NANOVESICULAR TOPICAL DELIVERY SYSTEMS FOR PSORIASIS MANAGEMENT: FROM LIPOSOMES TO INVASOMES—MECHANISTIC INSIGHTS, TRANSLATIONAL ADVANCES, AND FUTURE PERSPECTIVES.

Lingayat Pranali[1], Dr. Deshmukh Manish[2*], [3]Dr. Dhikale Rupali S.

[1]Research Scholar, Datta Meghe Institute of Higher education and research, DMIHER, Sawangi (Meghe) Wardha, MH, India 442001

[2]Professor, Datta Meghe College of Pharmacy, DMIHER (DU), Sawangi (Meghe), Wardha, MH, India 442001.

[3]HOD- Department of Pharmacognosy, SPES SNPT Institute of Pharmacy, Nashik, MH, India 422003.

****Corresponding author: Dr. Deshmukh Manish***

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ABSTRACT

Psoriasis is a chronic, relapsing, immune-mediated inflammatory dermatosis characterized by epidermal hyperproliferation, aberrant keratinocyte differentiation, angiogenesis, and sustained activation of the IL-23/Th17 inflammatory axis. Despite remarkable advances in systemic biologics and targeted immunotherapies, topical treatment remains the cornerstone for managing mild-to-moderate psoriasis and an essential adjunct in severe disease. However, conventional topical formulations often demonstrate limited therapeutic efficacy owing to inadequate penetration across the stratum corneum, poor drug retention, instability of active pharmaceutical ingredients, and dose-related adverse effects.

Recent advances in nanotechnology have revolutionized topical drug delivery through the development of nanovesicular systems capable of enhancing drug permeation, increasing epidermal retention, improving pharmacokinetic performance, and reducing systemic exposure. Liposomes, niosomes, transfersomes, ethosomes, transethosomes, glycerosomes, hyalurosomes, and invasomes represent successive generations of vesicular carriers specifically engineered to overcome the skin barrier. Among these systems, invasomes have emerged as highly promising ultradeformable vesicles owing to the synergistic action of phospholipids, ethanol, and terpenes, which collectively facilitate deeper skin penetration and improved therapeutic outcomes.

This review critically evaluates the evolution of nanovesicular technologies for psoriasis management, emphasizing mechanistic aspects of skin penetration, formulation design, physicochemical characterization, preclinical and clinical evidence, translational challenges, regulatory considerations, and future perspectives. Particular emphasis is placed on recent advances reported between 2020 and 2026 and their potential to bridge the gap between laboratory innovation and clinical application.

Keywords: Psoriasis, Liposomes, Transfersomes, Ethosomes, Invasomes, Nanovesicular systems, Topical drug delivery, Skin targeting, Nanomedicine, Transdermal delivery.

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1. INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder affecting approximately 2–3% of the global population and is increasingly recognized as a systemic immune-mediated disease rather than a purely dermatological condition[1,2]. The disease is characterized by sharply demarcated erythematous plaques covered with silvery scales, predominantly involving extensor surfaces, scalp, lumbosacral region, and nails. Plaque psoriasis accounts for nearly 85–90% of all cases and is frequently associated with metabolic syndrome, obesity, cardiovascular disorders, depression, and psoriatic arthritis [1–3].

The pathogenesis of psoriasis involves a complex interplay among genetic susceptibility, environmental triggers, immune dysregulation, and epidermal abnormalities. Activation of dendritic cells initiates a cytokine cascade that promotes differentiation and expansion of Th17 lymphocytes. Subsequently, pro-inflammatory mediators such as IL-17A, IL-22, IL-23, and TNF-α stimulate keratinocyte proliferation and chronic inflammation [4,5].

Although biologic therapies targeting these pathways have transformed psoriasis treatment, topical formulations remain indispensable because of their ease of administration, localized action, reduced systemic toxicity, and lower treatment cost [6]. Nevertheless, conventional creams, ointments, gels, and lotions frequently exhibit suboptimal clinical outcomes due to poor skin penetration and inadequate drug bioavailability.

The emergence of nanovesicular drug delivery systems has provided innovative opportunities for overcoming these limitations. These carriers can encapsulate hydrophilic, lipophilic, and amphiphilic drugs while enhancing penetration through the stratum corneum and promoting targeted deposition within diseased skin layers [7,8].

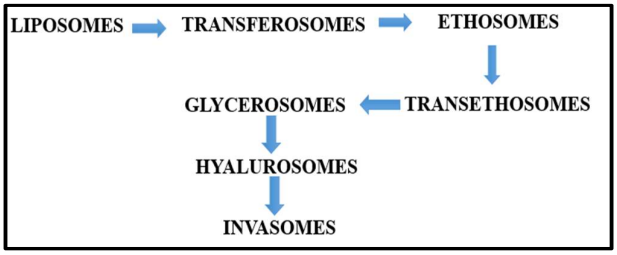

Figure 1: Evolution of Nanovesicular drug delivery systems for topical Psoriasis therapy.

2. GLOBAL BURDEN AND EPIDEMIOLOGY OF PSORIASIS:

Psoriasis exhibits marked geographical variation. Epidemiological studies indicate prevalence rates ranging from 0.09% to 11.4% worldwide, with higher incidence observed in Northern Europe and North America compared with Asian and African populations [2].

Recent epidemiological analyses suggest that the global burden of psoriasis continues to increase because of urbanization, lifestyle modifications, obesity, and environmental stressors. Furthermore, psoriasis contributes substantially to years lived with disability (YLDs), resulting in significant socioeconomic consequences [2]

Table 1. Global epidemiological characteristics of psoriasis.

Sr.No	Parameter	Observation
1	Global prevalence	0.09–11.4%
2	Most common subtype	Plaque psoriasis
3	Adult prevalence	Higher than pediatric population
4	Common comorbidities	Psoriatic arthritis, obesity, cardiovascular disease
5	Major risk factors	Genetics, smoking, alcohol, stress
6	Disease burden	Significant reduction in quality of life

The psychosocial burden associated with psoriasis frequently exceeds the physical manifestations. Anxiety, depression, social isolation, sleep disturbances, and work-related disability are commonly reported among patients [1,2].

3. IMMUNOPATHOGENESIS OF PSORIASIS

Understanding psoriasis pathophysiology is essential for designing effective topical nanomedicines.

Current evidence identifies the IL-23/Th17 axis as the central pathogenic pathway in psoriasis [4]. Upon exposure to environmental triggers, activated dendritic cells release IL-23 and TNF-α, promoting differentiation of naïve T cells into Th17 lymphocytes. These cells subsequently secrete IL-17A, IL-17F, IL-22, and TNF-α, which induce keratinocyte proliferation and inflammatory cell recruitment.

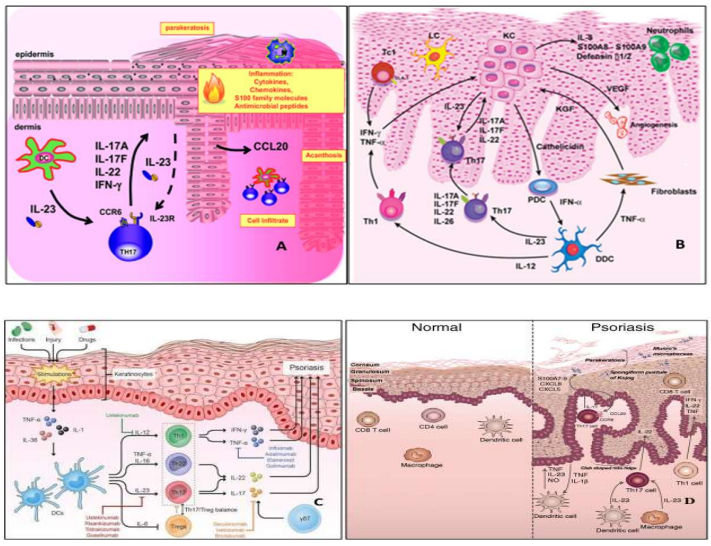

Figure 2. Immunopathogenic Mechanism of Psoriasis: A) IL-23/Th17 axis in the immunopathogenesis of psoriasis. B) Th 17 Lumphocytes and psoriasis cellular and molecular interactions with skin resident. C) The role of Helper T cells in Psoriasis. D) Normal skin and psoriatic plaque histology.

The molecular immunopathogenesis of psoriasis is complex and it involves series of following events and the same are depicted in figure 2.

- Dendritic cell activation
- IL-23 secretion
- Th17 differentiation
- IL-17A/IL-22 production
- Keratinocyte hyperproliferation

 Neutrophil infiltration Angiogenesis

Table 2. Key cytokines involved in psoriasis.

S.N	Cytokine	Cellular Source	Function
1	IL-23	Dendritic cells	Th17 differentiation
2	IL-17A	Th17 cells	Keratinocyte activation
3	IL-22	Th17 cells	Epidermal hyperplasia
4	TNF-α	Macrophages/T cells	Amplification of inflammation
5	IFN-γ	Th1 cells	Immune activation
6	IL-6	Keratinocytes	Inflammatory signaling

Recent molecular investigations further implicate NF-κB, MAPK, PI3K/Akt, and JAK/STAT pathways in disease progression [5]. Oxidative stress has also emerged as a critical contributor, with elevated reactive oxygen species (ROS) promoting inflammatory signaling and epidermal dysfunction.

4. CURRENT THERAPEUTIC APPROACHES AND THEIR LIMITATIONS

Psoriasis treatment is traditionally categorized into topical therapy, phototherapy, systemic therapy, and biologic therapy.

4.1 Topical Therapy

Topical corticosteroids remain first-line agents because of their potent anti-inflammatory effects. Vitamin D analogues, tazarotene, salicylic acid, coal tar, and calcineurin inhibitors are frequently used as monotherapy or in combination [6].

However, prolonged topical corticosteroid use may lead to skin atrophy, telangiectasia, tachyphylaxis, and rebound flare-ups.

4.2 Systemic Therapy

Methotrexate, cyclosporine, and acitretin remain widely prescribed systemic agents for moderate-to-severe disease. Although effective, these drugs are associated with hepatotoxicity, nephrotoxicity, teratogenicity, and systemic adverse effects.

4.3 Biological Therapy

Biologics targeting TNF-α, IL-17, IL-23, and IL-12/23 pathways have significantly improved clinical outcomes. Nevertheless, high cost, immunogenicity, injection-related issues, and long-term safety concerns continue to limit widespread use [6].

Table 3. Limitations of conventional anti-psoriatic therapies.

S.N	Therapy	Advantages	Limitations
1	Corticosteroids	Rapid symptom control	Skin atrophy
2	Vitamin D analogues	Good safety profile	Slow onset
3	Methotrexate	Effective systemic therapy	Hepatotoxicity
4	Cyclosporine	Rapid disease suppression	Nephrotoxicity
5	Acitretin	Useful in severe psoriasis	Teratogenicity
6	Biologics	High efficacy	Cost and immunogenicity

5. SKIN BARRIER AND CHALLENGES IN TOPICAL DRUG DELIVERY

The skin is composed of the epidermis, dermis, and hypodermis. The stratum corneum acts as the principal barrier limiting drug penetration.

The "brick-and-mortar" structure consists of corneocytes embedded within a lipid matrix primarily composed of ceramides, cholesterol, and free fatty acids. Although essential for maintaining homeostasis, this architecture restricts the permeation of most therapeutic molecules [7].

