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REVIEW ARTICLE

Mechanisms, Formulation and Therapeutic Applications of Surfactant-Mediated Nanocarriers for Transdermal Drug Delivery

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Abstract: Transdermal drug delivery systems (TDDS) represent a pivotal approach in modern therapeutics, offering the ability to bypass hepatic first-pass metabolism, maintain steady-state plasma concentration, and improve patient compliance compared to invasive routes. However, the stratum corneum functions as a formidable biological barrier, restricting the permeation of most pharmacological agents. Amphiphilic surfactants serve as critical functional excipients in overcoming this limitation by modulating the lipid bilayer structure and facilitating the partition of therapeutic agents. Physicochemical principles govern the efficacy of surfactant-based nanocarriers, including niosomes, transferosomes, transethosomes, nanoemulsions, and solid lipid nanoparticles, where structure-activity relationships dictate stability and skin permeability enhancement through mechanisms such as lipid extraction and keratin disruption. Methodological approaches for nanocarrier fabrication range from thermodynamic self-assembly to high-energy homogenization techniques, while critical quality attributes like particle size distribution, zeta potential, and entrapment efficiency directly influence biological performance. The therapeutic versatility of these systems extends to delivering hydrophilic and hydrophobic molecules for dermatological, systemic, and neurological conditions, positioning surfactant-based nanotechnology as a cornerstone of next-generation transdermal therapies.

Keywords: Transdermal delivery; Stratum corneum; Surfactants; Nanocarriers; Vesicular systems

1. Introduction

The skin is the largest organ of the human body, serving primarily as a protective interface against environmental insults. In the context of pharmaceutical sciences, transdermal drug delivery offers a non-invasive route of administration that circumvents the limitations associated with oral dosing, such as gastrointestinal degradation and presystemic metabolism [1]. Despite these advantages, the successful delivery of therapeutic agents across the skin is hindered by the stratum corneum (SC). This outermost layer consists of corneocytes embedded in a dense, mortar-like matrix of ceramides, cholesterol, and free fatty acids, creating a highly regulated barrier that restricts the passage of molecules larger than 500 Daltons or those possessing unfavorable hydrophilic-lipophilic balances [2].

To address these permeation challenges, pharmaceutical research has increasingly focused on the utilization of surface-active agents, or surfactants. These amphiphilic molecules possess the unique ability to interact with the stratum corneum components. By inserting their hydrophobic tails into the lipid bilayers and interacting with keratin filaments in corneocytes, surfactants can transiently increase membrane fluidity and permeability [3]. Beyond their role as penetration enhancers, surfactants are the fundamental building blocks of various nanocarrier systems. These nanocarriers, ranging from vesicular systems like niosomes to lipid-based nanoparticles, leverage the self-assembling properties of surfactants to encapsulate drugs, protect them from degradation, and facilitate their transport across the dermal barrier [4].

The selection of a specific surfactant whether anionic, cationic, non-ionic, or zwitterionic dictates the physicochemical stability, toxicity profile, and permeation efficacy of the nanocarrier. Recent advancements have seen the evolution of conventional liposomes into more sophisticated, surfactant-rich systems such as transferosomes and transethosomes, which possess deformability characteristics allowing them to squeeze through the narrow intercellular pores of the skin [5]. This review provides a critical analysis

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of these surfactant-based systems, detailing their structural composition, fabrication methodologies, and the mechanistic basis for their application in modern pharmacotherapy.

2. Merits and Demerits of Surfactant-Based Systems

The integration of surfactants into nanocarrier formulations provides distinct pharmaceutical advantages. Primarily, the amphiphilic nature of non-ionic surfactants allows for the successful sequestration of drugs with diverse solubility profiles; hydrophobic drugs partition into the lipid bilayer or oil core, while hydrophilic agents are encapsulated within the aqueous core [6]. Furthermore, surfactants play a thermodynamic role in reducing interfacial tension, which is essential for the stabilization of nanoemulsions and the prevention of particle aggregation in suspension. This interfacial activity also contributes to the wettability of the skin surface, ensuring uniform spreading of topical formulations. From a biomedical perspective, surfactant-coated nanoparticles have demonstrated utility in extending circulation half-life and facilitating targeted delivery to specific tissues, including the potential for nose-to-brain transport [7].

However, the clinical translation of these systems is not without challenges. The primary concern regarding surfactant usage is cytotoxicity. While non-ionic surfactants are generally regarded as safe and biocompatible, cationic and anionic surfactants can induce irritation or cellular damage depending on their concentration and alkyl chain length [8]. Manufacturing presents another hurdle; high-energy production methods often incur significant costs and may lead to the degradation of heat-sensitive active pharmaceutical ingredients (APIs). Additionally, the physical stability of these systems can be compromised by phenomena such as Ostwald ripening or sedimentation during long-term storage, necessitating rigorous optimization of the surfactant-to-lipid ratios and the inclusion of co-stabilizers [9].

