et al., 2003; Sintov and Botner, 2006; Kreilgaard, 2002).

In topical and transdermal formulations, microemulsions have increased the cutaneous absorption of both lipophilic and hydrophilic APIs when compared to conventional vehicles (emulsions, pure oils, aqueous solutions, etc). Due to their special features, microemulsions offer several advantages for pharmaceutical use, such as ease of preparation, long-term stability, high solubilization capacity for hydrophilic and lipophilic drugs, and improved drug delivery (Karasulu, 2008; Heusehkel et al., 2008).

Zhi and Jin (2011) prepared methotrexate loaded microemulsion and evaluated microemulsion quality and percutaneous penetration through the skin. Umezawa and Ozawa (2007) reported that cyclosporine microemulsion increased the percutaneous absorption in skin of patients with psoriasis. Baroli et al. (2000) reported that microemulsion for topical delivery of 8-methoxsalen increased the photostability and enhanced the percutaneous absorption of drug. Alvarez-Figueroa and Blanco-Mendez (2001) investigated the effectiveness of transdermal administration of methotrexate (MTX) by iontophoretic delivery from two types of hydrogel and passive delivery from two types of microemulsion by *in vitro* assays. Both iontophoretic delivery of MTX from hydrogels and passive delivery from microemulsions were more effective than passive delivery from aqueous solutions of the drug. In the passive delivery assays, both water/oil (w/o) and oil/water (o/w) microemulsions were used, and the effectiveness of delivery from o/w systems was higher. At the end of all assays, significant amounts of MTX were detected in the skin.

Raza et al. (2011) developed and characterised a novel dithranol-containing phospholipid microemulsion for enhanced skin permeation and retention. The microemulsion systems composed of isopropyl myristate and Tween 80, with mean particle diameter of 72.8nm showing maximum skin permeation (82.23%), skin permeation flux (0.281mg/cm²/h) along with skin retention (8.31%) with regard to systems containing tocopherol acetate and Tween 20.

Nanoemulsion and nanoemulsomes

Nanoemulsions are obtained when the dimension of an emulsion globule reaches approximately 20 to 500 nm. The small droplet size can resist the physical destabilization caused by gravitational separation, flocculation and/or coalescence. It also avoids the creaming process because the droplet's Brownian motion is enough to overcome the gravitational separation force. The size and polydispersity of nanoemulsions can affect properties such as particle stability, rheology, appearance, color, texture and shelf life. They are not formed spontaneously, and their properties depend on

the thermodynamic conditions and preparation methods. Nano/submicron emulsions are well accepted for their ability to increase skin permeation, prolonged action on the skin, and protection of the drug from instability (Solans et al., 2005; Weyenberg et al., 2007). Zhang et al. (2011) formulated 5-aminolevulinic acid (ALA) and methyl 5-aminolevulinic acid (mALA) at equimolar concentrations in o/w and w/o nanoemulsions for skin delivery and showed that apart from drug, the emulsion type and the oil phase are all important considerations when attempting to optimize topical drug permeation. The o/w soybean oil dispersions were most promising because of their ability to exert the highest *in vitro* ALA flux. The uniformity of drug flux by the emulsions was improved when compared to the aqueous control. The addition of α -terpineol, a penetration enhancer, as a part of the oil phase did not further increase drug permeation via the skin. Khandavilli and Panchagnula (2007) formulated a nanoemulsion (NE) to achieve penetration of paclitaxel into deeper skin layers while minimizing the systemic escape. Upon dermal application, the drug was predominantly localized in deeper skin layers, with minimal systemic escape. Bernardi et al. (2011) formulated rice bran oil nanoemulsions and evaluated it for irritation potential and moisturising activity on volunteers with normal and diseased skin types.

Optimized dithranol-loaded emulsomes were found to substantially enhance the antipsoriatic activity on a mouse-tail model with regard to marketed product (Raza et al., 2012). Also, the selected composition enhanced drug permeation and marked skin retention. The formulation was found to be quite non-irritant, stable and biocompatible in comparison to the marketed product.

Nanostructured lipid carrier

Nanostructured lipid carriers (NLCs) are the latest generation of Solid lipid nanoparticles (SLNs) possessing improved properties of drug loading, modulation of the release profile, and stable drug incorporation during storage. NLCs are produced by mixing solid lipids with spatially incompatible lipids leading to a lipid matrix with a special structure. A blend of a liquid and solid lipid creates a less perfect crystalline structure with many imperfections, providing more space for drug accommodation. Examples of solid lipids include triglycerides (tristearine, tripalmitine, trimyristine), fatty acids (stearic acid, palmitic acid), waxes (carnauba, cetyl palmitate), whereas liquid lipids include medium chain triglycerides, oleic acid, isopropyl myristate. Their suitability for dermatological applications was also confirmed by successful formulations of drugs for treatment of skin diseases. NLC systems are a promising carrier for the topical delivery of antipsoriatic drugs as revealed by enhanced skin permeation, negligible skin irritation, and the compatibility of the drugs (Muller et al., 2007).

Lin et al. (2010) combined calcipotriol and methotrexate in nanostructured lipid carriers for topical delivery, and reported efficient delivery of the drugs. Nam et al. (2007) investigated tacrolimus loaded nanostructured lipid carriers for topical delivery. The penetration rate of these NLCs through the skin of a hairless mouse was greater than a commercial dermal ointment containing tacrolimus. Fluticasone propionate in novel polyethylene glycol (PEG)-containing nanostructured lipid carriers in the presence of PEG in NLC composition improved the physicochemical stability of the developed NLC (Doktorovova et al., 2010).

