Infection and Drug Resistance

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REVIEW

Antimicrobial and Anti-Infective Potential of Herbal Creams in Dermatology: Efficacy, Safety, and Challenges in Skin Infection Management

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Abstract: Herbal creams are becoming increasingly popular in dermatology due to their potential to treat a variety of skin conditions, offering a natural, sustainable alternative to synthetic products. Derived from traditional medicine, these formulations contain plant-based bioactive compounds that provide anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties. Common ingredients such as Aloe vera, tea tree oil, calendula, turmeric, chamomile, and liquorice are known to address skin issues including acne, eczema, psoriasis, and aging. Despite these advantages, safety concerns remain, as the natural origin of these products does not guarantee safety; some may cause allergic reactions or skin irritation, while impurities and contaminants pose additional risks. This underlines the importance of comprehensive safety evaluations. Furthermore, regulatory and quality control challenges make the market difficult to navigate, reinforcing the need for standardized production and rigorous testing to ensure consistency and safety. Although clinical trials and marketed formulations demonstrate the efficacy of herbal creams, variability in ingredient concentrations and a lack of regulation can affect outcomes. Future perspectives call for the integration of traditional herbal knowledge with modern scientific advancements to enhance the safety and effectiveness of these products. This review explores the antimicrobial and anti-infective efficacy of herbal creams, their skin penetration mechanisms, safety considerations, and regulatory challenges, emphasizing clinical trials and marketed formulations. By integrating traditional herbal knowledge with modern scientific advancements, herbal creams offer a promising approach to managing skin infections while minimizing antibiotic resistance, provided robust regulatory frameworks ensure product safety and consistency.

Keywords: herbal drug, dermatology, nano-formulation, clinical trial, marketed formulation

Introduction

Skin infections are a global public health concern, with antimicrobial resistance, climate change, and lifestyle factors increasing their burden. Dermatological infections account for a significant proportion of outpatient visits, with bacterial and fungal infections being leading causes of morbidity. Skin diseases rank among the top ten causes of disability-adjusted life years, affecting quality of life and productivity. Fungal infections are a prevalent dermatological issue, affecting 40 million people worldwide. These infections can be superficial or systemic, with *Candida albicans* and *Aspergillus spp*. However, the use of antimicrobial agents must be limited due to potential toxic effects. Herbal materials, found in medicines, have gained popularity due to their strong antimicrobial properties and primary healthcare benefits. Herbal materials can replace nano silver as an antibiotic and antiviral agent due to their antioxidant activity.[1] Herbal creams are becoming more popular in dermatology because they can fight infections and bacteria. They are a natural alternative to traditional treatments for skin problems. These formulations contain a lot of phytoconstituents, like alkaloids, flavonoids, tannins, terpenoids, and essential oils. They work against a wide range of bacterial, fungal, and

