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A REVIEW OF LIPID-BASED NANOCARRIERS FOR TARGETED DERMAL DELIVERY AND ENHANCED SKIN RETENTION IN PSORIASIS

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ABSTRACT

Psoriasis is a chronic, immune-mediated inflammatory dermatosis that causes keratinocyte hyperproliferation and a weakened epidermal barrier. It affects about 2-3% of the world's population. While topical corticosteroids such as Clobetasol Propionate (CP) are still considered the "gold standard" for localized treatment, their clinical utility is frequently hampered by poor aqueous solubility, limited skin penetration through hyperkeratotic plaques, and significant side effects such as skin atrophy and systemic HPA-axis suppression.

This review investigates the emergence of lipid-based particulate systems, notably Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), and vesicular systems (ethosomes/transfersomes), as transformational vehicles for anti-psoriasis medication delivery. These carriers mirror endogenous skin lipids, allowing for a dual-action therapeutic approach: repairing the damaged lipid barrier while also delivering targeted, sustained drug release into the viable epidermis and dermis.

Key findings from the existing literature show that lipid nanoparticles (usually 100-300 nm) use an occlusive effect to prevent transepidermal water loss (TEWL), improving skin hydration and medication distribution. Advanced formulations of CP and methotrexate have showed entrapment efficiencies surpassing 85-94%, significant decreases in pro-inflammatory cytokines (TNF-α, IL-17A), and reduced systemic toxicity compared to standard creams. Despite strong preclinical evidence of enhanced dermatokinetic profiles and patient compliance, issues in large-scale production and long-term regulatory stability persist. This analysis finds that lipid-based nanocarriers provide a superior, safer alternative for long-term psoriasis therapy by concentrating powerful medicines within inflammatory reservoirs while maintaining skin integrity.

Keywords: Psoriasis, Clobetasol Propionate, Solid Lipid Nanoparticles, Curcumin.

1. INTRODUCTION

1.1 Overview of Psoriasis

Psoriasis is a chronic, immune-complexed, inflammatory dermatosis, which is involved in the excessive proliferation of keratinocytes, abverted differentiation, inflammatory cell invasion of the epidermis and dermis. Approximately 2-3 percent of the world population is impacted by the disease although this is relative, with an ethnicity related to an area and environmental exposure (Parisi et al., 2013). Psoriasis is clinically changeable. The percentage of plaque psoriasis (psoriasis vulgaris) cases amounts to approximately 80-90%, then there are guttate, inverted, erythrodermic and pustular forms. (Griffiths and Barker, 2007).

1. Psoriasis is a remitting and persistent inflammatory dermatosis. Clinically, which is macroscopically characterized by distinctly defined erythematous plaques, there is a molecular reality of a vicious cycle of inflammation.
2. The disorder is not contagious and lifetime course, alternating and remitting. Notably, psoriasis is currently classified as a systemic inflammatory disease associated with psoriatic arthritis, cardiovascular disease, Metabolic syndrome, metabolic bowel disease and psychological comorbidities, such as depression and anxiety (Boehncke and Schon, 2015). The apparent appearance of lesions in psoriatic patients adds substantially to a social stigma, as well as reduced life quality, which is usually on par with chronic illnesses like diabetes or cancer. (Rapp et al., 1999).
3. The IL-23/ Type 17 T-cell axis causes the disease. Unless stress-induced, the antimicrobial peptides secreted by the keratinocytes like LL-37 bind to the DNA/RNA and activate the plasmacytoid dendritic cells. Such cells travel to lymph nodes where they synthesize IL-23 that promotes the generation of Th17 cells.

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4. The resulting effect of the production of IL-17A and IL-22 acts directly on keratinocytes where they directly cause:
5. Acanthosis: It is epidermal thickening of the viable epidermis.
6. The stratum corneum thickening is referred to as hyperkeratosis.
7. The retention of nuclei in the stratum corneum is known as parakeratosis and it signifies poor maturation.
8. Drug delivery perspective As an aspect of drug delivery, this implies that the target site (viable epidermis and dermis) is concealed behind a far more hostile and disorganized barrier than that of normal skin.
9. Although there has been intensive research, psoriasis is an incurable disease with its therapies primarily aimed at the reduction of symptoms and inflammation in addition to remission of the disease. This points to the significance of optimized, long-term, safe as well as patient-friendly therapies methods.