Ethosome

Ethosomes are noninvasive delivery carriers that enable drugs to reach the deep skin layers and/or the systemic circulation. These are soft, malleable vesicles tailored for enhanced delivery of active agents. They are composed mainly of phospholipids, (phosphatidylcholine, phosphatidylserine, phosphatidic acid), high concentration of ethanol and water. It is reported that ethosomes penetrate the skin and allow enhanced delivery of various compounds to the deep strata of the skin or to the systemic circulation (Touitou, 2002).

The high concentration of ethanol in ethosomes causes disturbance of skin lipid bilayer organization, hence when incorporated into a vesicle membrane, it enhances the vesicle's ability to penetrate the stratum corneum. Also, because of their high ethanol concentration, the lipid membrane is packed less tightly than conventional vesicles but has equivalent stability, allowing a more malleable structure and improves drug distribution ability in stratum corneum lipids (Merdan et al., 1998). Trotta et al. (2004) prepared deformable liposomes for dermal administration of methotrexate, and these provided maximum dose administration through the skin that may be of value for topical administration of methotrexate in the treatment of psoriasis.

Novasome

Novasomes are the modified forms of liposomes or a variation of niosomes prepared from the mixture of monoester of polyoxyethylene fatty acids, cholesterol and free fatty acids at 74/22/4 ratio and are 0.1 to 1.0 μm in diameter.

They consist of two to seven layered shells that surround an unstructured space occupied by a large amorphous core of hydrophilic or any water-soluble molecules that have been mixed with the hydrophobic materials (Singh et al., 2011). An agonist of parathyroid hormone related peptide receptor, PTH (1-34), was formulated in Novasome A cream (Holick et al., 2003). Novasome A cream enhanced the percutaneous

absorption of PTH (1-34) in human skin in comparison with formulations in propylene glycol or normal saline. Psoriatic lesions treated with PTH (1-34) showed marked improvement in scaling, erythema and induration.

Solid lipid nanoparticle

During the last two decades, numerous reports have described various SLN formulations that may find applications in drug delivery. The SLN structure is composed of solid core, which may contain triglycerides, glyceride mixtures, or waxes that are solid at both room temperature and human body temperature. SLNs are interesting lipid based drug delivery carriers for a number of reasons, including their nanoscale particle size and their biocompatible and biodegradable components. Urban-Morlan et al. (2010) prepared and characterized solid lipid nanoparticle containing cyclosporine A (CyA) by emulsification-diffusion method. Gambhire et al. (2011) reported the preparation and optimization of dithranol loaded solid lipid nanoparticles. The results of the *ex vivo* penetration studies demonstrated about two-fold increase in localization of delayed type IV hypersensitivity (DTH) in skin with SLN entrapped ointment compared to plain DTH.

HERBAL DRUG USED FOR PSORIASIS

World Health Organization (WHO) notes that 74% of the plant derived medicines are used in modern medicine in a way that their modern application directly correlates with their traditional use as herbal medicines by native cultures (Kumar et al., 2003). WHO estimated that 65 to 80% of the world's population uses traditional medicines as their primary form of health care, and about 85% of traditional medicines involve the use of herbal preparations.

Various bioactives and phytoconstituents have been delivered using novel carriers in psoriasis as displayed in Table 4.

CONCLUSION

Despite the significant advances that have been made in understanding the pathomechanisms of psoriasis and in identifying effective treatment approaches, the search for optimum treatment strategies for psoriasis still remains a major challenge.

Numerous topical treatment modalities are available for psoriasis, but there is a dearth of uniformly acceptable approach for moderate-to-severe psoriasis. A variety of lipid based novel drug delivery systems like lipid nanoparticles, microemulsion, nanoemulsions, nanoemulsomes,

Table 4. Bioactives delivered through novel carriers for psoriasis.

Bioactives	Novel carrier	Effect observed	Reference
Psoralea corylifolia (babchi oil)	Microemulsion gel	Psoralea corylifolia seed oil was effective with improved stability	Kumar and Parmar (2003)
Curcuminoids	Nanoparticles	Enhanced skin uptake and better retention	Mulik et al. (2009)
Glycyrrhetic acid	Nanoemulsion	Increased the stability of formulation and better transdermal effect	Puglia et al. (2010)
Tea tree oil	Microemulsion	Potential in enhanced drug uptake	Khokhra and Diwan (2011)
Cholchicine	Liposome	Sustained delivery	Singh et al. (2009)
3,5-dihydroxy-4-isopropylstilbene	Nanoemulsion	Dramatically improved the DHPS transdermal effect, and the osmotic quantity of DHPS from the nanoemulsion formulations	Zhang et al., 2011

liposomes, niosomes and nanostructured lipid carriers clearly present a tool to overcome the many challenges associated with topical antipsoriatic drug therapy.

These novel carriers have been widely studied and have demonstrated an increment in the rate and extent of drug delivery and optimal therapeutic outcomes. Thus, there is need for further investigations with antipsoriatic drugs to establish the clinical utility and industrial scale-up of techniques for manufacturing these potential novel carriers.

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