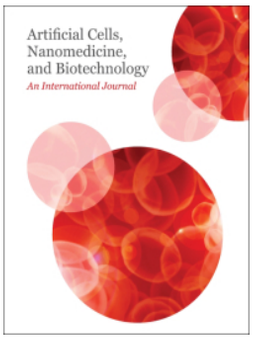

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# Nanotechnological approaches for the effective management of psoriasis

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**Abstract**

**Psoriasis is a chronic disorder with erythematous scaly patches, which typically affects the exposed surfaces of the body and scalp. Various factors such as bacterial infection, genetic and environmental factors, and immune disorders play an important role in causing psoriasis. Different types of psoriasis can be observed, such as guttate psoriasis, inverse psoriasis, pustular psoriasis, and psoriatic arthritis. Various ancient, topical, and systemic approaches have been used to control the disease, but have failed to achieve a complete reduction of the disease, besides causing toxic effects. Therefore, our main aim in this review article is to introduce the different advanced nanotechnological approaches for effective treatment of psoriasis.**

**Keywords:** drug delivery, ethosomes, liposomes, psoriasis

## Introduction

Psoriasis is an autoimmune disease of the epidermis and dermis, characterized by increased propagation of the epidermis with dilation of dermal capillaries (Garg et al. 2014b). The major symptoms of psoriasis are itchy, scaly, and flaky skin, swelling, pain, and disfiguring skin lesions. It can occur in any age group, but psoriatic arthritis usually develops between the ages of 30–50 years. More than 7 million people are mainly affected by this disease in the United States, and various cases have been observed in different countries such as Scandinavia (7–8%), Denmark (5–6%), North America (3–5%), Germany (4%), Canada (more than 1 million people), Russia, Northern Europe (2–3%), Great Britain (2%), China (0.37%), Kuwait (0.11%), Japan (less than 1%), and France (2 million people). The word psoriasis originates from a Greek word "psora", meaning itching. At present, various local and recent approaches such as topical, systemic, biological, and phototherapeutic are considered to reduce psoriasis for a duration of months to years. Psoriasis may be classified as localized or generalized, depending upon the type and severity of the disease. There are various types of psoriasis that can be observed, for example plaque, flexural, guttate, nail, inverse psoriasis, erythroderma, and psoriatic arthritis (arthritis might be present in 10% to 15% of psoriasis cases). Various ancient approaches (acupuncture, water treatment, dietary treatment, etc.) and recent approaches (such as topical, systemic, biological, and phototherapeutic) can induce reduction of psoriasis for months to years. However, complete reduction of psoriasis has not been observed using the above approaches. Therefore, various nanotechnological approaches are being mainly considered by researchers worldwide to achieve complete eradication of the disease (Mahapatra et al. 2014).

## Pathophysiology of psoriasis

Accumulation of dead cells on the skin due to imbalance in the normal cycle of replacing old skin cells with new ones is the main cause of psoriasis (Picardi et al. 2013). In this condition, the immune system (presence of abnormally large numbers of T cells in the skin) mistakenly attacks the cells, tissues, and organs of the person's own body. The other causes for psoriasis are heredity, gene mutations, weather, stress triggers, infection triggers, and skin injury (Gordon-Elliott and Muskin 2013), (Fraga et al. 2012). There are mainly three basic pathological events involved in psoriasis (Table I).

## Types of psoriasis

On the basis of causes, signs and symptoms, and characteristics, psoriasis is classified into 7 major categories. Each type of psoriasis will appear in response to a trigger. Typically, an individual has only one type of psoriasis at a time, and the signs and symptoms, which are typically identified by their hallmark appearance (Table II), vary from person to person.