In psoriatic skin, epidermal hyperplasia, altered lipid composition, increased transepidermal water loss (TEWL), and inflammatory infiltration further complicate topical drug delivery.

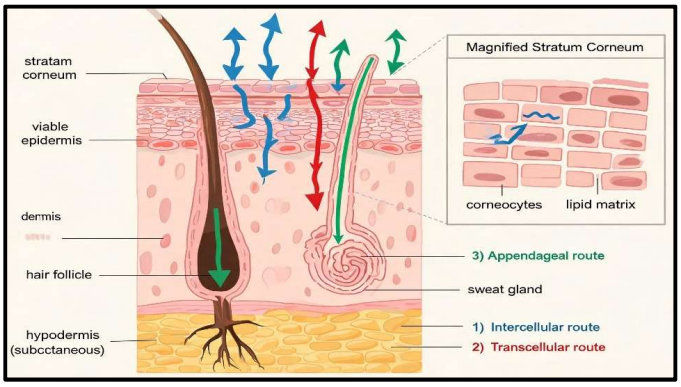

Figure 3. Skin structure and major pathways of drug permeation.

The three major pathways include:

1. Intercellular route
2. Transcellular route
3. Appendageal route

Several anti-psoriatic drugs such as methotrexate, cyclosporine, curcumin, boswellic acids, and tacrolimus possess poor aqueous solubility and limited skin permeability. Consequently, high drug concentrations and frequent applications are often required, reducing patient adherence.

6. RATIONALE FOR NANOVESICULAR DRUG DELIVERY SYSTEMS

Nanovesicular systems have emerged as a promising strategy to overcome the limitations associated with conventional topical formulations.

These carriers offer several advantages:

- Enhanced skin penetration
- Increased drug retention within epidermis
- Controlled drug release
- Improved physicochemical stability
- Reduced systemic exposure
- Improved patient compliance

Recent advances in vesicular engineering have generated a broad spectrum of nanovesicles, including liposomes, transfersomes, ethosomes, transethosomes, glycerosomes, hyalurosomes, and invasomes [7–10].

Table 4. Evolution of nanovesicular systems.

S.N	Vesicle Type	Distinguishing Feature
1	Liposomes	Phospholipid bilayers
2	Niosomes	Nonionic surfactants
3	Transfersomes	Edge activators
4	Ethosomes	High ethanol content
5	Transethosomes	Ethanol + surfactants
6	Glycerosomes	Glycerol enriched
7	Hyalurosomes	Hyaluronic acid modified
8	Invasomes	Ethanol + terpenes

Among these systems, invasomes have attracted particular attention because the incorporation of terpenes and ethanol enhances vesicular flexibility and penetration capability beyond that achieved by conventional liposomes [9,10].

NANOVESICULAR SYSTEMS IN PSORIASIS MANAGEMENT: LIPOSOMES, NIOSOMES, TRANSFERSOMES, ETHOSOMES AND TRANSETHOSOMES

7. NANOVESICULAR DRUG DELIVERY SYSTEMS FOR PSORIASIS: CLASSIFICATION AND DESIGN PRINCIPLES

The growing understanding of skin barrier physiology has accelerated the development of advanced nanovesicular carriers capable of overcoming the limitations of conventional topical formulations. Vesicular nanocarriers are colloidal systems composed of one or more amphiphilic bilayers enclosing an aqueous core. Their ability to encapsulate hydrophilic, lipophilic, and amphiphilic molecules simultaneously has made them particularly attractive for dermatological applications [11,12].

For psoriasis therapy, the primary objective of vesicular carriers is not merely drug transport across the skin but preferential deposition within inflamed epidermal and dermal layers. Such localized targeting improves therapeutic efficacy while minimizing systemic exposure and associated toxicities [13].

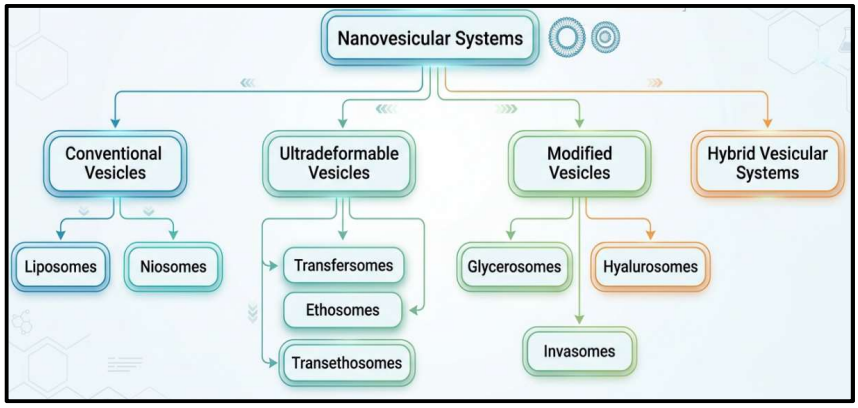

Figure 4. Classification of nanovesicular systems used in psoriasis management.

As shown in Figure 4, progressive modifications in vesicular composition have generated increasingly deformable systems capable of penetrating deeper skin layers.

8. LIPOSOMES

8.1 Historical Development

Liposomes were first described by Bangham and colleagues in the 1960s and subsequently became the first clinically successful lipid-based nanocarrier system [14]. Owing to their biocompatibility and structural resemblance to biological membranes, liposomes have been extensively investigated for topical psoriasis therapy.

Liposomes consist of phospholipid bilayers enclosing one or more aqueous compartments. Their amphiphilic architecture permits simultaneous loading of hydrophilic drugs within the aqueous core and lipophilic drugs within the phospholipid bilayer [15].

8.2 Composition and Structural Characteristics

Liposomes are typically composed of:

- Phosphatidylcholine

- Phosphatidylethanolamine
- Cholesterol
- Negatively charged phospholipids
- Surface modifiers

The composition shown in Figure 5 determines vesicle stability, encapsulation efficiency, membrane fluidity, and skin interaction properties [15].

8.3 Preparation Methods

Several preparation techniques have been employed for anti-psoriatic liposomes.

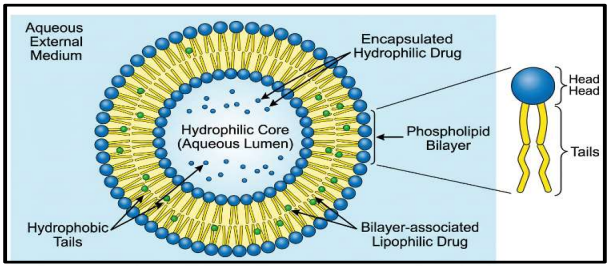

Figure 5. Structural organization of a liposome

Table 5. Common methods for liposome preparation.

S.N	Method	Principle	Advantages	Limitations
1	Thin-film hydration	Lipid film hydration	Simple	Broad size distribution
2	Reverse phase evaporation	Emulsion-based	High encapsulation	Organic solvent use
3	Ethanol injection	Solvent displacement	Reproducible	Limited loading
4	Microfluidization	High-pressure mixing	Scalable	Expensive
5	Extrusion	Membrane sizing	Uniform vesicles	Additional processing

As indicated in Table 5, thin-film hydration remains the most widely used laboratory-scale technique for psoriasis formulations because of its simplicity and versatility [16].

8.4 Mechanism of Skin Penetration

Liposomes improve topical delivery through multiple mechanisms:

1. Adhesion to stratum corneum
2. Lipid exchange with skin lipids
3. Hydration-induced penetration enhancement
4. Controlled drug release

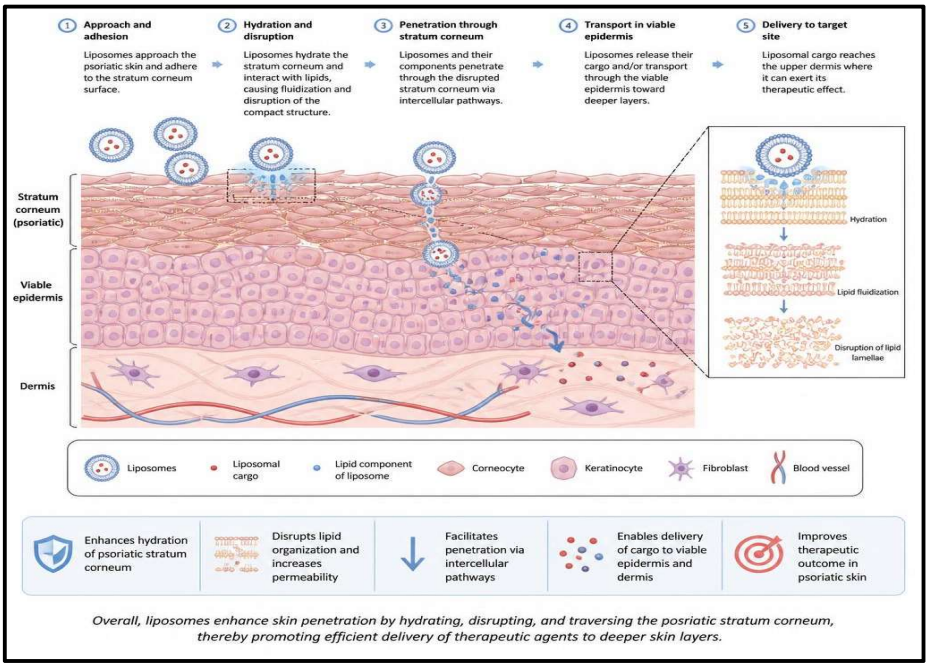

Figure 6. Proposed mechanism of liposomal penetration through psoriatic skin.

The mechanism illustrated in Figure 6 demonstrates that liposomes generally accumulate within superficial epidermal layers rather than penetrating intact skin as intact vesicles [17].

8.5 Liposomal Formulations Investigated for Psoriasis

Numerous anti-psoriatic agents have been incorporated into liposomal carriers.

Table 6. Representative liposomal formulations evaluated for psoriasis.

S.N	Drug	Therapeutic Purpose	Major Findings
1	Methotrexate	Antiproliferative	Improved epidermal retention
2	Cyclosporine	Immunosuppressive	Enhanced skin penetration
3	Curcumin	Anti-inflammatory	Reduced cytokine production
4	Tacrolimus	Immunomodulatory	Improved lesion targeting
5	Dithranol	Keratinocyte regulation	Reduced irritation

As summarized in Table 6, liposomes consistently improve local drug retention and reduce irritation compared with conventional formulations [18].

However, conventional liposomes often exhibit insufficient deformability and limited penetration beyond superficial epidermal layers.

9. NIOSOMES

9.1 Overview

Niosomes are vesicular systems composed of nonionic surfactants and cholesterol. Compared with liposomes, niosomes offer improved chemical stability, lower production cost, and enhanced storage characteristics [19].

9.2 Composition

Common surfactants include Span 20, Span 60, Span 80, Tween 20, Tween 60 and Tween 80.