Table 1. Common Surfactants Used in Transdermal Nanocarrier Formulation

Surfactant Class	Examples	Hydrophilic-Lipophilic Balance (HLB)	Role/Function in Nanocarrier	Toxicity/Safety
Non-ionic	Span 20, 40, 60, 80	Low (Lipophilic)	Membrane constituents for niosomes; stabilizers for w/o emulsions.	High biocompatibility; low irritation potential. Preferred for topical use.
	Tween 20, 80	High (Hydrophilic)	Edge activators in transferosomes; solubilizers in o/w emulsions.	Generally safe; can cause histamine release at high concentrations.
	Brij 35, 58, 72	Varied	Permeation enhancers; steric stabilizers.	Low toxicity.
Anionic	Sodium Lauryl Sulfate (SLS), Sodium Cholate	High (Hydrophilic)	Charge inducers (negative zeta potential); Edge activators.	Moderate to high skin irritation potential; disrupt protein structures.
Cationic	CTAB, DOTAP	High (Hydrophilic)	Charge inducers (positive zeta potential); promote bioadhesion.	Higher cytotoxicity; often used for gene delivery or antimicrobial effects.
Zwitterionic	Lecithin, Cocamidopropyl betaine	Amphoteric	Primary lipid component (Lecithin); co-surfactants.	Biocompatible; mimics natural cell membrane components.

3. Classification of Surfactant-Based Nanocarriers

Surfactant-based delivery systems act as distinct entities that differ in their supramolecular arrangement, composition, and rheological properties. The rational design of these carriers requires a precise understanding of the interplay between the surfactant, the lipid phase, and the hydration medium.

3.1. Vesicular Systems

3.1.1. Niosomes

Niosomes are microscopic lamellar structures formed by the self-assembly of non-ionic surfactants in an aqueous medium, typically stabilized by the addition of cholesterol. Unlike liposomes, which are comprised of phospholipids, niosomes utilize surfactants such

as Spans (sorbitan esters) or Tweens (polysorbate), making them more chemically stable and cost-effective [10]. Cholesterol acts as a membrane stiffening agent, preventing the leakage of the encapsulated drug and providing mechanical rigidity to the vesicle bilayer.

3.1.2. Transferosomes

Transferosomes, or elastic vesicles, represent the second generation of vesicular carriers. They are composed of phospholipids and an "edge activator," which is typically a single-chain surfactant like sodium cholate, Span 80, or Tween 80 [11]. The edge activator destabilizes the lipid bilayers, imparting a high degree of deformability to the vesicle. This elasticity allows transferosomes to traverse intercellular channels in the stratum corneum that are significantly smaller than the vesicle diameter, driven by the transdermal hydration gradient.

3.1.3. Transethosomes

Transethosomes combine the advantages of ethosomes and transferosomes. Their composition includes phospholipids, a high concentration of ethanol (up to 30%), and a surfactant edge activator [12]. The ethanol interacts with the polar head groups of the stratum corneum lipids, reducing their melting point and increasing fluidity, while the surfactant component provides flexibility to the vesicle itself. This synergistic mechanism results in superior permeation capabilities compared to conventional liposomes.

Table 2. Comparison of Various Surfactant-Based Nanocarrier Systems

Nanocarrier System	Composition	Structural Characteristics	Advantages	Disadvantages
Niosomes	Non-ionic surfactants, Cholesterol	Bilayer vesicular structure (Uni- or Multilamellar)	Chemically stable, cost-effective, biocompatible, versatile drug loading.	Physical instability (fusion/leakage) over time; lower drug loading compared to liposomes.
Transferosomes	Phospholipids, Edge Activators (Single-chain surfactants)	Highly deformable/elastic lipid bilayers	Superior skin penetration through narrow intercellular pores; high entrapment efficiency.	Complex manufacturing; potential for oxidative degradation of phospholipids.
Transethosomes	Phospholipids, High Ethanol content (20-40%), Surfactants	Malleable vesicles with fluidizing effect on SC lipids	Synergistic permeation enhancement via ethanol and surfactant; deep skin penetration.	Skin irritation potential due to high alcohol content; vesicle leakage.
Solid Lipid Nanoparticles (SLNs)	Solid Lipids (e.g., waxes), Surfactants	Solid lipid core stabilized by surfactant shell	Controlled release, improved stability of labile drugs, solvent-free production.	Low drug loading capacity; drug expulsion during storage (polymorphic transition).
Nanostructured Lipid Carriers (NLCs)	Solid Lipids, Liquid Lipids (Oils), Surfactants	Imperfect lipid matrix (amorphous structure)	Higher drug loading than SLNs; reduced drug expulsion; long-term stability.	Optimization of lipid ratios is complex.
Nanoemulsions	Oil, Water, Surfactant, Co-surfactant	Isotropic liquid dispersion (droplets <200 nm)	Thermodynamically (micro) or kinetically (nano) stable; large surface area for absorption.	Requires high surfactant concentration (toxicity risk); physical instability (Ostwald ripening).

