Research Article

Phytonanomedicine in Adolescent Dermatology: Formulation Advances, Therapeutic Potential and Future Perspectives

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Abstract

Adolescent skin health is integral to overall well-being, as dermatological conditions such as acne, psoriasis, atopic dermatitis, inflammatory skin disorders, and wound-related complications can arise during this developmental stage. Herbal medicines contain diverse bioactive phytochemicals with potential dermatological applications; however, their topical effectiveness is often limited by poor solubility, chemical instability, inadequate skin penetration, and inconsistent drug release. Phyto-nanomedicine offers an emerging approach to overcome these limitations by incorporating plant-derived bioactive compounds into specialized nanocarrier systems. This review explores advances in topical herbal Nanoformulations and their therapeutic potential for adolescent skin health, particularly for psoriasis, wound healing, and inflammatory skin disorders. Major formulation approaches, including liposomes, niosomes, phytosomes, nanoemulsions, solid lipid nanoparticles, and nanostructured lipid carriers, are discussed for their ability to enhance phytochemical stability, skin deposition, controlled release, and local bioavailability. Particular attention is given to the antioxidant, anti-inflammatory, antimicrobial, and wound-healing properties of nano-formulated herbal constituents. Experimental and preclinical evidence is evaluated to assess their potential to modulate inflammation, support tissue repair, and improve topical therapeutic outcomes. The review also addresses formulation characterization, skin permeation, stability, and dermal safety. Despite promising developments, challenges remain in phytochemical standardization, formulation variability, long-term toxicity, and limited clinical evidence. Furthermore, translating existing dermatological evidence into adolescent-specific applications requires careful assessment of age-related safety considerations. Phyto-nanomedicine therefore represents a promising platform for advanced topical therapies, warranting further standardized investigations and well-designed clinical studies to establish its safety and therapeutic effectiveness in adolescent dermatological care.

Keywords: Adolescent skin health; Phyto-nanomedicine; Herbal Nanoformulations; Topical drug delivery; Psoriasis; Wound healing; Inflammatory skin disorders; Phytochemicals.

1. INTRODUCTION

Adolescent skin health is an important component of overall well-being, as dermatological conditions, including acne, psoriasis, atopic dermatitis, inflammatory skin disorders, and wound-related complications, may arise or persist during this developmental stage. These conditions can involve persistent inflammation, impaired skin barrier function, altered tissue repair, and considerable physical and psychological discomfort. Although conventional topical therapies are widely used, their effectiveness may be limited by inadequate drug penetration, local adverse effects, poor patient adherence, and the need for prolonged treatment. These limitations have encouraged the exploration of plant-derived bioactive compounds as potential therapeutic agents for dermatological applications [1,2].

Medicinal plants contain diverse phytoconstituents, including flavonoids, polyphenols, terpenoids, and alkaloids, which have been reported to exhibit antioxidant, anti-inflammatory, antimicrobial, and wound-healing activities. These pharmacological properties offer considerable potential for addressing inflammatory skin conditions and supporting tissue repair. However, the topical application of conventional herbal preparations may be constrained by poor aqueous solubility, chemical instability, limited skin penetration, and inconsistent release of active constituents. Consequently, nanotechnology-based delivery systems have attracted growing attention as a means to improve the pharmaceutical performance and topical delivery of herbal bioactives [1].

Phyto-nanomedicine involves incorporating plant extracts or isolated phytoconstituents into nanoscale delivery systems, including liposomes, niosomes, ethosomes, transferosomes, nanoemulsions, solid lipid nanoparticles, and nanostructured lipid carriers. These systems can improve phytochemical stability, control drug release, enhance skin deposition, and increase local bioavailability. Their applications are particularly relevant to psoriasis, where localized delivery of anti-inflammatory phytochemicals is desirable; wound healing, where antioxidant, antimicrobial, and tissue-repair activities are important; and inflammatory skin disorders, where

modulation of inflammatory responses and restoration of skin barrier function are essential therapeutic considerations [2–4].

Despite promising experimental findings, the clinical translation of herbal Nanoformulations remains challenging. Variability in plant composition, formulation reproducibility, inadequate standardization, dermal safety concerns, and limited clinical validation require further investigation. Moreover, evidence from general dermatological studies cannot be automatically extrapolated to adolescent populations without accounting for age-specific safety requirements and clinical suitability. Therefore, this review explores advances in topical herbal Nanoformulations for adolescent skin health, with particular emphasis on psoriasis, wound healing, and inflammatory skin disorders. It further examines major nanocarrier systems, skin delivery characteristics, pharmacological potential, formulation evaluation, and translational challenges, highlighting future opportunities for developing safe and effective Phyto-nanomedicine-based topical approaches.

2. PATHOPHYSIOLOGICAL BASIS OF SELECTED DERMATOLOGICAL DISORDERS

2.1. Psoriasis

Psoriasis is a chronic, immune-mediated inflammatory skin disorder that can develop in childhood or adolescence and is associated with significant physical and psychosocial burden. It is characterized by excessive proliferation and abnormal differentiation of keratinocytes, along with infiltration of inflammatory cells into the skin. Its pathogenesis involves complex interactions among dendritic cells, T lymphocytes, keratinocytes, and inflammatory mediators. The interleukin-23 (IL-23)/T-helper-17 (Th17) signaling pathway plays a central role in disease progression. IL-23 promotes the activation and maintenance of Th17 cells, which release cytokines such as IL-17A, IL-17F, and IL-22. These mediators stimulate keratinocyte proliferation and induce the production of additional inflammatory cytokines and chemokines, thereby perpetuating the inflammatory response [5,6].