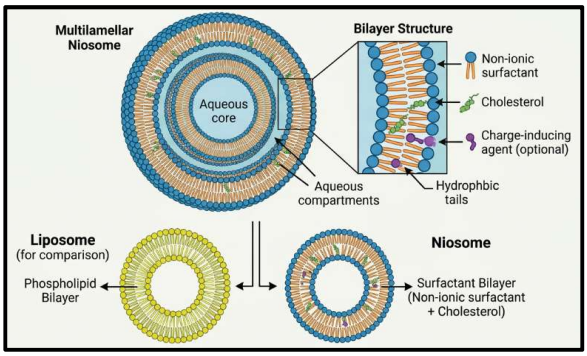

Figure 7. Structural Organization of Niosomes

The architecture illustrated in Figure 7 resembles liposomes but employs surfactant bilayers instead of phospholipid bilayers.

9.3 Advantages for Psoriasis Therapy

Niosomes provide:

- Improved drug stability
- Enhanced skin deposition
- Reduced irritation
- Controlled release

Table 7. Comparative characteristics of Liposomes and Niosomes.

S.N	Parameter	Liposomes	Niosomes
1	Cost	High	Lower
2	Stability	Moderate	Higher
3	Biocompatibility	Excellent	Good
4	Oxidative degradation	Possible	Reduced
5	Scalability	Moderate	Good

The advantages summarized in Table 7 explain the increasing interest in niosomal anti-psoriatic formulations [19].

10. TRANSFERSOMES

10.1 Concept of Ultradeformability

Transfersomes represent the first generation of ultradeformable vesicles specifically designed to overcome limitations associated with conventional liposomes [20].

These carriers contain:

- Phospholipids
- Edge activators
- Water

Edge activators destabilize the lipid bilayer, increasing elasticity and enabling passage through pores significantly smaller than vesicle diameter.

10.2 Role of Edge Activators

Common edge activators include:

- Sodium cholate
- Sodium deoxycholate
- Tween 80
- Span 80

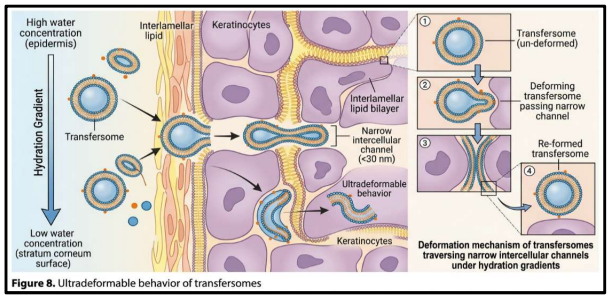

Figure 8. Ultradeformable behavior of transfersomes

The deformation mechanism illustrated in Figure 8 demonstrates how transfersomes traverse narrow intercellular channels under hydration gradients.

10.3 Mechanism of Skin Penetration

Transfersomes migrate through the skin via:

1. Osmotic gradient-driven transport
2. Intercellular diffusion
3. Vesicular deformation
4. Lipid interaction

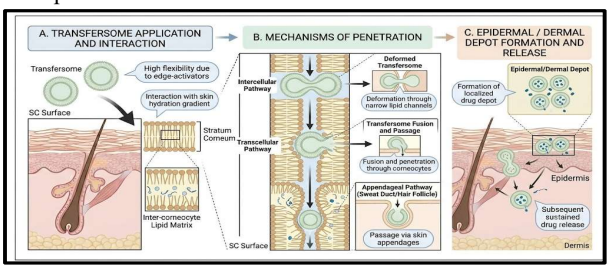

Figure 9. Penetration pathways of transfersomes through the stratum corneum.

As depicted in Figure 9, transfersomes penetrate considerably deeper than conventional liposomes [20].

10.4 Transfersomal Formulations for Psoriasis

Recent investigations have demonstrated enhanced therapeutic performance of transfersomal formulations containing:

- Methotrexate
- Curcumin
- Tacrolimus
- Cyclosporine

Table 8. Selected transfersomal formulations for psoriasis.

S.N	Drug	Vesicle Size (nm)	Entrapment (%)	Outcome
1	Methotrexate	120–180	70–85	Improved retention
2	Curcumin	150–220	>80	Reduced inflammation
3	Tacrolimus	100–170	>75	Enhanced penetration
4	Cyclosporine	130–210	>80	Better lesion targeting

The therapeutic improvements summarized in Table 8 have been attributed primarily to enhanced deformability and epidermal deposition [21].

11. ETHOSOMES

11.1 Introduction

Ethosomes are soft vesicular systems containing high concentrations of ethanol (20–45%) combined with phospholipids and water [22].

Their development represented a major breakthrough in topical delivery because ethanol simultaneously enhances skin permeability and vesicle flexibility.

11.2 Composition and Structural Characteristics

Typical ethosomal formulations comprise:

- Phospholipids
- Ethanol
- Water
- Optional stabilizers

The high ethanol content shown in Figure 10 differentiates ethosomes from conventional liposomes.

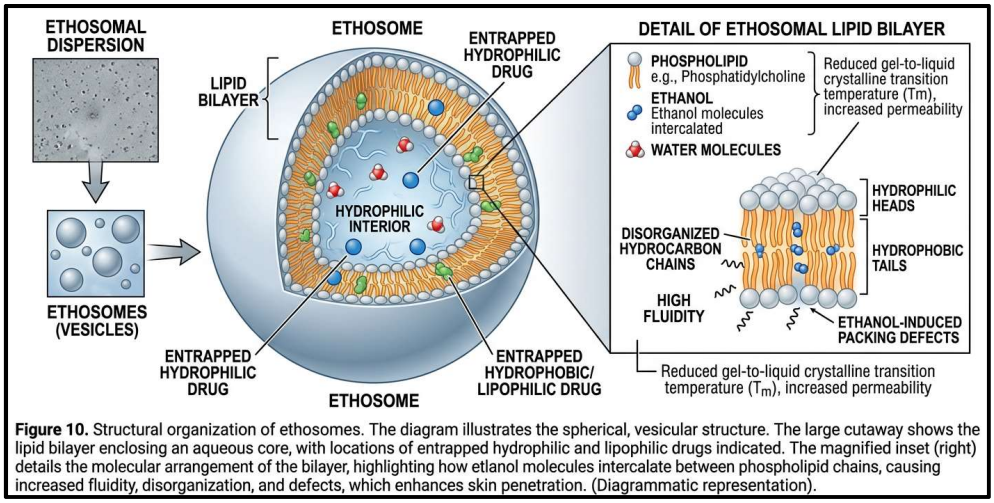

Figure 10. Structural organization of ethosomes. The diagram illustrates the spherical, vesicular structure. The large cutaway shows the lipid bilayer enclosing an aqueous core, with locations of entrapped hydrophilic and lipophilic drugs indicated. The magnified inset (right) details the molecular arrangement of the bilayer, highlighting how etlanol molecules intercalate between phospholipid chains, causing increased fluidity, disorganization, and defects, which enhances skin penetration. (Diagrammatic representation).

Figure 10. Structural organization of Ethosomes.

11.3 Ethanol-Mediated Penetration Enhancement

Ethanol improves delivery by:

- Fluidizing stratum corneum lipids
- Increasing membrane permeability
- Reducing lipid packing density
- Enhancing vesicle flexibility

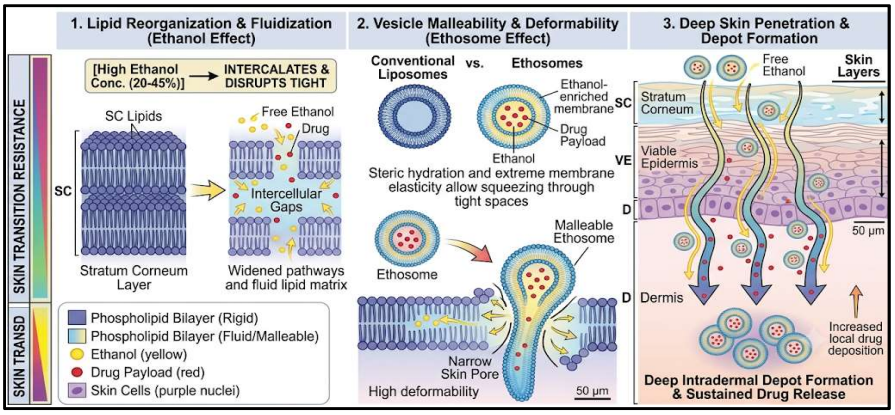

Figure 11. Mechanism of ethosomal penetration.

The dual penetration mechanism depicted in Figure 11 involves both ethanol-mediated lipid disruption and vesicular transport [22].

11.4 Ethosomal Systems for Psoriasis

Ethosomes have been investigated for delivery of:

- Acitretin
- Curcumin
- Tryptanthrin
- Methotrexate
- Cyclosporine

Table 9. Ethosomal formulations reported for psoriasis treatment.

S.N	Drug	Entrapment (%)	Major Outcome
1	Acitretin	>80	Improved lesion reduction
2	Curcumin	>85	Reduced inflammatory markers
3	Methotrexate	>75	Enhanced deposition
4	Tryptanthrin	>80	Significant anti-psoriatic activity

As shown in Table 9, ethosomal formulations consistently demonstrate superior penetration compared with conventional liposomes [23].

12. TRANSETHOSOMES

12.1 Evolution of Ethosomes

Transethosomes combine the advantages of ethosomes and transfersomes through incorporation of both ethanol and edge activators [24].

This design creates highly flexible vesicles with exceptional penetration capability.

12.2 Composition

Transethosomes generally contain:

- Phospholipids
- Ethanol
- Edge activators
- Water

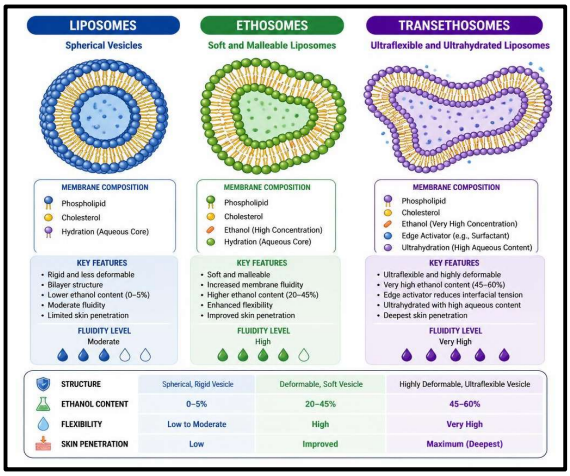

Figure 12. Comparative structure of Liposomes, Ethosomes and Transethosomes

The compositional differences illustrated in Figure 12 explain the progressively increasing deformability observed from liposomes to transethosomes.

12.3 Mechanism of Enhanced Delivery

Transethosomes improve delivery through:

1. Ethanol-induced lipid fluidization
2. Edge activator-mediated elasticity
3. Vesicular penetration
4. Enhanced drug deposition

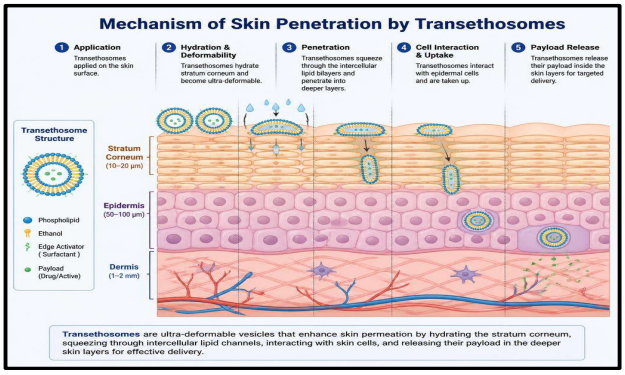

Figure 13. Skin penetration mechanism of transethosomes.

