INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Nano-Cosmeceuticals: A Comprehensive Review on Lipid-Based Nanoparticles (SLNS And NLCS) In Anti-Acne and Sunscreen Formulations

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ARTICLE INFO

Published: 26 Jun. 2026
Keywords:
Nano-cosmeceuticals, Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), Lipid-based Nanoparticles, Anti-Acne Therapy, Sunscreen Formulations, SPF Enhancement, Topical Drug Delivery, Stratum Corneum, High-Pressure Homogenization
DOI:
10.5281/zenodo.20924356

ABSTRACT

Nano-cosmeceuticals," a revolutionary paradigm in topical drug delivery systems, are the result of the convergence of nanotechnology and cosmetic science. Due to uncontrolled absorption, traditional skincare formulations frequently have systemic side effects, poor dermal penetration, and chemical instability of active ingredients. Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs), two lipid-based nanoparticles, have become highly effective biocompatible matrices that can overcome these formulation challenges. The structural characteristics, choice of lipid excipients, and stabilization mechanisms of SLNs and NLCs are all thoroughly assessed in this review article. It specifically examines their main clinical uses in sophisticated sunscreen systems and targeted anti-acne treatments. These lipid carriers reduce skin irritation, improve the deep follicular penetration of lipophilic molecules such as salicylic acid and retinoids, and offer sustained-release profiles in anti-acne formulations. SLNs and NLCs function as active physical blockers in UV protection systems, increasing the Sun Protection Factor (SPF) and successfully lowering the systemic absorption and photodegradation of chemical filters. Additionally, this paper offers a technical overview of industrial production techniques like microemulsion and high-pressure homogenization. A detailed examination of skin toxicity profiles, regulatory guidelines, and future commercial trajectories follows this. This review highlights the clear technological superiority of second-generation NLCs over conventional systems and offers a practical guide for advancing contemporary dermaceuticals.

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

INTRODUCTION

The human skin is the largest organ of the body, presenting an intricate cellular meshwork specialized to shield physiological homeostasis from external xenobiotics, physical injury, and solar radiation. The primary rate-limiting outermost stratum of this biological gatekeeper is the stratum corneum (SC). Often conceptually described by formulation scientists as a 'brick-and-mortar' configuration, the SC contains non-living, keratin-packed corneocytes (the bricks) firmly sealed within an ordered, continuous lamellar extracellular lipid matrix (the mortar). This intercellular matrix consists of a strict equitable ratio of free fatty acids, cholesterol, and ceramides. Because of this hydrophobic and tightly organized barrier, topically applied pharmaceutical or cosmetic ingredients with a molecular weight exceeding 500 Da or possessing extreme hydrophilic/lipophilic coefficients find it practically impossible to achieve passive dermal flux into deeper target tissues.

Conventional dermaceutical formulations such as macro-scale hydrogels, macrogol creams, water-in-oil (w/o) emulsions, and simple localized lotions routinely hit thermodynamic and mechanical boundaries. These conventional vehicles are prone to rapid environmental oxidation, phase inversion, syneresis, and erratic drug crystallization on the skin surface. Furthermore, aggressive active agents such as retinoic acid or organic UV filters cause immediate surface adverse events—including erythema, localized burning, desquamation, and barrier scaling—due to high localized concentration spikes on the non-target outer stratum corneum layer.

To overcome these historical limitations, Novel Drug Delivery Systems (NDDS) have entered mainstream aesthetic and clinical research. Over several decades, microparticles, liposomes, transfersomes, ethosomes, dendrimers, and polymeric nanostructures were introduced. However, polymeric systems carry lingering safety concerns due to organic solvent chemical residues and non-biodegradable polymer degradation accumulation inside vital epidermal cells. Liposomes possess high physiological compatibility but are heavily restricted by a low structural payload for hydrophobic molecules, rapid chemical leakage in aqueous bases, and extremely difficult or non-reproducible large-scale high-energy production cycles.

