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Review Article

Polyherbal Ethosomal Gel in Dermatology: A Review on Formulation, Evaluation, and Clinical Perspectives

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Abstract

Modern herbal medicine and the developed drug delivery systems are current possibilities in dermatological practice. The review is concerned with the formulation and testing of a polyherbal ethosomal gel using Curcuma caesia and Aloe Vera, which have topical skin care applications. Lipid vesicular carriers were chosen in the form of ethosomes, which improve the penetration and delivery of macromolecules to the skin because of their high ethanol concentration. The formulation using the cold method was optimized based on vesicle size, homogeneity, pH, viscosity, spreadability, and drug content. Curcuma caesia has a strong antioxidant, antimicrobial, and wound healing effect, whereas Aloe vera has moisturizing, anti-inflammatory, and skin regenerative effects, and there is a synergetic effect of them as a therapeutic action. The FTIR results and in vitro rates of diffusion showed the successful release of drugs and interrelated compatibility of the active components and excipients. Clinical orientations show increased patient compliance, decreased negative impact, and open possibilities of conditions in long-term skin diseases. However, commercialization remains a challenge for stability, scale production, and regulation standardization. The results show that polyherbal ethosomal gels have the potential to be safe, easily acceptable, and commercially viable as alternatives to synthetic topical agents, as the world is demanding safe, effective, and naturally derived skin care products.

1. Introduction

Skin care includes a wide range of activities meant to keep the skin healthy, look good, and work well. The skin is the body's largest organ and acts as a barrier to environmental damage, pathogens, and chemicals. It also plays an important role in the regulation of temperature, sensation, and metabolism. In the field of topical drug delivery, the goal is to deliver therapeutic agents directly to the skin to achieve localized effects such as anti-inflammatory, antimicrobial, wound-healing, and moisturizing actions or systemic delivery when the active ingredients penetrate deeply enough to enter the circulation. The advantages of this route include avoiding first-pass metabolism, targeting the application site, improving patient compliance, and bypassing gastrointestinal degradation(1).

Conventional topical formulations, such as creams, ointments, and lotions, face significant limitations owing to the formidable barrier presented by the stratum corneum, a highly organized lipid matrix that restricts the permeation of many therapeutic molecules, especially those that are hydrophilic, have a high molecular weight, or are chemically unstable, leading to subtherapeutic concentrations at the site of action. Other drawbacks of traditional formulations include cosmetic unacceptability due to greasiness; unpleasant odor; stickiness; poor spreadability; lack of controlled release necessitating frequent application; instability of sensitive compounds such as herbal phytoconstituents that may undergo oxidation, hydrolysis, or photodegradation before reaching the target layers; and the risk of irritation, sensitization, or allergic reactions, particularly when synthetic preservatives, fragrances, or strong penetration enhancers are included, further compounded by the variability of skin conditions in different individuals or disease states that can influence absorption and efficacy(2).

Prompting researchers to explore advanced delivery systems that can overcome these barriers and enhance therapeutic outcomes, one of the most promising of which is the ethosomal system, a novel lipid-based vesicular carrier composed primarily of phospholipids, ethanol, and water, where the high ethanol content imparts flexibility to the lipid bilayers and disrupts the ordered lipid structure of the stratum corneum(3), thereby enhancing skin permeability and allowing deeper penetration of the encapsulated actives, with the unique advantage that ethosomes can encapsulate both hydrophilic and lipophilic compounds as well as macromolecules like peptides and proteins, offering remarkable versatility in formulation design, and when incorporated into gels, ethosomes combine the superior penetration capability with patient-friendly characteristics such as non-greasiness, smooth texture, and ease of application, making ethosomal gels particularly attractive for dermatological and cosmeceutical use, especially in polyherbal formulations where the therapeutic synergy of multiple herbal extracts can be harnessed for enhanced efficacy, reduced side effects, and improved patient compliance, as in the case of combining *Curcuma caesia*, known for its potent anti-inflammatory, antioxidant, and wound-healing properties due to the presence of curcuminoids and volatile oils, with Aloe vera, which is rich in polysaccharides, vitamins, and enzymes that promote hydration, soothe irritation, and stimulate tissue regeneration(4).