## Diagnosis of psoriasis

Psoriasis is typically an easy condition for most dermatologists to identify. That is, it can characteristically be

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Table I. Pathological events involved in psoriasis.

| Steps | Pathological events |
|---|---|
| (A) T cell activation | • Human leukocyte antigen (HLA-1, HLA-4, & HLA-6) enter the human skin and activate the antigen-presenting cells.<br>• The activated cells reach the skin-associated lymphoid tissue and interact with T cells, resulting in their maturation, activation, and proliferation. |
| (B) Migration of activated T cells into skin | • The activated T cells express common leukocyte antigen (CLA), interact with E and P selection expressed by the vascular endothelium which undergoes extravasation into the skin, and migrate into the dermis and epidermis. |
| (C) Reactivation of T cells in dermis and epidermis | • Activated T cells undergo reactivation in the lymph nodes, resulting in the formation of memory T cells, which produce type-1 and type-2 cytokines.<br>• Type-1 cytokines (tumor necrosis factor-α, interleukin (IL)-2, interferon-γ) and type-2 cytokines (IL-4, IL-5 and IL-10) are predominant in psoriatic plaques and are responsible for the formation of new psoriatic lesions. |

diagnosed on sight, based on skin fluctuations or variations at the site of the condition on the body. For the diagnosis of psoriasis, the silvery white scales can be easily separated from the skin, which is filled with bright pink or red lesions with pronounced edges. Pinkish moist tender skin is seen under the scales and tiny blood droplets appear after scraping off the moist skin. At times, a skin biopsy or scraping and blood analysis may be desirable, because it is imperative to rule out other disorders and to approve the diagnosis (Table III).

## Approaches for treatment of psoriasis

There are a number of different treatment opportunities for psoriasis. Numerous ancient approaches have been used for initial stage or mild psoriasis; typically, topical approaches are used for mild disease, phototherapy for moderate disease, and systemic agents for severe disease. Complete reduction of psoriasis is not achieved by using the above approaches, therefore various nanotechnological approaches are mainly considered by the research

Table II. Characteristics, symptoms, and causes of various types of psoriasis.

| Types of psoriasis | Signs & symptoms | Causes |
|---|---|---|
| **Plaque psoriasis:** The most prevalent form of the disease. About 80–85% of those who have psoriasis have this type. It is typically found on the elbows, knees, scalp, and lower back. | The plaques are pinkish-red, round or oval, and covered with white silvery scales. The plaques itch or may be painful. | Rubbing of skin, infection, medicines, alcohol, stress, smoking, and sunlight. (Lee et al. 2012) |
| **Flexural psoriasis:** It is also known as inverse psoriasis. Inverse psoriasis is found in the armpits, groin, under the breasts, and in other skin folds around the genitals and the buttocks. About 18% of those who have psoriasis have this type. | Bright red lesions that are smooth and shiny. Irritation from rubbing and sweating. | Yeast overgrowth, high sensitivity to friction or sweating. (Syed and Khachemoune 2011) |
| **Guttate psoriasis:** Guttate psoriasis is usually triggered by a bacterial infection such as strep throat. This form of psoriasis that often starts in childhood or young adulthood. It often comes on quite suddenly. About 18% of those who have psoriasis have this type. | Itching and spots on skin. The spots may be covered with silvery, flaky skin called scales. It is marked by small water-drop-shaped sores on the trunk, arms, legs and scalp. | Streptococcal infection, bacterial or viral infections, injury to skin, e.g., cuts, burns, and insect bites, medicines, stress, sunburn, and alcohol. (Henley 2012) |
| **Nail psoriasis:** Psoriasis can affect fingernails and toenails, causing pitting, abnormal nail growth, and discoloration. About 50–80% of those who have psoriasis have this type. | Change in nail color, little pits in nails, lines across nails, white area on nail plate, thickening of skin under nail, loosening of nail. | Combination of genetic, environmental, and immune causes. (Aydin et al. 2012) |
| **Psoriatic arthritis:** Psoriatic arthritis (PSA) is an inflammatory condition that affects the joints of children and adults with psoriasis. About 1/3 of psoriasis patients have this type. | Red, swollen, tender, warm, and stiff joints, stroke, arthrosclerosis, myocardial infarction. | Trauma or injury on skin, like cuts or burns, medicines, alcohol, skin irritants, smoking. (Mease 2012) |
| **Erythrodermic psoriasis:** It is a particularly inflammatory form of psoriasis that affects most of the body surface. It is characterized by periodic, widespread, fiery redness of the skin and the shedding of scales in sheets, rather than smaller flakes. About 1–6% of those who have psoriasis have this type. | Heart rate increase, fluctuating body temperature, reddening and shedding of the skin. | Use of steroid, severe sun burn, emotional stress, alcoholism, infection, allergy. (Hawilo et al. 2011) |
| **Pustular psoriasis:** Pustular psoriasis can occur in widespread patches or in smaller areas on the hands, fingertips, or feet. Less than 5% of patients who have psoriasis have this type. | Reddening of the skin, followed by formation of pustules and scaling. Severe irritation, or light sensitivity. (Viguier et al. 2012) | Overexposure to UV light, pregnancy, systemic steroids, infections, stress, and sudden withdrawal of systemic medications or potent topical steroids. |