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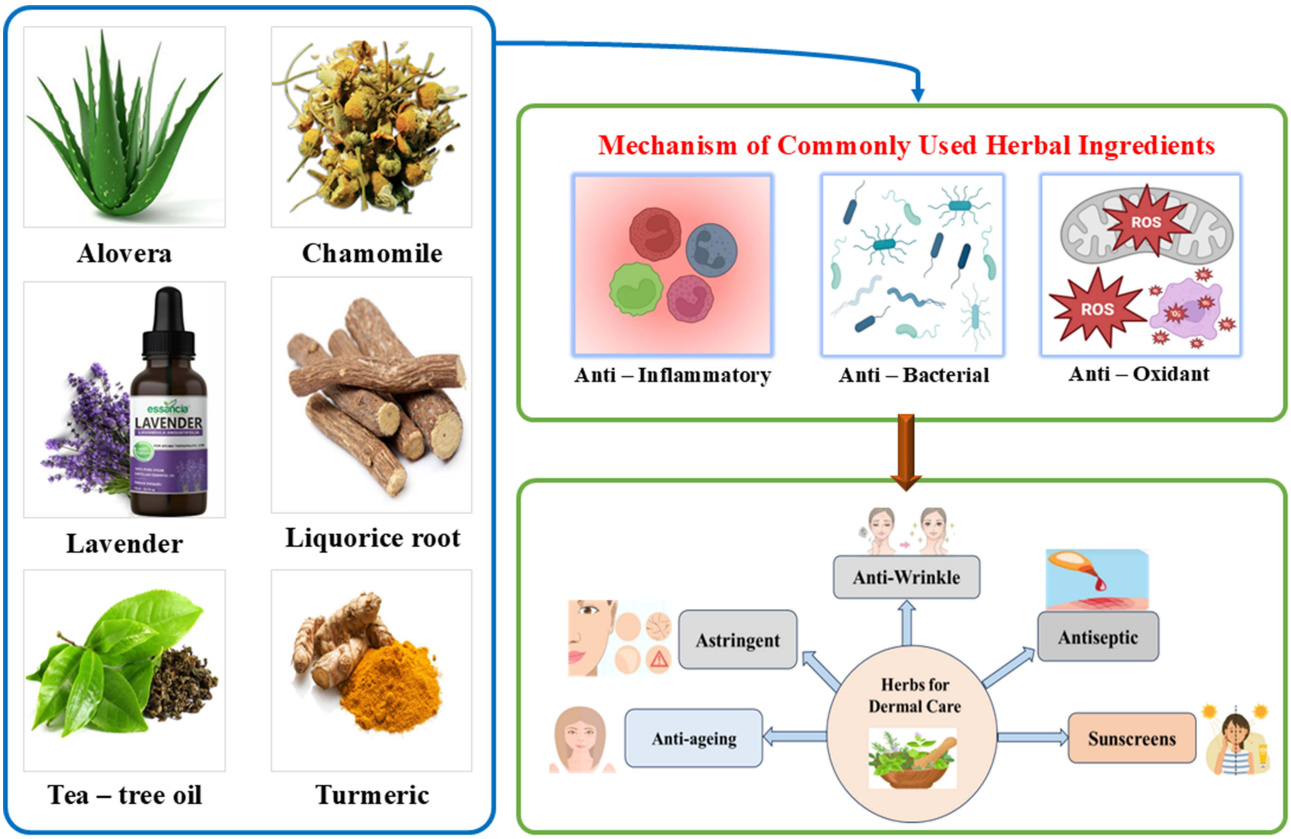
Graphical Abstract



viral pathogens by breaking down microbial membranes, stopping enzyme systems, and changing how the host's immune system works.[2] Clinical and experimental evidence indicates their effectiveness in disorders like as acne, atopic dermatitis, and superficial mycoses, demonstrating improved skin healing and reduced side effects relative to synthetic therapies.[3–5] Furthermore, their action on several targets lowers the chance of antimicrobial resistance and helps keep the skin microbiome in balance. Even with these benefits, there are still problems with the differences in phytochemical content, the lack of standardization, and the small number of large-scale clinical trials. To improve the antibacterial and anti-infective effects of herbal creams in dermatology, we need strong scientific proof, better formulations, and a way to combine phytopharmacology with modern dermatology.[6,7]

The use of herbal formulations for skin care has a rich history, deeply rooted in traditional medicine practices from cultures around the world. With the growing trend toward natural and organic products, there is renewed interest in herbal creams. As consumers become more conscious about the ingredients in their skincare routines, the shift towards plant-based remedies is seen as a safer and more sustainable alternative. The therapeutic potential of herbal creams lies in their composition, which often includes bioactive compounds derived from various plants. These compounds exhibit diverse pharmacological activities, including anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties.[8,9] As a result, herbal creams are utilized in treating conditions such as atopic dermatitis, psoriasis, acne vulgaris, rosacea, and skin ageing. Commonly used ingredients include Aloe vera which soothes and hydrates the skin, tea tree oil combats acne with antimicrobial action, and calendula aids in healing minor wounds. Furthermore, turmeric and chamomile reduce inflammation, while liquorice minimizes redness and pigmentation. Additionally, gotu kola helps in wound healing and scar management, and silibinin offers UV protection.[10,11] Other ingredients like borage oil hydrate, and green tea extract provide antioxidants, basil soothes, and onion extract enhances skin texture.[12,13] These components