As shown in Figure 13, transethosomes combine the penetration mechanisms of both transfersomes and ethosomes.

12.4 Application in Psoriasis

Recent studies indicate superior performance of transethosomes for delivering:

- Curcumin
- Tacrolimus
- Boswellic acids
- Methotrexate

Table 10. Advantages of transethosomes compared with other vesicles.

S.N	Parameter	Liposomes	Transfersomes	Ethosomes	Transethosomes
1	Deformability	Low	High	Moderate	Very High
2	Ethanol Content	No	No	Yes	Yes
3	Edge Activators	No	Yes	No	Yes
4	Penetration Ability	Moderate	High	High	Very High
5	Drug Retention	Moderate	High	High	Very High

The comparative analysis presented in Table 10 demonstrates why transethosomes are increasingly regarded as one of the most promising vesicular systems for psoriasis therapy [24].

The evolution from conventional liposomes to transethosomes reflects a continuous effort to improve penetration efficiency, vesicle flexibility, drug retention, and therapeutic performance.

13. COMPARATIVE ASSESSMENT OF FIRST- AND SECOND-GENERATION NANOVESICLES

Table 11. Comparative overview of nanovesicular systems.

S.N	Parameter	Liposomes	Niosomes	Trans fersomes	Ethosomes	Trans ethosomes
1	Flexibility	Low	Moderate	High	High	Very High
2	Stability	Moderate	High	Moderate	High	High
3	Skin Penetration	Moderate	Moderate	High	High	Very High
4	Drug Retention	Moderate	Good	High	High	Very High
5	Clinical Potential	Good	Good	Excellent	Excellent	Excellent

As summarized in Table 11, transethosomes currently represent one of the most advanced vesicular systems among those discussed in this section. Nevertheless, further modifications have led to the emergence of glycerosomes, hyalurosomes, and invasomes, which will be discussed in the next section.

ADVANCED NANOVESICULAR SYSTEMS FOR PSORIASIS MANAGEMENT: GLYCEROSOMES, HYALUROSOMES, INVASOMES AND PHYSICOCHEMICAL CHARACTERIZATION:

14. GLYCEROSOMES: AN EMERGING GENERATION OF SOFT NANOVESICLES

14.1 Introduction and Rationale

Despite significant advances in liposomes, transfersomes, and ethosomes, challenges related to vesicle stability, skin hydration, and drug retention continue to limit clinical translation. To address these limitations, researchers developed glycerosomes, a modified liposomal system enriched with glycerol. The incorporation of glycerol imparts increased membrane fluidity, enhanced hydration potential, and improved vesicle deformability, thereby facilitating deeper penetration into psoriatic skin lesions [25,26].

Psoriatic skin is characterized by excessive transepidermal water loss (TEWL), disrupted lipid organization, and impaired barrier function. Consequently, glycerol-containing vesicles are particularly attractive because glycerol acts as both a humectant and penetration enhancer. By maintaining skin hydration and improving vesicle elasticity, glycerosomes can promote prolonged retention of anti-psoriatic agents within diseased tissues [25].

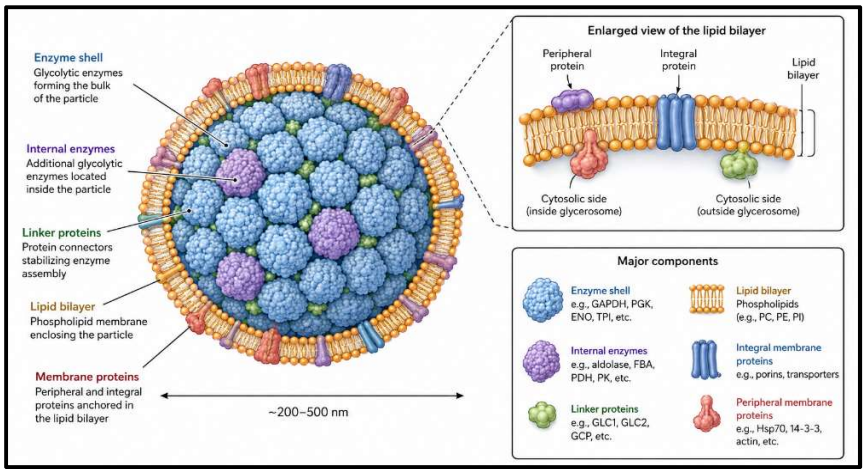

Figure 14. Structural organization of glycerosomes.

Figure 14 illustrate the following key parameters for glycerosomes:

- Phospholipid bilayer
- Glycerol molecules intercalated within the bilayer
- Encapsulated drug
- Enhanced membrane fluidity

As depicted in Figure 14, glycerol molecules alter phospholipid packing, producing a more flexible vesicular structure than conventional liposomes.

14.2 Composition and Preparation

Typical glycerosomal formulations consist of:

- Phosphatidylcholine
- Cholesterol (optional)
- Glycerol (10–30%)
- Water
- Active pharmaceutical ingredient

The most common preparation techniques include:

- Thin-film hydration
- Direct hydration method
- Sonication-assisted preparation
- Extrusion techniques

Table 12. Comparative characteristics of Liposomes and Glycerosomes.

S.N	Parameter	Liposomes	Glycerosomes
1	Glycerol content	Absent	Present
2	Membrane flexibility	Moderate	High
3	Hydration capacity	Moderate	Excellent
4	Skin retention	Moderate	Enhanced
5	Stability	Moderate	Improved

The comparative features summarized in Table 12 demonstrate the advantages of glycerosomes in treating inflammatory skin disorders [25].

14.3 Potential Applications in Psoriasis

Although glycerosomes have been more extensively investigated for antioxidant and anti-inflammatory compounds, recent evidence suggests considerable potential for psoriasis therapy.

Glycerosomal systems have demonstrated improved dermal localization of Curcumin, Resveratrol, Quercetin, Boswellic acids, Corticosteroids.

The enhanced hydration associated with glycerosomes may be particularly beneficial in psoriasis, where restoration of barrier function represents an important therapeutic objective [26].

15. HYALUROSOMES: HYALURONIC ACID-BASED VESICULAR SYSTEMS

15.1 Concept and Design

Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan widely distributed throughout the extracellular matrix. It plays essential roles in tissue hydration, wound healing, inflammation modulation, and cellular signaling.

Hyalurosomes are phospholipid vesicles modified with hyaluronic acid to improve biological interactions with skin tissues [27].

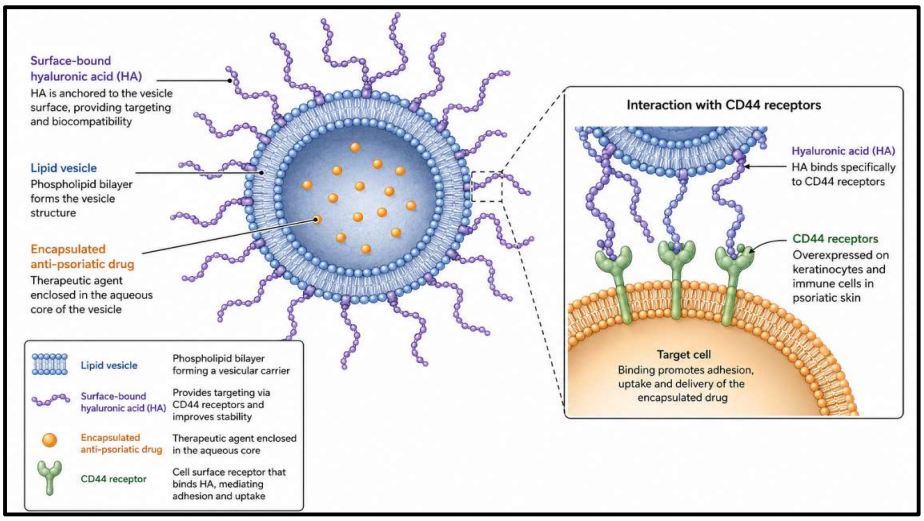

Figure 15. Structure of Hyalurosomes.

As shown in Figure 15, surface-associated hyaluronic acid facilitates receptor-mediated interactions with keratinocytes and immune cells.

15.2 Mechanisms Relevant to Psoriasis

Several characteristics make hyalurosomes attractive for psoriasis therapy:

1. Enhanced skin hydration

Hyaluronic acid exhibits remarkable water-retention capacity, improving hydration of psoriatic lesions.

2. Anti-inflammatory effects

HA can modulate inflammatory responses and support tissue repair processes.

3. Cd44 receptor interaction

Keratinocytes express CD44 receptors that bind hyaluronic acid. This interaction may facilitate enhanced localization of vesicles within epidermal tissues [27].

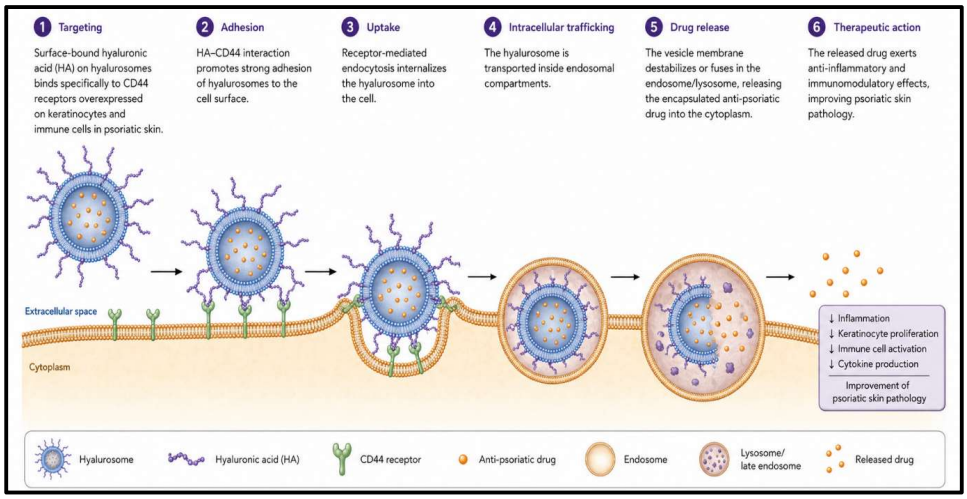

Figure 16. Proposed mechanism of hyalurosome-mediated drug delivery.

The interaction illustrated in Figure 16 demonstrates receptor-mediated retention and prolonged residence within diseased skin.

15.3 Applications in Dermatological Disorders

Studies have reported successful incorporation of following into hyalurosomal carriers.

- Curcumin
- Resveratrol
- Dexamethasone
- Natural polyphenols
- Antioxidants

Table 13. Advantages of hyalurosomes in topical drug delivery.

S.N	Advantage	Therapeutic Significance
1	Improved hydration	Restoration of barrier function
2	Receptor targeting	Enhanced retention
3	Anti-inflammatory activity	Reduced cytokine production
4	Biocompatibility	Excellent safety profile
5	Controlled release	Sustained therapeutic effect

The properties summarized in Table 13 suggest that hyalurosomes may represent promising carriers for future psoriasis formulations.