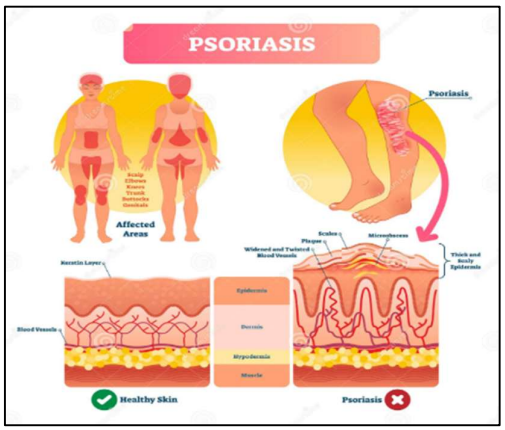
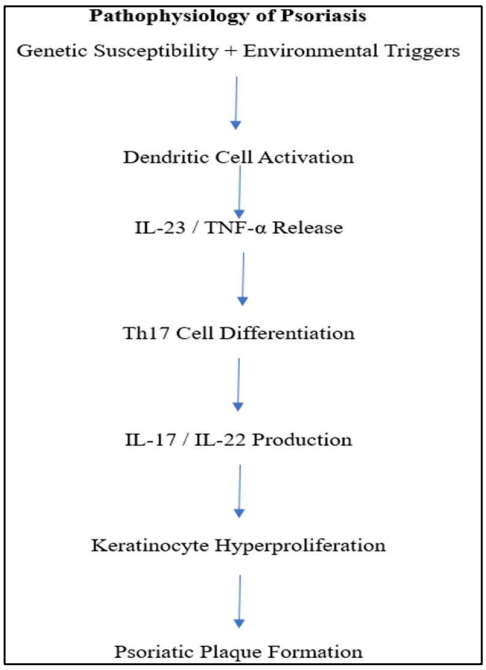


Fig 1. Effects of the Psoriasis on skin

1.2 Pathophysiology of Psoriasis

Etiology of psoriasis is multifactorial and intricate and involves both the genetic predisposition, the dysregulation in immunology and environments. Genome-wide association studies have also revealed several susceptibility loci, the most significant of which is PSORS1 locus within the major histocompatibility complex, which means that immunological systems are important (Nestle et al., 2009).

Abnormal activation of dendritic cells and T lymphocytes (Th1 and Th17 cells, in particular) among the cases leads to psoriasis. The activated dendritic cells release IL-23 that stimulates development and survival of Th17 cells leading to the release of pro-inflammatory cytokines, including IL-17A, IL-17F, IL-22 and TNF-α (Lowes et al., 2014). These cytokines cause hyper-proliferation, angiogenesis and



sustained inflammation in the keratinocytes leading to a vicious inflammatory circle.

Histopathological, the psoriatic skin is acanthotic, parakeratotic, telentosome of rete ridge, thinning of suprapapillary plates, neutrophil invasion leading to the Munro micro abscesses. Psoriasis has a much shorter epidermal turnover time, compared to the

Table 1. Pathophysiological Targets in Psoriasis and Delivery Requirements

Pathological Feature	Therapeutic Target	Delivery Requirement	Role of Lipid Particles
Keratinocyte hyperproliferation	Epidermal layers	Sustained local drug levels	Controlled release from lipid matrix
Immune cell infiltration	Dermis/follicles	Deep dermal penetration	Follicular targeting
Barrier dysfunction	Stratum corneum	Non-irritant modulation	Lipid exchange without damage
Chronic inflammation	Cytokine-rich microenvironment	Prolonged residence time	Occlusive film formation

normal skin (28 days), saying 3-5 days, which leads to immature keratinocytes and a lack of a protective barrier (Elias et al., 2014). Disrupted barrier integrity in psoriasis has imperative consequences in topical drug delivery since changing lipid content and augmentation of trans epidermal water loss (TEWL) could have implications in drug permeation and retention of the skin layers.

1.3 Current Therapeutic Approaches and Limitations

Treatment plans involving psoriasis hinge on the severity of the disease, skin affected and comorbidities as well as patient preferences. Topical therapy is generally the initial mode of treatment of mild to moderate psoriasis and biologics and systemic therapies are only used when the disease is more severe or is unresponsive (Menter et al., 2019).

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2. TOPICAL THERAPIES

Topical agents include corticosteroids, vitamin D analogues (calcipotriol), retinoids (tazarotene), calcineurin inhibitors, coal tar, salicylic acid and dithranol. Corticosteroids have anti-inflammatory and immunosuppressive properties, but extended use is associated with side effects such as skin shrinkage, telangiectasia, tachyphylaxis and hypothalamic-pituitary-adrenal axis suppression (Ference and Last, 2009).

Vitamin D analogues influence keratinocyte proliferation and differentiation but may produce discomfort and limited efficacy when administered alone (Menter et al., 2019). Moreover, typical topical formulations often fail to deliver sufficient medication concentrations to the deeper epidermal and dermal layers where immune activation continues.