collectively address various skin conditions, promoting overall skin health. However, safety remains a crucial concern despite the many advantages associated with herbal creams. The assumption that herbal products are inherently safe due to their natural origins can be misleading. Herbal creams can cause allergic reactions, irritations, or other adverse effects, highlighting the importance of thorough safety assessments.[14,15] Additionally, impurities or contaminants in herbal products can pose further risks such as redness, itching, swelling, skin irritation etc. Manufacturing herbal creams poses unique challenges due to the variability of plant materials. The stability of active compounds, such as curcumin in turmeric and aloin in Aloe vera, can be influenced by factors like origin, soil type, climate, and harvesting methods. This variability results in different potencies and purity levels in different batches, affecting therapeutic efficacy. Thus, maintaining stringent quality control is crucial to ensure product consistency and effectiveness.[16,17] Skin diseases, including alopecia, psoriasis, atopic dermatitis, vitiligo, hypertrophic scarring, melanoma, acne, and skin infections, are the fourth most prevalent non-fatal medical conditions worldwide. These diseases affect one in three individuals and have a significant global socioeconomic burden. Novel interventional approaches are needed to treat these diseases, as existing treatments lack effective options.[18,19] Dermatological diseases have been linked to increased psychological burden and suicidal behavior, with reviews and meta-analyses varying in their conclusions. Skin infections caused by bacteria, fungi, and viruses are a global health concern, and antimicrobial resistance (AMR) is limiting conventional therapies.[20] This review explores the antimicrobial and anti-infective potential of herbal creams in dermatology, with a focus on their efficacy, safety, mechanisms of action, formulation challenges, and regulatory considerations. It explains the commonly used herbal ingredients, their mechanisms of action, and the various pathways through which they penetrate the skin. Additionally, the review discusses important safety concerns and the measures that regulatory bodies can take to ensure product quality and minimize risks. It also presents clinical trial findings and marketed formulations, aiming to provide a comprehensive perspective on how herbal creams can be effectively and safely integrated into modern dermatological practice. In recent years, nano-formulations of herbal creams have emerged as a major advancement in dermatological therapeutics, addressing long-standing limitations associated with conventional plant-based topical preparations. Herbal actives often possess high molecular weight, poor aqueous solubility, and limited skin permeability, resulting in suboptimal therapeutic concentrations at the target site. Nanotechnology-based delivery systems —including nanoemulsions, nanostructured lipid carriers (NLCs), solid lipid nanoparticles (SLNs), polymeric nanocapsules, liposomes, and phytosomes enhance dermal retention, promote controlled release, and improve the stability of sensitive phytoconstituents such as flavonoids, terpenoids, polyphenols, and alkaloids. These nano-enabled herbal creams demonstrate superior penetration through the stratum corneum, prolonged residence time in deeper skin layers, and enhanced bioactivity compared with traditional formulations. Recent advances have shown significant improvements in managing inflammatory skin disorders, photoaging, pigmentation, psoriasis, wound healing, and microbial infections using nano-herbal systems. Incorporating this rapidly evolving field into the context of herbal dermatological therapy underscores the growing relevance of nano-phytopharmaceuticals and highlights the translational potential of nanotechnology in modern skin care and dermatology.

