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Review Article

Phyto - Transferosomes: Emerging Vesicular Nanocarriers for Topical Delivery of Phytoconstituents

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ABSTRACT

Skin disorders, including psoriasis, acne, fungal infections, chronic wounds, photoaging, and skin cancer, are major global health concerns that often require long-term treatment. Phytoconstituents derived from medicinal plants possess significant antioxidant, anti-inflammatory, antimicrobial, wound-healing, and anticancer properties, making them attractive candidates for topical therapy. However, their clinical effectiveness is frequently limited by poor aqueous solubility, low stability, photodegradation, inadequate skin permeation, and reduced bioavailability. To overcome these challenges, nanotechnology-based vesicular carriers have been extensively explored. Among them, transferosomes have emerged as promising ultra-deformable lipid vesicles capable of enhancing drug penetration across the stratum corneum. Incorporation of phytoconstituents into transferosomal systems, known as phyto-transferosomes, offers improved encapsulation efficiency, protection against degradation, sustained drug release, and enhanced therapeutic efficacy. This review discusses skin anatomy and barriers to topical drug delivery, the role of phytoconstituents in dermatological therapy, fundamentals and mechanisms of transferosomes, formulation components, preparation methods, and characterization techniques. Furthermore, therapeutic applications, safety and regulatory considerations, patents, commercialization prospects, and future perspectives are highlighted. Overall, phyto-transferosomes represent a promising strategy for improving the topical delivery and clinical performance of herbal therapeutics.

KEYWORDS: Phyto-transferosomes, Vesicular nanocarriers, Herbal nanomedicine, Nanoformulations, etc.**ARTICLE INFO:** Received 19 Jan. 2026; Review Complete 20 April, 2026; Accepted 29 May. 2026; Available online 15 June. 2026**Cite this article as:**

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INTRODUCTION

Skin disorders represent one of the most prevalent health concerns worldwide and continue to impose a substantial clinical, social, and economic burden. Conditions such as psoriasis, eczema, acne, fungal infections, chronic wounds, photoaging, and skin cancer affect millions of individuals globally and often require prolonged therapeutic intervention. According to recent global health reports, the incidence of inflammatory and malignant skin diseases has increased considerably due to environmental pollution, ultraviolet radiation exposure, microbial resistance, lifestyle changes, and aging populations. The skin, being the largest organ of the human body, serves as a protective barrier; however, this barrier property also restricts the effective penetration of therapeutic agents through the stratum corneum, thereby limiting the efficacy of topical formulations.

In recent years, phytoconstituents derived from medicinal plants have gained remarkable attention in dermatological therapy because of their potent antioxidant, anti-inflammatory, antimicrobial, anticancer, and wound-healing properties. Bioactive compounds such as curcumin, resveratrol, quercetin, catechins, aloe vera extract, and essential oils have demonstrated promising therapeutic potential in the management of various skin disorders. Herbal therapies are generally considered safer, biocompatible, and associated with fewer adverse effects compared to synthetic drugs, making them attractive candidates for topical and transdermal applications. Despite their therapeutic advantages, the clinical utility of phytoconstituents remains significantly limited due to several physicochemical and biopharmaceutical challenges. Most phytoconstituents exhibit poor aqueous solubility, low chemical stability, susceptibility to oxidation and photodegradation, limited skin permeation, rapid

metabolism, and inadequate bioavailability. Conventional topical formulations such as creams, gels, and ointments often fail to deliver sufficient concentrations of phytoconstituents into deeper skin layers, resulting in reduced therapeutic efficacy and poor patient outcomes. Therefore, the development of advanced carrier systems capable of enhancing skin permeation and improving drug stability has become an important area of pharmaceutical research.

Nanotechnology-based vesicular carriers have emerged as promising strategies to overcome the limitations associated with conventional topical delivery systems. Various nanocarriers including liposomes, niosomes, ethosomes, solid lipid nanoparticles, and nanostructured lipid carriers have been extensively investigated for improving dermal and transdermal drug delivery. Among these systems, transferosomes have gained considerable scientific interest due to their unique ultra-deformable and elastic characteristics. Transferosomes are phospholipid-based vesicles containing edge activators that provide remarkable flexibility, enabling them to squeeze through narrow intercellular spaces of the stratum corneum under osmotic gradients. This property significantly enhances drug permeation, dermal retention, and bioavailability compared to conventional vesicular systems.