3.2. Lipid-Based Nanoparticulate Systems

3.2.1. Solid Lipid Nanoparticles (SLNs)

SLNs act as an alternative to emulsions and liposomes, consisting of a solid lipid core stabilized by an interfacial surfactant layer. The lipids used such as triglycerides, fatty acids, or waxes remain solid at both room and body temperature [13]. The surfactant layer, often composed of lecithin or poloxamers, reduces the surface tension and prevents particle agglomeration. SLNs provide controlled release and protection of labile drugs but may suffer from low drug loading capacity due to the crystalline lattice of the solid lipid.

3.2.2. Nanostructured Lipid Carriers (NLCs)

To overcome the limitations of SLNs, NLCs incorporate a blend of solid and liquid lipids (oils). This disruption of the perfect crystal lattice creates imperfections and voids within the matrix, thereby increasing the drug loading capacity and preventing the expulsion of the drug during storage [14]. Surfactants remain a critical component in NLCs to stabilize the dispersion of lipid droplets in the aqueous phase.

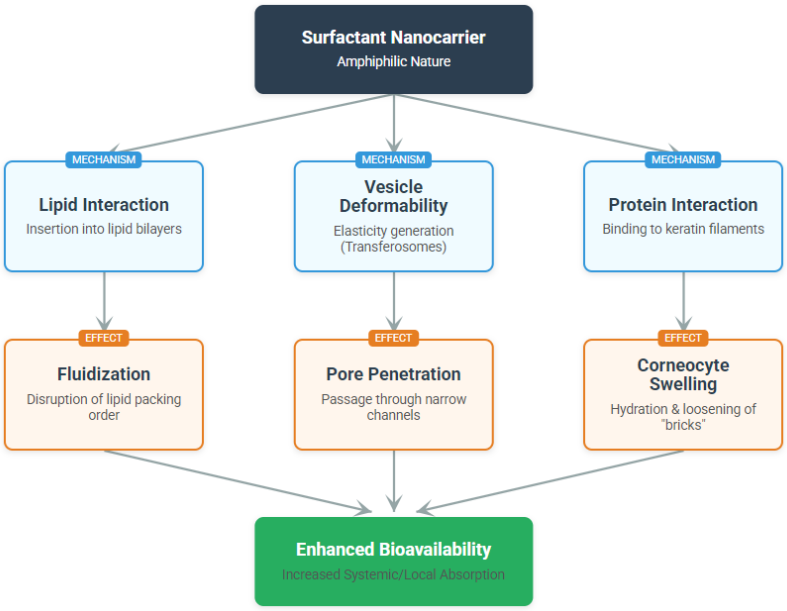

Figure 1. Mechanisms of Surfactant-Mediated Permeation

3.2.3. Microemulsions and Nanoemulsions

These are isotropic dispersions of oil and water stabilized by an interfacial film of surfactant and co-surfactant. While microemulsions are thermodynamically stable and form spontaneously, nanoemulsions are kinetically stable and typically require energy input for formation [15]. The surfactant reduces the interfacial tension to ultra-low levels, allowing for the formation of droplets in the nanometric range, which significantly increases the surface area available for drug absorption.

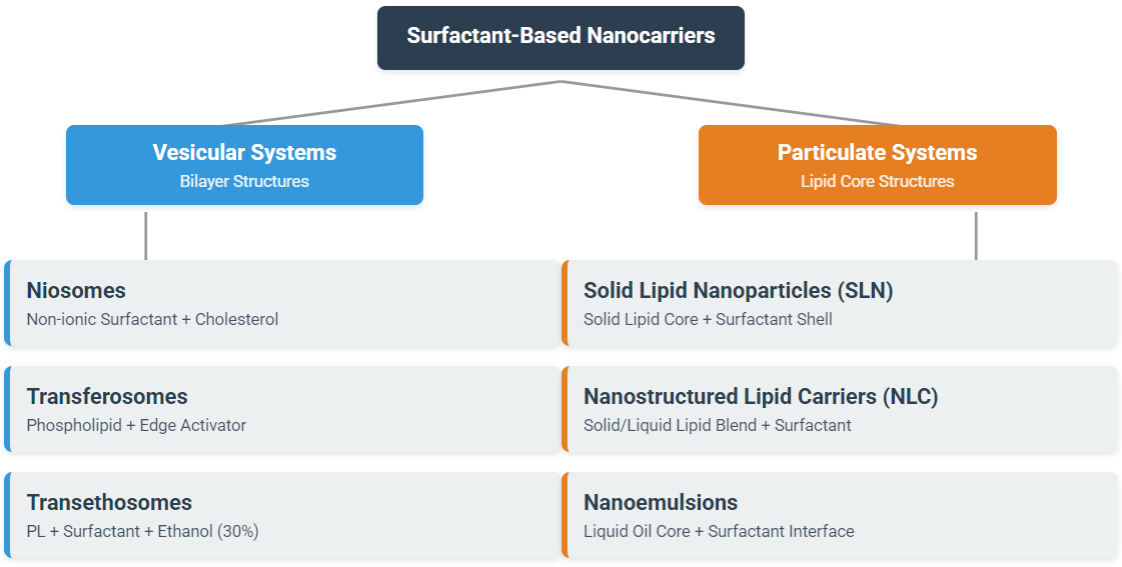

Figure 2. Classification of Surfactant Based Nanocarriers

4. Methods for Preparation

The fabrication of surfactant-based nanocarriers involves techniques that can be broadly categorized into bottom-up (self-assembly) and top-down (high-energy) approaches. The selection of a specific method depends on the physicochemical properties of the drug and the desired particle characteristics.