Other inflammatory mediators, particularly tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), contribute to the inflammatory microenvironment. These mediators drive characteristic epidermal changes, including acanthosis, parakeratosis, abnormal keratinocyte differentiation, and increased epidermal thickness. Disruption of epidermal barrier function further contributes to disease activity and may influence the penetration and retention of topical therapeutic agents [6,7].

From a therapeutic perspective, psoriasis is an important area for investigating topical phyto-nanomedicine. Plant-derived bioactive compounds such as curcumin, quercetin, and resveratrol have attracted research interest for their reported antioxidant and anti-inflammatory properties and their potential to modulate inflammatory signaling pathways. However, conventional topical application of these compounds is often limited by poor aqueous solubility, chemical instability, and inadequate skin penetration. Accordingly, lipid-based nanocarriers, including solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), liposomes, and nanoemulsions, are being explored to enhance formulation stability, improve local skin deposition, and regulate the release of phytoconstituents [3,9].

The therapeutic relevance of these systems should be evaluated through their ability to influence inflammatory mediators, regulate keratinocyte proliferation, reduce epidermal hyperplasia, and improve disease-associated skin changes. However, the available experimental findings should be distinguished from established clinical outcomes, particularly when considering their potential application in adolescent populations.

2.2. Wound Healing and Delayed Wound Repair

Wound healing is a complex biological process that involves coordinated cellular and molecular responses to restore the structural and functional integrity of damaged skin. It is conventionally divided into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling [10,11]. The hemostatic phase begins immediately after tissue injury and involves vasoconstriction, platelet aggregation, and fibrin clot formation. During the inflammatory phase, neutrophils and macrophages migrate to the wound site to clear microorganisms, damaged tissue, and cellular debris. The proliferative phase includes fibroblast migration, collagen deposition, angiogenesis, granulation tissue formation, and re-epithelialization. Finally, the remodeling phase involves collagen reorganization, extracellular matrix modification, and maturation of the newly formed tissue [10].

Delayed wound healing occurs when the normal progression of these phases is disrupted. Persistent inflammation, excessive oxidative stress, microbial infection, impaired angiogenesis, inadequate tissue perfusion, and defective extracellular matrix formation are key contributors to chronic wounds. Conditions such as diabetes mellitus, vascular insufficiency, and prolonged pressure may further compromise tissue repair. Excessive and prolonged production of reactive oxygen species can damage cellular components and interfere with fibroblast activity, angiogenesis, and re-epithelialization [11,12].

Medicinal plants containing flavonoids, phenolic compounds, terpenoids and polysaccharides have been studied for their wound-healing potential. Their reported pharmacological properties include antioxidant, antimicrobial, anti-inflammatory and tissue-repair effects. Examples include Aloe vera, Centella asiatica, Curcuma longa and Calendula officinalis [13]. Nanoformulations may improve the stability and local delivery of these constituents. Herbal-loaded nanogels, liposomes, polymeric nanoparticles and lipid nanoparticles are particularly relevant because they may facilitate sustained release, maintain a suitable wound environment and enhance the local availability of bioactive compounds. Nevertheless, the effectiveness of an individual formulation depends on its composition, wound type, release characteristics and biological compatibility.

2.3. Inflammatory Skin Disorders

Inflammatory skin disorders comprise a heterogeneous group of conditions characterized by immune dysregulation, inflammatory mediator release and alterations in epidermal barrier function. Atopic dermatitis, allergic contact dermatitis and irritant contact dermatitis are important examples. Although their initiating mechanisms differ, epidermal barrier disruption and interactions between keratinocytes, immune cells and environmental factors contribute to disease development and persistence [7,14].

Atopic dermatitis is characterized by impaired epidermal barrier function, reduced skin hydration, and immune responses that predominantly involve type 2 helper T cells (Th2). Cytokines such as IL-4 and IL-13 reduce the expression of barrier proteins, including filaggrin, while IL-31 is associated with pruritus. Barrier impairment increases susceptibility to irritants, allergens, and microbial colonization, resulting in a cycle of inflammation, itching, and further barrier damage [14,15]. Contact dermatitis develops after exposure to irritants or allergens. Irritant contact dermatitis involves direct damage to the epidermal barrier and activation of innate inflammatory responses, whereas allergic contact dermatitis is a delayed, T-cell-mediated hypersensitivity reaction. Both conditions may present with erythema, edema, itching and, in some cases, vesiculation and epidermal disruption [7]. Herbal bioactive compounds with anti-inflammatory, antioxidant, and skin-protective properties have been explored as potential topical agents for these disorders. Nanoemulsions, liposomes, niosomes, SLNs and NLCs may improve the solubilization and local delivery of poorly water-soluble phytochemicals. However, formulation selection must account for the sensitivity of inflamed skin, as surfactants, preservatives, and penetration enhancers may themselves cause irritation or sensitization. Therefore, dermal compatibility and barrier-function assessment are essential components of formulation evaluation.

3. HERBAL BIOACTIVE COMPOUNDS IN DERMATOLOGICAL MANAGEMENT

3.1. Major Phytochemical Classes

Medicinal plants contain several classes of secondary metabolites that contribute to their pharmacological activities. In dermatological applications, particular attention has been given to compounds possessing anti-inflammatory, antioxidant, antimicrobial, and wound-repair properties. Their activity depends on their chemical structure, concentration, stability, skin availability, and interactions with the formulation components.