Table 2. Classification of Topical Lipid Particulate Systems Used in Psoriasis

System	Typical Size Range	Key Lipids	Mechanism of Skin Interaction	Key Advantages	Limitations
Solid Lipid Nanoparticles (SLNs)	50–1000 nm	Glyceryl behenate, stearic acid, cetyl palmitate	Occlusion, lipid exchange with SC	Controlled release, high stability, reduced irritation	Limited drug loading, risk of drug expulsion
Nanostructured Lipid Carriers (NLCs)	80–500 nm	Solid + liquid lipids (e.g., glyceryl behenate + oleic acid)	Occlusion, enhanced partitioning	Higher drug loading, better stability	Formulation complexity
Liposomes	100–1000 nm	Phosphatidylcholine, cholesterol	Fusion with SC lipids	Biocompatible, versatile	Limited penetration depth
Ethosomes	70–400 nm	Phospholipids + ethanol	SC lipid fluidization	Deep penetration	Ethanol-induced irritation
Nanoemulsions	20–200 nm	Oils, surfactants	Enhanced wetting and diffusion	High surface area	Surfactant sensitivity

3. SYSTEMIC AND BIOLOGIC THERAPIES

Systemic treatments such methotrexate, cyclosporine and acitretin are beneficial, but they have limitations such as organ toxicity, teratogenicity and the requirement for close monitoring (Boehncke and Schön, 2015). Biologic treatments targeting TNF-α, IL-17, or IL-23 pathways have changed psoriasis treatment; nevertheless, their high cost, parenteral administration, immunosuppressive hazards and restricted accessibility limit widespread usage, particularly in impoverished countries (Lebwohl et al., 2018).

Such limitations have necessitated the development of innovative topical systems that have the potential to enhance therapeutic efficacy and minimize the exposure of systems to the body as well as reducing side effects.

4. CHALLENGES IN TOPICAL DRUG DELIVERY FOR PSORIASIS

The main barrier of the absorption of medication through the skin is the stratum corneum. The barrier of accessing hydrophilic molecules and lipophilic molecules lies in corneocytes organized in a lipid framework consisting of ceramides, cholesterol as well as free fatty acids (Barry, 2001).

Even though the skin of psoriasis has reduced barrier function, homogeneous drug entry may be inhibited by hyperkeratosis and thicker plaques. The traditional topical preparations are characterized by short residence time, rapid degradation of drugs, uncontrolled drug release and non-uniform combination of penetration (Prausnitz and Langer, 2008).

The chemical penetration enhancers may disrupt the skin barrier, though they will produce irritation and inflammation which is not desired on already inflamed psoriatic skin. Consequently, new carrier-based delivery mechanisms with the ability to alter contact with the skin but maintain its integrity are essential.

5. Lipid Particulate Systems: Concept and Classification

Physiological or biocompatible lipid-based colloidal carriers are called lipid particulate systems and are useful in encapsulating and delivering therapeutic agents. The topical application of these lipids of the skin, their nanoscale size and their ability to provide controlled drug release make them ideal in the treatment (Muller et al. 2000).

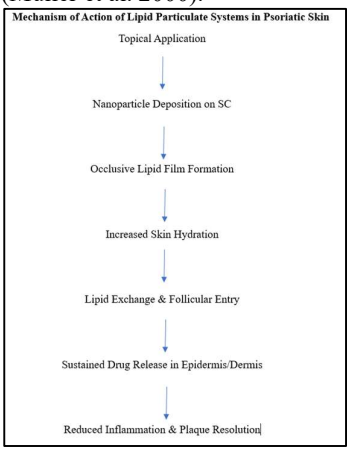
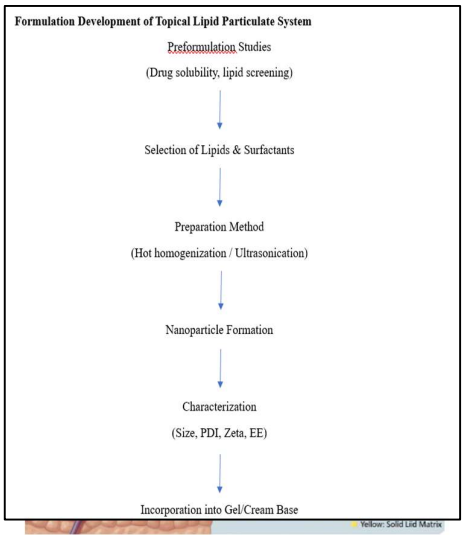


Fig 2. Lipid particulate system in Psoriatic skin



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6. SOLID LIPID NANOPARTICLES (SLNS)

Solid lipid nanoparticles consist of solid lipid core and surfactants. SLNs, proposed by Muller et al. (2000) as an alternative to polymeric nanoparticles first, have such advantages as biodegradability, low toxicity and scalability. SLN form an occlusive film on the skin surface which minimizes TEWL and maximizes skin moisture, thereby enhancing the penetration of medicines (Wissing et al., 2004).

Table 3. Critical Quality Attributes (CQAs) for Topical Lipid Particulate Systems

Attribute	Desired Range	Impact on Performance
Particle size	100–300 nm	Optimal penetrati on and retention
Polydispersity index	< 0.3	Uniform delivery and stability
Zeta potential	±20–30 mV	Colloidal stability
Entrapment efficiency	> 70%	Therapeutic dose adequacy
pH	5.0–6.5	Skin compatibility

Souto et al. (2007) observed that cutaneous delivery of anti-inflammatory drugs using SLNs produced better targeting and it led to a reduction in systemic concentrations, as well as, an increase in the systemic retention.