4.1. Thin Film Hydration (Hand Shaking Method)

This is the most fundamental technique for preparing vesicular systems like niosomes. The surfactant, cholesterol, and hydrophobic drugs are dissolved in a volatile organic solvent (e.g., chloroform or methanol) in a round-bottom flask. The solvent is removed under vacuum using a rotary evaporator, leaving a thin, dry lipid film on the flask wall. The film is subsequently hydrated with an aqueous buffer containing any hydrophilic drugs at a temperature above the gel-liquid transition temperature of the surfactant. Gentle agitation causes the film to peel off and self-assemble into multilamellar vesicles (MLVs) [16].

4.2. Ether Injection Method

In this technique, the surfactant and lipid components are dissolved in an organic solvent such as diethyl ether. This solution is injected slowly through a fine-gauge needle into an aqueous phase maintained at a temperature amenable to solvent vaporization (typically 60 °C). As the ether evaporates upon contact with the warm aqueous phase, the amphiphiles orient themselves at the interface to form unilamellar vesicles. This method allows for the production of vesicles with a defined size distribution but requires careful control of the injection rate [17].

Table 3. Preparation Methods for Surfactant-Based Carriers

Preparation Method	Principle Mechanism	Suitable For	Advantages	Disadvantages
Thin Film Hydration	Solvent evaporation followed by hydration of lipid film.	Lipophilic & Hydrophilic drugs; Niosomes.	Simple laboratory scale-up; proven technique.	Residual solvent risk; heterogeneous particle size requires sonication/extrusion.
Ether Injection	Slow injection of lipid-solvent phase into aqueous phase.	Niosomes; Liposomes.	Defined particle size distribution.	Use of volatile solvents; careful control of injection rate required.
High-Pressure Homogenization (HPH)	High shear and cavitation forces disrupt droplets.	SLNs, NLCs, Nanoemulsions.	Industrial scalability; avoids organic solvents.	High energy consumption; potential thermal degradation of sensitive drugs.
Phase Inversion Temperature (PIT)	Temperature-induced change in surfactant solubility (hydrophilic to lipophilic).	Nanoemulsions.	Low energy process; no high-shear equipment needed.	Limited to ethoxylated surfactants; requires careful temperature control.
Spontaneous Emulsification	Interfacial turbulence caused by solvent diffusion (Marangoni effect).	Nanoemulsions; NLCs.	Thermolabile drugs; simple equipment.	Requires water-miscible organic solvents; removal of solvent is necessary.

4.3. Reverse Phase Evaporation (REV)

The REV method is particularly effective for encapsulating a high percentage of the aqueous phase. Organic solvents containing surfactants are mixed with the aqueous phase to form a water-in-oil emulsion via sonication. The organic solvent is then removed under reduced pressure. As the solvent evaporates, the system converts from an emulsion to a gel-like state, and finally into a vesicular suspension upon further hydration. This method is advantageous for encapsulating both large macromolecules and small hydrophilic drugs [18].

4.4. High-Pressure Homogenization (HPH)

HPH is the industrial standard for producing SLNs, NLCs, and nanoemulsions. It involves passing a coarse emulsion through a narrow gap (homogenizing valve) at high velocity and pressure (100–1500 bar). The high shear stress, cavitation, and turbulence forces generated disrupt the droplets into the nanometric range [19].

4.4.1. Hot HPH

Performed at temperatures above the melting point of the lipid, resulting in smaller particle sizes due to lower viscosity.

4.4.2. Cold HPH

Designed for thermolabile drugs. The drug is dissolved in melted lipid, rapidly cooled to form microparticles, dispersed in a cold surfactant solution, and then homogenized.

4.5. Phase Inversion Temperature (PIT) Method

This low-energy method relies on the temperature-dependent solubility of non-ionic surfactants, particularly polyethoxylated types. At low temperatures, the surfactant is hydrophilic, stabilizing an oil-in-water (O/W) emulsion. As the temperature rises to the Phase Inversion Temperature (PIT), the surfactant becomes lipophilic due to the dehydration of the polymer chains. Rapid cooling from the PIT induces a phase transition that locks the droplets into a kinetically stable, fine nanoemulsion structure without the need for high shear equipment [20].

4.6. Spontaneous Emulsification

This technique exploits the chemical energy released during the dilution of a water-miscible organic solvent (containing oil and surfactant) into an aqueous phase. The rapid diffusion of the solvent into the water creates interfacial turbulence (the Marangoni effect), which spontaneously breaks the oil interface into nanodroplets. This method is simple and suitable for thermolabile compounds but requires the subsequent removal of the organic solvent [21].