Thereby, producing a formulation capable of addressing multiple skin concerns simultaneously, from inflammation and microbial infections to oxidative damage and dryness, and in such systems, ethosomes not only improve the penetration of these bioactives but also protect them from environmental degradation, maintaining their stability and bioavailability until they reach the target skin layers, which directly translates to better therapeutic outcomes, greater patient satisfaction, and potentially wider market acceptance, given the growing consumer preference for herbal and natural-based products supported by modern pharmaceutical technology. With their ability to provide controlled and sustained release, ethosomal gels can reduce the frequency of application, enhance treatment adherence, and minimize dose-related side effects, thereby making them suitable for chronic dermatological conditions, such as eczema, psoriasis, and chronic wounds, as well as for routine skincare applications in cosmeceuticals; however, this approach addresses many of the shortcomings of conventional topical formulations(5).

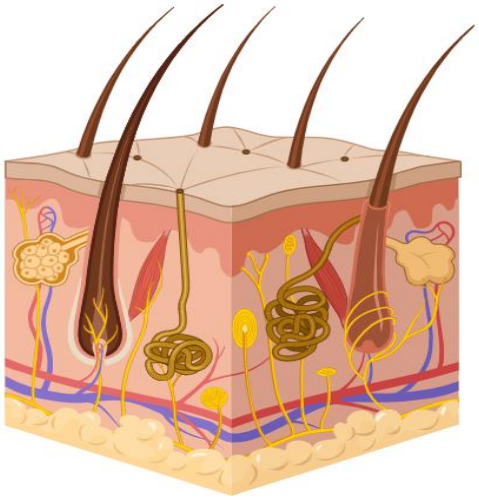

Figure 1 Structure of skin

Ongoing research continues to refine aspects such as vesicle size optimization, ethanol concentration adjustment, and excipient compatibility to further improve stability, loading capacity, and penetration efficiency, along with efforts to scale-up production for industrial applications without compromising vesicle integrity or performance. Considering the limitations of existing products along with the clinical and commercial potential of ethosomes, their integration into polyherbal gels represents a significant advancement in dermatology and skincare, offering a scientifically robust and patient-friendly alternative to conventional products capable of delivering multiple activities in a stable, effective, and aesthetically pleasing form that aligns with modern trends in personalized and natural medicine(6).

2. Polyherbal Approach in Skin Care

The polyherbal approach in skin care is based on the principle that combining multiple plant-derived ingredients in a single formulation can provide enhanced therapeutic efficacy, broad-spectrum activity, and synergistic effects compared to single-herb preparations. Diverse phytoconstituents from different botanical sources can act through complementary mechanisms to address multiple aspects of skin health such as inflammation, microbial invasion, oxidative damage, and impaired wound healing. This concept is deeply rooted in traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine, and Unani, which have long emphasized the use of multi-herb combinations for holistic healing, a philosophy that is increasingly embraced in modern dermatological research due to growing consumer demand for natural, safe, and multifunctional products(4).

The advantages of polyherbal formulations include the ability to harness synergistic pharmacological actions, where certain constituents enhance the bioavailability, stability, or penetration of others, and the potential to reduce individual component dosages while maintaining or improving efficacy(7).

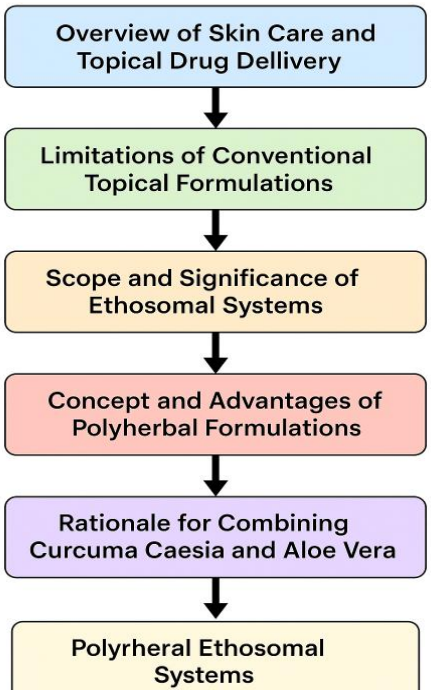

Figure 2 Conceptual flowchart illustrating the relationship between skin care, limitations of conventional topical formulations, significance of ethosomal systems, polyherbal advantages, and rationale for combining Curcuma caesia with Aloe vera.

