Review paper

Treatments in psoriasis: from standard pharmacotherapy to nanotechnology therapy

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Abstract

Psoriasis is a genetic chronic disease mediated by the immune system with systemic and cutaneous manifestations that can significantly deteriorate patients' quality of life. Two–three percent of the population worldwide suffer from psoriasis and it imposes a substantial economic burden on patients. The aetiology is mainly related with genes and environmental factors. The pathophysiology of psoriasis is characterized by T cells and dendritic cells, antimicrobial peptides, genetic predispositions, lipoprotein-2, galactosin-3, fractalkine, vaspin, and human neutrophilic peptides, etc. in the progression of psoriasis. For patients with psoriasis, the traditional treatments include corticosteroids, vitamin D_3 analogues, calcineurin inhibitors, methotrexate, cyclosporine, acitretin, phototherapy, and biological agents, etc. Nanodermatology is an emerging, multidisciplinary science that is gaining increasing recognition in the treatment of psoriasis. This review provides a summary of the pathophysiology, epidemiology, clinical diagnosis, and classical pharmacotherapy of psoriasis. The review also summarizes different nanotechnology therapies for effective treatment of psoriasis.

Key words: psoriasis, topical treatments, systemic treatments, nanocarriers.

Introduction

Psoriasis is a chronic genetic disorder that is mediated by the immune system; it mainly involves pathological changes in the skin and joints. The main symptoms include itching, flaky and scaly skin, pain, swelling, bleeding and skin damage [1]. However, the clinical course is difficult to predict [2]. Psoriasis poses many complications including physical disfigurement, chronicity, and its associated disability and comorbidities. Studying the pathophysiology of psoriasis can help control this complicated disorder whose impact on patients is far beyond the skin. To date there have been various standard local therapeutic approaches being applied that can help control the condition for months to years, such as corticosteroids, methotrexate, cyclosporine, acitretin, and phototherapy. However, complete recovery from psoriasis through these treatments has not been reported. Therefore, researchers worldwide are mainly considering to utilize various nanotechnology therapies to completely eradicate this condition [3–8]. New medication delivery carriers, particularly nanocarriers, may overcome certain disadvantages of conventional delivery methods, such as dose minimization, frequency of administration, and dose-dependent side effects.

Pathophysiology

Psoriasis is an autoimmune disease without any obvious immunogen identified, but the basic pathophysiology of psoriasis is considered to be too much activation of parts of the adaptive immune system [4], more specifically, it is the collective result of a variety of cell types, including keratinocytes, dendritic and T cells, which are in a chronic inflammatory state due to the production of cytokines [9–13]. Other reasons of developing psoriasis include genetic heredity and mutations, weather, infections, stress, and skin lesions [14, 15]. Basic pathological events involved in psoriasis are presented in Figure 1.

Epidemiology

Psoriasis affects at least 125 million people worldwide, making it a major public heath challenge. The prevalence

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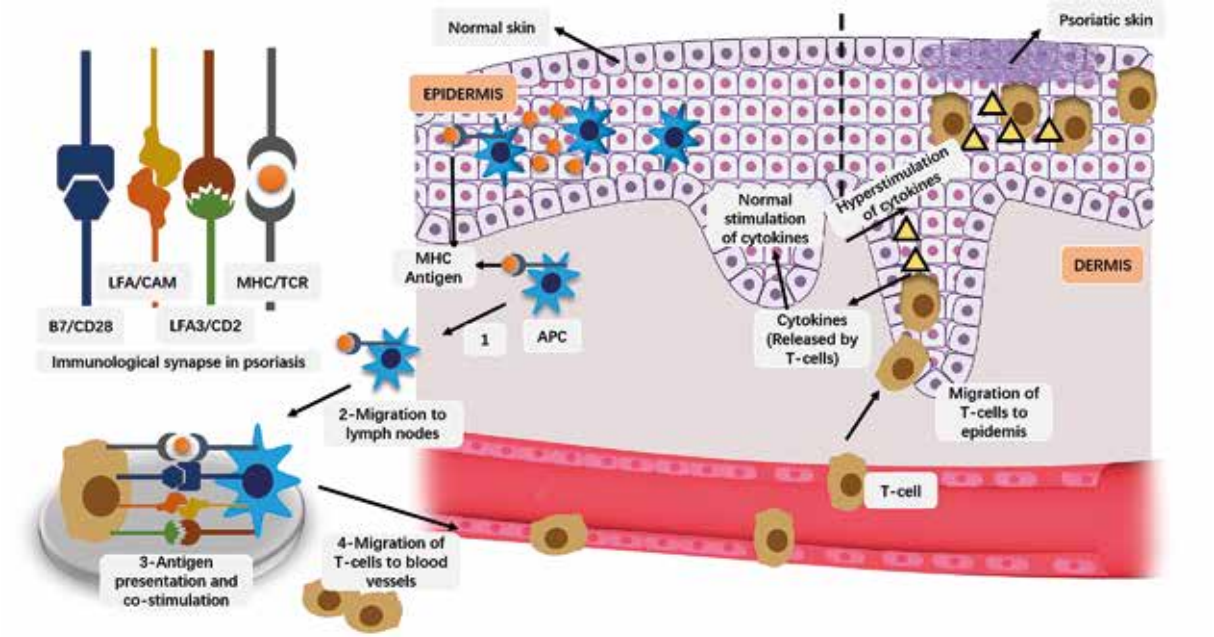

Figure 1. Basic pathological events involved in psoriasis. The antigen attaches to the major histocompatibility complex (MHC) of antigen presenting cells (MHC). Antigen-bound APC migrates to lymph nodes. Antigens are presented to T cells and co-stimulation via APC. The activated T cell clones are redirected to blood vessels

of psoriasis is equal among males and females [16], however it varies widely across different regions, ranging from as low as 0.5% (Asia) to as high as 8% in some European areas [16–18]. In the United States, approximately 3.2% of adults and 0.13% of children suffer from psoriasis [19–21].

The onset of psoriasis can be at any age, but is most common between the ages of 15 and 30 [22]. Environmental and genetic factors can influence the age of onset for psoriasis; for instance, the human leukocyte antigen (HLA)-C*06 allele has a strong correlation with early onset of psoriasis [23]. Besides, patient ethnicity, UV exposure, and the climate they live in are also considered to influence the prevalence of psoriasis, and recent studies have found a weak association between latitude and psoriasis prevalence [24].

Clinical diagnosis

Psoriasis is a typical skin disease that most dermatologists can easily identify based on its clinical manifestations, which are silver-white scales easily detaching from the skin, these scales usually are seen together with bright pink or red lesions with well-defined margins. The skin under the scales is pink, moist, and tender, and small bleeding spots will appear after the scales are scraped off from the moist skin. Normally, diagnosis would focus on investigation of any family history of psoriasis, and a clinical examination of the skin and nails, which includes an assessment of the distribution and morphology of psoriatic lesions. Sometimes, when psoriasis patients have atypical clinical presentations, dermatologists may also use skin biopsies or scrapes and blood analysis to eliminate other diseases and to verify the diagnosis. In addition, the Psoriasis Area and Severity Index (PASI) score is widely used to evaluate the severity of lesions in patients with psoriasis [25], and lattice system physician's global assessment (LS-PGA) or psoriasis global assessment (PGA) have been used in routine clinical practice [26].

Standard pharmacotherapy

Therapeutic targets include improving skin, joint, and nail lesions, as well as improving the quality of life for patients. Although modern medicine has not discovered the complete cure for psoriasis, many treatment modalities can be utilized (Figure 2). In general, conventional treatment of psoriasis includes topical treatments, systemic treatments. The preferred treatment for patients with mild psoriasis with less than 10% of body surface area (BSA) is local topical treatment [27]. Topical treatments include corticosteroids, calcineurin inhibitors, vitamin D_3 analogues, and other topical treatments (non-medicated moisturizers, coal tar, salicylic acid, and anthralin). Systemic treatments are commonly used for severe disease. The presence of comorbidities that are effectively treated and other patient-related factors should also be considered in the selection of systemic treatments.