4.7. Ultrasonication

Probe or bath sonication is frequently used to reduce the size of multilamellar vesicles or coarse emulsions. High-frequency sound waves generate acoustic cavitation the formation and collapse of microbubbles which imparts high energy to the system, breaking down particles into small unilamellar vesicles (SUVs) or nano-droplets. While effective for size reduction, sonication can generate heat and shed titanium particles from the probe, necessitating filtration and temperature control [22].

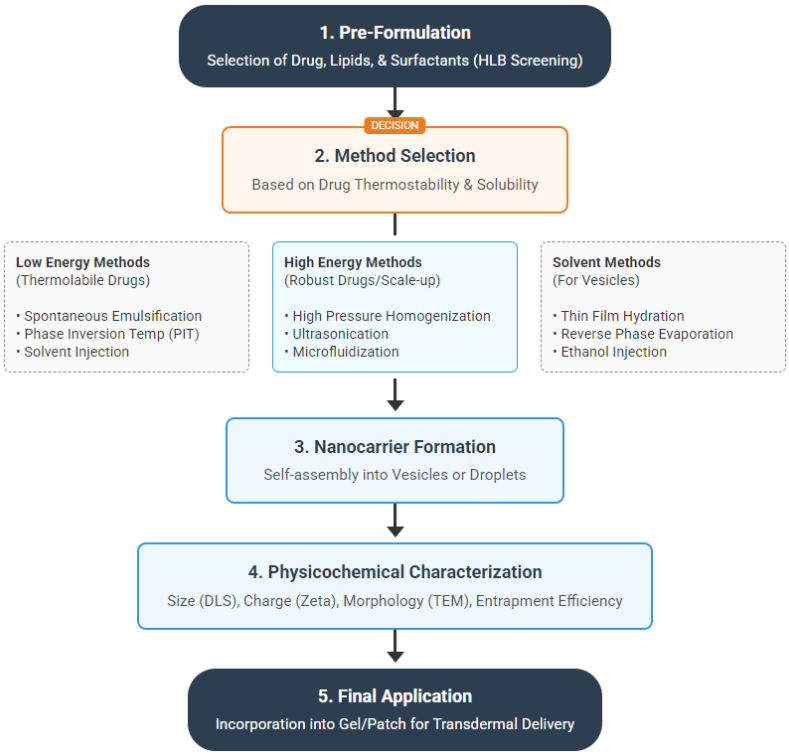

Figure 3. Formulation Development of Surfactant-Based Nanocarriers

5. Physicochemical Characterization of Surfactant-Based Nanocarriers

The clinical efficacy and safety of surfactant-based nanocarriers are intrinsically linked to their physicochemical attributes. Rigorous characterization is essential to ensure batch-to-batch consistency, stability, and predictable *in vivo* behavior.

5.1. Particle Size and Polydispersity Index (PDI)

The geometric diameter of nanocarriers is a determinant factor in their ability to penetrate the stratum corneum. For transdermal applications, a particle size generally below 300 nm is preferred to facilitate transport through the intercellular lipid matrix or hair follicles [23]. Dynamic Light Scattering (DLS), also known as Photon Correlation Spectroscopy (PCS), is the standard technique for measuring the hydrodynamic radius (Rh) of particles. This method analyzes the fluctuations in scattered light intensity caused by the Brownian motion of particles, correlating them to size via the Stokes-Einstein equation [24]:

$$D = \frac{k_B T}{C \pi \eta a}$$

Where D is the diffusion coefficient, k_B is the Boltzmann constant, T is the absolute temperature, and η is the solvent viscosity. The Polydispersity Index (PDI) provides a measure of the heterogeneity of the size distribution; a PDI value below 0.3 typically indicates a monodisperse and homogeneous population suitable for pharmaceutical use

5.2. Surface Charge and Zeta Potential

Zeta potential (ζ) reflects the electrokinetic potential at the slipping plane of the particle and is a critical indicator of colloidal stability. Surfactant-based systems rely on electrostatic repulsion to prevent aggregation and coalescence. A zeta potential magnitude greater than $\pm$30 mV is generally considered sufficient to maintain physical stability through electrostatic repulsion [25]. Furthermore, the surface charge influences the interaction with the negatively charged skin surface; cationic surfactants often demonstrate enhanced bioadhesion and cellular uptake compared to their anionic or neutral counterparts.

Table 4. Physicochemical Characterization Parameters

Parameter	Analytical Technique	Significance / Acceptance Criteria
Particle Size (Hydrodynamic Diameter)	Dynamic Light Scattering (DLS); Photon Correlation Spectroscopy (PCS)	Determines permeation depth. Ideal range for transdermal: 50–300 nm.
Polydispersity Index (PDI)	Dynamic Light Scattering (DLS)	Indicates uniformity of dispersion. Values <0.3 indicate a homogenous (monodisperse) population.
Zeta Potential (ζ)	Electrophoretic Light Scattering (ELS)	Predicts physical stability. Values > $\pm$30 mV indicate good stability (electrostatic repulsion).
Morphology	Transmission Electron Microscopy (TEM); Scanning Electron Microscopy (SEM); AFM	Confirms structure (vesicle vs. sphere); visualizes surface topography and lamellarity.
Entrapment Efficiency (EE%)	Ultrafiltration/Centrifugation followed by UV/HPLC	Measures % of drug encapsulated. Critical for dose calculation and cost-effectiveness.
Deformability / Elasticity	Extrusion through microporous filters	Essential for transferosomes/transethosomes. Higher elasticity index correlates with better skin penetration.
In Vitro Drug Release	Franz Diffusion Cell / Dialysis Bag	Determines release kinetics (e.g., zero-order, sustained release).