thereby lowering the risk of side effects and skin irritation, a benefit particularly relevant in topical applications where prolonged exposure to actives can lead to sensitization, and furthermore, polyherbal systems offer versatility in targeting different layers of the skin and multiple biological pathways, which is crucial for addressing complex skin conditions such as acne, eczema, psoriasis, or premature aging that involve a combination of inflammatory, microbial, and oxidative processes; phytoconstituents in dermatological applications span a vast range of bioactive classes including polyphenols, flavonoids, alkaloids, terpenoids, tannins, saponins, and glycosides, each contributing distinct therapeutic benefits, for example, polyphenols such as curcumin from turmeric and

catechins from green tea exhibit potent antioxidant(8) and anti-inflammatory(9) activity, scavenging reactive oxygen species that contribute to skin aging and disease progression, while flavonoids like quercetin and kaempferol strengthen capillaries, reduce inflammation, and protect against UV-induced damage, alkaloids in certain herbs act as antimicrobial agents inhibiting the growth of pathogenic bacteria and fungi, terpenoids contribute anti-inflammatory and wound-healing effects, and mucopolysaccharides from plants like Aloe vera provide hydration, enhance epidermal barrier function, and stimulate fibroblast activity, making them invaluable for skin repair(6).

the rationale for combining *Curcuma caesia* and Aloe vera in a polyherbal ethosomal gel lies in their complementary and synergistic dermatological actions, as *Curcuma caesia*, a species of black turmeric, is rich in curcuminoids, essential oils, and phenolic compounds that possess strong anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties, effectively reducing erythema, inhibiting microbial colonization, and promoting tissue regeneration, while Aloe vera contains a variety of bioactive compounds such as acemannan, glucomannans, vitamins C and E, amino acids, and enzymes that hydrate the skin, soothe irritation, and accelerate epithelialization, and together these two botanicals create a formulation capable of simultaneously addressing the primary pathological factors in many skin conditions, including infection control, inflammation reduction, oxidative stress neutralization, and enhancement of skin repair processes; moreover, *Curcuma caesia*'s lipophilic curcuminoids can benefit from Aloe vera's hydrophilic polysaccharides that may act as natural penetration enhancers and stabilizers, improving drug retention and delivery through the skin, and Aloe vera's inherent soothing effect can counterbalance any potential irritation from the bioactive oils of *Curcuma caesia*, making the combination more tolerable for long-term application, particularly in sensitive skin(6).

this synergy is further amplified when incorporated into ethosomal carriers, as the ethanol-phospholipid vesicles can encapsulate both the hydrophilic components of Aloe vera and the lipophilic curcuminoids of *Curcuma caesia*, protect them from degradation, and facilitate their transport into deeper skin layers, thereby maximizing therapeutic efficacy while maintaining stability and cosmetic acceptability; the modern consumer preference for natural, plant-based, and scientifically validated skincare solutions positions polyherbal ethosomal gels like the *Curcuma caesia* Aloe vera combination at the intersection of traditional herbal wisdom and advanced pharmaceutical delivery systems, enabling the formulation to serve not only as a treatment for various dermatological disorders but also as a premium cosmeceutical product for routine skin maintenance, anti-aging, and protection from environmental damage; the adoption of such polyherbal approaches also aligns with current regulatory trends and market demands, as botanical products with demonstrable safety and efficacy profiles are increasingly sought after in both developed and emerging markets, creating opportunities for commercialization while maintaining therapeutic integrity, and thus the integration of these two well-studied botanicals into an advanced ethosomal gel delivery system represents a logical, scientifically sound, and market-relevant innovation in the field of skin care(10,11).

Table 1 Source and their benifts

Herbal Source	Major Phytoconstituents	Dermatological Benefits	Ref.
Curcuma caesia	Curcumin, essential oils, alkaloids, phenolics	Antioxidant, antimicrobial, wound healing	(11,12)
Aloe vera	Aloin, aloesin, polysaccharides, vitamins	Moisturizing, anti-inflammatory, skin regeneration	(12,13)
Combined Use	Synergistic phytochemicals	Enhanced healing, hydration, and skin barrier repair	(14)

3. Ethosomes as a Novel Drug Delivery System

Ethosomes are advanced lipid-based nanocarriers designed to enhance the delivery of therapeutic agents across the skin; they were first introduced in the late 1990s by Elka Touitou and colleagues as an innovative modification of liposomal technology that incorporates high concentrations of ethanol into phospholipid vesicles to improve drug penetration through the stratum corneum, and since their inception, they have gained

considerable attention in pharmaceutical and cosmeceutical research owing to their unique ability to transport a wide variety of molecules, including hydrophilic, lipophilic, and amphiphilic compounds, as well as macromolecules such as peptides, proteins, and even genetic materials; in terms of composition, ethosomes typically consist of phospholipids such as phosphatidylcholine, a substantial amount of ethanol usually in the range of 20–45% v/v, and water, with optional additives such as cholesterol for stability, surfactants for flexibility, and penetration enhancers to further optimize delivery(14,15).