7. NANOSTRUCTURED LIPID CARRIERS (NLCS)

The second generation of lipid nanoparticles is known as nanostructured lipid carriers, which combine solid and liquid lipids to overcome the limitations of SLNs like release of drugs during storage (Muller et al., 2002). This is because the lipid matrix of NLCs is defective, which allows loading more drug and stability.

Topical preparations based in NLCs have been shown to have better skin deposition as well as long-lasting release of ant psoriatic agents including corticosteroids and immunomodulators. (Pardeike et al., 2009).

8. VESICULAR LIPID SYSTEMS

Vesicular lipid carriers that have been widely considered in cutaneous delivery are liposomes, ethosomes and transfersomes. Touitou et al. (2000) developed ethosomes, that are high ethanol levels that fluidize stratum corneum lipids and this enhances skin permeation significantly.

Methotrexate and calcipotriol ethosomal preparations were found to enhance the treatment of psoriasis and reduce symptoms in a psoriasis model (Dubey et al. 2007).

9. RELEVANCE OF LIPID PARTICULATE SYSTEMS IN PSORIASIS MANAGEMENT

The skin of a psoriatic patient provides an ideal environment to lipid particle carriers due to the lipid-rich environment. The devices are able to localize drugs in the epidermis and dermis, enhance therapeutic index as well as reduce frequency of doses-adaptable in the treatment of chronic diseases (Bseiso et al., 2016).

Moreover, the lipid nanoparticles have the ability to preserve labile drugs without their degradation, they can increase patient compliance using cosmetically appealing systems and even permit combination therapy whereby multiple drugs can be encapsulated.

10. MECHANISTIC ADVANTAGES OF LIPID PARTICULATE SYSTEMS IN PSORIATIC SKIN

The unique pathology of psoriatic skin, including lipid composition changes, loss of barrier integrity and increased levels of inflammatory mediators offer barriers and opportunities to administer topical medication in a targeted way. Due to their structural and physical resemblances to endogenous skin lipids, lipid particle system is specifically positioned to exploit the property (Pardeike et al., 2009).

One of the important ways through which lipid particles systems enhance topical medication is by occluding. The use of solid lipid nanoparticles and nanostructured lipid carriers results in the formation of a continuous lipid film on the stratum corneum surface decreasing the trans epidermal water loss as well as enhancing skin moisturization (Wissing et al., 2004). When hydration increases, it results in the enlargement and loosening of the intercellular lipid packing, which enables the encapsulated medicines to penetrate deeper (Barry, 2001).

In addition, there is follicular targeting of lipid nanoparticles, a significant advantage of psoriasis because hair follicles are the immune cell and inflammatory cells reservoirs. Lademann et al. (2007) discovered that localisation of nanoparticles occurs mostly in the hair follicles, which facilitates prolonged discharge of drugs and residence in inflammatory skin areas.

Lipid particle carriers affect stratum corneum lipids by lipid exchange mechanisms at the molecular level to enhance medication partitioning into the epidermis, but not irreversible disruption of the barrier (Muller et al., 2002). This forms a controlled alteration of barrier properties, particularly in psoriasis, in which inflammatory exacerbation can be exacerbated by violent inflammation of permeability.

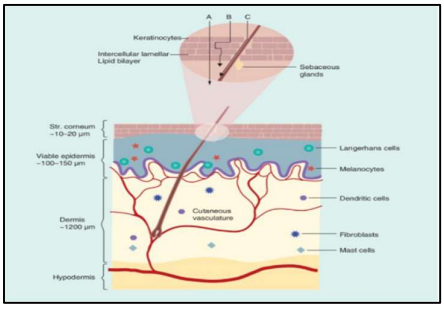

Fig 3. Topical particulate system on skin

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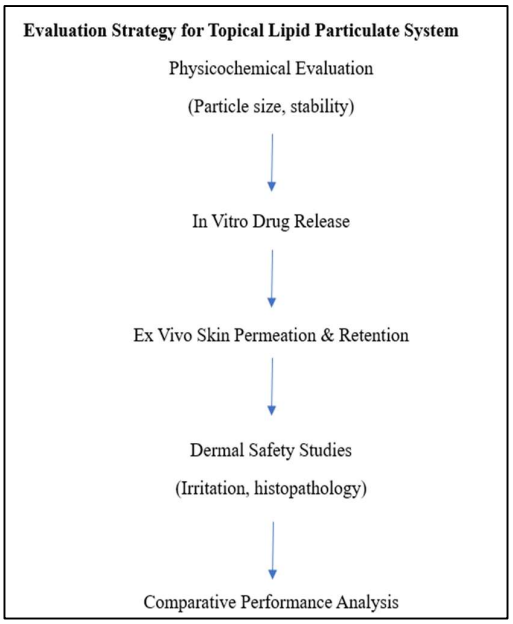
11 EVALUATION PARAMETERS FOR TOPICAL LIPID PARTICULATE SYSTEMS

The full investigation of the lipid particle systems is necessary to find out whether they can be applied in treating psoriasis or not. Typical characterization tests are physicochemical, in vitro, ex vivo and in vivo.