The incorporation of phytoconstituents into transferosomal systems, commonly referred to as phyto-transferosomes, represents an innovative and efficient approach for topical herbal drug delivery. Phyto-transferosomes improve encapsulation efficiency, protect phytoconstituents from degradation, provide controlled and sustained drug release, and enhance therapeutic efficacy. Moreover, these vesicular nanocarriers have shown promising applications in skin cancer therapy, wound healing, anti-aging treatment, inflammatory disorders, fungal infections, and cosmetic formulations.

The present review aims to comprehensively discuss the emerging role of phyto-transferosomes in the topical delivery of phytoconstituents. The review focuses on the fundamentals of transferosomes, formulation approaches, and mechanisms of skin permeation, preparation methods, characterization techniques, therapeutic applications, and recent research advancements. Furthermore, current challenges, regulatory considerations, and future prospects associated with the clinical translation and commercialization of phyto-transferosomal systems are critically highlighted.

SKIN ANATOMY AND BARRIERS TO TOPICAL DRUG DELIVERY

The skin is the largest organ of the human body and serves as the primary protective barrier between the internal physiological environment and the external surroundings. In addition to its protective role, the skin performs various essential physiological functions including thermoregulation, sensory perception, immune defense, vitamin D synthesis, and prevention of excessive water loss. Due to its extensive surface area and accessibility, the skin has become an attractive route for topical and transdermal drug delivery. However, the highly organized structure of the skin, particularly the stratum corneum, presents a significant barrier to the permeation of therapeutic agents. Understanding the anatomy of the skin and the mechanisms governing drug permeation is therefore essential for the successful development of advanced topical delivery systems such as phyto-transferosomes.

STRUCTURE OF SKIN

Human skin is a multilayered organ composed of three major layers: the epidermis, dermis, and hypodermis (subcutaneous tissue). Each layer possesses distinct structural and functional characteristics that collectively contribute to the barrier properties of the skin.