1. Flavonoids

Flavonoids, a diverse group of natural polyphenolic compounds, have garnered attention for their therapeutic potential as “food-derived medicines.” These compounds exhibit remarkable structural diversity, characterized by their common C6–C3–C6 carbon backbone, as illustrated in Figure 1 (Structural diversity and basic chemical backbone of flavonoids).

Flavonoids are polyphenolic compounds widely distributed in medicinal plants. Quercetin, luteolin, kaempferol, and catechin are representative members of this group. Their antioxidant activity is associated with free-radical scavenging and modulation of oxidative-stress-related pathways. Certain flavonoids have also demonstrated anti-inflammatory potential by affecting NF-κB signaling and the production of inflammatory mediators. These properties make them relevant candidates for investigations of psoriasis, dermatitis, and wound repair.

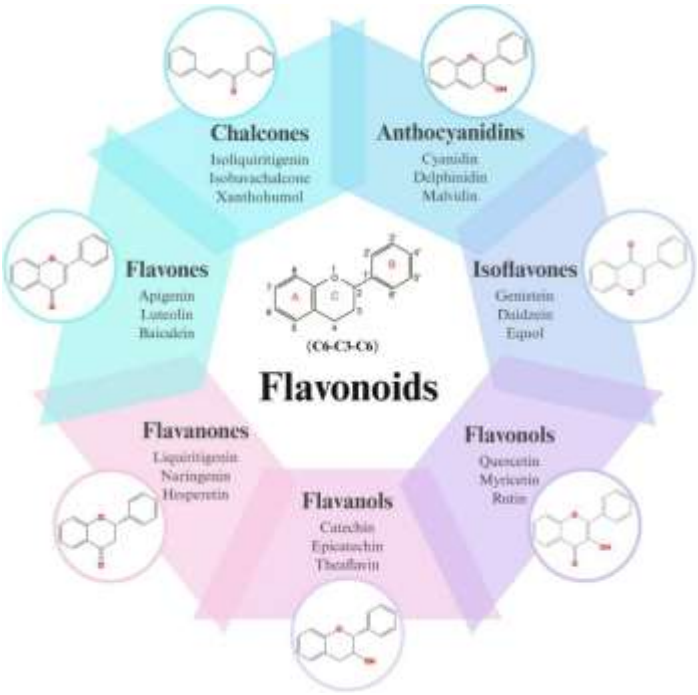


Figure 1. Structural diversity and basic chemical backbone (C6–C3–C6) of flavonoids.
Source: Adapted from Hao et al. (2025), Frontiers in Pharmacology.

2. Phenolic compounds and phenolic acids

Phenolic compounds include curcumin, resveratrol, gallic acid, caffeic acid, and related molecules. They have been investigated for antioxidant, anti-inflammatory, and antimicrobial properties. Curcumin, obtained from Curcuma longa, has received particular attention because of its reported influence on NF-κB-associated inflammatory signalling and cytokine production. Resveratrol has also been investigated for its antioxidant and anti-inflammatory effects. However, poor aqueous solubility and chemical instability restrict the topical pharmaceutical performance of several compounds in this category.

3. Terpenoids and essential-oil constituents

Terpenoids include monoterpenes, sesquiterpenes, diterpenes, and triterpenes. Compounds such as asiaticoside, madecassoside, thymol, and carvacrol have been investigated for their potential wound-healing, anti-inflammatory, or antimicrobial properties. Triterpenoid saponins from Centella asiatica, particularly asiaticoside and madecassoside, are of interest for fibroblast activity, collagen synthesis, and tissue repair. Essential-oil constituents may also exhibit antimicrobial effects, although their volatility, susceptibility to oxidation, and potential for dermal irritation require consideration.

4. Alkaloids

Alkaloids are nitrogen-containing plant metabolites with diverse pharmacological activities. Berberine, obtained from plants such as Berberis species, has been studied for antimicrobial and anti-inflammatory properties. Its potential dermatological relevance includes research on inflammatory skin conditions and microbial infections. However, topical application of alkaloids requires appropriate formulation development to improve their stability and local availability.

5. Tannins and plant-derived polysaccharides

Tannins are polyphenolic compounds with astringent, antioxidant, and antimicrobial properties. Their interaction with proteins may contribute to their traditional use in wound management. Plant-derived polysaccharides, particularly acemannan from Aloe vera, have been investigated for their potential roles in tissue repair, inflammation modulation, and wound hydration. These compounds may also be incorporated into hydrogel and nanogel systems to support topical delivery.

Overall, these phytochemical groups provide a pharmacological basis for exploring herbal Nanoformulations. Nevertheless, the activity of a crude plant extract cannot be attributed to a single phytochemical unless appropriate analytical and biological investigations establish its identity, concentration, and contribution [12,13].

3.2. Selected Medicinal Plants and Their Dermatological Relevance

Several medicinal plants have been investigated for their potential applications in psoriasis, wound healing, and inflammatory skin disorders. These plants represent important candidates for understanding the relationship between their phytochemical composition, pharmacological activities, and potential applications in nanotechnology-based topical delivery. The selected medicinal plants, their major bioactive constituents, and dermatological relevance are summarized in Table 1**.**

Table 1. Medicinal Plants, Their Bioactive Constituents and Potential Dermatological Applications