12. PHYSICAL AND CHEMICAL CHARACTERIZATION

Critical factors in the skin penetration and the stability are the particle size and the distribution. Nano-particles with a size width of 100-300 nm have already been bestowed with proper balance between epidermal penetration and retention (Souto et al., 2011). The colloidal stability is indicated by the zeta potential and contact with skin surfaces; the more negative the nanoparticles, the more stable and the less aggregation (Muller et al., 2000).

Entrapment efficiency measures the carrier's ability to integrate therapeutic substances and is impacted by lipid composition, drug solubility and production process. Because of their less ordered lipid matrix, nanostructured lipid carriers routinely outperform solid lipid nanoparticles in terms of entrapment efficiency.



13. IN VITRO DRUG RELEASE

In vitro release studies provide information on drug release kinetics and predict in vivo performance. Lipid particle systems often have biphasic release patterns, with an initial burst followed by continuous release, which are caused by surface-associated drug and matrix-embedded drug, respectively. Sustained release is especially useful in psoriasis to keep therapeutic medication levels stable and reduce dose frequency.

14. EX VIVO SKIN PERMEATION AND RETENTION

Ex vivo permeation investigations with human or animal skin models (such as Franz diffusion cells) are essential for determining dermal targeting efficacy. Schäfer-Korting et al. (2007) found that lipid nanoparticles considerably improve epidermal drug retention while limiting transdermal permeability, resulting in reduced systemic exposure.

Skin retention studies are especially important in psoriasis because therapeutic success is dependent on local medication concentration within the epidermal and dermal layers rather than systemic absorption.

15. SAFETY AND SKIN IRRITATION STUDIES

The safety of the psoriatic skin being weakened, it is of critical concern. Carriers made of lipids with physiological lipids are usually well tolerated and do not cause extensive irritation and sensitivity (Wissing et al., 2004). However, the excipients such as surfactants and penetration enhancers should be selected and tested well.

16. PRECLINICAL AND CLINICAL EVIDENCE SUPPORTING LIPID PARTICULATE SYSTEMS

A number of preclinical studies have indicated that there are lipid particle systems that are better than the conventional topical preparations in treating psoriasis. According to Bseiso et al. (2016), corticosteroid impregnated SLNs demonstrated the superiority of anti-inflammatory capacity and less erythema compared to commercial creams.

Similarly, NLC-based formulations of calcipotriol and methotrexate improved skin deposition and treatment results in imiquimod-induced psoriasis mice (Agrawal et al. 2019). Ethosomal systems have also shown that powerful ant psoriatic medicines penetrate better and cause less discomfort (Dubey et al., 2007).

Despite promising preclinical results, clinical translation is limited. Formulation scalability, long-term stability, regulatory constraints and cost-effectiveness must all be addressed to allow clinical adoption (Mehnert and Mader, 2012).

17. PHARMACOLOGICAL PROFILE OF CLOBETASOL PROPIONATE (CP)

Clobetasol Propionate (CP) is a synthetic, dihalogenated glucocorticoid that falls into the "super-potent" Class I group of topical corticosteroids. It is commonly recognized as the primary treatment for many corticosteroid-responsive dermatoses, most notably Psoriasis Vulgaris. (Pawar et al., 2021)

Mechanism of action

CP's therapeutic impact is achieved via binding to cytoplasmic glucocorticoid receptors. Once the clobetasol-receptor complex enters the nucleus, it binds to Glucocorticoid Response Elements (GREs), resulting in:

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Anti-inflammatory effect: Induction of phospholipase A2 inhibitory proteins (lipocortins), which regulate the release of arachidonic acid, an inflammatory precursor (Garg et al., 2016).
Antiproliferative effect: Inhibition of DNA synthesis and mitosis in keratinocytes, which substantially reduces the epidermal thickness associated with psoriatic plaques (Rafat and Singh, 2019).
Immunosuppressive effect: Reduces pro-inflammatory cytokines such IL-1, IL-6 and TNF-alpha.

18 PHYSICOCHEMICAL CHALLENGES

CP is a highly lipophilic molecule with a molecular weight of 466.97g/mol and extremely low water solubility ($\approx. 2 \text{µg/mL}$). (Rafat and Singh, 2019). While lipophilicity is beneficial for skin partitioning, low solubility results in poor bioavailability in typical aqueous carriers. Furthermore, the use of standard CP creams (such as Dermovate®) is limited to 14 days due to the danger of skin shrinkage, telangiectasia and HPA-axis suppression (Pawar et al., 2021).

18.1 Clobetasol Propionate drug for SLN's

The constraints of traditional therapy are addressed by the encapsulation of CP within SLNs through a number of clear advantages:

Epidermal Targeting: By selectively depositing the medication in the epidermis and dermis, SLNs lower the quantity of medication that enters the systemic circulation (Arora et al., 2012)

The Effect of Occlusion: SLNs create a hydrophobic coating on the skin because of their lipid composition. By lowering trans epidermal water loss (TEWL), this "occlusive" effect hydrates the stratum corneum and promotes deeper medication penetration (Wissing & Muller, 2003).