Topical treatments

Corticosteroids

Using corticosteroids topically is the standard primary treatment for the majority of patients with localized or mild psoriasis; these corticosteroids have anti-proliferative,

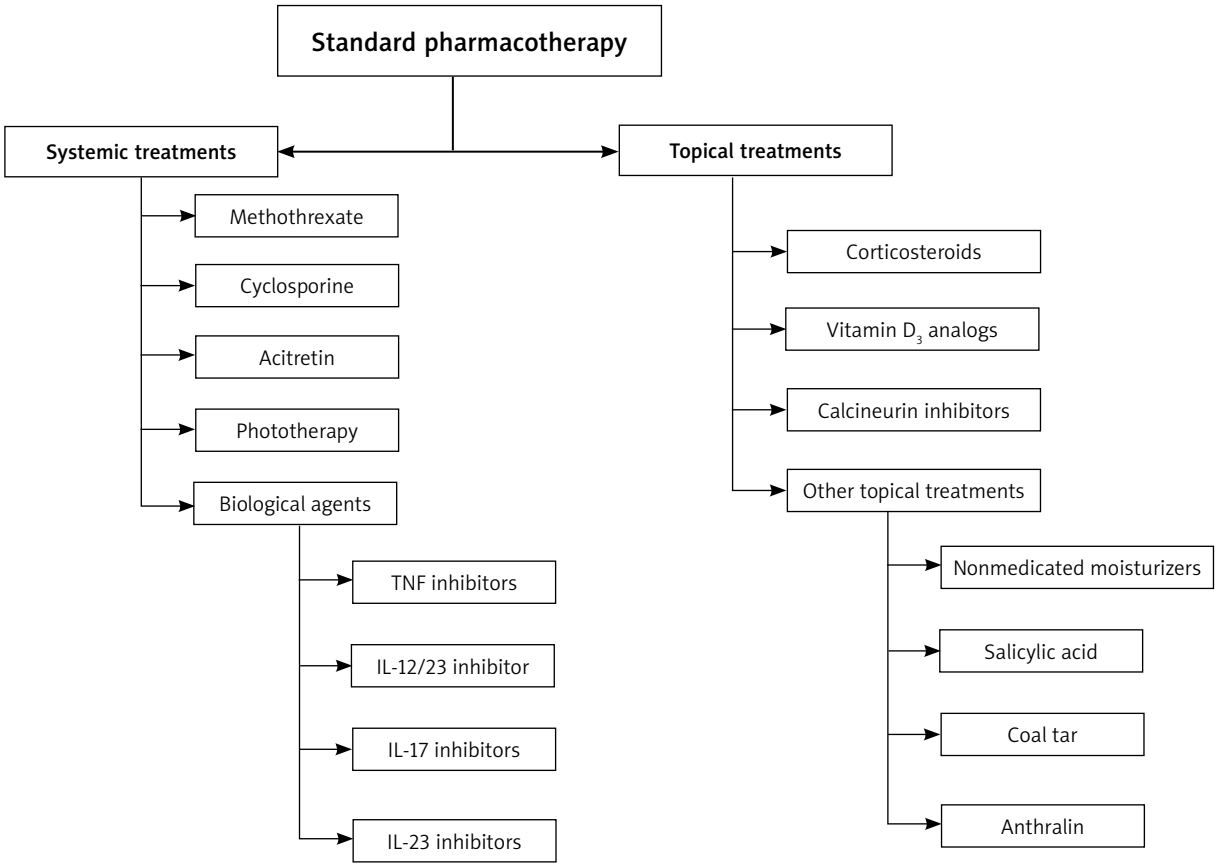

Figure 2. Standard pharmacotherapy used in psoriasis

anti-inflammatory, and locally vasoconstrictive properties through downregulating pro-inflammatory cytokines coding genes. The therapeutic effect of topical corticosteroids varies from classification (established using vasoconstrictive assays), with class I being the most potent, and class VII being the weakest. For mild or localized psoriasis, there are multiple options regarding using topical corticosteroids. During the acute phase of active psoriasis, topical agents are used twice daily; afterwards, patients can choose a topical agent (vitamin D analogue, topical corticosteroid, or calcineurin inhibitor) twice a week when the lesions become quiescent, which can reduce the risk of recurrence [28]. Besides, the results of a meta-analysis showed that corticosteroid combined with vitamin D_3 yielded the best outcomes for the scalp [29]. Other studies also found that combined formulations are more effective, producing less side effects and a recurrence is slower to return compared with monotherapy [30, 31]. However, long-term use can cause potential side effects, such as local skin alterations, hypothalamic-pituitary-adrenal axis suppression, and tachyphylaxis [32].

Vitamin D analogues

Another adjuvant for chronic psoriasis is vitamin D analogues. When applied topically, these analogues combine with vitamin D receptors on T cells and to those on keratinocytes to prevent the proliferation of keratinocytes and promote its differentiation. Topical agents include capotriol, calcitriol, etc. Among them, tacalcitol ointment is an efficient and harmless treatment for chronic plaque psoriasis that can be used for the long term, and systemic side effects at sensitive sites are minimal with overall satisfactory tolerability, but it is not as effective as capotriol [33]. Topical vitamin D agents have a modest effect when used on its own [34]. Vitamin D analogues are relatively safe and can be applied liberally on patients without any renal impairment. The major side effects include burning sensation and irritation seen in 35% of patients and usually diminish over time [35].

Calcineurin inhibitors

Inflammatory substance is considered to be an important factor in the pathogenesis of psoriatic skin lesions [36], and calcineurin inhibitors can inhibit the production of inflammatory substance. Tacrolimus ointment with difference strengths (0.03% and 0.1%) and pimecrolimus cream (1%) are the most commonly used topical calcineurin inhibitors that are commonly prescribed for the treatment of psoriasis in facial and intertriginous ar-

eas long-term without any adverse effect such as skin atrophy [37]. Clinically, it is recommended to increase permeability by blocking therapy or mixing these reagents with salicylic acid [38, 39]. Generally speaking, Tacrolimus and pimecrolimus are not thought to be teratogenic due to their low uptake systemically [40]. However, tacrolimus and pimecrolimus are present in breast milk, therefore not suggested for breastfeeding mothers.

Other topical treatments

Non-medicated moisturizers including salicylic acid, coal tar, and anthralin are less frequently used topical agents [41]. Moisturizers help to handle the pressure generated by the skin and the Koebner phenomenon [42]. Moisturizers can soothe dry skin, decrease desquamation, relieve itching, soften the skin cracks, and enhance the absorption of other topical drugs [43]. Moisturizers can be applied to pregnant women and children, but some patients may develop allergic symptoms due to sensitivity to moisturizing materials. Salicylic acid lowers the pH of the cuticle, thereby hydrates and softens the skin [44]. The combination of steroid hormone and salicylic acid can be used as first-line treatment for plaque psoriasis [45]. Side effects of salicylic acid include possible acute or chronic systemic poisoning, symptoms of the CNS, tinnitus, metabolic acidosis, and nausea and vomiting [46, 47]. Coal tar may inhibit DNA synthesis, thereby reducing keratinocyte overproliferation [48]. Side effects of using coal tar include bad odour, contact dermatitis, staining, erythema, folliculitis, tingling sensation, and corneal acanthoma formation; the use of PUVA and coal tar for treatment are not advocated to prevent the risk of skin cancer development [49, 50]. Anthralin may reduce keratinocyte proliferation through mitochondrial dysfunction to inhibit the activation of T cells and restore cell differentiation [51]. Furthermore, free radical production may enhance its action. Side effects of anthralin depend on the dose of treatment.