Medicinal plant	**Important bioactive constituents**	**Reported pharmacological relevance**	**Potential dermatological application**
Curcuma longa	Curcuminoids, particularly curcumin	Antioxidant and anti-inflammatory activity	Psoriasis, inflammatory skin conditions and wound repair
Aloe vera	Acemannan and other polysaccharides	Wound repair, hydration and inflammation modulation	Wound healing and irritated skin
Centella asiatica	Asiaticoside, madecassoside, asiatic acid	Collagen-related tissue repair and wound-healing potential	Wound healing and skin repair
Azadirachta indica	Limonoids, flavonoids and other phenolics	Antimicrobial and anti-inflammatory potential	Infected wounds and inflammatory skin conditions
Glycyrrhiza glabra	Glycyrrhizin, liquiritin and related flavonoids	Anti-inflammatory and antioxidant activity	Inflammatory skin conditions
Nigella sativa	Thymoquinone and volatile-oil constituents	Antioxidant and anti-inflammatory potential	Inflammatory skin disorders and wound management
Camellia sinensis	Catechins, particularly epigallocatechin gallate	Antioxidant and anti-inflammatory activity	Oxidative skin damage and inflammatory conditions
Calendula officinalis	Triterpenoids, flavonoids and carotenoids	Anti-inflammatory and wound-healing potential	Superficial wounds and skin irritation

These plants are of interest because their constituents span diverse chemical classes and pharmacological activities. For example, curcumin and thymoquinone are lipophilic compounds for which lipid-based delivery systems may be considered. In contrast, polysaccharide-rich Aloe vera preparations may be better suited to hydrogel or nanogel-based systems. Centella asiatica triterpenoids may also be explored using lipid or vesicular carriers, depending on the target formulation and intended skin deposition. However, therapeutic evidence is not uniform across these plants. Some activities are supported mainly by laboratory and animal studies, while clinical evidence varies by plant, extract, formulation, and dermatological indication. Therefore, plant selection for Nanoformulations should be based on authenticated botanical material, standardized phytochemical composition, and reproducible pharmacological evidence rather than traditional use alone [12,13].

4. NANOCARRIER SYSTEMS FOR TOPICAL HERBAL DRUG DELIVERY

The stratum corneum, consisting of corneocytes embedded within an intercellular lipid matrix, represents the principal barrier to topical drug delivery. Although topical formulations are intended to produce local effects, many phytochemicals exhibit inadequate penetration, limited skin retention or poor stability. Nanocarrier systems have therefore been investigated to improve the solubilization, protection, release and deposition of herbal bioactive compounds within the skin. Particle size, surface charge, lipid or polymer composition, drug-loading capacity, and interaction with the skin barrier influence their performance [8,9].

4.1. Liposomes and Niosomes

Liposomes are spherical vesicular carriers composed primarily of phospholipid bilayers surrounding an aqueous compartment. Their amphiphilic structure allows them to incorporate hydrophilic compounds in the aqueous core and lipophilic compounds in the lipid bilayer. This property makes liposomes suitable for encapsulating a range of herbal phytoconstituents. In topical applications, liposomes may improve the dispersion and stability of herbal compounds, facilitate their interaction with stratum corneum lipids, and promote local drug deposition. Depending on their composition and physicochemical characteristics, they may also serve as reservoirs for controlled release. Liposomes have consequently been investigated for delivering plant-derived compounds with anti-inflammatory, antioxidant, and wound-healing potential [16,17].

Niosomes are vesicular carriers primarily composed of non-ionic surfactants, typically combined with cholesterol. They resemble liposomes in structure but differ in their primary membrane-forming components. Niosomes can encapsulate both hydrophilic and lipophilic substances and are considered alternatives to

phospholipid-based vesicles. Their potential advantages include formulation flexibility, relatively good physical stability, and the ability to incorporate various herbal extracts and phytoconstituents. For dermatological applications, niosomes may improve the topical delivery of poorly soluble herbal constituents and enhance their retention within skin layers. However, their performance depends on surfactant selection, vesicle size, cholesterol concentration, and formulation stability. Potential surfactant-related irritation must also be assessed, particularly when formulations are intended for inflamed or damaged skin [16,18].

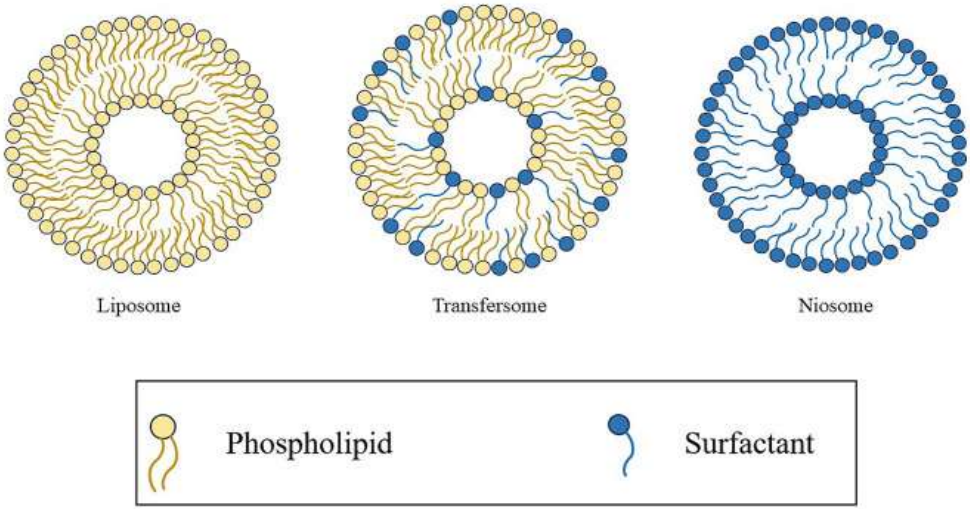


Figure 2. Structural representation of liposomes, transferosomes and niosomes.
Source: Adapted from Riccardi et al. (2024), Journal of Translational Medicine, 22, 339. https://doi.org/10.1186/s12967-024-05160-4

Liposomes, transferosomes and niosomes are vesicular nanocarrier systems that offer promising platforms for the topical delivery of herbal bioactive compounds. Their structural characteristics and composition influence drug encapsulation, skin penetration, stability, and controlled release, as illustrated in Figure 2.