Colloidal sub-micron lipid nanoparticles—specifically Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs)—represent the modern solution to this drug delivery paradox. Synthesized using physiological, completely biodegradable, non-toxic lipids that maintain a solid physical form at both ambient temperature and internal human body conditions, these systems create a highly uniform sub-micron distribution. They establish an occlusive nano-film over the stratum corneum, reducing trans-epidermal water loss (TEWL), triggering local cellular hydration, and aligning cleanly with the natural lipid pathways of the skin. This exhaustive review article highlights the structural, formulation, chemical, and regulatory landscape of lipid nanoparticles, focusing extensively on their high-

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impact clinical roles in anti-acne and sunscreen formulations.

4. COMPARATIVE TECHNICAL ANALYSIS OF DERMAL COLLOIDAL CARRIERS:

To clearly distinguish the advanced standing of SLNs and NLCs from other historical nanostructures, the following comprehensive structural comparison matrix outlines the thermodynamic parameters, advantages, and drawbacks of each system:

Nanocarrier classification	Structural architecture	Payload entrapment	Long-term thermodynamic stability	Key scale-up & processing bottlenecks
Liposomes	The aqueous inner core enveloped by a phospholipid double layer.	Restricted for lipophilic agents; moderate efficiency observed with water-soluble components.	Suboptimal; susceptible to membrane leakage, vesicle aggregation, and chemical degradation.	Technical hurdles in large-scale manufacturing; risks associated with toxic solvent residues.
Polymeric nanoparticles	Synthesized from biodegradable or natural macromolecules (e.g., PLA, PLGA).	Broadly high structural capacity to encapsulate diverse molecular structures.	Variable; ranges from intermediate to high depending on polymer-solvent processing parameters.	Potential toxicity from trace unreacted monomers; biological accumulation of non-cleavable matrices.
Solid Lipid Nanoparticles (SLN)	Solid crystalline lipid framework stabilized externally via tailored co-surfactants.	Restricted loading capacity owing to the highly ordered, rigid crystal arrangement.	Unstable long-term; polymorphic transitions over time trigger spontaneous drug expulsion.	Propensity for sudden formulation gelation; premature cargo release during thermal cooling cycles.
Nanostructured Lipid Carriers (NLC)	Spatially disordered matrix composed of blended solid lipids and liquid lipids (oils).	Exceptionally high; deliberate structural irregularities provide extensive molecular storage voids.	Superb; chaotic matrix design actively suppresses polymorphic rearrangement and leakage.	Demands highly precise and complex optimization of the exact solid-to-liquid lipid ratios.

5. STRUCTURAL ARCHITECTURE AND POLYMORPHIC DYNAMIC:

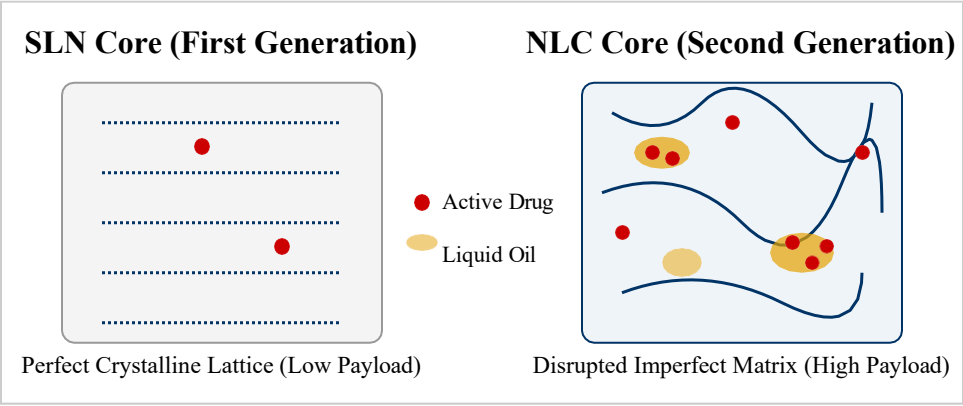
Lipid nanoparticles represent a highly specialized sub-micron colloidal class usually engineered with diameters between 50 nm and 1000 nm. Their core

structure features a highly hydrophobic internal lipid center enclosed by an amphiphilic shell of surfactants dispersed cleanly inside an aqueous continuous phase.