Table III. Diagnosis of psoriasis by skin biopsy and blood analysis.

| Findings revealed on skin biopsy of psoriasis (18) | Findings revealed on blood analysis of psoriasis (19) |
|---|---|
| • Thickening of skin<br>• Excess keratin formation<br>• Formation of continuous skin<br>• Expansion of capillaries<br>• Infiltration of skin due to macrophages<br>• Infiltration of skin due to lymphocytes<br>• Large Munro abscesses | • Increased erythrocyte sedimentation rate (ESR, CED rate)<br>• 10–20% increase in content of uric acid<br>• Below normal amount of red blood cells in severe psoriasis<br>• High erythrocyte sedimentation rate is noted in pustular psoriasis. |

scientists to achieve complete eradication of the disease worldwide.

## Ancient approaches

Various ancient approaches such as acupuncture (inserting needles at various depths at meridians), ayurveda, manipulation (massage), herbal treatment (garlic, jasmine, guggul, neem, turmeric, bogbean, Guaiacum), environmental or atmospheric treatment (sunlight), use of dietary supplements (vitamins, minerals), meditation, moisturizing treatments (aloe vera, neem oil, emu oil), water therapy, and other therapy (exercise, swimming) were used to control the various stages of psoriasis. The major limitations of these approaches are that they can be used only for mild disease. The other limitations are that they could causes allergic reactions, irritation, or darkening of skin, stain clothing, increase chances of infections as well as scarring, show limited efficacy and high toxicity, such as renal toxicity, and require patient monitoring. Miroddi et al. (2015) conducted a systematic review of clinical trials assessing the effectiveness and safety of aloe for the treatment of psoriasis (Miroddi et al. 2015). Xiong et al. (2015) investigated the effect of glycyrrhizin (GL) on psoriasis and explored the mechanisms involved. The results showed that GL treatment significantly reduced the levels of ICAM-1 in TNF-α-stimulated HaCaT cells, inhibited subsequent monocyte adhesion to keratinocytes, and suppressed the nuclear translation and phosphorylation of p65 following the degradation of inhibitor κB (IκB). GL treatment blocked the phosphorylation of extracellular signal-regulated kinase (ERK)/p38 MAPK. GL effectively delayed the onset of IPI in mice and ameliorated ongoing IPI, thereby reducing ICAM-1 expression in epidermal tissues. Conclusions: These results demonstrate that GL treatment ameliorates skin inflammation by inhibiting ICAM-1 expression via interference with the ERK/p38 MAPK and NF-κB signaling pathways in keratinocytes. Therefore, GL can be used as an anti-psoriatic drug (Xiong et al. 2015).