Antimicrobial and Anti-Infective Properties of Herbal Creams

Herbal creams, enriched with bioactive phytoconstituents, are increasingly being explored as antimicrobial and anti-infective agents in dermatology due to their multifaceted mechanisms of action, biocompatibility, and comparatively lower risk of resistance development. Extracts from plants such as *Azadirachta indica, Curcuma longa, Aloe vera, Ocimum sanctum*, and *Calendula officinalis* have demonstrated antibacterial, antifungal, antiviral, antioxidant, and anti-inflammatory activities.[21,22] These formulations are particularly beneficial for individuals suffering from chronic or recurrent infections, those with weakened immune systems, and patients who are hypersensitive to synthetic antibiotics. The combination of phytochemicals such as essential oils, polyphenols, flavonoids, and alkaloids helps inhibit or kill a variety of pathogenic microorganisms including bacteria, fungi, and viruses while also supporting skin repair and immune modulation.

Despite their promising therapeutic effects, several challenges limit their broader clinical application. Variability in plant species, extraction processes, and formulation techniques leads to inconsistencies in the concentration and stability of active ingredients. Additionally, the lack of standardization, limited randomized controlled trials, and insufficient

regulatory frameworks hinder the general acceptance of herbal creams in dermatological practice.[23] Addressing these gaps is crucial to fully realize the potential of these formulations. With robust scientific validation, standardized production protocols, and improved regulatory oversight, herbal creams can emerge as effective, safe alternatives or complements to conventional therapies.

Moreover, beyond the commonly used herbs, several other plant-based products have been traditionally employed for their antimicrobial and anti-infective properties. For example, Clove, rich in eugenol and caryophyllene, exhibits strong antioxidant, antimicrobial, and anti-inflammatory effects. Portulaca, containing ascorbic acid, quercetin, and omega-3 fatty acids, offers antioxidant, antimicrobial, anticancer, and neuroprotective benefits. Tribulus, with flavonoids and phenolic acids, provides antimicrobial, analgesic, and cardioprotective effects, while Eryngium, enriched with flavonoids, phenolic acids, and coumarins, supports antimicrobial, anticancer, and anti-inflammatory functions.[24] Similarly, Cinnamon (cinnamaldehyde and eugenol) and Turmeric (tumerone, zingiberene, and borneol) are widely recognized for their antimicrobial, anticancer, and immunomodulatory properties.[25] Ginger, abundant in gingerols and shogaols, supports antimicrobial, anti-inflammatory, and antihypertensive actions, while Thyme (carvacrol and thymol) and Pennyroyal (pulegone and menthone) offer antimicrobial and respiratory protective benefits.[26,27] Other herbal ingredients such as Fennel and Chamomile, rich in phenolic compounds, flavonoids, and apigenin, extend antimicrobial, hepatoprotective, and stress-reducing benefits. Mint and Burdock provide antimicrobial and anti-inflammatory actions through phenolic and caffeic acid derivatives, whereas Eucalyptus, with tannins and hydroxybenzoic acids, supports antimicrobial and antipyretic activities. Primrose, abundant in phenolic acids and flavonoids, and Lemon balm further contribute to antimicrobial, anticancer, and neuroprotective effects.[28] Additionally, Mallows, rich in flavonoids, polyphenols, and vitamins, offer hepatoprotective and anti-inflammatory benefits, while Garlic, containing allicin and organosulfur compounds, has strong antimicrobial, antidiabetic, and cardioprotective effects. Together, these phytochemicals provide a potent natural arsenal, making herbal creams highly promising candidates for antimicrobial therapy and overall skin health.[29] In nutshell herbal creams represent a compelling class of antimicrobial and anti-infective agents in dermatology. Their ability to act on multiple targets, support skin barrier function, and reduce microbial load makes them especially useful in managing infections where conventional treatments may fall short. To harness their full potential, future efforts must prioritize scientific research, standardized formulations, and robust regulatory practices. By bridging traditional herbal knowledge with modern scientific methodologies, herbal creams can be established as safe, effective, and evidence-based solutions for skin infection management.