Enhanced Stability: The encapsulated CP is shielded from environmental elements including light and moisture as well as chemical deterioration by the solid lipid matrix (Muller et al., 2011).

Controlled Release: The solid lipid hard structure allows a biphasic release pattern, which is a rapid initial dose to obtain instant relief and a slow release to support therapeutic concentrations at the site (Arora et al., 2012).

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19. REVIEW LITERATURE

- **Sahoo et al. (2025)** Hydrocortisone Acetate: Recent studies on NLC-hydrogels revealed an entrapment efficiency of 94%, resulting in a "reservoir effect" that reduced the requirement for frequent application and reduced textile discoloration
- **Patel et al. (2025)** study found that Hesperidin-Loaded NLCs (~125 nm) enhanced epidermal architecture and reduced erythema in imiquimod-induced psoriasis mice compared to standard gels
- **Upadhyay and Soni (2025)** SLNs have received extensive research into delivery of potent anti-psoriatic agents including methotrexate (MTX) and acitretin. In recent experiments the Box-Behnken type of designs were employed to optimize MTX-loaded SLNs giving Particle size of approximately 210 nm and a sustained release profile of approximately 24 hours. By concentrating the drug at the layers of the skin these formulations significantly decreased systemic toxicity which was a significant drawback of oral MTX.
- **Maiti et al. (2023)** engineered methotrexate-impregnated solid lipid nanoparticles against psoriasis. These nanoparticles were found to have a persistent, targeted anti-psoriatic effects and low systemic accommodation. This implies that topical delivery using SLN can increase the systemic toxicity of traditional methotrexate therapy.
- **Ganesan & Narayanasamy (2023)** Recent studies show that lipid particles significantly reduce pro-inflammatory cytokines including TNF-α, IL-17A and IL-22. The technique involves the "fusion" of nanoparticles with the stratum corneum's intercellular lipids, which allows even weakly soluble medicines to be partitioned into the deeper epidermis
- **Thomas et al. (2022)** determined that clobetasol propionate 0.025% cream was as clinically effective and with a better safer profile than higher-strength preparations. This explains the need to maximise the topical formulations in order to lessen the negative consequences of steroids.
- **Sharma et al. (2022)** isolated that topical psoriasis treatment with methotrexate loaded nanostructured lipid carriers was better in enhancing skin retention, sustained release and therapeutic effects without systemic toxicity.
- **Kaur et al. (2021)** found that co-loading these medicines into NLC-based nano emulsions resulted in greater anti-psoriatic efficacy in mice than commercial products.
- **Raharja et al. (2021)** psoriasis is a debilitating, chronic inflammatory immune-mediated disease associated with a high level of morbidity and disability across the globe. Here, the significance of patient-compliant, long-term and safe topical therapy methods is emphasized.
- **Patel et al. (2021)** established that tacrolimus-impregnated solid lipid nanoparticles enhancing and prolonging skin uptake, prolonging drug delivery and causing a substantial reduction in the exposure of psoriatic skin models to inflammation.
- **Pawar et al. (2021)** Still, the gold standard of treating moderate-to-severe psoriasis is clobetasol Propionate; however, the high doses of chemical enhancers are often necessitated by the fact that the molecule cannot easily diffuse through standard aqueous gel bases, further aggravating psoriatic

skin irritation. Their work led to the realization of the need to provide carriers with a so-called dermatokinetic benefit, i.e., it should increase the average period of stay of the drug in the skin and reduce the level of systemic absorption.