5.3. Morphological Analysis

While DLS provides an average size, it does not distinguish between different structural populations (e.g., micelles vs. vesicles). Electron microscopy techniques, specifically Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM), are employed to visualize the morphology and surface topography of the carriers . TEM is particularly valuable for confirming the vesicular nature of niosomes and transferosomes, revealing the number of concentric bilayers (lamellarity) and the integrity of the core-shell structure [26].

5.4. Entrapment Efficiency (EE%)

The capacity of the nanocarrier to encapsulate the active pharmaceutical ingredient is quantified as Entrapment Efficiency. This parameter is influenced by the surfactant's alkyl chain length, the hydrophilic-lipophilic balance (HLB), and the physicochemical properties of the drug. The EE% is typically determined by separating the unentrapped drug using techniques such as ultrafiltration, centrifugation, or dialysis. The concentration of the free drug in the supernatant is analyzed via UV-Visible spectrophotometry or HPLC, and EE% is calculated using the following equation [27]:

$$EE\% = \left(\frac{Encapsulated\ drug}{Total\ drug\ added}\right) x\ 100$$

5.5. *In Vitro* Drug Release Kinetics

The release profile of the drug from the nanocarrier determines the therapeutic duration and onset of action. *In vitro* release studies are commonly conducted using the dialysis bag method in phosphate-buffered saline (pH 7.4) at 37°C to mimic physiological conditions [28]. The release mechanism whether driven by diffusion, erosion, or swelling can be modeled using kinetic equations (e.g., Higuchi, Korsmeyer-Peppas) to predict *in vivo* performance.

6. Therapeutic and Biomedical Applications

The versatile architecture of surfactant-based nanocarriers has led to their adoption across a broad spectrum of therapeutic areas, ranging from local dermatological treatments to systemic delivery of biologics.

6.1. Dermatological and Cosmetic Applications

Surfactant vesicles are widely utilized in the treatment of skin diseases such as psoriasis, atopic dermatitis, and acne. For instance, niosomes loaded with dithranol or methotrexate have shown improved accumulation in the viable epidermis while reducing systemic absorption and associated side effects [29]. In the cosmetic sector, these carriers are employed to deliver antioxidants (e.g., Vitamin C, Vitamin E) and anti-aging agents. The surfactant bilayers protect these labile compounds from oxidation and facilitate their penetration into the deeper dermal layers, enhancing their efficacy in collagen synthesis and skin rejuvenation [30].

6.2. Transdermal Delivery of Systemic Therapeutics

One of the most significant advancements facilitated by transferosomes and transethosomes is the non-invasive delivery of systemic drugs.

6.2.1. Insulin Delivery

Transferosomes encapsulating insulin have demonstrated the ability to regulate blood glucose levels in diabetic models. The deformable vesicles squeeze through the stratum corneum pores, protecting the insulin peptide from enzymatic degradation in the skin and facilitating its uptake into the systemic circulation, offering a painless alternative to subcutaneous injections [31].

6.2.2. Pain Management

Transdermal delivery of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids via nanoemulsions allows for sustained pain relief with reduced gastrointestinal toxicity compared to oral administration.

6.3. Nose-to-Brain Drug Delivery

The olfactory and trigeminal nerve pathways in the nasal cavity provide a direct route to the central nervous system (CNS), bypassing the blood-brain barrier (BBB). Surfactant-based nanocarriers, particularly nanoemulsions and mucoadhesive niosomes, have shown promise in delivering neurotherapeutics for conditions such as Alzheimer's disease, Parkinson's disease, and epilepsy [32]. The small particle size (<200 nm) and the permeation-enhancing properties of surfactants facilitate the transport of drugs directly from the nasal mucosa to the brain, achieving higher cerebral concentrations than systemic administration.

Table 5. Applications of Surfactant-Based Nanocarriers in Pharmacotherapy

Therapeutic Area	Drug / Bioactive	Nanocarrier System	Benefit
Diabetes	Insulin	Transferosomes / Transethosomes	Non-invasive delivery; protection from enzymatic degradation; improved bioavailability.
Dermatology (Psoriasis)	Methotrexate / Dithranol	Niosomes	Enhanced accumulation in viable epidermis; reduced systemic toxicity and skin irritation.
Pain & Inflammation	Diclofenac / Ibuprofen	Nanoemulsions	Sustained release; deeper tissue penetration; avoidance of GI side effects.
Neurology (CNS)	Risperidone / Diazepam	Nanoemulsions (Nose-to-Brain)	Direct transport to brain via olfactory nerve; bypassing Blood-Brain Barrier (BBB).
Oncology	Doxorubicin / Curcumin	Niosomes (PEGylated) / SLNs	Passive targeting via EPR effect; reversal of multidrug resistance (MDR).
Cosmetics	Vitamin C / Retinol	Niosomes / Liposomes	Protection from oxidation; enhanced skin rejuvenation and collagen synthesis.