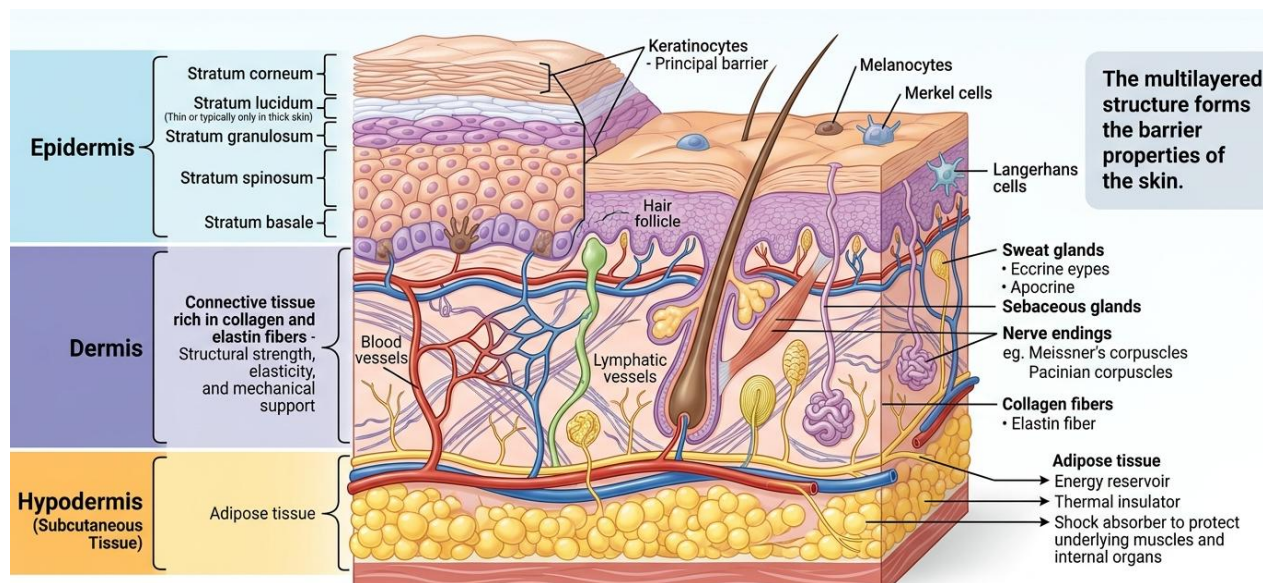


Figure 1: Structure of Skin

Epidermis

The epidermis is the outermost layer of the skin and acts as the principal barrier against environmental insults, pathogens, chemicals, and ultraviolet radiation. It is primarily composed of keratinocytes arranged in multiple differentiated layers. The epidermis is generally divided into five sublayers: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum.

Dermis

The dermis is located beneath the epidermis and is primarily composed of connective tissue rich in collagen and elastin fibers. It provides structural strength, elasticity, and mechanical support to the skin. The dermis contains blood vessels, lymphatic vessels, hair follicles, sweat glands, sebaceous glands, and nerve endings.

Hypodermis

The hypodermis, also known as subcutaneous tissue, is the deepest layer of the skin and mainly consists of adipose tissue and loose connective tissue. It acts as an energy reservoir, thermal insulator, and shock absorber that protects underlying muscles and internal organs.

STRATUM CORNEUM BARRIER

The stratum corneum is the outermost layer of the epidermis and represents the principal barrier to percutaneous drug permeation. It is approximately 10–20 μm thick and consists of highly keratinized corneocytes embedded within an organized extracellular lipid matrix. Despite its relatively small thickness, the stratum corneum effectively restricts the entry of exogenous substances and minimizes transepidermal water loss.

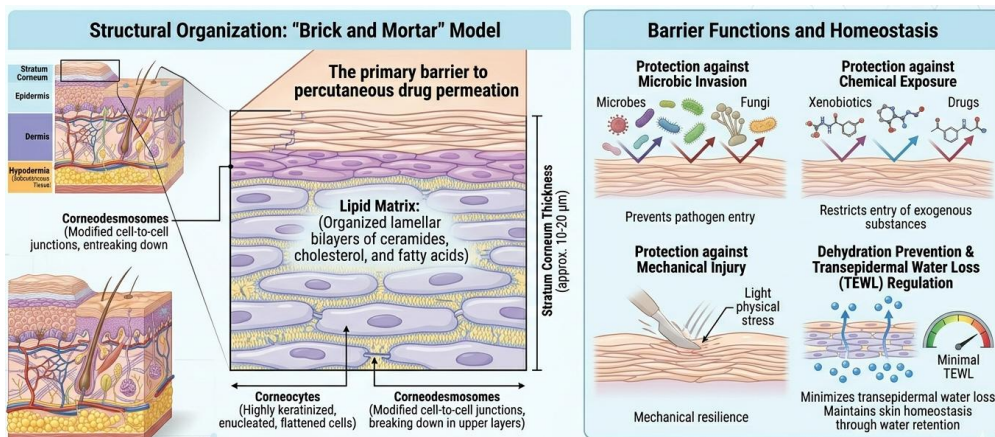


Figure 2: Stratum Corneum Barrier

Brick and Mortar Model

The structural organization of the stratum corneum is commonly explained using the “brick and mortar” model proposed by Elias. In this model, the corneocytes are represented as “bricks,” while the surrounding lipid matrix acts as the “mortar.”

Barrier Function

The stratum corneum serves several critical physiological functions, including protection against microbial invasion,

chemical exposure, mechanical injury, and dehydration. It maintains skin homeostasis by regulating water retention and preventing excessive transepidermal water loss.

PATHWAYS OF SKIN PERMEATION

Drugs can penetrate the skin through three main pathways: intercellular, transcellular, and follicular (appendageal) routes. The pathway utilized depends on the drug's physicochemical properties and formulation characteristics.