4.2. Phytosomes

Phytosomes are molecular complexes formed by associating plant-derived phytoconstituents, particularly polyphenols and flavonoids, with phospholipids such as phosphatidylcholine. Unlike conventional liposomes, in which the active compound is generally entrapped within an aqueous or lipid compartment, phytosomes feature a closer association between the phytoconstituent and the phospholipid. This association is intended to improve the compatibility of polar phytochemicals with lipid environments and may enhance their solubility, membrane interaction and absorption. Phytosome technology has been investigated for plant-derived compounds such as curcumin, silymarin and other polyphenol-rich extracts. In dermatology, phytosomes may be considered for topical delivery of herbal constituents with antioxidant and anti-inflammatory properties. Their relevance to psoriasis and inflammatory skin conditions lies in the potential to improve the local availability of poorly absorbed phytochemicals. Nevertheless, the improved systemic bioavailability reported for certain oral phytosome formulations should not automatically be interpreted as improved topical skin penetration. Skin permeation, epidermal deposition and dermal retention must be evaluated independently for each topical formulation.[16,18].

4.3. Nanoemulsions

Nanoemulsions are colloidal dispersions of oil and aqueous phases, stabilized by surfactants, with droplets typically in the nanometer range. Depending on their composition, they may be formulated as oil-in-water or water-in-oil systems. Their relatively large interfacial area and ability to incorporate lipophilic compounds make them suitable for topical delivery of poorly water-soluble phytochemicals. Nanoemulsions may improve the solubilization and dispersion of herbal constituents such as curcumin, essential oil components, and other lipophilic bioactives. Their small droplet size, together with suitable excipients, may enhance contact with the skin surface and facilitate drug deposition. They can also be incorporated into gels or creams to improve application characteristics and formulation retention. In dermatological research, nanoemulsions have been investigated for delivering herbal compounds with anti-inflammatory, antimicrobial, and antioxidant properties. They may be particularly relevant to inflammatory skin disorders and wound-associated microbial complications. However, their stability depends on droplet size distribution, surfactant concentration, phase composition, and

storage conditions. Excessive surfactant concentrations may also cause irritation, making dermal compatibility an important consideration [16,19].

4.4. Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs)

Solid lipid nanoparticles are colloidal carriers consisting of a solid lipid matrix stabilized by surfactants. They were developed to combine the advantages of lipid-based delivery systems with the physical stability of solid lipid matrices. Lipids used in their preparation may include triglycerides, fatty acids, waxes, and other physiologically acceptable lipid materials. SLNs may improve the stability of encapsulated lipophilic phytochemicals, provide controlled release, and increase local skin retention. Their lipid composition may also contribute to occlusive effects, which can improve skin hydration. These properties make SLNs relevant to topical formulations intended for inflammatory skin conditions and wound management [20,21].

However, the highly ordered crystalline structure of the solid lipid matrix may limit drug incorporation and, in some cases, lead to drug expulsion during storage. This limitation contributed to the development of nanostructured lipid carriers. NLCs contain a mixture of solid and liquid lipids, producing a less ordered lipid matrix than that of conventional SLNs. Structural imperfections within this matrix may provide additional space for drug incorporation, potentially improving loading capacity and reducing drug expulsion. NLCs may also provide controlled release and enhance the deposition of lipophilic phytochemicals within the skin [20,21]. For herbal dermatological applications, SLNs and NLCs are particularly relevant for compounds such as curcumin, thymoquinone, and other poorly water-soluble phytoconstituents. Their potential use in psoriasis is of interest because they may improve local delivery and retention of anti-inflammatory compounds. In wound management, their suitability depends on the wound type, the intended release profile, and the formulation's compatibility with damaged tissue. Evaluate evidence from individual formulations separately rather than assuming that all lipid nanoparticles produce equivalent therapeutic effects [22,23].

4.5. Polymeric Nanoparticles

Polymeric nanoparticles are colloidal delivery systems prepared from natural or synthetic polymers. Depending on their structure, they may be classified as nanospheres, in which the active compound is distributed throughout a polymeric matrix, or as nanocapsules, in which the active compound is contained within a core surrounded by a polymeric shell. Commonly investigated polymers include poly(lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), chitosan, and alginate. Their selection depends on biodegradability, biocompatibility, drug compatibility, and the intended release characteristics. Polymeric nanoparticles may protect phytochemicals from environmental degradation and provide controlled or sustained release. Surface properties can also be modified to influence interactions with skin components and to facilitate local delivery [15,24].

Natural polymers such as chitosan are of particular interest for wound-related applications because of their film-forming properties and potential biological compatibility. Chitosan-based nanocarriers may also be investigated for delivering plant-derived antimicrobial and wound-healing constituents. By contrast, PLGA-based nanoparticles provide a biodegradable matrix for the controlled delivery of selected phytochemicals. In psoriasis and other inflammatory skin disorders, polymeric nanoparticles may improve the stability and local availability of anti-inflammatory compounds. Their therapeutic potential depends on polymer composition, particle characteristics, encapsulation efficiency, and drug-release behavior. Potential limitations include manufacturing complexity, residual solvent concerns, polymer-related toxicity, and challenges in large-scale production. Therefore, polymer selection and dermal safety assessment are essential during formulation development.