16. INVASOMES: ADVANCED TERPENE-ENRICHED NANOVESICLES

16.1 Introduction

Among currently available vesicular systems, invasomes are considered one of the most advanced nanovesicular platforms for dermal and transdermal drug delivery. These carriers combine phospholipids, ethanol, and terpenes to achieve superior penetration enhancement and vesicle flexibility [28].

The term "invasome" reflects the ability of these vesicles to invade deeper skin layers more effectively than conventional liposomes and ethosomes.

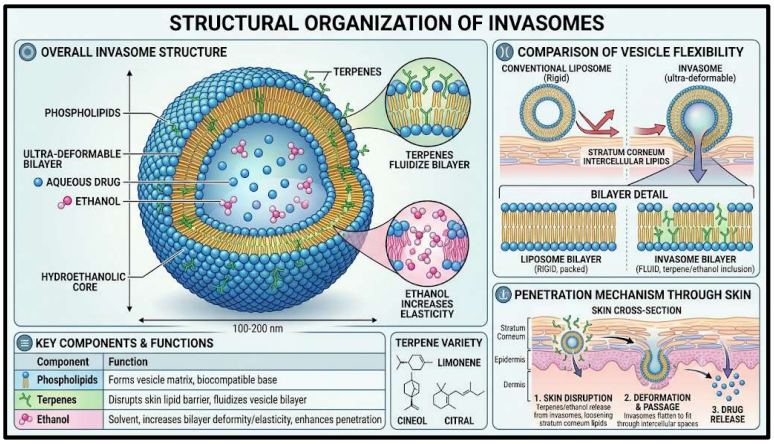

Figure 17. Structural organization of Invasomes.

The structure illustrated in Figure 17 highlights the synergistic combination responsible for enhanced skin penetration.

16.2 Composition of Invasomes

Typical invasomal formulations contain:

Phospholipids

Provide structural integrity and biocompatibility.

Ethanol

Enhances membrane fluidity and disrupts stratum corneum lipids.

Terpenes

Table 14. Common terpenes used in invasomal formulations.

S.N	Terpene	Source	Major Function
1	Limonene	Citrus oils	Lipid disruption
2	Cineole	Eucalyptus oil	Enhanced permeation
3	Citral	Lemongrass oil	Barrier modulation
4	Menthol	Peppermint oil	Penetration enhancement
5	Nerolidol	Essential oils	Lipid fluidization

Terpenes act as potent penetration enhancers. Common terpenes include Limonene, Cineole, Citral, Nerolidol, Menthol, Fenchone etc.

The terpenes listed in Table 14 possess distinct physicochemical properties that influence skin permeation behavior [29].

17. MECHANISMS OF INVASOMAL SKIN PENETRATION

The superior performance of invasomes results from three complementary mechanisms.

17.1 Ethanol-Induced Lipid Fluidization

Ethanol disrupts highly ordered lipid domains within the stratum corneum, increasing membrane permeability [30].

17.2 Terpene-Mediated Barrier Modification

Terpenes partition into intercellular lipid regions and reduce lipid packing density, creating transient permeation pathways.

17.3 Vesicle Deformability

Flexible invasomal membranes permit passage through microscopic skin channels. Figure 18 explain following triple penetration mechanism of inavasomes.

1. Ethanol-Induced Lipid Disruption

2. Terpene Penetration Enhancement

3. Deformable Vesicle Migration

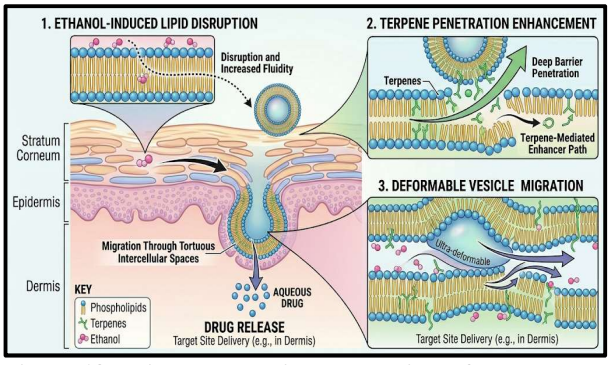

Figure 18. Triple penetration mechanism of Invasomes.

The synergistic effects explain the superior penetration performance of invasomes compared with earlier vesicular systems.

18. PREPARATION METHODS OF INVASOMES

Several approaches have been employed for invasome fabrication.

The methods summarized in Table 15 influence vesicle size, entrapment efficiency, and stability.

Table 15. Methods used for invasome preparation.

S.N	Method	Principle	Advantages
1	Thin-film hydration	Lipid film hydration	Simple
2	Mechanical dispersion	Direct mixing	Cost-effective
3	Ethanol injection	Solvent displacement	Reproducible
4	Sonication	Size reduction	Uniform vesicles
5	Extrusion	Controlled sizing	Narrow distribution

19. PHYSICOCHEMICAL CHARACTERIZATION OF NANOVESICULAR SYSTEMS

Successful development of vesicular formulations requires comprehensive physicochemical characterization.

19.1 Vesicle Size Analysis

Particle size significantly influences penetration behavior and drug deposition.

Recommended Technique

- Dynamic Light Scattering (DLS)

Desired Range: 100–300 nm.

Smaller vesicles generally demonstrate enhanced penetration through psoriatic skin [31].

19.2 Polydispersity Index (PDI)

PDI reflects size uniformity.

Acceptance Criteria and its interpretation for PDI is as below:

- IF PDI <0.2: Excellent uniformity
- If PDI =0.2- 0.3: Acceptable
- If PDI >0.4: Broad distribution

19.3 Zeta Potential

Zeta potential provides information regarding colloidal stability.

Table 16. Interpretation of Zeta potential.

S.N	Zeta Potential (mV)	Stability
1	±10	Poor
2	±20	Moderate
3	±30 or greater	Good
4	±40 or greater	Excellent

The values presented in Table 16 are widely accepted indicators of vesicular stability.

19.4 Morphological Characterization:

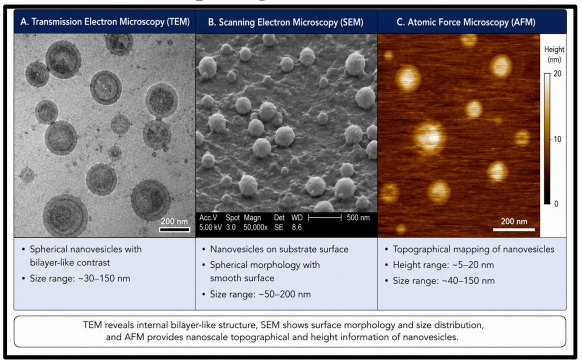

Figure 19. Representative microscopic evaluation of nanovesicles.

Techniques include:

- Transmission Electron Microscopy (TEM)
- Scanning Electron Microscopy (SEM)
- Atomic Force Microscopy (AFM)

The images shown in Figure 19 should confirm vesicle shape, surface morphology, and structural integrity.

19.5 Entrapment Efficiency

Entrapment efficiency reflects the percentage of drug successfully encapsulated.

Equation:

Entrapment Efficiency (%) = (Entrapped Drug / Total Drug) × 100

High entrapment efficiency is desirable for reducing dosing frequency and maximizing therapeutic outcomes.

19.6 Differential Scanning Calorimetry (DSC)

DSC evaluates:

- Drug–excipient compatibility
- Phase transitions
- Vesicle organization

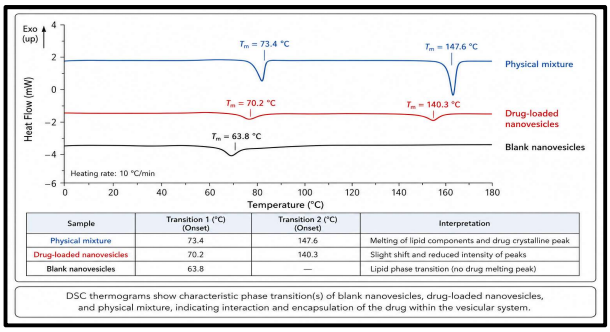

Figure 20. Representative DSC thermograms.

The thermograms depicted in Figure 20 provide evidence of successful drug incorporation.

19.7 FTIR Spectroscopy

FTIR analysis is employed to evaluate:

Functional group interactions

Chemical stability

Compatibility

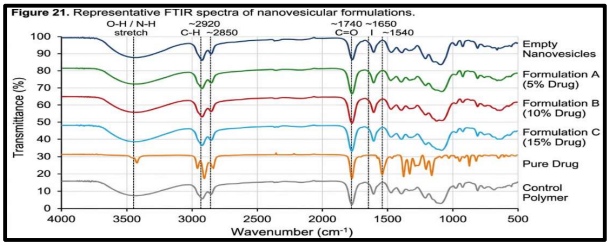

Figure 21. Representative FTIR spectra of nanovesicular formulations.

20. COMPARATIVE ASSESSMENT OF ADVANCED VESICULAR SYSTEMS

The comparison shown in Table 17 highlights invasomes as the most promising system for overcoming psoriasis-associated skin barriers.

Table 17. Comparative evaluation of advanced nanovesicles.

S.N	Parameter	Glycerosomes	Hyalurosomes	Invasomes
1	Hydration capability	Excellent	Excellent	Moderate
2	Targeting ability	Moderate	High	Moderate
3	Skin penetration	High	High	Very High
4	Deformability	High	Moderate	Very High
5	Psoriasis suitability	High	High	Outstanding
6	Clinical translation potential	Good	Good	Excellent

21. EMERGING ROLE OF BOSWELLIC ACID-LOADED INVASOMES IN PSORIASIS

Boswellic acids, particularly 3-O-acetyl-11-keto-β-boswellic acid (AKBA), possess potent anti-inflammatory activity through inhibition of 5-lipoxygenase, NF-κB signaling, and pro-inflammatory cytokine production [32].

However, poor aqueous solubility and limited skin permeation have restricted their therapeutic application.

Invasomal delivery offers several advantages:

- Enhanced epidermal deposition
- Improved penetration
- Sustained release
- Reduced systemic exposure

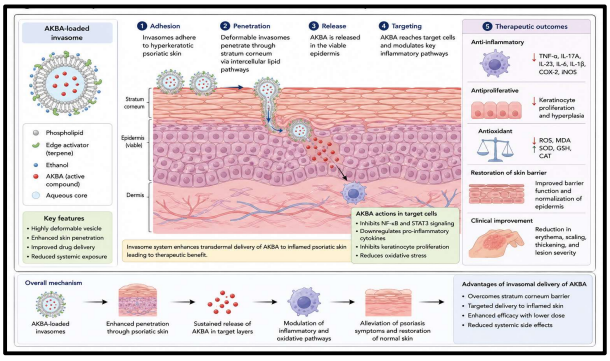

Figure 22. Proposed mechanism of AKBA-loaded invasomes in psoriasis.

The mechanism illustrated in Figure 22 depicts:

- Enhanced penetration
- Cytokine suppression
- Reduced keratinocyte proliferation
- Restoration of skin barrier function

These findings provide strong justification for continued investigation of AKBA-loaded invasomes as next-generation anti-psoriatic formulations.