5.1 Solid Lipid Nanoparticles (SLNs) & Crystal Packing:

Solid Lipid Nanoparticles represent the foundational first-generation phase of solid lipid colloids. They are produced by systematically replacing the fluid oil core of a classic oil-in-water (o/w) emulsion with a pure single lipid or lipid mixture that remains rigid and solid at room and body temperature. When cooled, these pure lipid ingredients (such as pure tristearin or palmitic acid) arrange into a highly organized, perfect crystalline lattice. While this rigid core protects the embedded active drug from ambient air exposure, it drastically limits drug loading capacity. Because the crystal lattice is highly symmetric, there are very few structural defects or molecular gaps where the active drug molecules can fit. Over time, these solid matrices experience a natural thermodynamic shift known as a polymorphic transition. The lipids slowly transform from an unstable high-energy alpha-polymorph (α-form) into a highly compressed, perfectly stable beta-polymorph (β-form). This shifting lattice reduces the intermolecular distances within the lipid matrix, squeezing out the embedded active ingredients and causing phase separation and product sedimentation.**5.2 Nanostructured Lipid Carriers (NLCs) & The Spatial Disruption:**

To overcome the structural instability and low capacity of SLNs, second-generation Nanostructured Lipid Carriers (NLCs) were developed. The core of an NLC is engineered by blending a solid lipid with a liquid lipid (a liquid oil) at a controlled ratio, typically between 70:30 and 99:1. Because the liquid oil molecules have very different chain lengths and structures compared to the solid lipid crystals, their inclusion completely disrupts the formation of a perfect crystal lattice. Instead, the resulting NLC matrix contains highly imperfect, distorted, and unorganized crystalline regions. These structural defects provide ample space to trap and hold high concentrations of active cosmetic ingredients, dramatically increasing the loading capacity. Furthermore, the liquid oil domains within the core suppress the polymorphic shift to the tight beta-form during long-term storage, keeping the system stable and preventing drug expulsion over time.



6. TECHNICAL PROCESS CHART: STRUCTURAL MECHANISM OF ACTION

The functional pathway of NLC dermal delivery can be mapped out step-by-step through the following architectural operational flow sequence:

NLC Dermal Delivery Operational Workflow

Step 01: Topically apply NLC Cream Base to the skin stratum corneum

↓

Step 02: Sub-micron particles form a tight occlusive nano-film on the surface

↓

Step 03: Block Evaporation → Reduce TEWL → Local Skin Hydration

↓

Step 04: Corneocytes swell & loosen intercellular lipid layers

↓

Step 05: Passive diffusion of active molecules down the concentration gradient

↓

Step 06: Preferential accumulation and sustained release in shunt follicles

7. CHEMICAL REACTION SCHEMA AND ACTIVE AGENT PROFILE:

The performance of lipid nanoparticles relies heavily on the chemical structure of the active ingredients and their interaction with the lipid matrix. The following comprehensive profile highlights the key chemical parameters, molecular configurations, and stabilization reactions of the primary actives used in anti-acne and sunscreen systems:

7.1 Salicylic Acid (Anti-Acne Active)

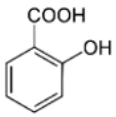
Salicylic acid is a beta-hydroxy acid (BHA) widely used in anti-acne formulations. It exfoliates the skin, unclogs pores, reduces inflammation, and helps prevent acne lesions. In SLNs and NLCs, it can provide controlled release and improve skin penetration.

Salicylic Acid chemical blueprint

Chemical formula: C7H6O3 Simplified Structure: HO-C6H4-COOH

Molecular weight: 138.12 g/mol

Chemical structure:



Stabilization Mechanism: The carboxyl group and benzene ring readily fit into the voids of NLC matrices (such as Compritol 888 combined with Miglyol 812). By preventing the acidic carboxyl group from coming into direct contact with the epidermal surface, this encapsulation significantly lessens topical irritation while preserving continuous therapeutic release.