Systemic treatments

Methotrexate

Methotrexate is a folic acid analogue that stops the synthesis of DNA by blocking the production of purine and thymidine. Initially, the recommended dosage is 7.5–10 mg/week and increased to of 25 mg/week maximally [52]. Despite being widely used in clinical practice, there is a lack of substantial well-structured clinical research to evaluate the efficacy and safety of methotrexate. A placebo-controlled, randomized, double-blinded study found that nearly 40% of patients taking methotrexate improved 75% in the Psoriasis Area and Severity Index score, compared with only 18.9% improvement in 16 weeks for patients receiving placebo treatment [53]. The use of methotrexate for the treatment of psoriasis in children has not been approved [54]. The common side effects include feeling tired and nauseous, diarrhoea, and vomiting. A more serious side effect is hepatotoxicity [55].

Cyclosporine

Cyclosporine is an immunosuppressant of calcineurin inhibitor that suppresses T cells and is used for moderate to severe psoriatic patients [56]. It has also been shown to be effective in treating psoriatic arthritis [57–59]. Cyclosporine can rapidly relieve symptoms, but its many adverse effects and drug interactions restrict its long-term use. Hypertension, nephrotoxicity and non-melanoma skin cancer are obvious potential side effects.

Acitretin

Acitretin is an oral retinoid to treat moderate to severe psoriasis. As an adjuvant therapy to other systemic agents, acitretin has been established as an agent that improves efficacy, lowers dosage, and reduces the incidence of side effects [60–62]. However, acitretin is teratogenic, so women are advised not to plan any birth for three years after discontinuing the medication [63]. Mucocutaneous dryness, photosensitivity gastrointestinal troubles, and arthralgia are commonly seen side effects of acitretin; sometimes it can even induce elevated triglyceride levels and transaminitis.

Phototherapy

Phototherapy is often used for the treatment of moderate to severe psoriasis, particularly for psoriasis that is unresponsive to topical agents [64]. In addition, phototherapy can be combined with biologic agents for the treatment of severe psoriasis [65]. The main types of phototherapy used to treat psoriasis include psoralen plus UVA, broadband UVB, and narrowband UVB (NB-UVB). Generally, the frequently used first-line treatment is NB-UVB therapy because it is more effective and safer [66]. No evidence suggests that NB-UVB predisposes patients to skin malignancies [67]. Another treatment of psoriasis is targeted phototherapy, for instance excimer light. Although it is safe, the limited availability of phototherapy centres and the need for frequent treatments make this option very inconvenient for patients.

Biological agents

In recent years, the development and approval of biological agents for the treatment of moderate and severe psoriasis and psoriatic arthritis have received wide attention. There are four classes of biologic agents for the treatment of psoriasis: IL-12/23 inhibitor, TNF inhibitors, IL-23 inhibitors, and IL-17 inhibitors. Monoclonal antibodies used in the treatment of psoriasis and psoriatic arthritis that can achieve the inhibition of TNF include adalimumab (Humira) and infliximab (Remicade), and another TNF inhibitor used is etanercept (Enbrel). Ustekinumab is a drug that blocks interleukin 12 and 23 through inhibiting their shared p40

subunit, and it is also approved for treating both psoriasis and psoriatic arthritis. IL-17 inhibitors are a class of biological agents that target the IL-17 ligand or its receptor rapidly and generate powerful response and yield satisfactory sustainability in the treatment of plaque psoriasis patients. IL-23 inhibitors, including guselkumab, tildrakizumab and risankizumab (approved by the US FDA to treat adult plaque psoriasis), are a class of biological agents that precisely inhibit the p19 subunit of IL-23. Among biologic therapies, infliximab produces the fastest clinical response, with sustained response and improved quality of life in clinical trials. It seems that the biological effects of short-term treatment are more superior to these of traditional systemic medications [53], to date no previous evidence has suggested that biologics cause cumulative toxicity or drug interactions in long-term treatment.

Nanotechnology

Advantages of nanotechnology in treating psoriasis

Nanotechnology could not only simplify diagnosis, but also make treatment more precise. In general, nanotechnology offers a better controlled, nontoxic, more secure and localized delivery of drugs than traditional treatments. A variety of nanotechnology colloidal carriers are popular for treating and controlling psoriasis because of their distinctive characteristics, such as liposomes, niosomes, transmitters, microspheres, micelles, dendrimers, glycosomes, solid lipid nanoparticles, etc. (Figure 3) [68–76].

Conventional topical treatments, such as ointments, creams, and gels have poor penetration and low absorption because of the barrier effect of the skin. Local administration of drug-loaded nanocarriers showed better permeability and efficacy at lower doses with minimum systemic side effects. As the particle size becomes smaller, the interaction with skin becomes better. Particles less than 20 nm can penetrate intact skin, however, diseased imperfect skin with a weaker barrier can allow larger particles to penetrate. Particles with the size between 50 and 100 nm are still on the stratum corneum layer [77, 78].

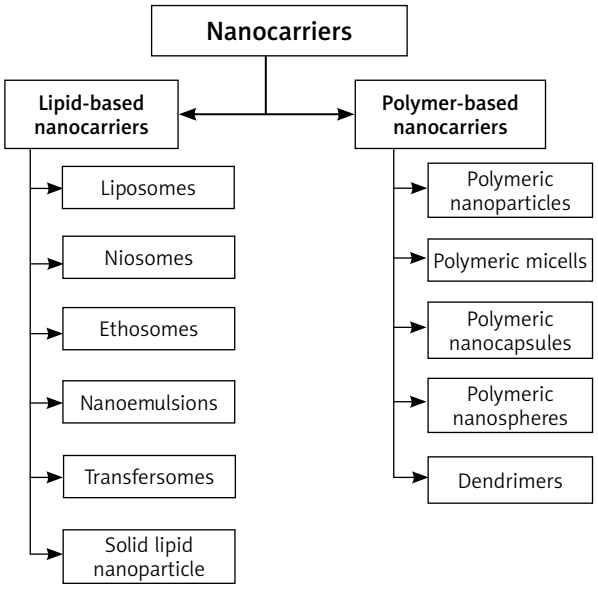

Figure 3. Nanotechnology for psoriasis treatment modalities

At present, these nanocarriers are becoming increasingly popular as delivery agents for anti-psoriasis drugs because of their non-toxicity, natural degradation, excellent biocompatibility and biodegradability; they do not cause any harmful inflammatory reaction and are easily excreted from the body. The performance of nanocarriers is stable, their porosity is adequate, their pore size distribution is ideal, and their interconnectivity, easy processability and malleability into desired shape, etc. [79–84] all contribute to their reputation.

Nanocarriers for psoriasis

Reports of nanocarrier delivery for psoriasis suggested that it improved efficacy and reduced toxicity compared to standard pharmacotherapy. To better elucidate the application of nanotechnology in the treatment of psoriasis, various nanocarrier-based formulations will be summarized [85, 86].