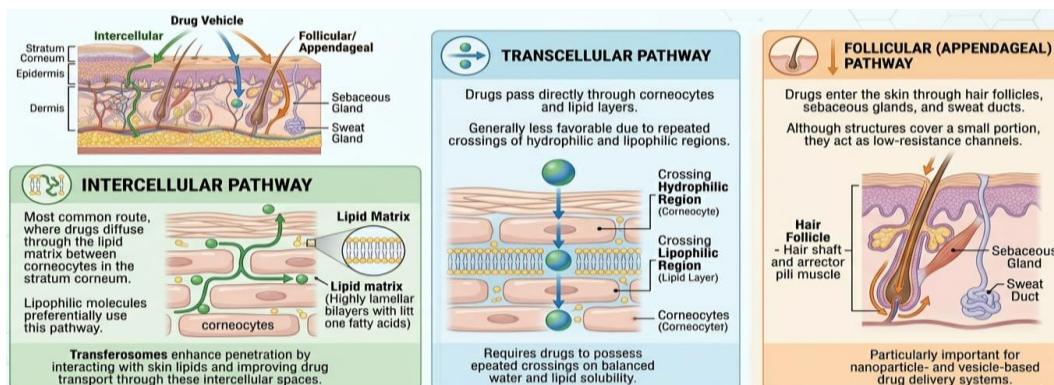


Figure 3: Pathways of Skin Permeation

Intercellular Pathway:

This is the most common route, where drugs diffuse through the lipid matrix between corneocytes in the stratum corneum. Lipophilic molecules preferentially use this pathway. Transfersomes enhance penetration by interacting with skin lipids and improving drug transport through these intercellular spaces.

Transcellular Pathway:

In this route, drugs pass directly through corneocytes and lipid layers. Since molecules must repeatedly cross both

hydrophilic and lipophilic regions, this pathway is generally less favorable and requires drugs to possess balanced water and lipid solubility.

Follicular (Appendageal) Pathway:

Drugs enter the skin through hair follicles, sebaceous glands, and sweat ducts. Although these structures cover only a small portion of the skin surface, they act as low-resistance channels and can be particularly important for nanoparticle- and vesicle-based drug delivery systems.

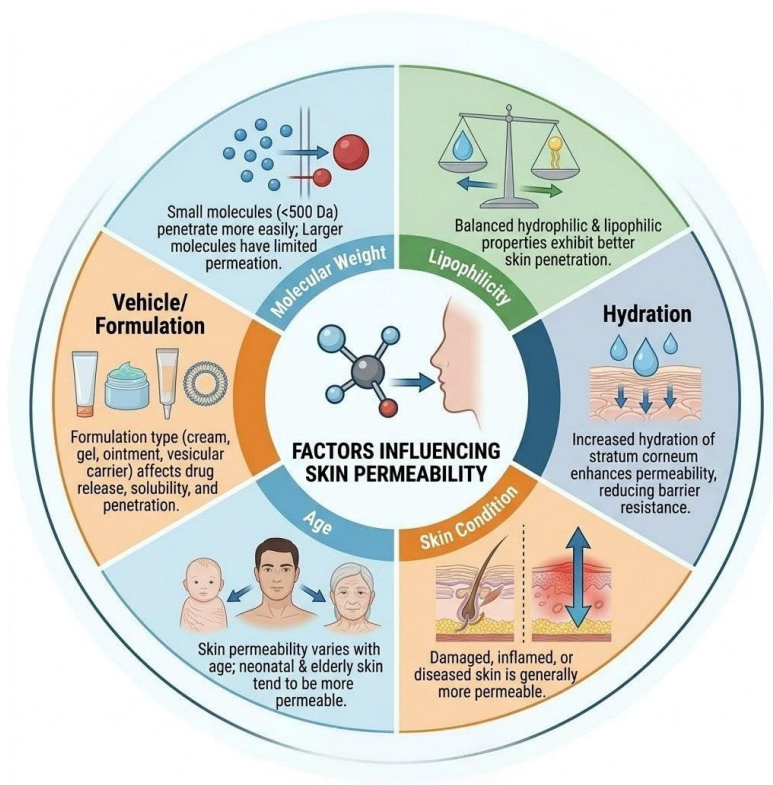


Figure 4: Factors Affecting Topical Absorption

Several physiological and formulation-related factors influence drug absorption through the skin.