5. Comparative summary of nanocarrier systems: Various nanocarrier systems have been explored to enhance the topical delivery of herbal bioactive compounds, improving their stability, skin penetration, controlled release, and therapeutic efficacy. The principal nanocarrier platforms differ in their structural characteristics, drug-loading capacity, delivery mechanisms, and potential dermatological applications. A comparative overview of these systems is presented in the following Table 2.

Table 2. Nanocarrier Systems, Their Composition, Formulation Advantages and Potential Dermatological Applications

Nanocarrier	Principal composition	Main formulation advantage	Potential dermatological relevance
Liposomes	Phospholipids and cholesterol	Encapsulation of hydrophilic and lipophilic constituents	Psoriasis, dermatitis and wound healing
Niosomes	Non-ionic surfactants and cholesterol	Flexible vesicular delivery system	Inflammatory skin disorders

Phytosomes	Phospholipids complexed with phytoconstituents	Improved compatibility of selected phytochemicals with lipid environments	Delivery of polyphenols and flavonoids
Nanoemulsions	Oil, water, and surfactants	Solubilization of poorly water-soluble constituents	Inflammatory skin conditions and topical antimicrobial delivery
SLNs	Solid lipids and surfactants	Lipid-based protection and controlled release	Psoriasis and topical skin repair
NLCs	Solid and liquid lipids with surfactants	Less ordered lipid matrix and potentially improved drug loading capacity.	Psoriasis and local delivery of lipophilic phytochemicals
Polymeric nanoparticles	Natural or synthetic polymers	Protection and controlled release of bioactives	Wound healing and inflammatory skin conditions

5. MECHANISMS AND STRATEGIES OF SKIN DELIVERY

5.1. Skin penetration pathways

The stratum corneum, consisting of corneocytes embedded in an intercellular lipid matrix, represents the principal barrier to topical drug delivery. Topically applied compounds may penetrate through three major pathways: intercellular (between corneocytes), transcellular (through corneocytes), and trans-appendageal (through hair follicles and sweat ducts). Penetration extent depends on molecular size, lipophilicity, skin hydration, formulation composition, and barrier integrity [23,24].

Importantly, nanoparticles do not necessarily penetrate intact through the entire skin barrier. In many formulations, nanocarriers remain on the skin surface or within superficial layers and release their incorporated phytochemicals, which subsequently penetrate deeper skin compartments.

5.2. Mechanisms of nanocarrier-mediated delivery

Nanocarriers may improve topical delivery through the following mechanisms:

1. **Occlusive effect:** Lipid-based carriers such as SLNs and NLCs may reduce trans-epidermal water loss and increase stratum corneum hydration.
2. **Lipid interaction:** Certain vesicular systems may interact with intercellular lipids and facilitate phytochemical penetration.
3. **Improved solubilization:** Encapsulation improves the dispersion and protection of poorly water-soluble compounds such as curcumin.
4. **Controlled release:** Nanocarriers may provide sustained release and prolonged local availability of phytochemicals.
5. **Enhanced skin deposition:** Appropriate carrier composition and surface characteristics may improve epidermal or dermal deposition.
6. **Follicular targeting:** Hair follicles may act as reservoirs for certain particulate delivery systems [23,24].

5.3. Disease-specific delivery strategies

Effective topical nanocarrier-based delivery requires disease-specific formulation approaches that account for the distinct pathological features, skin barrier alterations, and therapeutic requirements of different dermatological conditions. Selecting appropriate nanocarriers, drug-release characteristics, and penetration-enhancing strategies is essential for optimizing therapeutic outcomes. The major dermatological conditions, targeted drug delivery strategies, and key formulation considerations are summarized in Table 3.

Table 3. Dermatological Conditions, Targeted Drug Delivery Strategies and Key Formulation Considerations

Condition	Desired delivery strategy	Important considerations
Psoriasis	Local epidermal and viable skin deposition	Penetration through hyperkeratotic skin and anti-inflammatory release
Wound healing	Local retention at wound surface and repair tissue	Moisture balance, biocompatibility and sustained release
Atopic dermatitis	Local delivery with minimal irritation	Skin hydration and barrier compatibility

Contact dermatitis	Local delivery to inflamed epidermis	Low irritation and sensitization potential

6. THERAPEUTIC APPLICATIONS AND AVAILABLE EVIDENCE

6.1. Psoriasis

Psoriasis involves persistent inflammatory signalling, keratinocyte hyperproliferation and epidermal hyperplasia, with the IL-23/Th17 pathway playing a central role. Curcumin, a major constituent of Curcuma longa, has demonstrated anti-inflammatory potential in experimental psoriasis models. Sun et al. reported that topical curcumin reduced imiquimod-induced psoriasis-like inflammation in mice, accompanied by reductions in epidermal hyperplasia and inflammatory mediators, including IL-17A, IL-17F, IL-22, IL-1β, IL-6 and TNF-α [25]. Curcumin-loaded nanostructured lipid carriers incorporated into cellulose nanofibre films demonstrated increased epidermal deposition and improvement in psoriasis-like dermatitis in mice [26]. Similarly, a curcumin nanoemulsion incorporated into an oligopeptide hydrogel was investigated for enhanced skin penetration and anti-inflammatory activity in an imiquimod-induced psoriasis model [27]. These findings support the potential of topical Nanoformulations to improve curcumin delivery. However, the evidence remains predominantly preclinical.