Lipid-based nanocarriers

Liposomes

Liposomes or lipid-based vesicles, which are produced by phospholipid, cholesterol and long chain fatty acids, are unilamellar or multilayer vesicles that can be seen microscopically [87, 88]. Drugs containing liposomes can be delivered in a variety of ways to treat psoriasis, such as IV injection, oral inhalation, topical application, and ocular delivery. The main advantages of the system include nontoxicity, non-immunogenicity, biocompatibility and biodegradability, increased stability, and ensuring that the encapsulated drugs are shielded from the external environment [89]. Sathe *et al*. examined a liposomic gel loaded with dithranol (particle size = 203.3 ±1.20 nm, PDI = 0.29 ±0.04 and zeta = –0.97 ±0.08) on an IMQ-treated mice model, and discovered an optimal anti-psoriatic property along with significant reductions in PASI and IL-17, IL-22, and IL-23 serum levels compared with controls [90]. Walunj *et al*. used a liposome-based gel containing cyclosporine (size = 111 ±1.62 nm, PDI 0.27 ±0.08, Z 41.12 ±3.56 mV) on an IMQ-treated murine model, and found a significant reduction in the severity of skin problems, along with IL-17, IL-22, and TNF-α [91]. Through the film hydration method, Gupta *et al*. developed liposomes, niosomes, and emulsomes containing capsaicin (CAP). Nanospheres allowed the maximum skin retention, especially in emulsified-gel for-

mulations [92]. Srisuk *et al*. designed methotrexate (MTX) entrapped oleic acid-containing deformable liposomes, used for in vitro trans-epidermal delivery in psoriasis treatments, and the results suggested a promising use of liposomes to enhance the permeability of MTX in psoriasis treatment [93].

Niosomes

Niosomes (Nio) are non-ionic liposomes which constitute mainly of non-ionic surfactant, cholesterol, and other lipids [94]. They are available for parenteral, oral, and administration topically, and can also enhance the drug's oral bioavailability and its penetration into skin [95]. Nio can be prepared as unilamellar or multilamellar vesicles in a similar way to liposomes [96, 97]. Nio also contain more surfactants than liposomes and may also provide a stronger penetrability [98]. Abdelbary *et al*. studied and discovered that MTX niosomes may have profound therapeutic application in topical delivery to treat psoriasis [99]. Abu Hashim *et al*. investigated the advantages of the Act nano niosomal gel as a topical drug delivery system, which includes significantly enhanced drug penetration and deposition into deeper skin layers, and reduced systemic uptake [100]. Meng *et al*. prepared Nio hydrogels containing Cel, which was effective in the treatment of IMQ-induced psoriasis-like mouse models. Encapsulation of Cel into Nio improved the water-solubility and permeation of Cel in the skin, and the anti-psoriasis activity was significantly improved in the mice model [101].

Ethosomes

Ethosomal carriers are constituted mainly of alcohol (ethanol & isopropyl alcohol at relatively high concentrations), phospholipids (phosphatidylserine, phosphatidylcholine, phosphatidic acid), and water; these carriers are able to catch hydrophilic, lipophilic, and amphiphilic drug molecules with varying characteristics [102, 103]. Ethosomes range from 30 nanometres to a few microns long [104]. Dubey *et al*. found that the enhanced accumulation of MTX in the skin through ethosomal carriers could help to improve targeted drug delivery to sites within the epidermis and dermis, thereby producing new methods for regulated and contemporary topical use of MTX for psoriasis [105]. Compared with an equivalent ethanol solution, the ethosomes demonstrated superior biocompatibility with human embryonic skin fibroblasts, which implies that the presence of phosphatidylcholine in ethosomal vesicles can enhance biocompatibility. Based on the research, Zhang *et al*. concluded that ethosomes might improve the trans-dermal delivery of psoralen as well as other drugs that probably require deep skin delivery [106]. Moreover, the increased penetration and deposition of psoralen delivered by ethosomes are advantageous as it can reduce toxicity and enhance the efficacy of psoralen long-term treatment [107]. In addition, as skin vitality decreases, the amount of penetration of psoralen delivered by liposomes is increased, while the deposition of psoralen from liposomes and ethosomes into skin is decreased. This study also showed that there was less deposition of ethosomes- or liposomes-delivered psoralen in the skin, which could relate to decreased cellular uptake [108].

Nanoemulsions

Nanoemulsion is a transparent/translucent, isotropic, heterogeneous system consisting of two immiscible liquids in which drugs are finely dispersed as nanodroplets. An interfacial layer of emulsifier and co-emulsifier are used to stabilize it [109–111]. Somagoni *et al*. used Vitamin E TPGS through using the solvent evaporation method, and prepared nanoemulsion by the high-pressure homogenization method. They found that nanomiemgel is released in a controlled manner, and induced permeation of aceclofenac and capsaicin that were 2.02 and 1.97-fold higher than Ace-Proxyvon, respectively, via dermatomed human skin. In the rat skin microdialysis study, nanomiemgel also showed that 2.94 and 2.09-fold greater Cmax of aceclofenac and capsaicin, respectively, than Ace Proxyvon [112]. Rajitha *et al*. found an elevated anti-psoriasis efficacy in low methotrexate nanoemulsion formulations compared with the oral methotrexate formulation [113].

Transfersomes

Cevc first proposed the concept of Transfersomes in 1992. Transfersomes are an ultra-deformable carrier, facilitating the efficient distribution of a wide variety of drugs through the skin barrier [114]. There are two different interdependent mechanisms adopted by transfersomes, which are the use of electromechanics (pressing through intercellular gaps and pores) and the use of the gradient in water activity across the epidermis (dehydration and rehydration cycles) [115]. Eline *et al*. prepared transfersomes of RNA interferon by solvent evaporation method to certify its effectiveness in the treatment of psoriasis, and found that transfersomes of RNA interferon could effectively improve the pathological conditions of psoriasis [116].

Solid lipid nanoparticle

Solid lipid nanoparticles (SLNs) are an innovative generation of the nanoparticle system composed of a mix of physiological lipids and surfactants [117]. SLNs have unique characteristics including their compact size, high drug loading capacity, large surface area, and prolonged drug release profile consequent to the slow degradation of lipid matrices [118]. The small particle size of SLNs ensures the close contact between the nanocarrier and the stratum cuticle, thus promoting penetration into the skin

[119]. Treatment of various skin diseases, including psoriasis, has also utilized SLNs. Sonawane *et al*. prepared gel formulation that contained calcipotriol and betamethasone dipropionate loaded SLNs (CT-BD-SLNs) to achieve effective treatment of psoriasis [120]. Pradhan *et al*. established, improved, and tested the Fluocinolone acetonide (FA) combined with SLNs for its anti-psoriatic activity, and they suggested that FA containing SLNs might be a promising carrier for the treatment of psoriasis [121].

Polymer-based nanocarriers

Polymeric nanoparticles

Polymeric nanoparticles (NPs) have excellent biodegradability and biocompatibility that can shield drugs from being degraded and can also envelope both hydrophobic and hydrophilic drugs. Khalid *et al*. demonstrated that enhancement of bioavailability and long-term retention of the apremilast-loaded PLGA nanoparticles might contribute to once-daily regimen treatment [122]. Tomoda *et al*. prepared spherical and indomethacin-loaded PLGA nanoparticles through the use of emulsion solvent evaporation method and employed the nanoparticles to transdermal delivery [123]. Shah *et al*. prepared surface modified bilayered nanoparticles with oleic acid by PLGA and chitosan. Spantide II was added to the inner core of PLG and ketoprofen A to the outer layer of chitosan. Hydroxypropyl methylcellulose (HPMC) and Carbopol were used to produce the nano gel formulation to further boost the delivery of drugs to the deeper skin layers through increasing the contact time with skin and preventing the loss of water [124].

Polymeric micelles

Polymer micelles enhance drug solubility and enhance the distribution of water-soluble drugs and their localization in the skin layer. Polymer micelles have the specific ability to encapsulate hydrophilic drugs. In dermatological diseases such as psoriasis and acne, polymeric micelles could enhance drugs deposition in targeted sites of the skin [125]. Ehrlich *et al*. investigated the efficacy and safety of paclitaxel in the treatment of severe psoriasis, and found that micellar paclitaxel has a certain therapeutic effect on severe psoriasis [126]. Skin deposition studies showed that the formation of polymer micelle (1.50 ±0.59 μg/cm^2) had a higher retention rate than traditional tacrolimus ointment (0.47 ±0.20 μg/cm^2), and it was also found that polymeric micelles improved the topical permeability of tacrolimus in psoriasis patients [127].