Molecular Weight: Small molecules (generally <500 Da) penetrate the skin more easily, while larger molecules show limited permeation.

Lipophilicity: Drugs with balanced hydrophilic and lipophilic properties exhibit better skin penetration than extremely hydrophilic or highly lipophilic compounds.

Hydration: Increased hydration of the stratum corneum enhances permeability by reducing barrier resistance and facilitating drug diffusion.

Skin Condition: Damaged, inflamed, or diseased skin is generally more permeable than healthy skin due to disruption of the skin barrier.

Age: Skin permeability varies with age; neonatal and elderly skin tends to be more permeable than adult skin.

Vehicle/Formulation: The type of formulation (e.g., cream, gel, ointment, or vesicular carrier) affects drug release, solubility, and penetration into the skin.

PHYTOCONSTITUENTS IN TOPICAL THERAPY

Phytoconstituents are naturally occurring bioactive compounds derived from medicinal plants and herbal sources that possess diverse pharmacological activities. Over the past few decades, phytoconstituents have gained substantial attention in topical and transdermal drug delivery owing to their antioxidant, anti-inflammatory, antimicrobial, anticancer, and wound healing properties. These compounds are widely utilized in dermatological and cosmeceutical formulations for the management of skin disorders such as psoriasis, acne, eczema, skin infections, premature aging, and skin cancer.

CLASSIFICATION OF PHYTOCONSTITUENTS

Phytoconstituents are naturally occurring bioactive compounds produced by plants. Based on their chemical structure and biological functions, they are mainly classified into the following groups:

Polyphenols: Plant compounds rich in phenolic groups, commonly found in fruits, vegetables, tea, and medicinal

herbs. They are known for their strong antioxidant and anti-inflammatory properties.

Flavonoids: A major subclass of polyphenols widely present in plants and fruits. They exhibit antioxidant, antimicrobial, anti-inflammatory, and anticancer activities.

Alkaloids: Nitrogen-containing compounds with diverse pharmacological effects, including antimicrobial, analgesic, anti-inflammatory, and anticancer activities.

Terpenoids: Bioactive constituents of essential oils that possess antioxidant, antimicrobial, anti-inflammatory, and anticancer properties.

Curcuminoids: Polyphenolic compounds derived from turmeric, with curcumin being the most studied. They are recognized for their potent antioxidant, anti-inflammatory, antimicrobial, and anticancer effects.

THERAPEUTIC APPLICATIONS OF PHYTOCONSTITUENTS IN TOPICAL THERAPY

Phytoconstituents exhibit diverse biological activities that make them valuable for the treatment of various skin disorders and for cosmeceutical applications.

Anti-inflammatory activity: Reduce inflammation by inhibiting pro-inflammatory mediators such as TNF- α , interleukins, prostaglandins, and cyclooxygenase enzymes, helping manage conditions like psoriasis, eczema, and acne.

Antioxidant activity: Protect the skin from oxidative stress caused by UV radiation and environmental pollutants by scavenging free radicals and enhancing antioxidant defenses.

Antimicrobial activity: Exhibit broad-spectrum activity against bacteria, fungi, and other pathogens responsible for skin infections and acne.

Anti-aging activity: Delay skin aging by reducing oxidative damage, preserving collagen, and improving skin elasticity.

Wound-healing activity: Accelerate tissue repair through enhanced fibroblast proliferation, collagen synthesis, and re-epithelialization.

Anti-psoriatic activity: Modulate immune responses and suppress inflammatory pathways involved in psoriasis.

Anticancer activity: Demonstrate chemopreventive and anticancer effects against melanoma and non-melanoma skin cancers through antioxidant, anti-inflammatory, and antiproliferative mechanisms.

CHALLENGES IN TOPICAL DELIVERY OF PHYTOCONSTITUENTS

Despite their promising therapeutic benefits, the topical delivery of phytoconstituents is often limited by several physicochemical and biological challenges.