- **Bakshi et al. (2020)** conducted a safety and satisfaction analysis of the available psoriasis medications and discovered that patients were not satisfied and expressed safety concerns on the same. Their conclusion was that the psoriasis is promise to deliver drugs and be successful and focused when it is achieved using nanocarrier-based approaches of drug delivery.
- **Khan et al. (2020)** concluded that nanostructured lipid carriers (NLCs) exhibit a greater drug loading, increased sustained release and skin retention relative to conventional SLNs suggesting their potential as novel carriers of chronic inflammatory skin diseases like psoriasis.
- **Gupta et al. (2020)** developed curcumin-loaded nanostructured lipid carriers for topical administration, demonstrating improved skin penetration, anti-inflammatory efficacy and photostability.
- **Kumar et al. (2019)** developed topical preparations on anti-psoriatic medicines in the form of nano emulsions, which enhanced better penetration and bioavailability and minimized systemic exposure.
- **Rafat and Singh (2019)** applying emulsification-homogenization technique, focused their attention on optimization of CP-loaded SLNs on the technical level. Their study showed the lipid-drug ratio and the choice of surfactant (e.g. Tween 80 vs. Poloxamer 188) to be the primary determinants of Entrapment Efficiency (EE). They received an EE of over 85, which means that since CP spontaneously separates into the lipid melt during the production process, it is highly lipophilic to be incorporated as a part of the the solid lipid matrix.
- **Gupta et al. (2018)** found that topical formulations containing nano emulsions are better in skin penetration and patient acceptability, which render them a useful delivery system to lipophilic anti-psoriatic drugs.
- **Mohan et al. (2018)** found that solid lipid nanoparticles containing calcipotriol had higher skin deposition and regulated release than traditional formulations for treating psoriasis.
- **Ranjan et al. (2017)** developed lipid-based nanoparticles for anti-inflammatory drug delivery, which demonstrated improved efficacy, reduced irritation and increased patient compliance.
- **Griffiths et al. (2017)** found that psoriasis has a significant global disease burden, highlighting the need for effective topical therapies for long-term control.
- **Garg et al. (2016)** investigated the molecular constraints of CP and discovered that in many cases, local adverse reactions dominate the anti-inflammatory effect of CP. Their study revealed that the formulations made by the drug that interact with the stratum corneum are altered when CP is made into a lipidic nanoparticle. They have discovered that although nanocarriers provide a more product-controlled release that mimics physiological needs of inflammatory tissue conventional vehicles fail to counter the rebound effect of psoriasis.
- **Santos et al. (2016)** found that lipid-based nanoparticles improve skin retention and lower systemic exposure over traditional psoriasis treatments.
- **Singh et al. (2016)** developed nano-lipid carriers for topical methotrexate delivery, resulting in enhanced skin retention, tailored distribution and lower systemic toxicity.
- **Boehncke and Schon (2015),** psoriasis is a chronic, recurrent inflammatory illness that requires persistent local medication delivery to suppress immune-mediated disease development.
- **Patel et al. (2015)** found that ethosomal administration of calcipotriol improved epidermal penetration and accumulation, making it a promising treatment option for psoriasis.
- **Choudhary et al. (2014**) developed lipid-based vesicular systems for corticosteroid delivery, resulting in improved skin bioavailability and sustained anti-inflammatory effects.
- **Lowes et al. (2014)** established the IL-23/Th17 axis as a significant mechanism in the pathogenesis of psoriasis, which requires long-term use of the anti-inflammatory effect.
- **Kaur et al. (2013)** found that solid lipid nanoparticles of clobetasol propionate provided regulated release, reduced irritation and enhanced cutaneous targeting for treating psoriasis.
- **Shakeel et al. (2013)** found that nano emulsion-based topical solutions improve skin drug penetration and bioavailability, making them effective carriers for lipophilic anti-psoriatic medicines.
- **Labouta and Schneider (2013),** targeted nanoparticle-based therapies for inflammatory skin illnesses can be designed based on disease-specific skin changes.
- **Mehnert and Mader (2012)** published a global review of the nanoparticle production, physique and applications of solid lipids. They identified important variables in formulation that enhance effective cutaneous drug administering.
- **Menon et al. (2012)** described the composition and structure of the stratum corneum and the role it plays in the process of adopting lipid-based delivery systems by diseased skin due to a change of architecture of its lipids.