the presence of ethanol plays a critical dual role by imparting high fluidity to the vesicle membrane, making the ethosomes more deformable, and by interacting with the polar head groups of stratum corneum lipids to disrupt their tightly packed structure, thereby reducing the skin's barrier function and enabling deeper penetration of the vesicles; the mechanism of skin penetration involves ethanol-mediated lipid fluidization, vesicle deformability allowing passage through intercellular pathways, and fusion or adsorption of ethosomes with skin lipids that facilitates the release of the encapsulated drug into the viable epidermis and dermis, resulting in significantly higher drug deposition compared to conventional liposomes or other vesicular systems, and this process ensures that both the vesicle and the drug are delivered efficiently to the target layers, which is particularly advantageous for topical and transdermal applications; compared to liposomes, ethosomes demonstrate several advantages, including superior penetration capability due to the ethanol effect, higher drug loading efficiency especially for lipophilic compounds, greater stability against aggregation, and better entrapment efficiency for a broad range of actives(16).

Liposomes often fail to penetrate beyond the upper layers of the stratum corneum; ethosomes can reach deeper skin strata or even systemic circulation if required, making them suitable for both localized dermatological treatments and systemic drug delivery, and in addition to improved penetration, ethosomes can be easily incorporated into different dosage forms, such as gels, creams, and patches, offering formulation flexibility, better patient compliance, and compatibility with various therapeutic and cosmetic agents. Their production process is relatively simple, scalable, and cost-effective compared to other nanocarrier systems, and the ability to modulate vesicle size, ethanol concentration, and lipid composition allows for precise tailoring to meet specific therapeutic goals, making ethosomes not just an incremental improvement over liposomes but a significant leap forward in the design of vesicular drug delivery systems for dermatology and beyond(17).

Table 2 Comparative Advantages of Ethosomes Over Liposomes and Other Vesicular Systems

Feature	Liposomes	Ethosomes	Ref.
Ethanol Content	Absent or very low	High (20–45%), enhances skin penetration	(1)
Vesicle Size	Larger (up to 1000 nm)	Smaller (100–300 nm), improves dermal delivery	(2)
Skin Permeability	Limited	High, due to ethanol-induced lipid fluidization	(7)
Drug Loading Capacity	Moderate	Higher for both lipophilic and hydrophilic drugs	(6)
Stability	Moderate	Improved stability in hydroalcoholic systems	(12)
Release Profile	May be burst release	Sustained and controlled drug release	(14)
Patient Compliance	Average	High, due to better efficacy and comfort	(16)

(Placeholder1)**3.1 Mechanism of Ethosomal Gel**

Ethosomal gel works on the principle of enhanced transdermal and dermal drug delivery using ethosomes soft, malleable vesicular carriers composed of phospholipids, high concentrations of ethanol, and water. The unique mechanism begins with ethanol's ability to fluidize the lipid bilayers of the stratum corneum, thereby decreasing its rigidity and enhancing permeability. Ethanol also imparts flexibility to the phospholipid vesicles, allowing ethosomes to deform and squeeze through the narrow intercellular spaces of the skin. Once applied, the ethanol-rich ethosomal vesicles penetrate deeply into the epidermal and dermal layers, carrying the encapsulated drug in both lipophilic and hydrophilic forms. The phospholipid bilayer of ethosomes merges with skin lipids, facilitating drug release directly into the target layers or systemic circulation, depending on the therapeutic need. The gel base provides a sustained release platform, ensuring prolonged contact of ethosomes with the skin and gradual drug release over time(4,6).

This dual mechanism ethanol-induced permeability enhancement and vesicular carrier-mediated penetration results in higher drug deposition at the site of action, improved bioavailability, and reduced dosing frequency. Ethosomal gels are particularly advantageous for delivering drugs with poor skin permeability, achieving non-invasive delivery, and avoiding gastrointestinal or first-pass metabolism issues associated with oral administration(14,17).