PRECLINICAL EVALUATION, SKIN PENETRATION ASSESSMENT, IN VIVO ANTI-PSORIATIC EFFICACY, AND SAFETY EVALUATION OF NANOVESICULAR SYSTEMS

22. PRECLINICAL EVALUATION STRATEGIES FOR NANOVESICULAR ANTI-PSORIATIC SYSTEMS

Successful translation of nanovesicular formulations from laboratory development to clinical application requires comprehensive preclinical evaluation. Unlike conventional topical formulations, nanovesicular systems must demonstrate not only drug release and stability but also enhanced skin penetration, selective deposition within diseased tissues, biological efficacy, and safety. The preclinical evaluation workflow typically includes:

1. In vitro drug release studies
2. Ex vivo skin permeation studies
3. Skin deposition studies
4. Confocal imaging investigations
5. Cellular uptake studies
6. In vivo efficacy studies
7. Histopathological assessment
8. Toxicological evaluation

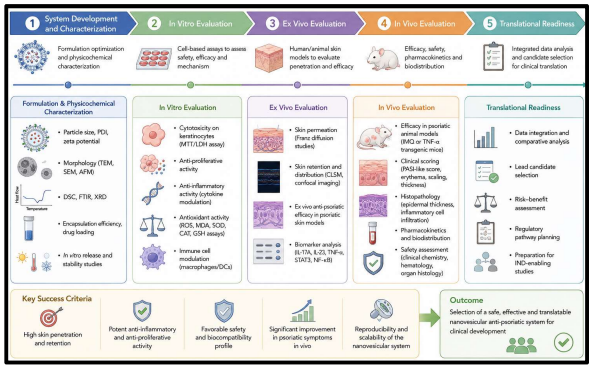

Figure 23. Preclinical evaluation roadmap for nanovesicular anti-psoriatic systems.

As shown in Figure 23, comprehensive evaluation is necessary to establish both efficacy and safety before advancing toward clinical studies [33].

23. IN VITRO DRUG RELEASE STUDIES

23.1 Importance of Drug Release Evaluation

Drug release studies provide critical information regarding:

- Release kinetics
- Diffusion behavior
- Stability of drug encapsulation
- Prediction of therapeutic performance

For psoriasis treatment, sustained release is particularly desirable because it minimizes dosing frequency and improves patient compliance [34].

23.2 Experimental Methodologies

The most frequently employed methods include:

Dialysis Bag Method

Drug-loaded vesicles are enclosed within a dialysis membrane and immersed in release medium.

Franz Diffusion Cell Method

Widely accepted for topical formulations.

USP Apparatus-Based Methods

Useful for comparative studies.

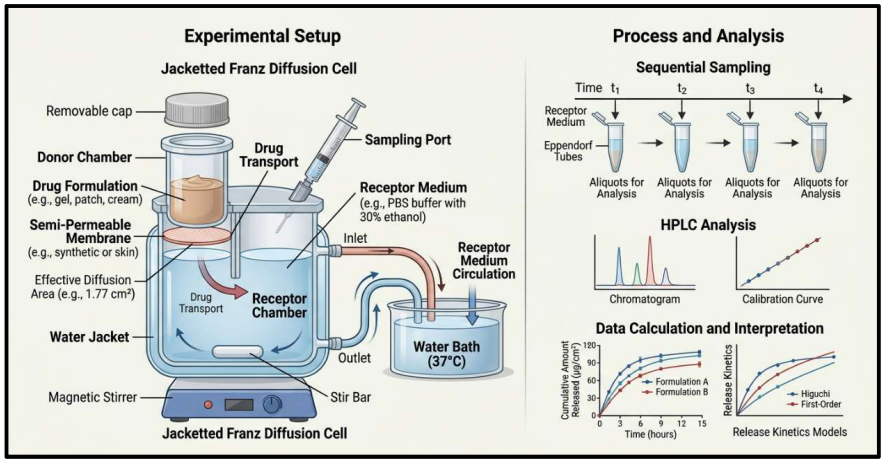

Figure 24. Schematic representation of drug release evaluation using Franz diffusion cells.

The experimental setup illustrated in Figure 24 is commonly used for comparing release profiles of nanovesicular formulations and conventional products.

23.3 Release Kinetics Models

Drug release data are generally fitted to various mathematical models which are summarized in Table 18.

Table 18. Mathematical models used in release kinetics analysis.

S.N	Model	Equation	Interpretation
1	Zero-order	$Qt = Q0 + K0t$	Constant release
2	First-order	Log Qt	Concentration dependent
3	Higuchi	$Qt = KH\sqrt{t}$	Diffusion-controlled
4	Korsmeyer-Peppas	$Mt/M\infty = Ktn$	Mechanistic analysis

The models summarized in Table 18 assist in understanding the mechanisms governing drug release from vesicular systems [35].

24. EX VIVO SKIN PERMEATION STUDIES

24.1 Importance

Ex vivo permeation studies bridge the gap between in vitro testing and in vivo evaluation.

These studies determine:

- Drug permeation rate
- Skin retention
- Flux
- Permeability coefficient

The information obtained is particularly important for psoriasis because local skin deposition is generally preferred over systemic absorption [36].

24.2 Skin Models Used

As shown in Table 19, porcine skin is frequently considered the most appropriate surrogate for human skin [36].

Table 19. Biological membranes employed in permeation studies.

S.N	Model	Advantages	Limitations
1	Human skin	Closest to clinical condition	Limited availability
2	Porcine skin	Similar permeability to human skin	Variability
3	Rat skin	Readily available	Different barrier properties
4	Mouse skin	Convenient	More permeable than human skin

24.3 Franz Diffusion Cell Studies

The Franz diffusion cell remains the gold standard for evaluating skin permeation. Figure 25 depicts the different parts like:

- Donor compartment
- Skin membrane
- Receptor compartment
- Sampling port
- Magnetic stirring system

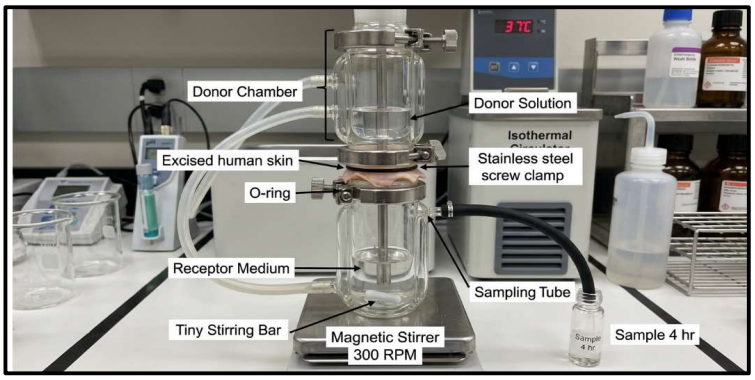

Figure 25. Franz diffusion cell setup for skin permeation studies.

The arrangement illustrated in Figure 25 enables quantitative assessment of drug transport through skin tissues.

Numerous investigations have demonstrated superior permeation characteristics for ultradeformable vesicles.

24.4 Comparative Permeation of Nanovesicles

Table 20. Relative skin penetration capability of nanovesicular systems.

S.N	Vesicle Type	Relative Penetration
1	Liposomes	Moderate
2	Niosomes	Moderate
3	Transfersomes	High
4	Ethosomes	High
5	Transethosomes	Very High
6	Invasomes	Very High

The comparative trends summarized in Table 20 consistently support the superior performance of invasomes and transethosomes [37].

25. SKIN DEPOSITION STUDIES

25.1 Significance

For psoriasis treatment, therapeutic success depends largely on drug accumulation within:

- Stratum corneum
- Epidermis
- Dermis

rather than systemic circulation.

Consequently, skin deposition studies are considered more clinically relevant than permeation studies alone [38].

25.2 Tape Stripping Technique

The tape stripping method is widely employed for quantifying drug distribution within different skin layers.

Figure 26. Tape stripping procedure for determination of skin deposition.

The process illustrated in Figure 26 allows sequential removal of stratum corneum layers for drug analysis.

25.3 Findings from Recent Studies

Recent investigations involving Methotrexate, Curcumin, Tacrolimus, Acitretin, Boswellic acids have demonstrated significantly higher epidermal retention following encapsulation within nanovesicular systems compared with conventional formulations [39].

26. ADVANCED SKIN IMAGING TECHNIQUES

26.1 Confocal Laser Scanning Microscopy (CLSM)

CLSM has become one of the most powerful tools for visualizing vesicular penetration.

Fluorescent dyes such as Rhodamine B, Nile Red and Coumarin-6 are frequently incorporated into vesicles.

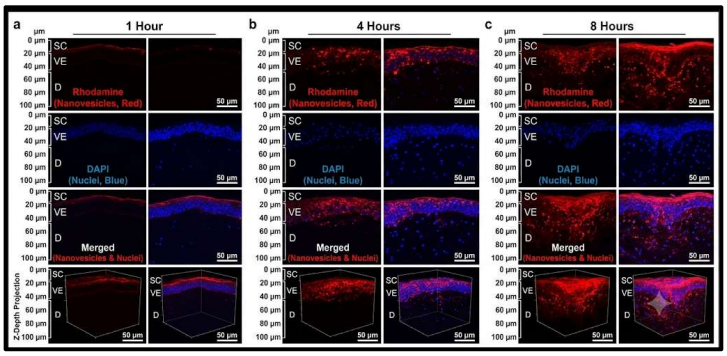

Figure 27. Representative CLSM images of nanovesicle penetration through skin.

The images shown in Figure 27 should demonstrate progressively deeper penetration of transfersomes, ethosomes, transethosomes, and invasomes compared with conventional liposomes.

26.2 Multiphoton Microscopy

Advantages include:

- High spatial resolution
- Minimal photodamage
- Real-time imaging

This technique provides valuable information regarding vesicle localization within skin tissues [40].

26.3 Raman Imaging

Confocal Raman microscopy enables non-invasive evaluation of following parameter without requiring fluorescent labels.

- Drug distribution
- Lipid organization
- Skin hydration

The techniques illustrated in Figure 28 collectively provide mechanistic evidence supporting enhanced penetration of ultradeformable vesicles.

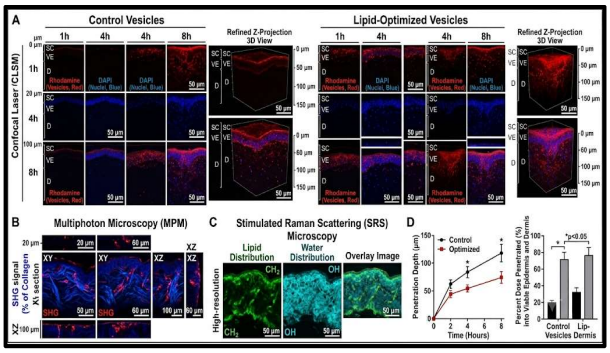

Figure 28. Advanced imaging techniques used for nanovesicular penetration studies.

27. CELLULAR EVALUATION OF NANOVESICULAR SYSTEMS

27.1. Keratinocyte-Based Models

Human keratinocyte cell lines such as HaCaT cells, NHEK cells are frequently employed. These models help evaluate Cytotoxicity, Cellular uptake and Anti-inflammatory activity.