Poor Solubility: Many phytoconstituents are poorly soluble in water, resulting in low drug release and limited bioavailability.

Chemical Instability: They are prone to degradation by heat, oxygen, pH changes, and enzymes, which can reduce their effectiveness and shelf life.

Photodegradation: Exposure to UV light can degrade compounds such as curcumin and resveratrol, leading to loss of biological activity.

Poor Skin Penetration: The stratum corneum acts as a strong barrier, restricting the penetration of many phytoconstituents into deeper skin layers.

Rapid Metabolism: Some phytoconstituents undergo rapid enzymatic breakdown, reducing their availability and therapeutic efficacy.

TRANSFEROSOMES: FUNDAMENTALS AND MECHANISM

Introduction to Transferosomes

Definition: Transferosomes are ultra-deformable lipid vesicles that enhance drug delivery through the skin by penetrating the stratum corneum efficiently.

Historical Development: They were introduced in the early 1990s as an advanced carrier system for topical and transdermal drug delivery.

Composition

- **Phospholipids:** Form the vesicle bilayer and carry the drug.
- **Edge Activators:** Surfactants that provide flexibility and deformability.
- **Cholesterol:** Improves membrane stability and reduces drug leakage.
- **Hydration Medium:** Aqueous phase used for vesicle formation.

Mechanism of Elasticity and Penetration

- **Deformability:** Flexible vesicles can squeeze through skin pores smaller than their size.
- **Osmotic Gradient:** Natural hydration differences in the skin drive transferosomes into deeper layers.

Advantages over Conventional Vesicles

- Greater skin penetration.
- Enhanced drug bioavailability.
- High membrane flexibility.
- Improved targeting of drugs to deeper skin layers.

Limitations

- Limited physical and chemical stability.
- Phospholipids are prone to oxidation.
- Large-scale manufacturing can be challenging.

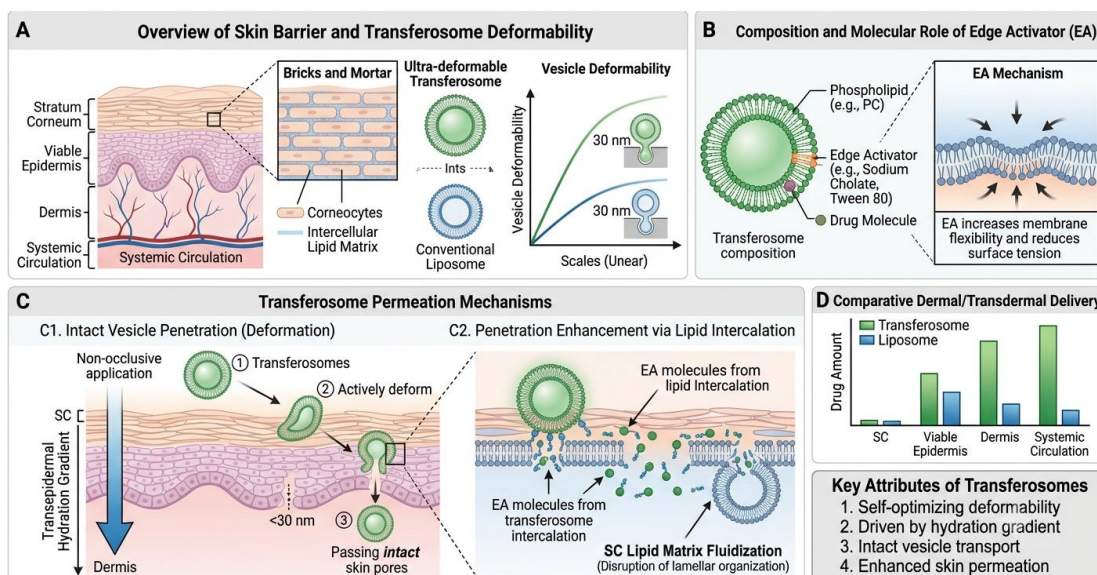


Figure 5: Mechanism of transferosomal penetration through skin

PHYTO-TRANSFEROSOMES

Concept and Definition

Phyto-transferosomes are ultra-deformable lipid vesicles containing herbal bioactive compounds. They are designed to enhance the delivery of phytoconstituents through the skin, improving their stability, penetration, and therapeutic effectiveness.