4. Formulation of Polyherbal Ethosomal Gel

The formulation of a polyherbal ethosomal gel involves a systematic approach beginning with the careful selection of herbal extracts and excipients, where the choice of herbs is based on their proven dermatological benefits, compatibility, and potential for synergistic action, as in the case of *Curcuma caesia* and Aloe vera, where the former contributes potent anti-inflammatory, antioxidant, antimicrobial, and wound-healing effects due to its curcuminoids and essential oils, and the latter offers hydration, soothing, and tissue-regenerating properties through its polysaccharides, vitamins, and enzymes, and excipients are selected not only for their functional roles but also for their safety and compatibility with herbal actives(5,12).

with phospholipids such as phosphatidylcholine serving as the vesicle-forming agents, ethanol acting as both a penetration enhancer and vesicle fluidizer, distilled water forming the aqueous phase, and optional components such as cholesterol for membrane stability, carbopol or hydroxypropyl methylcellulose as gelling agents, triethanolamine for pH adjustment, and preservatives such as methylparaben to prevent microbial contamination. The preparation is typically carried out using the cold method, a simple yet effective technique that preserves the integrity of the heat-sensitive phytoconstituents. Initially, the phospholipid was dissolved in ethanol under continuous magnetic stirring at a moderate speed, followed by the addition of herbal extracts in appropriate ratios to ensure uniform dispersion. In a separate vessel, phosphate buffer saline (PBS) of the desired pH, commonly around 6.4, was preheated to approximately 30 ± 1 °C to mimic skin conditions, after which it was slowly introduced into the ethanolic phospholipid-herbal solution at a controlled rate while maintaining constant stirring to promote vesicle formation(2,6).

After complete mixing, the suspension was stirred for an additional period, often approximately 10 min, before being stored at a low temperature (approximately 4 °C) to allow vesicle maturation. To reduce vesicle size and improve uniformity, the ethosomal suspension may be subjected to probe sonication for a short duration under controlled cooling to prevent the thermal degradation of the actives(14,15).

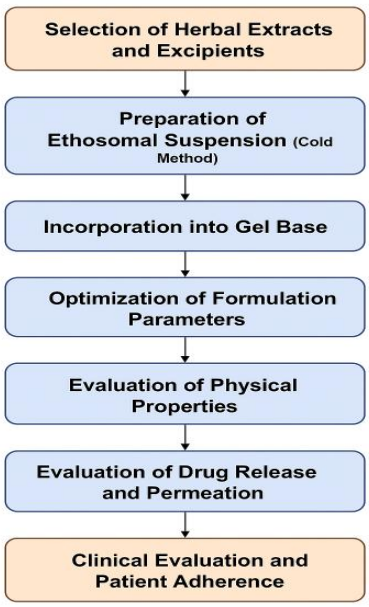

Figure 3: Stepwise flowchart depicting the formulation and evaluation process of polyherbal ethosomal gel for topical skin care.

once the ethosomal suspension is prepared, it is incorporated into the gel base by gradual mixing with the prehydrated gelling agent under gentle stirring to avoid vesicle rupture, followed by neutralization with triethanolamine to achieve the desired gel consistency, and optimization parameters are then evaluated to ensure the formulation meets the desired quality attributes, including vesicle size and size distribution, which influence penetration efficiency, zeta potential to assess stability, entrapment efficiency to quantify the amount of active retained within vesicles, pH to ensure skin compatibility, viscosity and spreadability for ease of application, and homogeneity to ensure a uniform product, while drug content analysis confirms accurate dosing and in vitro diffusion studies predict release behavior, and additional optimization may involve adjusting ethanol concentration to balance penetration enhancement with skin tolerability, modifying phospholipid levels to control vesicle rigidity, and fine-tuning the herbal extract ratio to

maximize synergistic effects without compromising stability, culminating in a polyherbal ethosomal gel that combines the therapeutic richness of botanical actives with the advanced delivery capabilities of ethosomal technology for effective, stable, and cosmetically acceptable skin care applications(5,6).

5. Evaluation of Ethosomal Gel

The evaluation of an ethosomal gel is a critical step to ensure that the formulation meets all the necessary quality parameters for safe and effective topical application, beginning with the assessment of physical appearance and homogeneity, where the gel is visually inspected under adequate illumination for color, clarity, and the presence of any particulate matter or phase separation, and tactile examination is carried out to verify smoothness, absence of grittiness, and uniform consistency, as a physically appealing and homogeneous product greatly influences patient acceptance(16,17).