7.2 Retinol (Vitamin A Derivatives)

Retinol (Vitamin A) promotes skin cell turnover, reduces acne formation, improves skin texture, and helps minimize signs of aging. Lipid nanoparticles improve their stability against light and oxidation while enhancing dermal delivery.

Retinol chemical blueprint

Chemical formula: C20H30O

Molecular weight: 310.39 g/mol

Simplified structure: β- Ionone ring - Polyene chain- OH

Stabilization mechanism: Retinol is highly unstable because light, air, and heat easily break down its chemical structure, rendering it ineffective. To protect it, cosmetic chemists rely on physical encapsulation (trapping retinol inside microscopic lipid or polymer shells to shield it and control its release) and chemical antioxidant networks (using sacrificial ingredients like Vitamin E and C to neutralize oxygen before it can degrade the retinol). Combined with waterless formulas, airless packaging, and a neutral pH, these mechanisms ensure the molecule remains active and potent until it is absorbed into your skin.

7.3 Avobenzone (Chemical UV Filter)

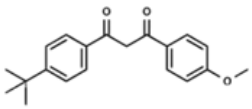
Avobenzone is a UVA sunscreen agent that protects the skin from long-wave UV radiation. Encapsulation in SLNs and NLCs improves photostability, reduces degradation, and enhances sunscreen performance.

Avobenzone chemical reaction matrix

Chemical formula: C20H22O3

Molecular weight: 310.39 g/mol

Chemical structure:



Stabilization matrix: An avobenzone stabilization matrix is a carefully engineered chemical environment within a sunscreen that prevents the primary UVA filter, Avobenzone, from rapidly breaking down when exposed to sunlight. By itself, avobenzone is highly photounstable, losing up to half of its sun-protection capacity within a single hour of UV exposure because it breaks apart after absorbing light energy. To fix this, formulators create a "matrix" by pairing it with strategic co-ingredients—such as Octocrylene, Tinosorb S, or Solastay S1—which act as energy sponges that safely absorb and dissipate that destructive energy as heat before it can destroy the avobenzone. This complex chemical teamwork ensures the sunscreen maintains its protective UVA barrier on the skin for the full recommended two hours.

8. ADVANCED CO-ENCAPSULATION AND HYBRID SYSTEM:

A modern paradigm shift in nano-cosmeceuticals involves the simultaneous entrapment of multiple synergistic active ingredients within a single engineered nanocarrier, known as co-encapsulation or hybrid nanostructures. Traditional formulation strategies are highly restricted by individual active solubilities, where dual incorporation of a highly lipophilic compound alongside an extremely hydrophilic counterpart causes inevitable phase separation, uneven topical coverage, and molecular competition for lipidic domains. For instance, in severe clinical acne treatment, combining an antimicrobial agent like Clindamycin Phosphate (hydrophilic) with a powerful comedolytic retinoid like Tretinoin (lipophilic) represents the gold standard. However, putting these together into a conventional gel network often results in rapid degradation of the retinoid and reduced skin penetration of the antibiotic.

To circumvent this challenge, lipid-polymer hybrid nanoparticles (LPHNs) and core-shell dual lipid particles have emerged. LPHNs feature a hydrophobic polymeric core (such as poly-lactic-co-glycolic acid, PLGA) that encapsulates the highly lipophilic active, surrounded by an outer monolayer or bilayer of physiological solid lipids that shield the inner core and act as a secondary depot for hydrophilic molecules. This spatial architecture provides distinct compartmentalization, meaning both actives can

be deployed harmoniously without direct chemical incompatibility. In anti-acne therapeutics, this architecture ensures a dual-stage kinetic profile: the hydrophilic antibiotic is released from the surface outer lipid coat in an immediate burst to rapidly reduce superficial Propionibacterium acnes populations, followed by a sustained, zero-order slow release of the retinoid from the deep core to modulate cell differentiation over an extended 24-hour period. Similarly, in advanced sunscreen designs, co-encapsulating an organic chemical filter like Avobenzone within the core and dispersing inorganic physical blockers like Zinc Oxide within the outer surfactant mantle maximizes light attenuation via simultaneous absorption and scattering, yielding unprecedented Sun Protection Factor (SPF) metrics without requiring heavy chemical loads.