Advantages for Herbal Delivery

Enhanced Permeation:

Their flexible structure allows efficient transport of herbal compounds across the skin barrier.

Protection of Phytoconstituents:

Encapsulation protects sensitive plant compounds from degradation and improves their stability.

Sustained Release:

Phyto-transferosomes provide controlled release of herbal actives, maintaining therapeutic levels for a longer duration.

Improved Therapeutic Efficacy:

Enhanced penetration and retention increase bioavailability and overall treatment effectiveness.

Components Used in Phyto-Transferosomes

Natural Phospholipids: Form the vesicular bilayer and improve biocompatibility.

Edge Activators: Surfactants that impart flexibility and deformability to the vesicles.

Herbal Actives: Plant-derived compounds such as resveratrol, curcumin, quercetin, and other phytoconstituents incorporated for therapeutic action.

METHODS OF PREPARATION FOR PHYTO - TRANSFEROSOMES

Thin Film Hydration Method

Phospholipids, edge activators, and the phytoconstituent are dissolved in organic solvents. The solvent is evaporated to form a thin lipid film, which is then hydrated with an aqueous phase to produce phyto-transferosomes. This is the most commonly used method.

Reverse Phase Evaporation Method

Lipids and plant-derived compounds are dissolved in an organic solvent and mixed with an aqueous phase to form an emulsion. Removal of the solvent results in the formation of phyto-transferosomal vesicles with high drug entrapment.

Ethanol Injection Method

Lipids and phytoconstituents are dissolved in ethanol and slowly injected into an aqueous phase under continuous stirring. Vesicles form spontaneously as ethanol diffuses into the water.

Sonication Method

Ultrasonic energy is applied to reduce the size of the vesicles and obtain a more uniform distribution, improving stability and skin penetration.

Extrusion Method

The vesicle suspension is passed through membrane filters of specific pore sizes to obtain phyto-transferosomes with a uniform and controlled size.

Optimization Approaches

Quality by Design (QbD): Helps identify critical formulation parameters and ensures consistent product quality.

Design of Experiments (DOE): Uses statistical tools to optimize formulation variables and achieve the desired characteristics with fewer experimental trials.

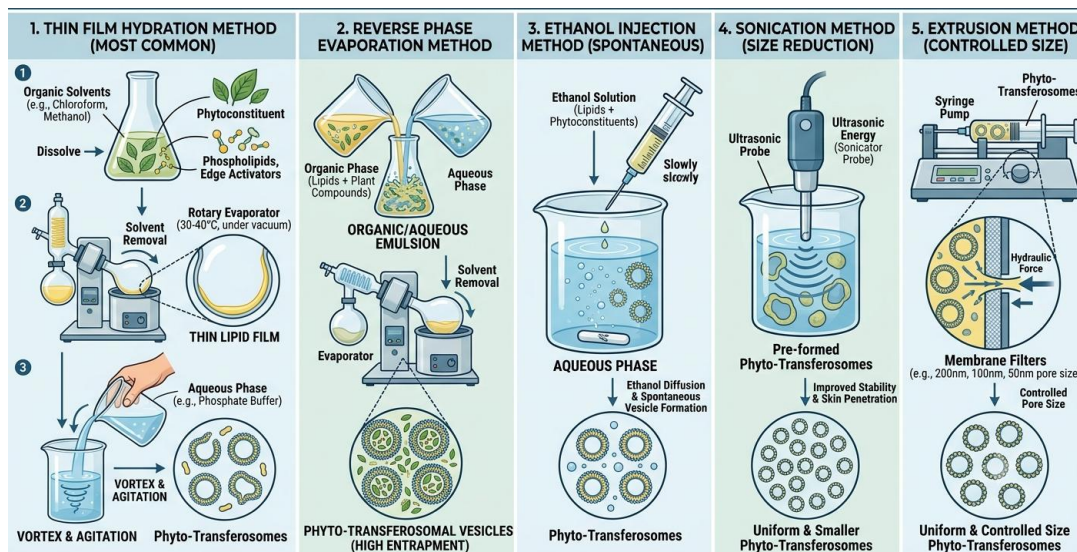


Figure 6: Methods of Preparation for Phyto - Transfersomes

CHARACTERIZATION OF PHYTO-TRANSFEROSOMES

Table 1: Analytical techniques and significance.