6.4. Targeted Cancer Therapy

In oncology, surfactant-based carriers are engineered to exploit both passive and active targeting mechanisms.

6.4.1. Passive Targeting

Nanosized carriers (specifically SLNs and NLCs) accumulate in tumor tissues due to the Enhanced Permeability and Retention (EPR) effect caused by leaky tumor vasculature [33].

6.4.2. Active Targeting

The surface of niosomes can be functionalized with ligands such as folic acid or antibodies that specifically bind to receptors overexpressed on cancer cells (e.g., folate receptors, EGFR). This targeted approach maximizes drug cytotoxicity within the tumor while sparing healthy tissues. Furthermore, certain surfactants used in these formulations, such as Pluronics and TPGS, have been shown to inhibit P-glycoprotein efflux pumps, thereby reversing multidrug resistance (MDR) in cancer cells [34].

6.5. Delivery of Biologics and Macromolecules

The transdermal delivery of high-molecular-weight biologics (proteins, peptides, vaccines) is historically challenging. However, ultra-deformable vesicles like transethosomes have successfully delivered therapeutic proteins and genetic material (siRNA, DNA plasmids) across the skin barrier [35]. These systems protect the biological payload from degradation and facilitate cellular transfection, opening new avenues for transcutaneous immunization and gene therapy.

7. Conclusion

Surfactant-based nanocarriers represent a transformative leap in transdermal drug delivery technology. By intelligently combining the amphiphilic properties of surfactants with lipid-based structures, researchers have developed systems that not only overcome the formidable barrier of the stratum corneum but also provide controlled release, improved stability, and targeted delivery capabilities. From the robust stability of niosomes to the remarkable deformability of transferosomes and the high drug-loading capacity of lipid nanoparticles, each system offers unique advantages tailored to specific therapeutic needs. While significant progress has been made, challenges regarding long-term physical stability, scale-up manufacturing, and the need for comprehensive nanotoxicology profiles remain. Future research must focus on the development of biocompatible, "green" biosurfactants and the integration of smart, stimuli-responsive features to create the next generation of intelligent transdermal systems. Ultimately, these nanocarriers hold the potential to redefine standard of care across oncology, endocrinology, and dermatology, making non-invasive therapy a tangible reality for complex medical conditions.

References

[1] Kuznetsova DA, Gaynanova GA, Vasilieva EA, Pavlov RV, Sapunova AS, Buzyurova DN, et al. Enhancement of the transdermal delivery of nonsteroidal anti-inflammatory drugs using W/O/W multiple emulsions: *in vitro* and *in vivo* studies. Nanomaterials. 2022;12(24):4403.

[2] Bami MS, Olesen CM, Arora S, Lomstein SBA, Franzyk H, Thakur A, et al. Potential of biosurfactant as green pharmaceutical excipient for drug delivery in microneedle-based transdermal delivery systems: safety, formulation, and regulatory perspectives. AAPS PharmSciTech. 2024;25(6):164.

[3] Strati F, Neubert RHH, Opálka L, Kerth A. Non-ionic surfactants as innovative skin penetration enhancers: insight in the mechanism of interaction with simple 2D stratum corneum model system. Eur J Pharm Sci. 2021;157:105620.

[4] Tapfumaneyi P, Imran M, Mohammed Y, Roberts MS, Benson HAE, Grice JE. Recent advances and future prospective of topical and transdermal drug delivery systems. Front Drug Deliv. 2022;2:950891.

[5] Nadim N, Jamei A, Zadeh MT, Fathi H, Dastmalchi S, Afshar M. A narrative review on potential applications of Spanlastics in drug delivery and biomedical sciences. Adv Colloid Interface Sci. 2025;335:103341.

[6] Ashutosh S. Comparative analysis of liposomal and surfactant-based drug delivery systems. J Pharm Sci. 2023.

[7] Miyazawa T, et al. A critical review of the use of surfactant-coated nanoparticles in nanomedicine and food nanotechnology. Int J Nanomed. 2021;16:3937–3999.

[8] Ridout G, Hinz RS, Hostynek JJ, Reddy AK, Wiersema RJ, Hodson CD, et al. The effects of zwitterionic surfactants on skin barrier function. Toxicol Sci. 1991;16(1):41–50.

[9] Alshawwa SZ, et al. Nanocarrier drug delivery systems: characterization, limitations, future perspectives and implementation of artificial intelligence. Pharmaceutics. 2022;14(4):883.

[10] Yeo PL, Lim CL, Chye SM, Ling AK, Koh RY. Niosomes: a review of their structure, properties, methods of preparation, and medical applications. Asian Biomed. 2017;11(4):301–314.