## Topical approaches

Topical agents such as Epsom salts, moisturizers, mineral oil, and petroleum jelly may offer support by soothing inflamed or elevated skin and diminishing the dryness which accompanies the build-up of skin on psoriatic plaques (Sarker 2005). They also help to normalize skin cell production and reduce inflammation. Typically, topical approaches are mainly used for control and treatment of the mild form of the disease. Various anti-psoriatic drugs such as tacrolimus, clocortolone pivalate, zinc pyrithione, methotrexate (MTX), betamethasone dipropionate, Acitretin, adalimumab, dapsone, valrubicin, etc. are successfully delivered to the target site through different dosage forms such as cream, gel, paste, lotion, ointment, and spray. The major advantages of topical approaches are that they are safe, effective, cause minimum inflammation, reduce skin turnover, remove built-up scale, and can be applied directly to the target site. However, they suffer from various limitations such as having a greasy feel, staining clothes and bedding, having an unpleasant odor like coal tar (Colombo et al. 2012), and being time consuming. Del Rosso and Kircik (2012) prepared clocortolone pivalate-loaded cream to control skin diseases. The results showed excellent control of atopic dermatitis and other eczematous dermatoses at the target site (Del Rosso and Kircik 2012). Colombo et al. (2012) prepared Dovobet gel incorporating calcipotriol and betamethasone dipropionate, and the results showed better overall adherence and treatment of patients with mild-to-moderate psoriasis (Colombo et al. 2012).

## Systemic approaches

Systemic approaches are mainly used in severe conditions or when the psoriasis is resistant to topical treatment. The three main traditional systemic treatments are the use of MTX, cyclosporine, and retinoids. The main mechanisms of systemic approaches are to suppress the immune system and slow the growth of skin cells (Jadhav et al. 2006). Various anti-psoriatic drugs such as dithranol, ammonium glycyrrhizinate, ketoprofen, betamethasone 17-valerate, bortezomib, simvastatin, cyclosporine, retinoids, etc. are successfully administered through the systemic route to the target site. The major advantages of systemic treatment are good skin tolerability, effectiveness against various types of psoriasis, and activity in severe conditions (Tarun et al. 2011). Despite their advantages, they suffer from some limitations such as causing nausea or fatigue, abdominal pain, diarrhea and headaches, damaging the liver and blood cells, impairing kidney function, and increasing blood pressure. Hazarika (2009) developed a cyclosporine-incorporated solution and administered it to psoriatic patients by the systemic route. The result showed an excellent management of pustular psoriasis of pregnancy or psoriasis with pustulation in pregnancy (Hazarika 2009).

## Nanotechnological approaches

An ancient approach has been used for initial stage or mild psoriasis, but has not been successful in the case of moderate and severe conditions of psoriasis. Topical and systemic approaches provide effective control of various types of disease, but show numerous side-effects and toxicity (Chaudhary et al. 2015a, Chaudhary et al. 2015b). Therefore,

various nanotechnological colloidal carriers including vesicular and particulate systems like liposomes (Garg 2014, Garg and Goyal 2014b), transfersomes (Garg and Goyal 2012), niosomes (Garg and Goyal 2014a), ethosomes (Garg et al. 2012a), solid lipid nanoparticles (Garg et al. 2014a), microspheres (Garg and Rath 2015), micelles (Garg et al. 2014d), dendrimers (Garg et al. 2014c), etc. are widely used for the prevention and control of psoriasis, due to their unique characteristics (Chaudhary et al. 2014). These nanotechnological approaches can be delivered by various routes such as topical (Garg and Goyal 2014c), dermal (Garg et al. 2011a), transdermal (Garg et al. 2011b), or systemic, in a single form (Singh et al. 2014c) or a combined form (Gagandeep et al. 2014).

### Characteristics of nanocarriers

Nanocarriers play a critical role in drug delivery to the target site for control (Garg et al. 2015) and prevention of the disease (Garg and Goyal 2014c). Nowadays, these carriers have become the first choice to deliver anti-psoriatic drugs, due to their various characteristics such as:

- Excellent biocompatibility as well as biodegradability (Goyal et al. 2013a)
- Free from harmful inflammatory reactions (Goyal et al. 2013b)
- Non-toxic and degradable in nature (Goyal et al. 2014a)
- Easily eliminated from the body (Goyal et al. 2013a)
- Stable at physiological and atmospheric conditions (Goyal et al. 2013b, Kaur et al. 2015a)
- Stability retained for a longer duration of time (Goyal et al. 2014a)
- Adequate porosity, pore size distribution, and interconnectivity (Goyal et al. 2014b)
- Reproducible microscopic and macroscopic structure (Hussain et al. 2014)
- Easy processability and malleability into desired shape (Johal et al. 2014)
- Provide protection of encapsulated substances from physiological and atmospheric conditions (Joshi et al. 2014a)
- Sustained and controlled drug release to the target site (Joshi et al. 2014b)
- Prevent dose dumping and associated side effects (Kalia et al. 2014)
- Similarity to implantation site (Garg et al. 2012b)

## Nanotechnological carriers

Various nanotechnological colloidal carriers including vesicular and particulate systems like liposomes, transfersomes, niosomes, ethosomes, solid lipid nanoparticles, microspheres, micelles, dendrimers, etc. are widely used for the prevention and control of psoriasis.