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- **Arora et al. (2012)** emphasized once again the Quality by Design (QbD). There was a particle size of 100-200 nm that exhibited a targeting of particles in the follicles, which demonstrated particle size as an important quality attribute (CQA) of psoriasis. They proved that with the help of SLNs, the CP could reach the viable epidermis where the inflammatory cascade is active the most by circumventing the thickened psoriatic stratum corneum, through the hair follicle shunts.
- **Patzelt et al. (2011)** stylesheet that nanoparticles can be delivered to hair follicles making topical delivery of medications long-term possible.
- **Korting and Schäfer-Korting (2010)** determined that resorting to advanced carriers like lipid nanoparticles can improve the effectiveness of topical dermatological therapy and minimize irritation/systemic exposure.
- **Nestle et al. (2009)** provided a detailed clinical and immunological overview of psoriasis, emphasizing the need for localized therapy options to minimize systemic consequences.
- **Pardeike et al. (2009)** found that lipid nanoparticles in cutaneous applications had scalability, durability and regulatory approval, indicating their potential for translation.
- **Soto and Muller (2008)** examined cosmetic and medicinal applications of lipid nanoparticles, confirming their safety, biocompatibility and appropriateness for long-term cutaneous use.
- **Elias (2008)** inflammatory dermatoses are caused by decreased skin barrier function. Lipid-based carriers can help restore the barrier and deliver therapeutic medicines.
- **Lademann et al. (2008),** found that nanoparticles can effectively carry drugs into follicles, indicating their potential for improved skin targeting and long-term release.
- **Schafer-Korting et al. (2007),** lipid nanoparticles form an occlusive film with stratum corneum lipids, increasing penetration and reducing irritation.
- **Uner and Yener (2007)** highlighted the safety and applicability of solid lipid nanoparticles for topical treatment.
- **Elsayed et al. (2007)** discovered that deformable liposomes and ethosomes were more effective than regular liposomes with respect to permeability of the skin.
- **Bouwstra and Ponec (2006)** determined that pathological conditions lead to the alteration of the epidermal barrier, which underlies lipid-based psoriasis therapy.
- **Kogan and Garti (2006)** found that microemulsions improve the solubility and penetration of lipophilic medicines for transdermal and cutaneous application.
- **Honeywell-Nguyen and Bouwstra (2005**) identified vesicular carriers as effective methods for bypassing the stratum corneum barrier in cutaneous medication delivery.
- **Barry (2004)** highlighted carrier-based approaches to improve topical medication penetration.
- **Williams and Barry (2004)** found that lipid-based and vesicular carriers are safer than chemical enhancers for topical medication delivery.
- **Wissing and Muller (2003)** It made a contribution of a seminal study on the physical interaction between SLNs and the skin surface. They have applied in vivo research to show the existence of a significant mechanism by which SLNs produce an effect which is an occlusive effect. These nanoparticles reduce the trans epidermal water loss (TEWL), due to the formation of a monolithic lipid coating on the skin. This increased hydration is itself good in the psoriatic patients whose skin is usually scaly and dry. The reason being that it facilitates the uptake of the drug in further epidermal layers and scales regulating themselves to desquamate.
- **Muller et al. (2002)** identified solid lipid nanoparticles and nanostructured lipid carriers as advanced dermal carriers with controlled release and enhanced skin compatibility.
- **Cevc and Blume's (2001)** study found that employing deformable vesicular systems improved topical medication delivery and increased local drug availability.
- **Elias and Feingold (2001)** indicated lipid abnormalities in inflammatory skin diseases and urged to restore lipid organization in the form of therapeutic intervention. This also indirectly endorses the use of lipid-based topical delivery systems to psoriasis.
- **Touitou et al. (2000)** identified ethosomes as vesicular carriers that enhance cutaneous penetration via ethanol-induced lipid fluidization.
- **Jenning et al. (2000)** found that vitamin A-loaded solid lipid nanoparticles had strong occlusive characteristics and targeted upper skin layers, indicating the potential for SLN-mediated dermal targeting.
- **El Maghraby et al. (1999)** found that deformable vesicles provide better drug transport to the skin than rigid liposomes, leading to the development of elastic vesicular systems for dermal therapy.
- **Zur Muhlen et al. (1998)** discovered that drug release from solid lipid nanoparticles is controlled by diffusion and erosion, paving the way for long-term topical drug administration with SLNs.
- **Barry (1987)** emphasized the importance of carrier systems in overcoming stratum corneum resistance, which influenced the creation of lipid-based nanoparticles today.
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20. CONCLUSION AND FUTURE PERSPECTIVES

The substantial body of evidence reviewed herein confirms a paradigm shift in psoriasis management, from traditional topical vehicles to sophisticated lipid-based nanocarriers. For decades, the fundamental issue in treating psoriasis has been the "dual barrier": the thicker, hyperkeratotic stratum corneum that resists drug penetration, as well as the potential of systemic toxicity from powerful treatments such as clobetasol propionate and methotrexate.

The most promising answers to these issues, according to the data from both seminal and modern studies, are Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs). Key findings from the literature indicate four critical therapeutic benefits:

Occlusion and Barrier Restoration: According to Wissing and Muller (2003), lipid nanoparticles actively create an occlusive layer that lowers transepidermal water loss (TEWL), rather than only serving as passive carriers. Because it naturally encourages desquamation and enables deeper medication partitioning, this moisture effect is essential for psoriatic skin. Enhanced Dermatokinetics: Recent research shows that nanocarriers offer a "reservoir effect," concentrating active molecules within the viable dermis and epidermis (Pawar et al., 2021; Upadhyay & Soni, 2025). Strong steroids and anti-inflammatory drugs are guaranteed to reach the IL-23/Th17 axis, the immunological "engine" of psoriasis, thanks to this localization, which also considerably lowers the systemic absorption that causes side effects.

Synergistic Co-loading: The development of NLC technology has made it possible to successfully co-incorporate natural antioxidants (curcumin) and lipophilic medications (clobetasol). Compared to single-drug therapy, this dual-action strategy offers a more comprehensive treatment profile by addressing both oxidative stress and the inflammatory cascade. Targeted Delivery via Appendages: According to more recent studies particles in the 100–200 nm range can use hair follicles as "shunt" channels to get beyond the thicker skin barrier and increase local bioavailability.

In conclusion, the shift from straightforward creams to hydrogels based on lipid nanoparticles is a big step toward safer, more patient-friendly psoriasis treatment. The field's future depends on the clinical translation of these formulations, even if the technical optimization of these carrier using Quality by Design (QbD) and contemporary homogenization techniques—is well-documented. Large-scale regulatory approval and the creation of "smart" nanocarriers that can react to the particular pH or temperature changes of inflammatory psoriatic lesions must become the main priorities as we approach 2030. In the end, lipid-based nanotechnology presents the most practical way to turn psoriasis from a crippling long-term battle into a controllable localized ailment.

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