9. DETAILED EXCIPIENT MATRIX FOR LIPID NANO PARTICLES:

To build a stable structural architecture for Nanostructured Lipid Carriers (NLCs), choosing the right combination of excipients is essential. The table below outlines the core components typically evaluated during formulation development, highlighting their physical characteristics and specific functional roles within the lipid matrix.

Table: Structural components and functional roles of essential excipients used in NLC engineering.

STRUCTURAL COMPONENT	REPRESENTATIVE EXAMPLE	PHYSICOCHEMICAL ATTRIBUTES	FUNCTIONAL MECHANISM IN NLCs
Solid Lipid base	Glyceryl Behenate (Compritol 888 ATO), Cetyl Palmitate, Stearic Acid, Cetyl Alcohol	Melting Point Range: 55°C to 85°C	Establishes the fundamental solid hydrophobic core matrix. Key factor in sustaining drug release kinetics and preventing premature burst release.
Liquid Lipid (Oil Profile)	Caprylic/Capric Triglycerides (Miglyol 812), Oleic Acid, Isopropyl Myristate, Castor Oil	Maintains a fluid state at room temperature	Strategically distorts the highly crystalline lattice of the solid lipid base. This structural imperfection creates more space to maximize drug payload and prevents drug expulsion during storage.
Surfactants and Co-surfactants	Polysorbate 80 (Tween 80), Poloxamer 188, Soy Lecithin, Span 60	HLB Value Range: 4.0 to 16.0	Reduces interfacial tension at the oil-water boundary. Minimizes surface free energy to effectively prevent particle aggregation, flocculation, and coalescence.

10. ADVANCE MANUFACTURING AND SCALE-UP METHODOLOGIES:

To produce high-quality lipid nanoparticles with an extremely narrow size distribution, formulation scientists utilize high-energy or low-energy manufacturing techniques:

10.1 Hot High-Pressure Homogenization (Hot HPH)

The industry standard for producing lipid nanoparticles is hot HPH. At a temperature that is approximately 5–10°C higher than the solid lipid's melting point, the liquid and solid lipids are combined and melted. Retinol or Avobenzone are examples of active cosmeceutical ingredients that are dissolved straight into this molten lipid phase. To make a coarse hot pre-emulsion, an aqueous surfactant solution is simultaneously heated to the same temperature and combined with the lipid melt using a high-shear mixer. After that, this pre-emulsion is sent through a high-pressure homogenizer for several cycles at pressures ranging from 500 to 1500 bar. The emulsion droplets are broken down to the nanoscale by the strong shear pressures, cavitation, and turbulent impacts. Upon cooling to room temperature, the nano-droplets solidify, forming stable SLNs or NLCs.

10.2 Cold High-Pressure Homogenization (Cold HPH)

In order to manage highly heat-sensitive or water-soluble active substances that are unable to endure the high temperatures of the hot homogenization process, cold HPH was created. This method dissolves or evenly distributes the active medication into the melted lipid phase. After that, dry ice or liquid nitrogen is used to quickly cool this mixture. Phase separation is prevented by this quick cooling, which distributes the medication evenly and solidly throughout the lipid block. After the drug-lipid block has formed, it is mechanically ground into tiny microparticles, usually between 10 and 100 microns. Stable, sub-micron lipid nanoparticles are produced by passing these microparticles through a high-pressure homogenizer at or below room temperature while suspended in an ice-cold surfactant solution.