### Liposomes

Liposomes or lipid-based vesicles are microscopic (unilamellar or multilamellar) vesicles (Kataria et al. 2014). They are produced from phospholipids, cholesterol, and long-chain fatty acids (Kaur et al. 2014a). Liposomes containing drugs can be administered by various routes (intravenous, oral inhalation, local application, ocular) for the treatment of psoriatic conditions. The main advantages of this system are biocompatibility and biodegradability, nontoxicity, non-immunogenicity, increased stability (Wilczewska et al. 2012), and the ability to protect the encapsulated drug from the external environment. Knudsen et al. (2012) investigated the stabilizing effect of liposomes with the lipopolymer poly(ethylene glycol)-distearoyl phosphoethanolamine (PEG-DSPE) on the physicochemical properties of the liposomes and their ability to deliver membrane-intercalated calcipotriol into the skin for topical treatment of psoriasis (Knudsen et al. 2012). Srisuk et al. (2012) fabricated MTX-entrapped oleic acid-containing deformable liposomes for in vitro transepidermal delivery in targeted treatment for psoriasis. The results showed that the liposomes are one of the promising candidates to enhance the permeability of MTX for the treatment of psoriasis (Srisuk et al. 2012). Gupta et al. (2014) evaluated the potential of capsaicin (CAP)-containing liposomes, niosomes, and emulsomes in providing localized and controlled delivery, to improve the topical delivery of the drug. Based on the results, we concluded that these carrier systems may be a potential approach for the topical delivery of CAP, for an effective therapy for psoriasis (Gupta et al. 2014).

### Niosomes

Niosomes (non-ionic surfactant-based liposomes) are microscopic lamellar structures obtained on hydration of non-ionic surfactant, cholesterol, and other lipids (Kaur et al. 2014b). The vesicle holds hydrophilic and hydrophobic drugs within the space enclosed in the vesicle, and within the bilayer itself, respectively (Kaur et al. 2014c). Based on the size of the vesicle, niosomes can be classified into three groups: (i) small unilamellar vesicles (SUV, size = 0.025–0.05 μm), (ii) multilamellar vesicles (MLV, size = > 0.05 μm) and (iii) large unilamellar vesicles (LUV, size = > 0.10 μm) (Kaur et al. 2014d). They can be used for oral, parenteral, as well as topical administration, and can increase the oral bioavailability and the skin penetration of drugs (Azeem et al. 2009). They are biodegradable, biocompatible, non-immunogenic, and do not require any special condition for handling or storage. They provide protection from the biological environment and improve the therapeutic performance of the drug. Lakshmi et al. (2007) studied the preparation of niosomal MTX in chitosan gel, and tested the same for irritation and sensitization on healthy human volunteers, assessed the efficacy of the gel through double-blind placebo-controlled study on psoriasis patients, and also compared its efficacy with a marketed MTX gel. The results showed a reduction in total score, from 6.2378+/− 1.4857 to 2.0023+/− 0.1371 at week 12, and suggested that niosomal MTX gel is more efficacious than placebo and marketed MTX gel (Lakshmi et al. 2007). Marianecci et al. (2012) investigated the potential application of niosomes for the delivery of ammonium glycyrrhizinate (AG), useful for the treatment of various inflammatory diseases such as psoriasis. The results showed

that the AG-loaded non-ionic surfactant vesicles showed no toxicity, good skin tolerability, and were able to improve the drug's anti-inflammatory activity in mice (Marianecci et al. 2012). Abdelbary and AbouGhaly (2015) designed topical MTX-loaded niosomes for management of psoriasis to avoid systemic toxicity. An in vivo skin deposition study showed that the highest values for percentage of drug deposited (22.45%) and AUC0-10 (1.15 mg.h/cm$^2$) of MTX were significantly greater with the use of niosomes than those seen with the drug solution (13.87% and 0.49 mg.h/cm$^2$, respectively). Moreover, in vivo histopathological studies confirmed the safety of topically applied niosomes. Summing up, the results showed that targeted MTX delivery might be achieved using topically applied niosomes for enhanced treatment of psoriasis (Abdelbary and AbouGhaly 2015).