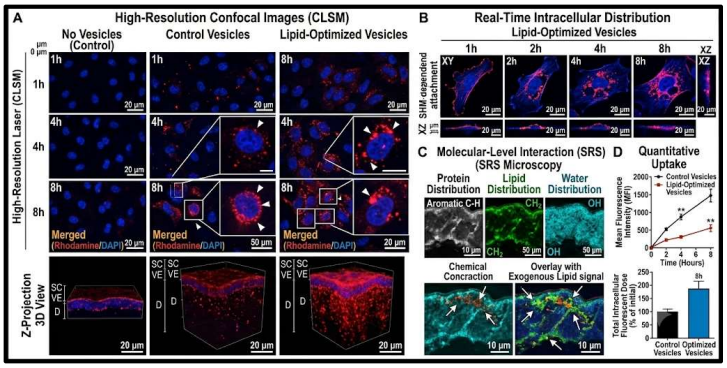

Figure 29. Cellular uptake of fluorescent nanovesicles by keratinocytes.

The uptake process illustrated in Figure 29 demonstrates enhanced internalization of nanosized vesicles.

27.2 Cytotoxicity Assessment

Common cytotoxicity assays are included in Table 21.

Table 21. Cytotoxicity assays used in nanovesicular research.

S.N	Assay	Endpoint
1	MTT	Cell viability
2	Alamar Blue	Metabolic activity
3	LDH release	Membrane integrity
4	Annexin V	Apoptosis

The assays summarized in Table 21 are routinely used to establish formulation safety [41].

28. ANIMAL MODELS FOR PSORIASIS RESEARCH

28.1 Importance of In Vivo Models

Animal models remain indispensable for evaluating following factors before human studies:

- Anti-inflammatory activity
- Psoriasis-like lesion reduction
- Drug deposition
- Safety

28.2 Imiquimod-Induced Psoriasis Model

The imiquimod (IMQ)-induced model is currently considered the most widely accepted experimental model. Application of IMQ cream induces Epidermal hyperplasia, Scaling Erythema, Cytokine overexpression closely resembling human plaque psoriasis [42].

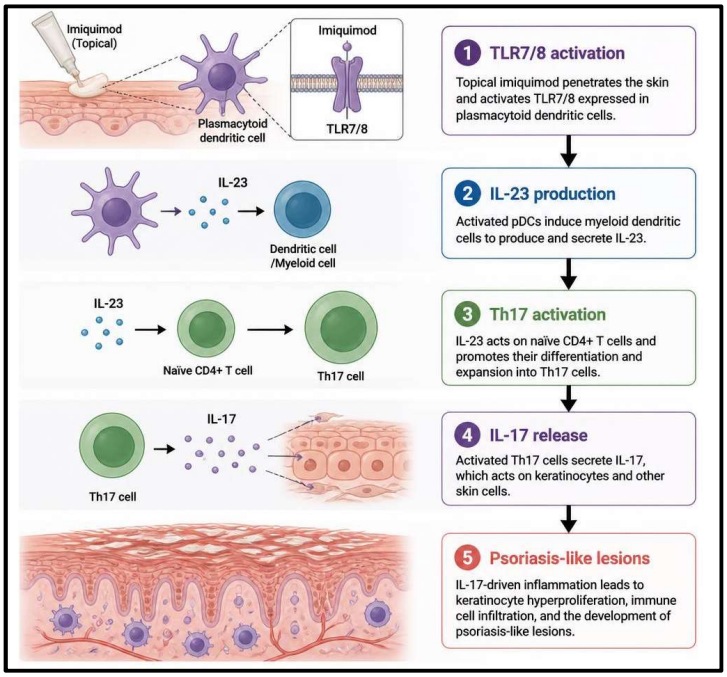

Figure 30. Pathogenesis of the imiquimod-induced psoriasis model.

28.3 Other Animal Models:

Table 22. Commonly employed animal models.

S.N	Model	Application
1	Imiquimod-induced	Plaque psoriasis
2	Xenograft model	Human skin evaluation
3	Transgenic model	Mechanistic studies
4	Cytokine-induced model	Pathway analysis

The IMQ model remains the most frequently reported model in contemporary nanovesicular psoriasis research.

29. IN VIVO ANTI-PSORIATIC EFFICACY OF NANOVESICULAR SYSTEMS

Recent studies have demonstrated significant therapeutic benefits associated with vesicular carriers.

Observed improvements include:

- Reduced erythema
- Reduced scaling
- Reduced epidermal thickness
- Lower PASI-like scores
- Decreased cytokine expression

Table 23. Comparative anti-psoriatic efficacy of nanovesicular systems.

S.N	Parameter	Conventional Formulation	Nanovesicular Formulation
1	Skin retention	Low	High
2	Epidermal deposition	Moderate	High
3	Cytokine suppression	Moderate	Significant
4	Therapeutic efficacy	Moderate	Superior
5	Dosing frequency	Frequent	Reduced

The outcomes summarized in Table 23 support the therapeutic superiority of nanovesicular formulations [43].

30. HISTOPATHOLOGICAL EVALUATION

Histological examination remains a critical endpoint in psoriasis studies.

Parameters Evaluated

- Epidermal thickness
- Hyperkeratosis
- Parakeratosis
- Inflammatory infiltration

- Angiogenesis

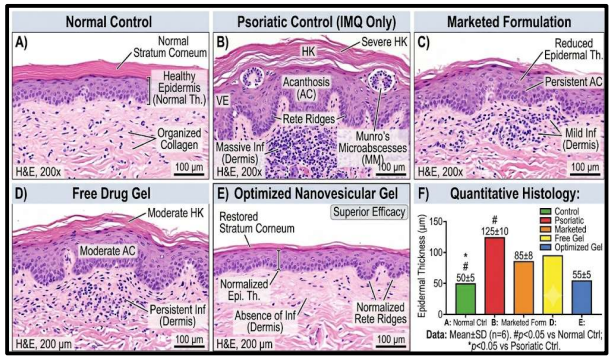

Figure 31. Histopathological comparison of normal, psoriatic, and treated skin.

The micrographs shown in Figure 31 should demonstrate reversal of pathological alterations following treatment.

31.1 Skin Irritation Studies

Skin irritation is commonly assessed according to OECD guidelines.

Parameters

- Erythema
- Edema
- Sensitization

Most phospholipid-based vesicular systems demonstrate excellent dermal compatibility [44].

31.2 Hemocompatibility

Although topical administration minimizes systemic exposure, evaluation of hemocompatibility is often performed during translational development.

31.3 Long-Term Safety

The safety parameters listed in Table 24 are essential components of preclinical assessment.

31. SAFETY AND TOXICOLOGICAL EVALUATION

Table 24. Safety parameters evaluated during preclinical studies.

S.N	Parameter	Purpose
1	Skin irritation	Local safety
2	Histopathology	Tissue compatibility
3	Cytotoxicity	Cellular safety
4	Hemocompatibility	Systemic compatibility
5	Stability studies	Product quality

32. COMPARATIVE PERFORMANCE OF NANOVESICULAR SYSTEMS IN PSORIASIS:

The comparative assessment presented in Table 25 indicates that invasomes and transethosomes currently represent the most promising nanovesicular platforms for psoriasis therapy.

Table 25. Overall comparison of nanovesicular systems investigated for psoriasis.

S.N	Parameter	Liposomes	Niosomes	Transfersomes	Ethosomes	Trans ethosomes	Invasomes
1	Skin Penetration	Moderate	Moderate	High	High	Very High	Very High
2	Retention	Moderate	Good	High	High	Very High	Very High
3	Deformability	Low	Moderate	High	Moderate	High	Very High
4	Stability	Moderate	High	Moderate	High	High	High
5	Psoriasis Potential	Good	Good	Excellent	Excellent	Excellent	Outstanding

CLINICAL TRANSLATION, REGULATORY LANDSCAPE, PATENTS, QUALITY BY DESIGN (QBD), ARTIFICIAL INTELLIGENCE, RESEARCH GAPS, FUTURE PERSPECTIVES AND CONCLUSIONS:

33. CLINICAL TRANSLATION OF NANOVESICULAR SYSTEMS FOR PSORIASIS MANAGEMENT

33.1 Current Status of Clinical Development

Although numerous nanovesicular systems have demonstrated promising outcomes in preclinical psoriasis models, successful clinical translation remains limited. The gap between laboratory findings and clinical implementation is attributable to challenges related to scale-up, manufacturing reproducibility, long-term stability, regulatory approval, and cost-effectiveness [45,46].

The majority of published studies involving liposomes, transfersomes, ethosomes, transethosomes, and invasomes remain at the preclinical stage. Only a limited number of vesicular formulations have progressed beyond the translational stages. Nevertheless, increasing evidence suggests that nanovesicular systems can significantly improve drug localization within psoriatic lesions while minimizing systemic exposure.

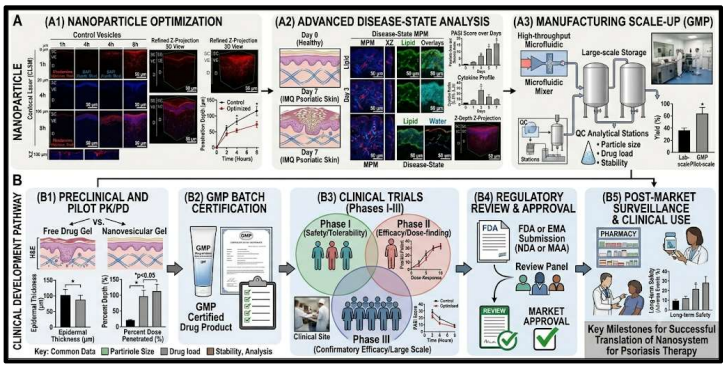

Figure 32. Translational pathway of nanovesicular anti-psoriatic systems.

33.2 Human Studies of Vesicular Systems

Clinical investigations involving topical vesicular formulations have reported:

- Improved skin hydration
- Enhanced lesion targeting
- Reduced erythema
- Improved patient compliance
- Reduced corticosteroid-associated adverse effects

However, large multicentric randomized controlled trials remain scarce [46].

Table 26. Clinical advantages of nanovesicular systems over conventional topical formulations.

S.N	Parameter	Conventional Formulations	Nanovesicular Systems
1	Skin penetration	Limited	Enhanced
2	Drug retention	Moderate	High
3	Dosing frequency	Frequent	Reduced
4	Systemic exposure	Possible	Minimized
5	Patient compliance	Moderate	Improved

The advantages summarized in Table 26 support continued clinical development of nanovesicular psoriasis therapies.

34. COMMERCIALLY AVAILABLE VESICULAR AND NANOCARRIER-BASED DERMATOLOGICAL PRODUCTS:

Although few products are specifically approved for psoriasis, several nanocarrier-based dermatological formulations have successfully reached the market, demonstrating the commercial feasibility of lipid-based delivery systems.

Table 27. Examples of marketed lipid-based dermatological products.

S.N	Product Type	Therapeutic Application
1	Liposomal formulations	Skin hydration and anti-inflammatory therapy
2	Nanoemulsion-based products	Dermal delivery
3	Lipid nanoparticles	Cosmetic and dermatological applications
4	Vesicular carriers	Localized skin targeting

The successful commercialization of these products indicates the feasibility of translating advanced vesicular systems into clinical practice [47].

35. PATENT LANDSCAPE IN NANOVESICULAR PSORIASIS THERAPY

35.1 Increasing Patent Activity

The past decade has witnessed substantial growth in intellectual property filings related to:

- Liposomal anti-psoriatic formulations
- Transfersomal drug delivery systems
- Ethosomal technologies
- Invasomal vesicles
- Hybrid nanocarriers

The trend illustrated in Figure 33 demonstrates increasing commercial interest in advanced vesicular technologies.