Polymeric nanocapsules

Polymeric nanocapsules, as a potential drug delivery system, have been extensively studied in recent years. Much research has been carried out to investigate the therapeutic ability of nanocapsules for innocuous and useful delivery of drugs used in different diseases (including psoriasis) [128, 129]. Cationic nanocapsules containing dexamethasone were prepared by Eudragit RS 100 polymers, and the *in vitro* drug release and skin permeability were assessed. Surprisingly, as a result of their excellent ability to permeate skin to regulate drug release across skin, these nanocapsules have received much attention [130]. Studies on skin permeation using porcine skin indicated that a large number of drugs are present in the viable epidermis – the primary target site for dexamethasone to exert its action against psoriasis. This study implies that suitability of cationic nanocarriers for targeting the epidermis in psoriatic skin as the negatively charged skin surface expedites the penetration of the positively charged particles when applied topically [131]. Beber *et al*. also produced cationic polymeric nanocapsules containing dexamethasone in a hydrogel formulation. They suggested that nanocapsules are expected to become the transporter for the delivery of dexamethasone [131].

Polymeric nanospheres

Nanospheres are nanocompounds, which are biodegradable, biocompatible, and synthetic polymers-based. Nanospheres (TyroSpheres) have been successfully used to deliver drugs to the skin. Nanospheres provide better solubility with chemicophysical protection of the therapeutic moiety, enhanced absorption and drug release in a controlled manner [132]. Batheja *et al*. prepared lipophilic drugs that are loaded with tyrosine-derived nanospheres for topical application, and found that the drug permeation of TyroSphere was enhanced compared with aqueous nanosphere formulation. Therefore, TyroSphere is also a useful delivery medium for lipophilic drugs when treating skin conditions such as acne and psoriasis [133]. Another vitamin D_3 loaded polymeric nanospheres (TyroSpheres) proposed by Ramezanli *et al*. also improved drug loading [134]. Jain *et al*. discussed the antipsoriatic and anti-inflammatory properties of thymoquinone (TMQ), which is an element of the hydroalcoholic extract of Nigella sativa (N. sativa) and is conveyed via nanospheres/lipoglobules (particle size < 70 nm). They supported the potential of TMQ lipospheres for patients with psoriasis [135].

Dendrimers

Dendrimers are monodisperse, multivalent, and typically spherical macromolecules that has a hyperbranched and regular structure, including manageable internal cavities and external border with 3D multifunctional moieties that can be useful for dual drug delivery, as well as increasing the solubility and recognition of drugs [136, 137]. Compared with other polymers, dendrimers have several advantages, such as being less readily absorbed by the reticuloendothelial system, being easy to modify, aiming at specific sites in the body, protecting the repro-

ductive pharmacokinetic behaviour, and supplying different structures to minimize production costs [138]. The dendrimer solution has a unique viscosity generation property that allows a very concentrated formulation to be applied on the skin [139]; dendrimers have been used successfully to deliver anti-psoriatic drugs. Gras *et al*. investigated whether the second-generation ammonium terminated carbosilane dendrimer (2G-NN16) was a possible agent for the treatment of Th17 deregulated pathologies. They concluded that 2G-NN16-carbosilane dendrimer could be a potential system for the management of IL17-involved autoimmune diseases, such as psoriasis in which IL17 is the main cause of the disease [140].

Conclusions

Psoriasis is a skin disease that is the consequence of a variety of autoimmune cellular processes, including keratinocytes, dendritic cells, T cells, etc. There are various treatments for psoriasis, none of which is completely safe and effective with great patient compliance. So far, existing drugs suppress the condition and ease symptoms but do not completely cure psoriasis, such as methotrexate and cyclosporine. Therefore, a newer drug delivery method has been widely used for antipsoriatic drug delivery, especially nanocarriers. Nanotechnology therapies have improved efficacy and patient compliance without producing adverse events. These methods can enhance the penetration of drug molecules to target sites hence can treat psoriasis of different types. In addition, several nanocarrier-based antipsoriatic agents have been patented, demonstrating the potential functions of such nanocarriers in the treatment of psoriasis. Therefore, nanocarriers is a promising agent to transform the field of clinical dermatology and will eventually become an important treatment for patients with psoriasis.

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Baohua Zhu, Mingyi Jing, Qianying Yu, Xiaopei Ge contributed equally to this work and are co-first authors.

Conflict of interest

The authors declare no conflict of interest.

References

1. Louis D, Mrowietz U, Ranki A, et al. European patient perspectives on the impact of psoriasis: the EUROPSO patient membership survey. Br J Dermatol 2006; 155: 729-36.
2. Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. Ann Rheum Dis 2005; 64: 18-23.
3. Mahapatra AK, Murthy PN, Samoju S, Mohapatra AK. Tiny technology proves big: a challenge at engineering, medicine and pharmaceutical sciences interface. Crit Rev Ther Drug Carrier Systems 2014; 31: 1-47.
4. Nestle FO, Kaplan DH, Barker J. Mechanisms of disease: psoriasis. N Engl J Med 2009; 361: 496-509.
5. Cesare AD, Meglio PP, Nestle FO. The IL-23/Th17 axis in the immunopathogenesis of psoriasis. J Investig Dermatol 2009; 129: 1339-50.
6. Saubermann LJ, Beck P, De Jong YP, et al. Activation of natural killer T cellsby alpha-glactosylceramide in the presence of CD1d provides protection against colitis in mice. Gastroenterology 2000; 119: 119-28.
7. Singh AK, Wilson MT, Hong S, et al. Natural killer T cell activation protects mice against experimental autoimmune encephalomyelitis. J Exp Med 2001; 194: 1801-11.
8. Campos RA, Szczepanik M, Itakura A, et al. Cutaneous immunization rapidly activates liver invariant Valpha 14 NKT cells stimulating B-1 B cells to initiate T cell recruitment for elicitation of contact sensitivity. J Exp Med 2003; 198: 1785-96.
9. Bos JD, Rie MAD, Teunissen MBM, Piskin G. Psoriasis: dysregulation of innate immunity. Br J Dermatol 2005; 152: 1098-107.
10. Deguchi M, Aiba S, Ohtani H, et al. Comparison of the distribution and numbers of antigen-presenting cells among T-lymphocyte-mediated dermatoses: CD1a+, factor XIIIa+, and CD68+ cells in eczematous dermatitis, psoriasis, lichen planus and graft-versus-host disease. Arch Dermatol Res 2002; 294: 297-302.
11. Nickoloff BJ. The cytokine network in psoriasis. Arch Dermatol 1991; 127: 871-84.
12. Trefzer U, Hofmann M, Sterry W, Asadullah K. Cytokine and anticytokine therapy in dermatology. Exp Opin Biol Ther 2003; 3: 733-43.
13. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet 2007; 370: 263-71.
14. Gordon-Elliott JS, Muskin PR. Managing the patient with psychiatric issues in dermatologic practice. Clin Dermatol 2013; 31: 3-10.
15. De Azevedo Fraga NA, De Oliveira MDFP, Ivonise F, et al. Psoriasis and uveitis: a literature review. An Brasil Dermatol 2012; 87: 877-83.
16. Parisi R, Symmons DPM, Griffiths CEM, Ashcroft DM. Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Investig Dermatol 2013; 133: 377-85.
17. World Health Organization. Global Report on Psoriasis: World Health Organization (https://apps.who.int/iris/handle/10665/204417).
18. Tsai TF, Wang TS, Hung ST, et al. Epidemiology and comorbidities of psoriasis patients in a national database in Taiwan. J Dermatol Sci 2011; 63: 40-6.
19. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol 2017; 31: 205-12.
20. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol 2014; 70: 512-6.
21. Paller AS, Singh R, Cloutier M, et al. Prevalence of psoriasis in children and adolescents in the United States: a claims-based analysis. J Drugs Dermatol 2018; 17: 187-94.
22. Gudjonsson JE, Elder JT. Psoriasis: epidemiology. Clin Dermatol 2007; 25: 535-46.
23. Nair RP, Stuart PE, Nistor I, et al. Sequence and haplotype analysis supports HLA-C as the psoriasis susceptibility 1 gene. Am J Human Genet 2006; 78: 827-51.