the pH and viscosity measurements are equally important, with pH determined using a calibrated digital pH meter to confirm compatibility with the skin's natural range (approximately 5.5–6.5) to minimize the risk of irritation, while viscosity is measured using a Brookfield viscometer or similar rheological instrument to evaluate the gel's flow characteristics, ensuring it is neither too runny, which may cause wastage, nor too stiff, which may hinder application; spreadability and extrudability are then examined to assess patient convenience, with spreadability determined by placing a fixed quantity of gel between two glass plates and measuring the diameter or area covered under a standardized weight, indicating ease of application over the skin, and extrudability evaluated by determining the force required to expel the gel from a collapsible tube, which reflects both packaging suitability and user comfort; entrapment efficiency, a crucial parameter in ethosomal systems, is assessed by separating the unentrapped drug from vesicles using ultracentrifugation or dialysis and quantifying the drug content in the supernatant, allowing calculation of the percentage of drug successfully encapsulated within ethosomes, which directly correlates to sustained release potential and therapeutic effectiveness; drug content analysis is carried out to ensure dose accuracy and uniformity within the gel, typically by dissolving a known weight of gel in a suitable solvent, followed by appropriate dilution and spectrophotometric or chromatographic measurement against a standard calibration curve ensuring batch-to-batch consistency(13,15).

In vitro diffusion studies were performed using Franz diffusion cells with synthetic membranes or excised animal skin to simulate drug release through the skin. Samples were withdrawn at predetermined intervals and analyzed for drug concentration to construct release profiles and determine kinetic models, such as zero order, first order, or Higuchi, providing insight into the release mechanism. Finally, FTIR spectroscopy was employed for drug-excipient compatibility studies, where the characteristic peaks of the pure drug, excipients, and the final gel were compared to detect any significant shifts, disappearance, or formation of new peaks that may indicate chemical interaction, and a lack of such changes confirms the stability of the drug within the formulation, ensuring that the ethosomal gel retains its intended pharmacological properties throughout its shelf life. Together, these evaluations provide a comprehensive understanding of the physical, chemical, and functional performance of the gel, ensuring that it meets regulatory and therapeutic standards for topical dermatological applications(10,11).

6. Pharmacological Aspects

The pharmacological aspects of a polyherbal ethosomal gel containing *Curcuma caesia* and Aloe vera stem from the individual therapeutic properties of each plant and their synergistic effects when combined, beginning with the wound-healing potential of *Curcuma caesia*, which is attributed to its rich phytoconstituents such as curcuminoids, essential oils, alkaloids, and phenolic compounds that exhibit strong antioxidant activity, neutralizing free radicals at the wound site and thus preventing oxidative stress-induced tissue damage, while its anti-inflammatory properties inhibit the production of pro-inflammatory cytokines like TNF-α and interleukins, reducing edema and erythema, and its antimicrobial action, particularly against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, helps prevent secondary infections in wounds, thereby accelerating tissue repair(6,14).

additionally, *Curcuma caesia* enhances fibroblast proliferation, collagen synthesis, and

angiogenesis, all of which are vital processes in granulation tissue formation and epithelialization, leading to faster wound closure; Aloe vera, on the other hand, plays a crucial moisturizing and anti-inflammatory role in skin care, with its mucilaginous gel containing polysaccharides such as acemannan that form a protective hydrating layer over the skin, preventing transepidermal water loss while maintaining optimal moisture for cell regeneration, and its vitamins (A, C, E) and amino acids nourish skin cells and stimulate repair, while enzymes like bradykinase help reduce inflammation by modulating the activity of inflammatory mediators; Aloe vera's phytosterols and gibberellins contribute to its anti-inflammatory activity, reducing swelling and redness, while its glucomannan interacts with growth factor receptors to promote fibroblast proliferation and collagen deposition, improving tensile strength of newly formed tissue; when combined in a polyherbal ethosomal gel, the synergistic effects of *Curcuma caesia* and Aloe vera become evident, as the antioxidant,(9) antimicrobial,(10) and collagen-stimulating actions of *Curcuma caesia* complement the hydrating, soothing, and anti-inflammatory effects of Aloe vera, resulting in a formulation that not only accelerates wound healing but also maintains skin softness, elasticity, and barrier integrity during the repair process; the ethosomal delivery system further enhances this synergy by improving skin penetration and sustaining drug release, ensuring prolonged bioavailability of active constituents at the site of application, thereby reducing dosing frequency and improving patient compliance; this combination also addresses multiple skin concerns simultaneously, from treating minor cuts, burns, and abrasions to reducing post-healing hyperpigmentation and scar formation, making it suitable for both therapeutic and cosmetic dermatological applications(13).

The integration of these botanicals into an ethosomal gel represents a scientifically grounded approach that leverages traditional herbal medicine and modern nanocarrier technology to achieve superior pharmacological outcomes in skin care and wound management(15).