### Microspheres

Microspheres are solid polymeric spherical particles (1–1000 μm), in which the drug is dispersed throughout the polymer matrix (Kaur et al. 2015b). Microspheres (free-flowing powders) characteristically consist of biodegradable proteins or synthetic polymers (Kaur et al. 2014f). Microspheres are used for efficiently delivering therapeutic substances to the target site in a sustained and controlled fashion of release (Kaur et al. 2014e). The major advantages of this system are that it protects the unstable drug before and after administration, improves the bioavailability, reduces the incidence or intensity of adverse effects, provides prolonged therapeutic effect, and improves patient compliance (Kaur et al. 2014g). Gomes et al. (2008) prepared psoralen-loaded poly (DL-lactide-co-glycolide) (PLGA) microspheres to be used in PUVA therapy (psoralen and UVA irradiation (ultraviolet A, 320–400 nm) for the treatment of psoriasis in rat skin (Gomes et al. 2008). Chlapanidas et al. (2014) evaluated the effect of the combined use of the racemic flavanone naringenin (NRG) and the protein sericin as TNF-α blockers against psoriasis. The results of this study provide the proof of concept that sericin-based microspheres loaded with TNF-α-blockers could contribute to the downregulation of cytokine, and represent the starting point for the development of new topical formulations for the treatment of middle-stage psoriasis (Chlapanidas et al. 2014).

### Hydrogels

Hydrogels are a hydrophilic polymeric network of three-dimensional crosslinked structures based on ionic interaction and hydrogen bonding (Kaur et al. 2014h). The network structure of hydrogels can be macroporous (pores of dimension 0.1–1 μm), microporous (pore size in the range of 100–1000A°), or nonporous (10–100 A°) (Kaur et al. 2014i). The advantages of hydrogels include their biocompatibility and their ability to sense changes of pH, temperature, or other stimulation, and the fact that they can be injected, can absorb water nearly 10–20 times the molecular weight, and are easy to modify (Goyal et al. 2013b). Ali et al. (2008) prepared liposomal MTX hydrogels for the treatment of localized psoriasis. The results showed that gels showed zero order kinetic release and were beneficial in relieving psoriasis, and did not exert systemic toxicity (Ali et al. 2008). Patel et al. (2011) studied the efficacy and safety of an occlusive hydrogel dressing. In this research study, participants were treated with a calcipotriene 0.005%–betamethasone dipropionate 0.064% ointment, with and without a hydrogel patch. No adverse effects, including skin irritation, were observed or reported in the study, and hydrogel dressings were found to provide an effective and safe occlusive option to enhance topical therapy for psoriasis (Patel et al. 2011). Park et al. (2013) proposed the hydrogel patch as an innovative approach to complete barrier repair. The results after the 2-week no-treatment follow-up showed that the hydrogel patch had notable efficacy, and was comparable to TAC 0.1% cream (Park et al. 2013).

### Nanoparticles

Nanoparticles are particulate dispersions or solid particles (size range 10–1000 nm), in which the drug is dissolved, entrapped, encapsulated, or attached to a nanoparticle matrix (Kaur et al. 2014j). Hydrophilic substance-coated biodegradable polymeric nanoparticles have been used as potential drug delivery devices (Kaur et al. 2014k). Polymeric nanoparticles offer some specific advantages such as aiding the increase in stability of drugs/proteins, easy manipulation of particle size and surface characteristics, ability to circulate for a prolonged period of time, ability to target a particular organ (Kumar et al. 2015) and to control and sustain the release of the drug during transportation (Malik et al. 2014), reduction in side effects, high drug loading, site-specific targeting, and possibility of administration by various routes (Coaker 2012). Lin et al. (2011) evaluated time-correlated single photon counting (TCSPC) for simultaneous monitoring of zinc oxide nanoparticles (ZnO-NP) and the metabolic state of volunteers' skin (Lin et al. 2011). Kato (2012) developed photodegradable nanoparticles for phototherapy of psoriasis vulgaris (Kato 2012).