24. Jacobson CC, Kumar S, Kimball AB. Latitude and psoriasis prevalence. Dermatology 2011; 65: 870-3.
25. Schmitt J, Wozel G. The psoriasis area and severity index is the adequate criterion to defifi ne severity in chronic plaque-type psoriasis. Dermatology 2005; 210: 194-9.
26. Langley RG, Ellis CN. Evaluating psoriasis with psoriasis area and severity index, psoriasis global assessment, and lattice system physician's global assessment. J Am Acad Dermatol 2004; 51: 563-9.
27. van de Kerkhof PC, Barker J, Griffiths CE, et al. Psoriasis: consensus on topical therapies. J Eur Acad Dermatol Venereol 2008; 22: 859-70.
28. Ito K, Koga M, Shibayama Y, et al. Proactive treatment with calcipotriol reduces recurrence of plaque psoriasis. J Dermatol 2016; 43: 402-5.
29. Mason AR, Mason JM, Cork MJ, et al. Topical treatments for chronic plaque psoriasis of the scalp: a systematic review. Br J Dermatol 2013; 169: 519-27.
30. Leonardi C, Bagel J, Yamauchi P, et al. Efficacy and safety of calcipotriene plus betamethasone dipropionate aerosol foam in patients with psoriasis vulgaris – a randomized phase III study (PSO-FAST). J Drugs Dermatol 2015; 14: 1468-77.
31. Gold LS, Lebwohl MG, Sugarman JL, et al. Safety and efficacy of a fixed combination of halobetasol and tazarotene in the treatment of moderate-to-severe plaque psoriasis: results of 2 phase 3 randomized controlled trials. J Am Acad Dermatol 2018; 79: 287-93.
32. Canadian Psoriasis Guidelines Committee. 2009. Canadian Guidelines for the Management of Plaque Psoriasis. Ottawa, ON, Canadian Dermatology Association.
33. Van De Kerkhof PC, Berth-Jones J, Griffiths CE, et al. Long-term efficacy and safety of tacalcitol ointment in patients with chronic plaque psoriasis. Br J Dermatol 2002; 146: 414-22.
34. Lebwohl M, Menter A, Weiss J, et al. Calcitriol 3 microg/g ointment in the management of mild to moderate plaque type psoriasis: results from 2 placebo-controlled, multicenter, randomized double-blind, clinical studies. J Drugs Dermatol 2007; 6: 428-35.
35. Oranjea AP, Marcouxb D, Svenssonc Å, et al. Topical calcipotriol in childhood psoriasis. J Am Acad Dermatol 1997; 36: 203-8.
36. Marsland AM, Griffiths CE. The macrolide immunosuppressants in dermatology: mechanisms of action. Eur J Dermatol 2002; 12: 618-22.
37. Wang C, Lin A. Efficacy of topical calcineurin inhibitors in psoriasis. J Cutan Med Surg 2014; 18: 8-14.
38. Gupta AK, Chow M. Pimecrolimus: a review. J Eur Acad Dermatol Venereol 2003; 17: 493-503.
39. Carroll CL, Clarke J, Camacho F, et al. Topical tacrolimus ointment combined with 6% salicylic acid gel for plaque psoriasis treatment. Arch Dermatol 2005; 141: 43-6.
40. Tauscher AE, Fleischer AB, Jr Phelps KC, Feldman SR. Psoriasis and pregnancy. J Cutan Med Surg Incorporating Med Surg Dermatol 2002; 6: 561-70.
41. Menter A, Korman NJ, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriaticarthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol 2009; 60: 643-59.
42. Fluhr JW, Cavallotti C, Berardesca E. Emollients, moisturizers, and keratolytic agents in psoriasis. Clin Dermatol 2008; 26: 380-6.
43. Gelmetti C. Therapeutic moisturizers as adjuvant therapy for psoriasis patients. Am J Clin Dermatol 2009; 10: 7-12.
44. Lebwohl M. The role of salicylic acid in the treatment of psoriasis. Int J Dermatol 1999; 38: 16-24.
45. Torsekar R, Gautam MM. Topical therapies in psoriasis. Indian Dermatol Online J 2017; 8: 235-45.
46. Zesch A. Short and long-term risks of topical drugs. Br J Dermatol 1986; 115: 63-70.
47. Chapman BJ, Proudfoot AT. Adult salicylate poisoning: deaths and outcome in patients with high plasma salicylate concentrations. Quarterly J Med 1989; 72: 699-707.
48. Arbiser JL, Govindarajan B, Battle TE, et al. Carbazole is a naturally occurring inhibitor of angiogenesis and inflammation isolated from antipsoriatic coal tar. J Investig Dermatol 2006; 126: 1396-402.
49. Lin AN, Moses K. Tar revisited. Int J Dermatol 1985; 24: 216-8.
50. Stern RS, Zierler S, Parrish JA. Skin carcinoma in patients with psoriasis treated with topical tar and artificial ultraviolet radiation. Lancet 1980; 315: 732-5.
51. McGill A, Frank A, Emmett N, et al. The anti-psoriatic drug anthralin accumulates in keratinocyte mitochondria, dissipates mitochondrial membrane potential, and induces apoptosis through a pathway dependent on respiratory competent mitochondria. FASEB J 2005; 19: 1012-4.
52. Saurat JH, Stingl G, Dubertret L, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol 2008; 158: 558-66.
53. Saurat JH, Stingl G, Dubertret L, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol 2008; 158: 558-66.
54. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol 2009; 61: 451-85.
55. Malatjalian DA, Ross JB, Williams CN, et al. Methotrexate hepatotoxicity in psoriatics: report of 104 patients from Nova Scotia, with analysis of risks from obesity, diabetes and alcohol consumption during long term follow-up. Canad J Gastroenterol 1996; 10: 369-75.
56. Canadian Psoriasis Guidelines Committee. 2009. Canadian Guidelines for the Management of Plaque Psoriasis. Ottawa, ON, Canadian Dermatology Association.
57. Mahrle G, Schulze HJ, Brautigam M, et al. Anti-inflammatory efficacy of low-dose cyclosporin A in psoriatic arthritis: a prospective multicenter study. Br J Dermatol 1996; 135: 752-7.
58. Salvarani C, Macchioni P, Olivieri I, et al. A comparison of cyclosporine, sulfasalazine, and symptomatic therapy in the treatment of psoriatic arthritis. J Rheumatol 2001; 28: 2274-82.
59. Ho VC, Griffiths CE, Albrecht G, et al. Intermittent short courses of cyclosporin (Neoral(R)) for psoriasis unresponsive to topical therapy: a 1-year multicentre, randomized study. The PISCES Study Group. Br J Dermatol 1999; 141: 283-91.
60. Lebwohl M, Drake L, Menter A, et al. Consensus conference: Acitretin in combination with UVB or PUVA in the treatment of psoriasis. J Am Acad Dermatol 2001; 45: 544-53.
61. Roenigk HHJ. Acitretin combination therapy. J Am Acad Dermatol 1999; 41: S18-21.
62. Koo J. Systemic sequential therapy of psoriasis: a new paradigm for improved therapeutic results. J Am Acad Dermatol 1999; 41: S25-8.

63. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol 2009; 61: 451-85.
64. Canadian Psoriasis Guidelines Committee. 2009. Canadian Guidelines for the Management of Plaque Psoriasis. Ottawa, ON, Canadian Dermatology Association.
65. Calzavara-Pinton PG, Sala R, Arisi M, et al. Synergism between narrowband ultraviolet B phototherapy and etanercept for the treatment of plaque-type psoriasis. Br J Dermatol 2013; 169: 130-6.
66. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. J Am Acad Dermatol 2010; 62: 114-35.
67. Weischer M, Blum A, Eberhard F, et al. No evidence for increased skin cancer risk in psoriasis patients treated with broadband or narrowband UVB phototherapy: a first retrospective study. Acta Dermatol Venereol 2004; 84: 370-4.
68. Garg T, Goyal AK. Liposomes: Targeted and controlled delivery system. Curr Drug Deliv 2014; 4: 62-71.
69. Garg T, Goyal AK. Iontophoresis: drug delivery system by applying an electrical potential across the skin. Curr Drug Deliv 2012; 2: 270-80.
70. Garg T, Goyal AK. Biomaterial-based scaffolds–current status and future directions. Exp Opin Drug Deliv 2014; 11: 767-89.
71. Garg T, Goyal AK, Arora S, et al. Development, optimization & evaluation of porous chitosan scaffold formulation of gliclazide for the treatment of type-2 diabetes mellitus. Drug Deliv Lett 2012; 2: 251-61.
72. Garg T, Kumar A, Rath G, Goyal AK. Gastroretentive drug delivery systems for therapeutic management of peptic ulcer. Crit Rev Ther Drug Carrier Systems 2014; 31: 531-57.
73. Kaur R, Garg T, Goyal AK, Rath G. Development, optimization and evaluation ofelectrospun nanofibers: tool fortargeted vaginal delivery of antimicrobials against urinary tract infections. Curr Drug Deliv 2015; 13: 754-63.
74. Garg T, Rath G, Goyal AK. Comprehensive review on additives of topical dosage forms for drug delivery. Curr Drug Deliv 2014; 13: 754-63.
75. Garg T, Rath G, Goyal AK. Biomaterials-based nanofiber scaffold: targeted and controlled carrier for cell and drug delivery. J Drug Targeting 2014; 23: 202-21.
76. Chaudhary S, Garg T, Murthy RS, et al. Recent approaches of lipid-based delivery system for lymphatic targeting via oral route. J Drug Targeting 2014; 22: 871-2.
77. Rapalli VK, Waghule T, Hans N, et al. Insights of lyotropic liquid crystals in topical drug delivery for targeting various skin disorders. J Mol Liquids 2020; 315: 113771.
78. Rapalli VK, Kaul V, Waghule T, et al. Curcumin loaded nanostructured lipid carriers for enhanced skin retained topical delivery: optimization, scale-up, in-vitro characterization and assessment of ex-vivo skin deposition. Eur J Pharm Sci 2020; 152: 105438.
79. DNA and RNA Nanobiotechnologies in Medicine: Diagnosis and Treatment of Diseases. Erdmann VA, Barciszewski J (eds.). Springer, Berlin Heidelberg 2013; 67-120.
80. Goyal G, Garg T, Malik B, et al. Development and characterization of niosomal gel for topical delivery of benzoyl peroxide. Drug Deliv 2013; 22: 1027-42.
81. Goyal G, Garg T, Rath G, Goyal AK. Current nanotechnological strategies for an effective delivery of drugs in treatment of periodontal disease. Crit Rev Ther Drug Carrier Systems 2014; 31: 89-119.
82. Kaur G, Garg T, Rath G, Goyal AK. Archaeosomes: an excellent carrier for drug and cell delivery. Drug Deliv 2015; 23: 2497-512.
83. Goyal G, Garg T, Rath G, Goyal AK. Current nanotechnological strategies for treating glaucoma. Crit Rev Ther Drug Carrier Systems 2014; 31: 365-405.
84. Johal HS, Garg T, Rath G, Goyal AK. Advanced topical drug delivery system for the management of vaginal candidiasis. Drug Delivery 2016; 23: 550-63.
85. Pradhan M, Alexander A, Singh MR, et al. Understanding the prospective of nano-formulations towards the treatment of psoriasis. Biomed Pharmacother 2018; 107: 447-63.
86. Martins AM, Ascenso A, Ribeiro HM, Marto J. Current and future therapies for psoriasis with a focus on serotonergic drugs. Mol Neurobiol 2020; 57: 2391-419.
87. Kataria K, Sharma A, Garg T, et al. Novel technology to improve drug loading in polymeric nanofibers. Drug Deliv Letters 2014; 4: 79-86.
88. Kaur M, Garg T, Narang RK. A review of emerging trends in the treatment of tuberculosis. Artif Cells Nanomed Biotechnol 2014; 44: 478-84.
89. Wilczewska AZ, Niemirowicz K, Markiewicz KH, Car H. Nanoparticles as drug delivery systems. Pharmacol Rep 2012; 64: 1020-37.
90. Sathe P, Saka R, Kommineni N, et al. Dithranolloaded nanostructured lipid carrier-based gel ameliorate psoriasis in imiquimod-induced mice psoriatic plaque model. Drug Develop Industrial Pharm 2019; 45: 826-38.
91. Walunj M, Doppalapudi S, Bulbake U, Khan W. Preparation, characterization, and in vivo evaluation of cyclosporine cationic liposomes for the treatment of psoriasis. J Liposome Res 2020; 30: 68-79.
92. Gupta R, Gupta M, Mangal S, et al. Capsaicin-loaded vesicular systems designed for enhancing localized delivery for psoriasis therapy. Artif Cells Nanomed Biotechnol 2016; 44: 825-34.
93. Srisuk P, Thongnopnua P, Raktanonchai U, Kanokpanont S. Physico-chemical characteristics of methotrexate-entrapped oleic acid-containing deformable liposomes for in vitro transepidermal delivery targeting psoriasis treatment. Int J Pharm 2012; 427: 426-34.
94. Kaur M, Garg T, Rath G, Goyal AK. Current nanotechnological strategies for effective delivery of bioactive drug molecules in the treatment of tuberculosis. Crit Rev Ther Drug Carrier Systems 2014; 31: 49-88.
95. Azeem A, Anwer MK, Talegaonkar S. Niosomes in sustained and targeted drug delivery: some recent advances. J Drug Targeting 2009; 17: 671-89.
96. Pando D, Gutiérrez G, Coca J, Pazos C. Preparation and characterization of niosomes containing resveratrol. J Food Engineering 2013; 117: 227-34.
97. Waddad AY, Abbad S, Yu F, et al. Formulation, characterization and pharmacokinetics of Morin hydrate niosomes prepared from various non-ionic surfactants. Int J Pharm 2013; 456: 446-58.
98. Sharma R, Mahatma R, Bharkatiya M, Goyal A. Niosomes – as potential drugdelivery system. Int J Drug Res Technol 2017; 2: 8.
99. Abdelbary AA, AbouGhaly MH. Design and optimization of topical methotrexate loaded niosomes for enhanced management of psoriasis: application of box-Behnken design,