11. RIGOROUS CHARACTERIZATION AND QUALITY CONTROL PARAMETERS:

To secure regulatory approvals from bodies like the FDA or EMA, lipid nanoparticle formulations must undergo strict quality control testing. The following matrix details the critical parameters and analytical methods used:

Characterization Parameter	Standard Analytical Instrument used	Acceptable Limits & Quality Specifications
Particle Size Analysis	Dynamic Light Scattering (DLS) / Photon Correlation Spectroscopy	Ideally, between 100 nm and 300 nm for deep follicular skin targeting
Polydispersity Index (PDI)	Laser Diffraction Particle Size Analyzers	Less than 0.25 indicates a highly uniform and stable distribution
Zeta Potential (Surface Charge)	Zetasizer / Electrophoretic Light Scattering Instruments	Greater than +30 mV or less than -30 mV for strong electrostatic stability

Entrapment Efficiency (EE%)	Ultracentrifugation followed by HPLC Analysis	Greater than 85% for lipophilic active agents and UV filters
Crystalline Polymorphism	Differential Scanning Calorimetry (DSC) & X-ray Diffraction (XRD)	Identifies crystal defects, amorphous regions, and polymorphic shifts

12. REGULATORY LANDSCAPES, TOXICOLOGICAL PROFILES, AND FUTURE MILESTONES:

Because nano-scale materials possess an incredibly high surface-area-to-volume ratio, they exhibit radically altered physicochemical properties compared to standard macro-scale ingredients. Consequently, regulatory agencies (such as the USFDA and the European Cosmetics Regulation EC 1223/2009) enforce strict guidelines on products containing engineered particles under 100 nm. The primary regulatory concern is the risk of unexpected systemic absorption, where ultra-small nanoparticles could breach local dermal tissues, enter the bloodstream, and accumulate in internal organs like the liver or kidneys, potentially triggering systemic oxidative stress.

Fortunately, because SLNs and NLCs are fabricated using physiological, biodegradable lipids that are safely broken down by the skin's natural enzymes (like lipases), they boast an exceptionally safe biocompatibility profile. Extensive in-vitro cytotoxicity testing on human skin models (HaCaT cell lines) and in vivo human patch testing have repeatedly proven that lipid nanoparticles cause negligible irritation compared to polymeric nanostructures or raw chemical solutions. The remaining industrial hurdles include ensuring long-term physical stability beyond two years, avoiding gelation during storage, and preventing structural degradation during large-scale manufacturing.

The future of lipid-based nano-cosmeceuticals is incredibly promising. Current research is focusing on 'smart', stimuli-responsive lipid matrices that can release active anti-acne compounds only when triggered by specific environmental cues, such as a shift in skin pH or an increase in enzyme concentrations secreted by acne-causing bacteria. Additionally, combining lipid nanoparticles with 3D-printed hydrogel patches and biomimetic skin carriers represents the next major milestone in personalized, clinical-grade dermatology.

13. CONCLUSION:

Lipid-based nanoparticles represent a major technological breakthrough in the field of formulation science and nano-cosmeceuticals. By elegantly resolving the performance limitations of conventional topical vehicles, Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) provide an uncompromised platform for targeted, controlled, and stable drug delivery. In anti-acne therapies, encapsulation shields sensitive active ingredients from degradation and modulates their release kinetics, maximizing target uptake within hair follicles while successfully preventing surface skin irritation. In sunscreen systems, the intrinsic UV-scattering properties of the solid lipid core create a powerful physical-chemical defensive synergy, maximizing SPF protection while minimizing the concentration and systemic absorption of chemical filters. While first-generation SLNs paved the way, second-generation NLCs—with their imperfect crystal matrices, superior drug loading capacities, and absolute stability against drug

expulsion—stand out as the definitive vehicle for next-generation cosmetic and dermatological products. As regulatory guidelines clear up and manufacturing technologies standardize, lipid-nanoparticle-driven formulations will undoubtedly redefine the standards of clinical skincare worldwide.

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HOW TO CITE: Harshkumar Parmar*, Aditi Tyagi, Nano-Cosmeceuticals: A Comprehensive Review on Lipid-Based Nanoparticles (SLNS And NLCS) In Anti-Acne and Sunscreen Formulations, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 6652-6663. https://doi.org/10.5281/zenodo.20924356