### Transfersomes

Transfersomes are colloidal particles having a water-filled core surrounded by a wall of lipids and surfactants (amphiphiles) arranged in a bilayer (Marwah et al. 2014). With the help of various forces such as electrostatic and/or hydrophobic forces, amphiphilic and lipophilic drugs get entrapped in the bilayered wall and hydrophilic drugs get placed in the internal aqueous environment (Rajan et al. 2011). These systems have been found to be much more efficient at delivering a low and high molecular weight drug to the skin by systemic as well as topical routes (Modgill et al. 2014a). These systems protect the encapsulated drug from metabolic degradation and act as a depot, releasing their contents slowly and gradually (Modgill et al. 2014b). Absence of toxicity, drug targeting, ability to provide sustained-release action of drugs, and ease of scaling up are other associated advantages related to these vesicles (Patel and Parikh 2012).

### Ethosomes

Ethosomal carriers are systems composed mainly of phospholipids (phosphatidyl choline, phosphatidylserine, phosphatidic acid), alcohol (ethanol & isopropyl alcohol at

relatively high concentrations), and water (Morie et al. 2014). The size of ethosomes can be modulated to range anywhere from 30 nm to a few microns (Pabreja et al. 2014). They can trap hydrophilic, lipophilic, or amphiphilic drug molecules with various physicochemical characteristics (Rohilla et al. 2014a). The major advantages of these carrier systems are high patient compliance, enhanced permeation of drugs, content of non-toxic raw materials, and simple technique of drug delivery (Rohilla et al. 2014b). Therefore, these carrier systems have been found to be suitable for various applications within the pharmaceutical, biotechnology, veterinary, cosmetic and nutraceutical markets (Bhalaria et al. 2009). Fang et al. (2009) employed a highly potent ethosomal carrier (phosphatidylethanolamine; PE) to investigate the penetration behavior of 5-aminolevulinic acid-photodynamic therapy (ALA-PDT) and the recovery of skin in a hyperproliferative murine model. The results demonstrated that the ethosomal carrier significantly improved the delivery of ALA and the formation of PpIX in both normal and hyperproliferative murine skin samples, and the expression level of tumor necrosis factor (TNF)-alpha was reduced after the ALA-ethosomes were applied to treat hyperproliferative murine skin (Fang et al. 2009). Zhang et al. (2014) developed a novel system for the transdermal delivery of psoralen employing ethosomes—flexible vesicles that can penetrate the stratum corneum and target deep skin layers. An in vitro skin permeation study showed that the permeability of psoralen-loaded ethosomes was superior to that of liposomes. The ethosomes and liposomes were found to be safe, following daily application to rat skin in vivo for 7 days. The ethosomes showed better biocompatibility with human embryonic skin fibroblasts than did an equivalent ethanol solution, indicating that the phosphatidylcholine present in the ethosomal vesicles improved their biocompatibility. These findings indicated that ethosomes could potentially improve the dermal and transdermal delivery of psoralen and possibly of other drugs requiring deep skin delivery (Zhang et al. 2014).

### Micelles

A micelle is an aggregate of surfactant molecules disseminated in a liquid colloid (Sharma et al. 2014a). A characteristic micelle forms a complex with the hydrophilic head regions in contact with surrounding solvent, sequestering the hydrophobic tail region in the micelle center in aqueous solution (Sharma et al. 2015). The hydrophilic and hydrophobic blocks form the corona and the core of the micelles respectively (Valerii et al. 2013). The main merits of poly(ethylene oxide)-block-poly(ester) are the biocompatibility, unaltered biological activity, sustained release of encapsulated materials, ability to act as long-circulating drug carriers, non-toxicity, increased solubility of hydrophobic drugs, ability to function in site-specific delivery, and ability to be used for delivery of therapeutic proteins as well as small molecules (Sharma et al. 2014b). Ehrlich et al. (2004) explored the safety and efficacy of paclitaxel in individuals with severe psoriasis. The results showed that micellar paclitaxel demonstrates therapeutic activity in patients with severe psoriasis (Ehrlich et al. 2004).