in-vitro evaluation and in-vivo skin deposition study. Int J Pharm 2015; 485: 235-43.
100. Abu Hashim II, Abo El-Magd NF, El-Sheakh AR, et al. Pivotal role of Acitretin nanovesicular gel for effective treatment of psoriasis: ex vivo-in vivo evaluation study. Int J Nanomed 2018; 13: 1059-79.
101. Meng SK, Sun L, Wang L, et al. Loading of water-insoluble celastrol into niosome hydrogels for improved topical permeation and anti-psoriasis activity. Colloids Surf B Biointerfaces 2019; 182: 110352.
102. Morie A, Garg T, Goyal AK, Rath G. Nanofibers as novel drug carrier – an overview. Artif Cells Nanomed Biotechnol 2014; 44: 135-43.
103. Rohilla R, Garg T, Bariwal J, et al. Development, optimization and characterization of glycyrrhetinic acid-chitosan nanoparticles of atorvastatin for liver targeting. Drug Deliv 2016; 23: 2290-7.
104. Pabreja S, Garg T, Rath G, Goyal AK. Mucosal vaccination against tuberculosis using Ag85A-loaded immunostimulating complexes. Artif Cells Nanomed Biotechnol 2014; 44: 532-9.
105. Dubey V, Mishra D, Dutta T, et al. Dermal and transdermal delivery of an anti-psoriatic agent via ethanolic liposomes. J Control Release 2007; 123: 148-54.
106. Zhang YT, Shen LN, Wu ZH, et al. Comparison of ethosomes and liposomes for skin delivery of psoralen for psoriasis therapy. Int J Pharm 2014; 471: 449-52.
107. Zhang YT, Shen LN, Zhao JH, Feng NP. Evaluation of psoralen ethosomes for topical delivery in rats by using in vivo microdialysis. Int J Nanomed 2014; 9: 669-78.
108. Zhang YT, Shen LN, Wu ZH, et al. Evaluation of skin viability effect on ethosome and liposome-mediated psoralen delivery via cell uptake. J Pharm Sci 2014; 103: 3120-6.
109. Sood S, Jain K, Gowthamarajan K. Optimization of curcumin nanoemulsion for intranasal delivery using design of experiment and its toxicity assessment. Colloids Surf B Biointerfaces 2014; 113: 330-7.
110. Gorain B, Choudhury H, Kundu A, et al. Nanoemulsion strategy for olmesartan medoxomil improves oral absorption and extended antihypertensive activity in hypertensive rats. Colloids Surf B Biointerfaces 2013; 115: 286-94.
111. Zhao L, Wei YM, Huang Y, et al. Nanoemulsion improves the oral bioavailability of baicalin in rats: in vitro and in vivo evaluation. Int J Nanomed 2013; 8: 3769-79.
112. Somagoni J, Boakye CH, Godugu C, et al. Nanomiemgel – a novel drug delivery system for topical application-in vitro and in vivo evaluation. PLoS One 2014; 9: e115952.
113. Rajitha P, Shammika P, Aiswarya S, et al. Chaulmoogra oil based methotrexate loaded topical nanoemulsion for the treatment of psoriasis. J Drug Deliv Sci Technol 2019; 49: 463-76.
114. Opatha SAT, Titapiwatanakun V, Chutoprapat R. Transfersomes: a promising nanoencapsulation technique for transdermal drug delivery. Pharmaceutics 2020; 12: 855.
115. Rajan R, Jose S, Mukund VP, Vasudevan DT. Transferosomes – a vesicular transdermal delivery system for enhanced drug permeation. J Adv Pharm Technol Res 2011; 2: 138-43.
116. Desmet E, Bracke S, Forier K, et al. An elastic liposomal formulation for RNAi-based topical treatment of skin disorders: proof-of-concept in the treatment of psoriasis. Int J Pharm 2016; 500: 268-74.
117. Muller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. Adv Drug Deliv Rev 2002; 54: 131-55.
118. Hanumanaik M, Kumar S, Sree K. Solid lipid nanoparticles: a review. Int J Pharm Sci Res 2013; 6: 928-40.
119. Pardeike J, Hommoss A, Muller RH. Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. Int J Pharm 2009; 366: 170-84.
120. Sonawane R, Harde H, Katariya M, et al. Solid lipid nanoparticlesloaded topical gel containing combination drugs: an approach to offffset psoriasis. Exp Opin Drug Deliv 2014; 11: 1833-47.
121. Pradhan M, Singh D, Singh MR. Development characterization and skin permeating potential of lipid based novel delivery system for topical treatment of psoriasis. Chem Phys Lipids 2015; 186: 9-16.
122. Khalid MA, Mohammad M, Ezzeldin E, et al. Preparation of sustained release apremilast-loaded PLGAlga nanoparticles: in vitro characterization and in vivo pharmacokinetic study in rats. Int J Nanomed 2019; 14: 1587-95.
123. Tomoda K, Terashima H, Suzuki K, et al. Enhanced transdermal delivery of indomethacin-loaded PLGA nanoparticles by iontophoresis. Colloids Surf B Biointerfaces 2011; 88: 706-10.
124. Shah PP, Desai PR, Patel AR, Singh MS. Skin permeating nanogel for the cutaneous co-delivery of two anti-inflammatory drugs. Biomaterials 2012; 33: 1607-17.
125. Makhmalzade BS, Chavoshy F. Polymeric micelles as cutaneous drug delivery system in normal skin and dermatological disorders. J Adv Pharm Technol Res 2018; 9: 2-8.
126. Ehrlich A, Booher S, Becerra Y, et al. Micellar paclitaxel improves severe psoriasis in a prospective phase II pilot study. J Investig Dermatol 2004; 50: 533-40.
127. Lapteva M, Mondon K, Möller M, et al. Polymeric micelle nanocarriers for the cutaneous delivery of tacrolimus: a targeted approach for the treatment of psoriasis. Mol Pharm 2014; 11: 2989-3001.
128. Pegoraro NS, Mattiazzi J, da Silveira EF, et al. Improved photostability and cytotoxic effffect of coenzyme Q10 by its association with vitamin E acetate in polymeric nanocapsules. Pharm Dev Technol 2018; 23: 400-6.
129. Liakos IL, Grumezescu AM, Holban AM, et al. Polylactic acid-lemongrass essential oil nanocapsules with antimicrobial properties. Pharmaceuticals 2016; 9: 42.
130. Teixeira Z, Zanchetta B, Melo BA, et al. Retinyl palmitate flflexible polymeric nanocapsules: characterization and permeation studies. Colloids Surf B Biointerfaces 2010; 81: 374-80.
131. Beber TC, De Andrade DF, Chaves PDS, et al. Cationic polymeric nanocapsules as a strategy to target dexamethasone to viable epidermis: Skin penetration and permeation studies. J Nanosci Nanotechnol 2016; 16: 1331-8.
132. Sheihet L, Chandra P, Batheja P, et al. Tyrosinederived nanospheres for enhanced topical skin penetration. Int J Pharm 2008; 350: 312-9.
133. Batheja P, Sheihet L, Kohn J, et al. Topical drug delivery by a polymeric nanosphere gel: formulation optimization and in vitro and in vivo skin distribution studies. J Control Release 2011; 149: 159-67.
134. Ramezanli T, Kilfoyle BE, Zhang Z, Michniak-Kohn BB. Polymeric nanospheresfor topical delivery of vitamin D3. Int J Pharm 2017; 516: 196-203.
135. Jain S, Addan R, Kushwah V, et al. Liposphere mediated topical delivery of thymoquinone in the treatment of psoriasis. Nanomedicine 2017; 13: 2251-62.

136. Gajbhiye V, Palanirajan VK, Tekade R, Jain NK. Dendrimers as therapeutic agents: a systematic review. J Pharm Pharmacol 2009; 61: 989-1003.
137. Gupta S, Tyagi R, Parmar VS, et al. Polyether based amphiphiles for delivery of active compounds. Polymer 2012; 53: 3053-78.
138. Singh B, Garg T, Goyal AK, Rath G. Recent advancements in the cardiovascular drug carriers. Artif Cells Nanomed Biotechnol 2014; 44: 216-25.
139. Cheng YY, Man N, Xu TW, et al. Transdermal delivery ofnonsteroidal anti-inflflammatory drugs mediated by polyamidoamine (PAMAM) dendrimers. J Pharm Sci 2007; 96: 595-602.
140. Gras R, Relloso M, García MI, et al. The inhibition of Th17 immune response in vitro and in vivo by the carbosilane dendrimer 2G-NN16. Biomaterials 2012; 33: 4002-9.