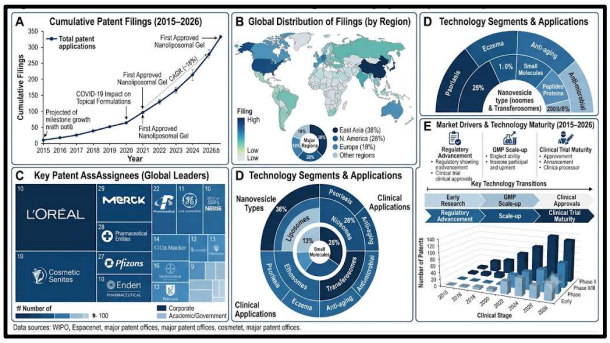

Figure 33. Global patent trends for nanovesicular dermatological delivery systems (2015-26).

35.2 Areas of Patent Protection

Commonly protected innovations include:

- Novel phospholipid compositions
- Terpene-based invasomes
- Combination drug therapies
- Controlled release systems

 Vesicle stabilization technologies

Table 28. Major areas of patent activity.

S.N	Technology Area	Commercial Interest
1	Liposomes	High
2	Transfersomes	High
3	Ethosomes	High
4	Invasomes	Very High
5	Hybrid Vesicles	Very High

The data summarized in Table 28 suggest that invasomes represent one of the most rapidly expanding intellectual property domains in dermal drug delivery.

36. REGULATORY CONSIDERATIONS FOR NANOVESICULAR DRUG DELIVERY SYSTEMS:

36.1 Challenges in Regulatory Approval

Unlike conventional topical formulations, nanomedicines require extensive characterization because therapeutic performance depends on multiple physicochemical parameters.

Critical quality attributes include:

 Particle size

 Polydispersity index

 Zeta potential

 Entrapment efficiency

 Morphology

 Stability

The framework illustrated in Figure 34 include Physicochemical Characterization, Safety Assessment, Efficacy Evaluation, Quality Control, and Regulatory Submission as a key steps for nanovascular products.

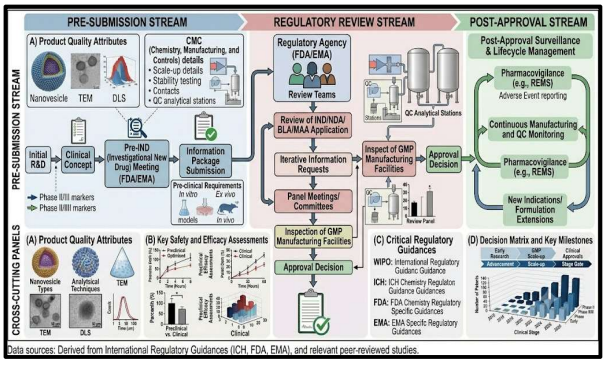

Figure 34: Regulatory evaluation framework for nanovesicular products

36.2 Regulatory Agencies

Major regulatory authorities involved in nanomedicine approval include:

 United States Food and Drug Administration (FDA)

 European Medicines Agency (EMA)

 International Council for Harmonisation (ICH)

 Central Drugs Standard Control Organization (CDSCO)

These agencies increasingly emphasize a risk-based approach for nanomedicine evaluation [48].

36.3 Regulatory Challenges Specific to Invasomes

Several challenges remain and some are stated in Table 29.

Table 29. Regulatory barriers for invasomal products.

S.N	Challenge	Regulatory Concern
1	Terpene variability	Batch-to-batch consistency
2	Vesicle deformability	Lack of standardized testing
3	Long-term stability	Product shelf life
4	Scale-up processes	Manufacturing reproducibility
5	Characterization methods	Analytical standardization

The issues presented in Table 29 represent major hurdles in commercialization.

37. QUALITY BY DESIGN (QBD) IN NANOVESICLE DEVELOPMENT

37.1 Concept of QbD:

Quality by Design (QbD) has emerged as a systematic approach for pharmaceutical product development. QbD involves:

 Defining target product profiles

 Identifying critical quality attributes (CQAs)

 Determining critical material attributes (CMAs)

 Establishing critical process parameters (CPPs)

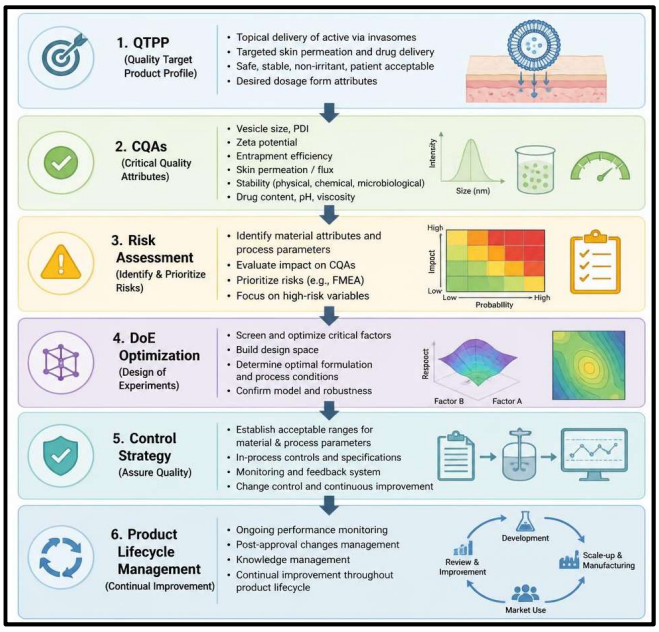

Figure 35. QbD framework for invasomal formulation development.

37.2 Critical Quality Attributes for Invasomes

The parameters listed in Table 30 are frequently incorporated into QbD-based optimization studies [49].

Table 30. Critical quality attributes of invasomal formulations.

S.N	CQA	Importance
1	Vesicle size	Skin penetration
2	PDI	Uniformity
3	Zeta potential	Stability
4	Entrapment efficiency	Drug loading
5	Deformability index	Penetration capability
6	Drug release profile	Therapeutic efficacy

38. ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN NANOVESICLE DESIGN

38.1 Emerging Role of AI

Artificial intelligence (AI) and machine learning (ML) are increasingly being applied to pharmaceutical formulation development.

Applications include:

- Formulation optimization
- Prediction of particle size
- Stability forecasting
- Drug release modeling
- Process optimization

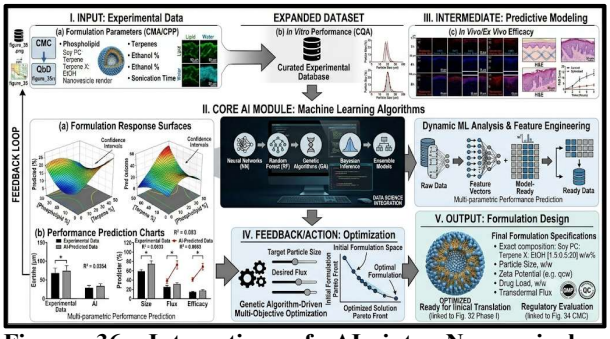

Figure 36. Integration of AI into Nanovesicular formulation development

38.2 Potential Applications in Psoriasis Nanomedicine

AI-assisted approaches may facilitate:

- Optimization of AKBA-loaded invasomes
- Prediction of skin permeation
- Identification of optimal terpene combinations
- Personalized topical therapy

Table 31. Potential AI applications in nanovesicular psoriasis research.

S.N	Application	Expected Benefit
1	Formulation optimization	Reduced experimentation
2	Stability prediction	Faster development
3	Skin permeation modeling	Improved targeting
4	Clinical response prediction	Personalized therapy

The applications summarized in Table 31 are expected to accelerate translational nanomedicine research.

39. RESEARCH GAPS IN NANOVESICULAR PSORIASIS THERAPY

Despite encouraging progress, several gaps remain.

Table 32. Research gaps and future opportunities.

S.N	Research Gap	Future Direction
1	Limited clinical trials	Multicentric RCTs
2	Lack of standardized characterization	Harmonized guidelines
3	Scale-up challenges	Continuous manufacturing
4	Regulatory uncertainty	Specific nanomedicine frameworks
5	Long-term safety data	Chronic exposure studies
6	Comparative clinical studies	Head-to-head evaluations

The research gaps identified in Table 32 highlight areas requiring further investigation before widespread clinical adoption.

40. FUTURE PERSPECTIVES

Several emerging trends are expected to shape the next generation of psoriasis nanomedicines.

40.1 Stimuli-Responsive Vesicles

Future vesicles may respond to:

- pH
- Temperature
- Oxidative stress
- Inflammatory mediators

40.2 Targeted Nanovesicles

Potential targets include:

- CD44 receptors
- IL-17 signaling pathways
- Keratinocyte-specific receptors

40.3 Combination Therapy

Co-delivery of drugs may provide synergistic therapeutic benefits.

- AKBA
- Curcumin
- Methotrexate
- Biologics

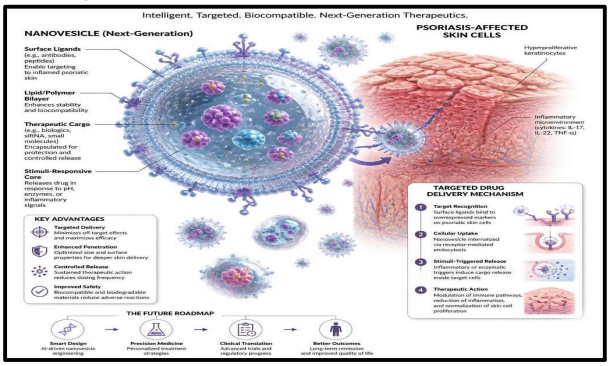

Figure 37. Future evolution of nanovesicular systems for psoriasis.

The roadmap shown in Figure 37 should illustrate progression from conventional liposomes toward intelligent, targeted, AI-assisted nanovesicular systems.

41. CONCLUSIONS

Psoriasis remains a chronic inflammatory disease requiring long-term management and improved topical therapeutic strategies. Conventional formulations often fail to achieve adequate skin penetration, resulting in suboptimal clinical outcomes and poor patient adherence.

The evolution of nanovesicular systems—from liposomes and niosomes to transfersomes, ethosomes, transethosomes, glycerosomes, hyalurosomes, and invasomes—has significantly expanded the possibilities for targeted topical drug delivery. Among these technologies, invasomes have emerged as particularly promising carriers because of their unique combination of phospholipids, ethanol, and terpenes, which collectively enhance deformability and skin penetration.

Evidence accumulated from physicochemical characterization studies, ex vivo permeation investigations, confocal imaging analyses, and in vivo psoriasis models consistently demonstrates superior therapeutic performance of invasomal systems compared with earlier generations of vesicular carriers. These advantages are especially relevant for poorly permeable anti-psoriatic agents such as methotrexate, tacrolimus, cyclosporine, curcumin, and boswellic acids.

Despite substantial progress, challenges related to scale-up, long-term stability, regulatory approval, and clinical validation continue to hinder widespread commercialization. Future integration of QbD principles, artificial intelligence, predictive modeling, and targeted delivery approaches is expected to accelerate clinical translation.

Overall, nanovesicular systems—and particularly invasomes—represent a highly promising platform for next-generation psoriasis management and may ultimately bridge the gap between laboratory innovation and patient-centered therapy.

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