Analytical Technique	Parameter Evaluated	Significance
Dynamic Light Scattering (DLS)	Particle Size	Determines vesicle size distribution and formulation uniformity.
Zeta Potential Analysis	Surface Charge	Evaluates physical stability and aggregation tendency of vesicles.
Scanning Electron Microscopy (SEM)	Surface Characteristics	Examines surface morphology and vesicle appearance.
Entrapment Efficiency (%)	Drug Loading Capacity	Measures the amount of phytoconstituent encapsulated within vesicles.
Fourier Transform Infrared Spectroscopy (FTIR)	Chemical Interactions	Identifies functional groups and possible interactions among formulation components.
In Vitro Drug Release Study	Drug Release Profile	Evaluates the rate and extent of phytoconstituent release from vesicles.
Stability Studies	Storage Stability	Determines formulation stability under different storage conditions.

SKIN CANCER

Phyto-transfersomes enhance the skin delivery of anticancer phytoconstituents, improving therapeutic effectiveness.

Psoriasis

They improve the penetration of anti-inflammatory herbal compounds, reducing redness, scaling, and irritation.

Acne

Phyto-transfersomes deliver antimicrobial and anti-inflammatory phytochemicals effectively, helping control acne and inflammation.

Fungal Infections

They enhance the penetration of antifungal herbal agents, improving treatment outcomes.

Wound Healing

Phyto-transfersomes promote tissue repair and accelerate wound healing by delivering bioactive compounds to the affected site.

Anti-aging and Cosmeceuticals

They improve the delivery of antioxidants, helping protect the skin and reduce signs of aging.

SAFETY, TOXICITY AND REGULATORY CONSIDERATION

Skin Irritation Studies

Skin irritation studies are essential to ensure that phyto-transfersomal formulations are safe and well tolerated after topical application.

Cytotoxicity

Cytotoxicity evaluation helps determine the safety of formulations and their effects on skin cells.

Regulatory Concerns

Regulatory approval requires evidence of safety, efficacy, quality, and reproducibility of the formulation.

Herbal Formulation Standardization

Standardization ensures consistent quality, potency, and therapeutic performance of herbal ingredients.

GMP Considerations

Good Manufacturing Practices (GMP) are necessary to maintain product quality, safety, and batch-to-batch consistency.

PATENTS AND COMMERCIAL PERSPECTIVES

Recent Patents

Several patents have been filed for transferosomal and phyto-transferosomal systems to improve topical drug delivery.

Marketed Vesicular Products

A number of vesicular formulations have reached the market, demonstrating the commercial potential of this technology.

Industrial Challenges

Major challenges include stability issues, production costs, and maintaining formulation consistency.

Scale-Up Approaches

Advanced manufacturing techniques are being explored to enable large-scale and cost-effective production.

CURRENT CHALLENGES AND FUTURE PERSPECTIVES

Stability Enhancement

Improving the physical and chemical stability of phyto-transferosomes remains a key research focus.

Clinical Translation

More clinical studies are needed to confirm safety and therapeutic efficacy in humans.

AI-Assisted Formulation Optimization

Artificial intelligence can help optimize formulation variables and accelerate product development.

Green Nanotechnology

Eco-friendly materials and sustainable manufacturing methods are gaining increasing attention.



Figure: 7 Current Challenges and Future Perspectives

CONCLUSION

Phyto-transferosomes are promising nanocarriers that enhance the topical delivery of herbal bioactives by improving skin penetration, stability, and therapeutic efficacy. Despite challenges related to stability and large-scale production, advances in nanotechnology, artificial intelligence, and personalized medicine offer significant opportunities for their future development. Their strong translational potential makes them attractive candidates for next-generation topical and transdermal therapies.

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