Efficacy of Herbal Creams

The effectiveness of creams produced from natural herbs continues to be an area of discussion for both conventional and complementary systems of treatment, especially as people increasingly embrace natural remedies. Most herbal creams contain extracts from plants that have medicinal functions, including essential oils, antioxidants, anti-inflammatory substances, and antimicrobial agents.[30] These ingredients have long been used in traditional medicine and applied for the care of various skin diseases such as inflammation, infections, wounds, rashes, and even chronic skin conditions like eczema and psoriasis (Figure 1). Currently, herbal creams are marketed globally as risk-free, organic substitutes for chemical-based cosmetic products, reflecting the growing preference for natural healthcare solutions. The therapeutic potential of these creams is largely attributed to the bioactive compounds found in the plants used as raw materials during their preparation.[31] For instance, oils such as lavender, tea tree, and eucalyptus are widely appreciated for their ability to fight off harmful bacteria and reduce inflammation. Many of these oils have proven effective against both bacterial and fungal infections, while also helping to minimize skin irritation and redness. Similarly, popular herbs and flowers such as calendula, chamomile, and aloe vera contain antioxidants and bioactive elements that promote wound healing and tissue regeneration. These components work synergistically to reduce inflammation, prevent infections, and accelerate tissue repair, making them suitable for managing abrasions, superficial burns, and dermatitis.[32]

However, the efficacy of these creams depends on several critical factors. The choice of ingredients and their concentrations play a significant role in determining therapeutic outcomes. For example, if the content of active plant extracts is too low, the desired benefits may not be achieved, whereas excessively high concentrations may result in undesirable effects such as skin irritation or allergic reactions.[33] Thus, proper formulation is essential to balancing

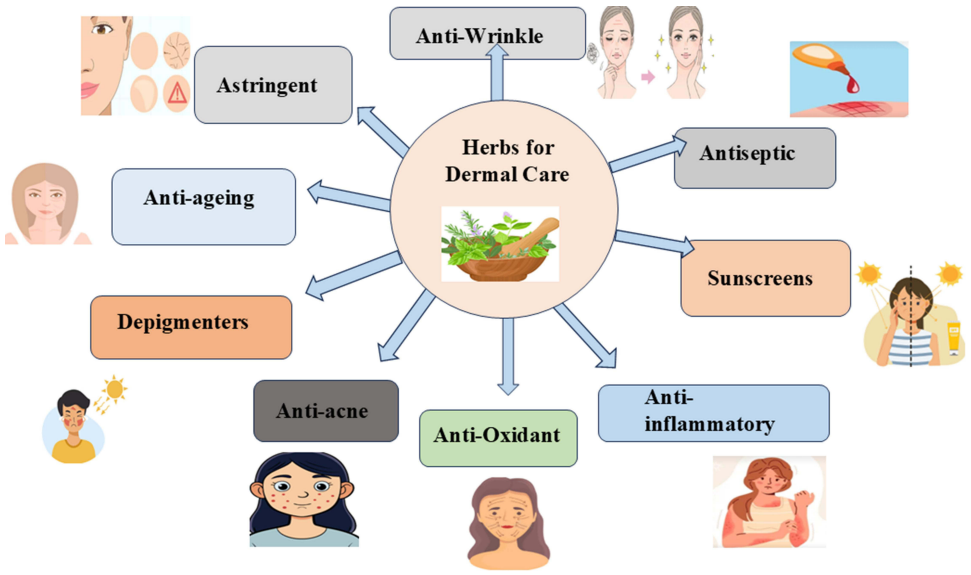


Figure 1 Figure illustrating the various beneficial effects of herbal drugs in dermatological applications, highlighting their roles in skin protection, hydration, antioxidant action, anti-inflammatory action, and antimicrobial properties.

effectiveness with safety. One of the major challenges in assessing the efficacy of herbal creams is the lack of standardized guidelines and regulatory policies governing their production and sale. Unlike synthetic medications, herbal products are often not subject to stringent controls, resulting in significant variability in quality and safety. Differences in manufacturing methods can lead to inconsistent levels of active ingredients, or even the presence of harmful contaminants.[34] To protect consumers and ensure the efficacy of these products, comprehensive testing and regulatory oversight are crucial. Experimental validation is necessary to demonstrate the effectiveness of various formulations and ensure they meet market safety standards.