Clinical Perspectives, Patient Compliance, Challenges, and Future Prospects

From a clinical perspective, polyherbal ethosomal gels offer significant advantages in the management of chronic skin conditions such as psoriasis, eczema, chronic ulcers, and dermatitis, where prolonged therapy is often required, because the ethosomal delivery system enhances the penetration of active phytoconstituents through the stratum corneum, enabling sustained drug release and maintaining therapeutic levels for extended periods, thereby reducing the need for frequent applications and improving patient adherence; the combination of *Curcuma caesia* and Aloe vera further addresses the multifactorial nature of chronic skin disorders by simultaneously reducing inflammation, combating microbial infections, enhancing skin hydration, and promoting tissue regeneration, which makes them particularly suitable for long-term use(10,12).

compared to synthetic formulations, the polyherbal ethosomal gel significantly reduces the risk of side effects such as skin irritation, allergic reactions, and systemic toxicity, because it uses biocompatible, naturally derived actives and excipients, and its targeted delivery limits systemic absorption; this safety profile not only improves patient comfort but also broadens the formulation's suitability across different age groups, including elderly patients and children; market potential for such a product is strong, given the growing global preference for herbal and natural-based therapeutics, especially in the personal care and cosmeceutical sectors, where consumers value products that combine scientific validation with traditional herbal wisdom, and the enhanced efficacy, appealing texture, and ease of application further support its acceptability;(11) however, despite these promising aspects, there are notable challenges that must be addressed for successful translation into large-scale commercial products, with stability concerns being a major issue, as ethosomal systems can be sensitive to temperature changes, pH variations, and long-term storage, which may lead to vesicle aggregation, leakage of the entrapped drug, or degradation of active phytoconstituents; ensuring consistent vesicle size distribution and preventing oxidation or microbial growth in the herbal components are critical for maintaining product integrity.

Large-scale manufacturing presents additional difficulties because the precise conditions required for ethosome formation, such as controlled temperature, ethanol concentration, and sonication parameters, must be replicated

consistently in industrial settings without compromising quality, which demands investment in specialized equipment and robust quality control protocols. Regulatory challenges may arise in standardizing herbal extracts, ensuring batch-to-batch consistency, and meeting international guidelines for the safety and efficacy of nanoformulated herbal products(8,13).

Future research should focus on developing more stable ethosomal formulations with advanced lipid compositions, incorporating natural antioxidants to prevent phytoconstituent degradation, and exploring lyophilization techniques for long-term storage, while also investigating novel polyherbal combinations tailored for specific dermatological indications. Clinical trials with larger patient populations are essential to validate the therapeutic claims and establish dosage regimens. Exploring bioactive-loaded ethosomes in combination with stimuli-responsive delivery systems, such as temperature- or pH-sensitive gels, could further enhance the therapeutic performance. Overall, the integration of polyherbal ethosomal gels into modern dermatological practice holds immense promise; however, overcoming stability, manufacturing, and regulatory challenges is crucial for their full-scale adoption and sustained market success(4,10,17).

Conclusion

The development and evaluation of a polyherbal ethosomal gel incorporating *Curcuma caesia* and Aloe vera represents an innovative approach that merges the therapeutic depth of traditional herbal medicine with the advanced capabilities of modern vesicular drug delivery systems. Ethosomes, owing to their unique ethanol–phospholipid composition, enhance skin penetration and prolong drug release, thereby addressing the limitations of conventional topical formulations. The selected herbal actives bring complementary pharmacological actions *Curcuma caesia* offers potent antioxidant, antimicrobial, and wound-healing properties, while Aloe vera provides exceptional moisturizing, anti-inflammatory, and skin-repair benefits. When formulated using the cold method and optimized for parameters such as vesicle size, entrapment efficiency, and homogeneity, the resulting ethosomal gel exhibited desirable physicochemical characteristics, effective drug release, and compatibility between components. Evaluation studies have confirmed its stability, spreadability, and potential for improved therapeutic outcomes. Clinical perspectives highlight its suitability for chronic skin disorders, with a reduced risk of irritation or systemic side effects compared to synthetic formulations. The formulation also aligns with market trends that favor natural, safe, and effective skincare solutions. Nevertheless, challenges remain in ensuring long-term stability, scaling up production without compromising quality, and meeting regulatory standards for herbal nanoformulations. Future studies should emphasize stability enhancement, advanced manufacturing techniques, and robust clinical trials to establish its efficacy in diverse dermatological conditions. Overall, polyherbal ethosomal gel is a promising, patient-compliant, and commercially viable alternative in dermatology, offering a multi-targeted, science-backed, and naturally derived solution for skin care and wound management.