### Dendrimers

Dendrimers are three-dimensional macromolecular architectural classes (linear, crosslinked, and branched) with an initiator core, several branching units, and multiple active terminal groups (Sharma et al. 2014c). Drug molecules can be loaded both in the interior of dendrimers as well as attached to surface groups. Dendrimers offer various advantages over other polymers, such as less susceptibility to uptake by the reticuloendothelial system, ease of modification, targeting to particular sites in the body, ensuring reproductive pharmacokinetic behavior, and providing a large variety of structures with reduced cost of production (Singh et al. 2014a). These systems can be administered by various routes including intravenous, oral, transdermal, pulmonary, and ocular (Wang et al. 2003). Agrawal et al. (2013) explored the potential of polypropylene imine (PPI) dendrimers to deliver dithranol (DIT) topically and evaluated its encapsulation, permeation, and skin irritation potential. DIT–PPI showed a significantly enhanced permeation rate constant and less skin irritation ($11.61 \pm 1.80$ μg/cm(2)/h and 1.0, respectively) when compared with the plain DIT solution ($2.72 \pm 0.31$ μg/cm(2)/h and 2.3, respectively). The enhanced accumulation of DIT via dendrimer carriers within the skin might help optimize targeting of this drug to the epidermal and dermal sites, thus creating new opportunities for well-controlled, modern topical application of DIT for the treatment of psoriasis (Agrawal et al. 2013b).

### Solid lipid nanoparticle (SLN)

A solid lipid nanoparticle (SLN) is typically spherical, with an average diameter between 10 to 1000 nanometers (Singh et al. 2014b). SLNs possess a solid lipid core matrix that can solubilize lipophilic molecules. The lipid core is stabilized by surfactants (emulsifiers) (Singh et al. 2012a). The term lipid is used here in a broader sense and includes triglycerides (e.g., tristearin), diglycerides (e.g., glycerol behenate), monoglycerides (e.g., glycerol monostearate), fatty acids (e.g., stearic acid), steroids (e.g., cholesterol), and waxes (e.g., cetyl palmitate) (Singh et al. 2012b). All classes of emulsifiers (with respect to charge and molecular weight) have been used to stabilize the lipid dispersion. It has been found that the combination of emulsifiers might prevent particle agglomeration more efficiently (Bikkad et al. 2013). Due to their unique size-dependent properties, lipid nanoparticles offer the possibility to develop new therapeutics. The ability to incorporate drugs into nanocarriers offers a new prototype in drug delivery that could hold great promise for attaining enhanced bioavailability along with controlled and site-specific drug delivery. Agrawal et al. (2013) explored the potential of SLNs and nanostructured lipid carriers (NLCs) in improving the topical delivery of capsaicin (CAP), by in vitro and in vivo studies. 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 (Agrawal et al. 2013a). Pradhan et al. (2014) developed SLNs of triamcinolone acetonide (TA), to study the effect of various process variables in order to optimize the formulation for effective delivery. The SLNs exhibited prolonged drug release, following Higuchi release

kinetics ($R^2 = 0.9909$). An in vitro skin distribution study demonstrated systemic escape of the drug from TA-loaded SLNs, which might eliminate side effects associated with systemic exposure (Pradhan et al. 2014).

## Conclusion

Recent nanotechnological approaches are being successfully used to reduce symptoms in advanced stages of psoriasis for months to years, without producing side effects. These approaches increase the penetration of drug molecules to the target site and control the various types of psoriasis. Besides the nanotechnological techniques, some combination therapies which may involve the use of corticosteroids along with non-corticosteroids with PUVA therapy play an important role in the treatment of psoriasis.

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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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