6.2. Wound healing

Wound healing involves hemostasis, inflammation, proliferation, and remodeling. Herbal compounds with antioxidant, antimicrobial, and anti-inflammatory activities may support various stages of tissue repair. Curcumin-loaded chitosan nanoparticles have been investigated for sustained phytochemical release and wound-healing potential. Experimental findings included improved cell migration in an in vitro scratch assay [28]. Other relevant formulation approaches include herb-loaded nanogels, polymeric nanoparticles, lipid nanoparticles, and vesicular systems. Their evaluation should include wound closure, re-epithelialization, collagen deposition, angiogenesis, inflammatory markers, and microbial burden. For chronic and diabetic wounds, particular attention should be given to persistent inflammation, oxidative stress, and impaired tissue repair.

6.3. Inflammatory skin disorders

Atopic and contact dermatitis involve inflammatory responses and alterations in epidermal barrier function. Phytochemicals such as curcumin, quercetin, glycyrrhizin, and selected terpenoids have been investigated for their antioxidant and anti-inflammatory properties. Liposomes, niosomes, nanoemulsions, and polymeric nanoparticles may improve the stability and local delivery of these compounds. In atopic dermatitis, formulations should also support skin hydration and barrier recovery while minimizing irritation. For contact dermatitis, surfactants, preservatives, and penetration enhancers require particular safety assessment because they may cause irritation or sensitization. Although emerging studies indicate potential benefits of herbal nanocarriers in inflammatory skin disorders, further disease-specific preclinical and clinical investigations are required [29].

6.4. Summary of representative therapeutic evidence

Several herbal bioactive compounds have demonstrated promising therapeutic potential in dermatological applications through nanocarrier-based formulations. These formulations aim to enhance the stability, skin penetration, bioavailability, and targeted delivery of phytoconstituents, thereby improving their therapeutic effectiveness. The representative herbal bioactives, nanocarrier-based formulations, and their reported therapeutic evidence in dermatological applications are summarized in Table 4.

Table 4. Representative Herbal Bioactives, Nanocarrier-Based Formulations and Reported Therapeutic Evidence in Dermatological Applications

Herbal bioactive	Nanocarrier/formulation	Application	Reported evidence
Curcumin	NLC-loaded cellulose nanofiber film	Psoriasis	Increased epidermal deposition and improvement in mouse model
Curcumin	Nanoemulsion-embedded oligopeptide hydrogel	Psoriasis	Improved skin delivery and evaluated anti-inflammatory activity in mice
Curcumin	Chitosan nanoparticles	Wound healing	Sustained release and improved in-vitro cell migration
Herbal phytochemicals	Liposomes, noisome and polymeric carriers	Atopic dermatitis	Emerging preclinical evidence

7. CHARACTERIZATION, DERMAL SAFETY AND QUALITY EVALUATION [30,31]

7.1. Physicochemical characterization

Comprehensive physicochemical characterization is essential to establish the quality, stability, safety and reproducibility of herbal Nanoformulations. It provides critical information regarding particle size, surface characteristics, drug-loading efficiency, morphology and release behaviour, which collectively influence formulation performance and therapeutic effectiveness. Table 5 presents the key characterization parameters, analytical techniques, and their respective purposes in evaluating herbal nanocarrier formulations.

Table 5. Characterization Parameters, Analytical Techniques and Their Purpose in Herbal Nanocarrier Formulations

Parameter	Analytical technique	Purpose
Particle size and PDI	Dynamic light scattering (DLS)	Particle-size distribution and uniformity
Zeta potential	Zeta potential analyzer	Surface charge and colloidal stability
Morphology	SEM, TEM, AFM	Particle shape and surface characteristics
Encapsulation efficiency	Validated analytical assay	Percentage of phytochemical incorporated
Drug loading capacity	HPLC/UV-visible spectroscopy	Quantity of active constituent in the carrier
Functional groups	FTIR	Chemical interactions between carrier and phytochemical
Thermal properties	DSC	Thermal behavior and physical state
Crystallinity	XRD	Crystalline or amorphous characteristics
Phytochemical profile	HPTLC, HPLC, LC-MS	Extract fingerprinting and marker quantification

Encapsulation efficiency (EE%) and Loading Capacity (LC%) may be calculated using the following equations

Encapsulation efficiency (EE%) and loading capacity (LC%) may be calculated using the following equations, based on the drug distribution within the liposomal system, as illustrated in Figure 3.

1. Encapsulation Efficiency (EE%)

$$EE\ (\%) = \frac{\text{Amount of drug encapsulated}}{\text{Initial amount of drug added}} \times 100$$

2. Loading Capacity (LC%)

$$LC\ (\%) = \frac{\text{Amount of drug encapsulated}}{\text{Total weight of nanoparticles}} \times 100$$

Note: EE% indicates the proportion of the initially added drug successfully entrapped, whereas LC% indicates the proportion of drug in the final nanoparticle formulation. Ensure consistent units and a clearly defined nanoparticle mass basis throughout the calculation.

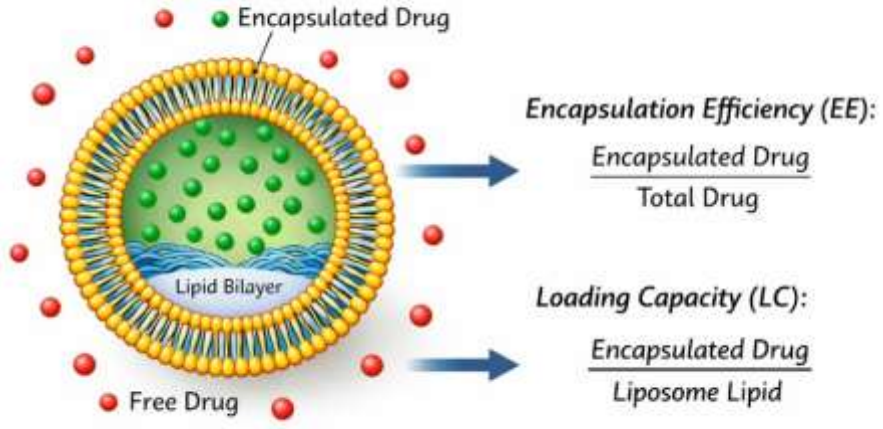


Figure 3. Schematic representation of drug distribution in liposomes for calculating Encapsulation Efficiency (EE%) and Loading Capacity (LC%).