Ethical Approval

NA

Informed Consent

Not Applicable.

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Conflict of Interest

There are no apparent conflicts of interest between the authors' personal relationships or financial interests that may have affected the results of this study, the authors state. There is no conflict of interest, according to the writers. All ideas and opinions expressed in this article are those of the authors.

Financial Interests

The authors declare they have no financial interests.

References

1. Yadav T, Yadav HKS, Raizaday A, Alam MS. The treatment of psoriasis via herbal formulation and nano-polyherbal formulation: A new approach. BioImpacts BI. 2024;15:30341.

2. Mishra R, Singh S, Mishra S, Bhatt S. Planterosomal Gel designed by different Polyherbal Herbs: A Novel Method for Skin Healing. J Drug Discov Heal Sci. 2024;1(02):62–8.

3. Shree D, Patra CN, Sahoo BM. Novel herbal nanocarriers for treatment of dermatological disorders. Pharm Nanotechnol. 2022;10(4):246–56.

4. Ansari SA, Qadir A, Warsi MH, Mujeeb M, Aqil M, Mir SR, et al. Ethosomes-based gel formulation of karanjin for treatment of acne vulgaris: in vitro investigations and preclinical assessment. 3 Biotech. 2021;11(11):456.

5. Hariharanb S, Justinc A. Topical delivery of drugs using ethosomes: A review. Indian drugs. 2019;56(08):7.

6. Arora S, Rathore C. Potential role of herbal nanoformulations for skin disorders: a review. Ther Deliv. 2023;14(8):511–25.

7. Jena J, Mahendrakar S, Sahu D, Sahu B, Patro N, Sahoo BM, et al. Nanovesicle ethosome: A potential carrier of microwave assisted polyherbal extracts as Cosmecueticals. Curr Nanomater. 2021;6(1):31–42.

8. Jufri M. Hair growth activity and safety test of ethosomal gel ethyl acetate fraction of nothopanax leaves (Nothopanax scutellarium merr.). Asian J Pharm Clin Res. 2017;

9. Khogta S, Patel J, Barve K, Londhe V. Herbal nano-formulations for topical delivery. J Herb Med. 2020;20:100300.

10. Maheshwari N, Maheshwari N, Mishra DK, Goyal A. Phytotherapeutic potential of natural herbal medicines for management of psoriasis: current status. Pharmacognosy Res. 2023;15(1).

11. Shiven A, Alam A, Dewangan HK, Shah K, Alam P, Kapoor DN. Optimisation and in-vivo evaluation of extracted Karanjin loaded liposomal topical formulation for treatment of psoriasis in tape-stripped mouse model. J Microencapsul. 2024;41(5):345–59.

12. Sarma SK, Subba T, Hazra N, Pradhan A, Bhattacharjee T. Anti-aging activity of various topical nano herbal formulations. Univers J Pharm Sci Res. 2023;9(1):21–7.

13. Biswasroy P, Pradhan D, Haldar J, Kar B, Ghosh G, Rath G. Recent Advancements in Herbal Bioactive-based Nanoformulations for the Treatment of Psoriasis. Curr Bioact Compd. 2023;19(4):94–103.

14. Chopra H, Tsagkaris C, Matthews L, Gautam RK, Kamal MA. Novel approaches for the application of herbs for skin care. Curr Pharm Biotechnol. 2023;24(1):164–87.

15. Mardiyanti S, Anwar E, Desmiaty Y, Sadiah S. Novel Enhalus acoroides Phytosomes: Formulation, Characterization, and Bioavailability Enhancement. Biosci Med J Biomed Transl Res. 2025;9(7):8019–32.

16. Kumar S, Alsaidan OA, Alzarea SI, Kumar A, Kondaveeti SB, Sharma D, et al. Integrating Quality by Design (QbD) in Phytosomal Drug Delivery: A New Era in Precision Phytotherapy. AAPS PharmSciTech. 2025;26(7):198.

17. Mishra R, Singh S, Mishra SS, Bhatt S, Shree D, Patra CN, et al. Development and optimization of a novel nanocarrier SabiWhite-loaded ethosomal gel for targeted skin inflammation complicated by multidrug-resistant pathogens. Front Cell Infect Microbiol. 2025;6(4):1640799.