[11] Opatha SA, Titapiwatanakun V, Chutoprapat R. Transfersomes: a promising nanoencapsulation technique for transdermal drug delivery. Pharmaceutics. 2020;12(9):855.

[12] Verma S, Kumar S. Transethosomes: a versatile tool for transdermal drug delivery of insulin. J Control Release. 2021;330:456-469.

[13] Viegas C, Patrício AB, Prata JM, Nadhman A, et al. Solid lipid nanoparticles vs. nanostructured lipid carriers: a comparative review. Pharmaceutics. 2023;15(3):939.

[14] Khan S, Sharma A, Jain V. An overview of nanostructured lipid carriers and its application in drug delivery through different routes. Adv Pharm Bull. 2022;12(1):164–177.

[15] Salama AA, et al. Nanoemulsions: formulation, characterization, biological fate, and potential role against COVID-19 and other viral outbreaks. PMC. 2023;11945362.

[16] Thabet Y, Elsabahy M, Eissa NG. Methods for preparation of niosomes: a focus on thin-film hydration method. Methods. 2022;199:9–15.

[17] Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M, et al. Niosome: a future of targeted drug delivery systems. J Adv Pharm Technol Res. 2010;1(4):374–380.

[18] Shafiepour M, Razavi SH, Khanniri E, Jahan FM, Nouri M, Afraei M. Nanocarriers for foods: a review of niosomes and proniosomes in bioactive compounds. Food Humanit. 2025;100623.

[19] Julio LM, Copado CN, Diehl BW, Tomás MC, Ixtaina VY. Development of chia oil-in-water nanoemulsions using different homogenization technologies and the layer-by-layer technique. Colloids Surf A. 2019;583:123927.

[20] Soni M, et al. Nanoemulsion formation by low-energy methods: a review. OUCI. 2023;12(21):401.

[21] Pereir SF, Barroso A, Mourão RH, Fernandes CP. A low energy approach for the preparation of nano-emulsions with a high citral-content essential oil. Molecules. 2021;26(12):3666.

[22] Javed S, Mangla B, Almoshari Y, et al. Nanostructured lipid carrier system: a compendium of their formulation development approaches, optimization strategies by quality by design, and recent advances. Nanotechnol Dev. 2022;12(1):2100018.

[23] Iacob AT, Ababei-Bobu A, Chirliu OM, Lupascu FG, Vasincu IM, Apotrosoaei M, et al. A state-of-the-art review on recent biomedical application of polysaccharide-based niosomes as drug delivery systems. Polymers. 2025;17(11):1566.

[24] Rodriguez-Loya J, Lerma M, Gardea-Torresdey JL. Dynamic light scattering and its application to control nanoparticle aggregation in colloidal systems: a review. Micromachines. 2023;15(1):24.

[25] Ibrahim AH, et al. Transethosomes for enhanced transdermal delivery of tizanidine hydrochloride: formulation, *in-vitro*, and *in-vivo* evaluation. Drug Deliv. 2022;29(1):123-135.

[26] Lens M. Niosomes as vesicular nanocarriers in cosmetics: characterisation, development and efficacy. Pharmaceutics. 2025;17(3):28.

[27] Bakand A, Moghaddam SV, Naseroleslami M, André H, Mousavi-Niri N, Alizadeh E. Efficient targeting of HIF-1α mediated by YC-1 and PX-12 encapsulated niosomes: potential application in colon cancer therapy. J Biol Eng. 2023;17(1):58.

[28] Agbaje KO, Adesina SK, Adebayo AS. Development and characterization of optimized drug-loaded niosomes for delivery of 5-FU and irinotecan. Pharmaceutics. 2025;17(7):900.

[29] Singh D, et al. Development of transethosomes for enhanced permeation of an anti-psoriatic drug, dithranol. Pharm Dev Technol. 2022;27(3):299-311.

[30] Gupta V, Mohapatra S, Mishra H, Farooq U, Kumar K, Ansari MJ, et al. Nanotechnology in cosmetics and cosmeceuticals a review of latest advancements. Gels. 2022;8(3):173.

[31] Jasmin MKP, Battu S, Vishwanath BA. Transferosomes for effective transdermal drug delivery. J Pharm Res Int. 2024.

[32] Lorenzett AK, Lima VA, Fonseca CO, Mainardes RM. Nanoemulsions and microemulsions for intranasal drug delivery: a bibliometric analysis and emerging trends (2004–2024). Pharmaceutics. 2025;17(9):1104.

[33] Sivadasan D, Ramakrishna K, Mahendran J, et al. Solid lipid nanoparticles: applications and prospects in cancer treatment. Int J Mol Sci. 2023;24(20):15112.

[34] Bashkeran T, Kamaruddin AH, Ngo TX, Suda K, Umakoshi H, Watanabe N, et al. Niosomes in cancer treatment: a focus on curcumin encapsulation. Heliyon. 2023;9(8):e18532.

[35] Sharma G, et al. Transethosomes as a vesicular carrier for enhanced transdermal delivery of methotrexate. J Microencapsul. 2021;38(4):245-258.