Source: BOC Sciences. Liposome drug encapsulation efficiency measurement.
Available at: https://liposomes.bocsci.com/solution/liposome-drug-encapsulation-efficiency-measurement.html

7.2. In vitro release and skin delivery

In vitro release studies assess the rate and extent of phytochemical release using membrane-based methods. Release profiles can be analyzed using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. Franz diffusion cells are commonly used to evaluate skin permeation and deposition. Drug retention in the stratum corneum, epidermis, and dermis should be distinguished from drug that permeates completely through the skin. Tape stripping and tissue extraction, followed by HPLC or another validated analytical method, can help quantify skin deposition. OECD Test Guideline 428 provides a framework for in vitro skin absorption studies using excised skin and diffusion cells [30].

7.3. Dermal Safety

The natural origin of herbal constituents does not automatically ensure the safety of their Nanoformulations, especially when intended for adolescent skin. Dermal safety assessment is essential to establish the tolerability of topical Phytonanomedicine, given repeated application, prolonged exposure, and the potential sensitivity of developing skin. Key safety parameters include cytotoxicity assessments in human keratinocytes and dermal fibroblasts; skin irritation and sensitization potential; epidermal barrier integrity and transepidermal water loss; histopathological evaluation of skin tissues; systemic absorption following topical application; and repeated-dose dermal toxicity. Particular attention should be given to nanoparticle-associated irritation, sensitization, and potential systemic exposure. OECD Test Guideline 439 describes an in vitro reconstructed human epidermis method for assessing skin irritation, whereas OECD Test Guideline 428 provides guidance for evaluating dermal absorption [30–33]. These assessments are important for establishing the safety profile of herbal Nanoformulations and their suitability for adolescent dermatological applications.

7.4. Stability and Quality Control

Stability and quality control are essential to ensure the safety, consistency, and therapeutic reliability of herbal Nanoformulations for adolescent dermatological applications. Evaluation should include particle size, polydispersity index (PDI), zeta potential, drug content, encapsulation efficiency, phytochemical degradation, pH, viscosity, drug-release profile, and microbial quality. Long-term and accelerated stability studies are necessary to identify potential formulation changes, including particle aggregation, drug leakage, phase separation, and chemical degradation during storage. Quality assessment should incorporate botanical authentication, phytochemical standardization, nanocarrier characterization, and batch-to-batch reproducibility [32–34]. Particular attention should be given to maintaining formulation stability, microbial safety, and consistent drug delivery throughout the intended shelf life, thereby supporting the development of reliable and safe topical phyto-nanomedicines for adolescent skin health.

8. CHALLENGES, RESEARCH GAPS AND FUTURE PERSPECTIVES

Despite the promising potential of Phytonanomedicine in dermatological applications, several challenges continue to hinder its clinical translation. These include variability in phytochemical composition, inadequate standardization of herbal extracts, formulation instability, batch-to-batch variation, and difficulties in large-scale manufacturing. Furthermore, limited long-term dermal safety data, potential nanoparticle-related toxicity, inconsistent skin penetration, and the scarcity of well-designed clinical trials remain significant concerns. These limitations are particularly important for adolescent applications, where age-appropriate dermal safety and long-term tolerability require careful evaluation.

Future research should prioritize developing standardized herbal extracts, reproducible formulation methods, comprehensive physicochemical characterization, and disease-specific skin models. Comparative studies evaluating Nanoformulations against conventional topical preparations are needed to establish their relative therapeutic advantages. Particular attention should be given to adolescent-relevant dermatological conditions, including acne, psoriasis, atopic dermatitis, inflammatory skin disorders, and wound healing, while distinguishing preclinical findings from clinical evidence. Long-term dermal toxicity assessments and appropriately designed clinical investigations are essential to establish safety and therapeutic effectiveness.

Emerging approaches, including stimuli-responsive nanocarriers, combination formulations, nanogels, polymeric films, and nanoparticle-based wound dressings, may further enhance localized drug delivery and therapeutic performance. Integrating scalable, cost-effective manufacturing processes, robust quality control, and early

regulatory considerations will be crucial to translating promising experimental findings into safe, reproducible, and clinically relevant dermatological products.

9. CONCLUSION

Phyto-nanomedicine offers a promising approach to improving the stability, local bioavailability, and topical delivery of plant-derived bioactive compounds. Various nanocarrier systems can enhance the therapeutic potential of herbal constituents for psoriasis, wound healing, and inflammatory skin disorders. Their relevance to adolescent skin health warrants further investigation, particularly regarding age-appropriate formulation design, dermal safety, and clinical suitability. However, challenges related to phytochemical standardization, formulation reproducibility, long-term toxicity, and limited clinical evidence must be addressed. Standardized preclinical investigations, comparative formulation studies, and well-designed clinical trials are essential to establish the safety, efficacy, and future therapeutic applications of Phytonanomedicine in adolescent dermatological care.

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Abdul Kabeer: Conceptualization, Methodology, Validation.
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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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