It is important to highlight that natural creams, formulated from plant extracts, offer a viable category of cosmetic products distinct from synthetic analogues. They can be used to treat a wide range of skin diseases and conditions, but their effectiveness varies based on formulation, concentration, and individual skin sensitivity. Importantly, their use should not be regarded as conclusive proof of efficacy, as they lack the rigorous regulatory testing applied to pharmaceutical drugs. Addressing this challenge requires individualized assessments, where the impact of each herb is evaluated for every customer based on existing data regarding skin response and sensitivity.[35] Herbal materials derived from diverse medicinal plants have long been recognized for their broad spectrum of biological activities, including antioxidant, anti-inflammatory, antimicrobial, and antiviral properties. These phytoconstituents not only serve as the foundation of traditional healing systems but also contribute significantly to modern drug discovery and development. Applications have been demonstrated in cancer therapy, cardiovascular and neural disease treatments, and skin regeneration.[30,31] Historically, herbal medicines have been the primary therapeutic resources in ancient cultures across Africa, Europe, the Americas, and particularly Asia, and they continue to play a vital role in infection management in many developing regions. Extracts from these plants remain a crucial source of novel compounds with potential antibacterial and antiviral activity, reflecting global efforts to combat resistant pathogens. Numerous studies have confirmed that herbal medicines are rich in diverse bioactive molecules that possess radical-scavenging and antimicrobial effects, helping to protect the human body against microbial invasion while mitigating oxidative cellular damage. Importantly, these phytochemicals often exhibit low cytotoxicity, making them promising candidates for new antimicrobial drug development. Considering the rapid emergence of bacterial and viral resistance, the exploration of herbal-based antibacterial and antiviral therapies with minimal side effects has become a central focus in biomedical research.[34,35]

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Commonly Used Herbal Ingredients in Herbal Creams in Dermatology

Current dermatology treatments face challenges such as side effects from synthetic medications, antibiotic resistance, issues with chronic conditions requiring long-term treatment, and skin sensitivity or allergies to harsh chemicals.[36] Additionally, some patients experience adverse reactions to the chemicals and preservatives used in preparation of conventional creams. Herbal creams offer a promising alternative by using natural ingredients like Aloe Vera, Neem, and Chamomile, which provide anti-inflammatory, antibacterial, and soothing effects without harsh side effects.[37] They also have a low risk of resistance, are gentle for long-term use, and have hypoallergenic properties, making them suitable for patients with sensitive skin or allergies. Thus, herbal creams provide a safer, more sustainable, and gentle option for managing dermatological conditions.[38] Various herbal ingredients that have been mostly used are discussed below.

Aloe Vera

Known for its soothing, moisturizing, and anti-inflammatory properties, often used for treating burns, dry skin, and eczema. Amaral et al developed a new technique to formulate membranes by using chitosan, aloe vera extract and silver nanoparticles for new wound dressings which are useful in fast healing and reducing infection. The membranes were developed by using casting method. The test confirmed that the membrane containing Aloe vera and nanoparticles absorbed the least amount of water but degraded more quickly than the pure chitosan membrane. It was found that when it came to contact with hazardous microbes like Staphylococcus aureus and E. coli, both varieties responded effectively. Because of their antibacterial qualities, these novel membranes have potential for the treatment of wounds.[39] Dhamary et al conducted a study on excision wounds of animals in Sana'a city. Animals were divided into four groups the first group was denoted as a controlled group, second was treated with a placebo (petroleum jelly), a conventional wound-healing drug called Mebo was given to the third group, and fourth group was treated with fresh aloe vera gel. After three weeks of the experiment, results showed that Aloe vera group had considerably better and faster wound healing capacity for open wound treatment compared to the other groups. Wounds treated with aloe vera showed 100% contraction by the sixteenth day; in comparison, the Mebo group showed 97.6% contraction, while the control and placebo groups showed 76.6% and 73.8% shrinkage, respectively. Aloe vera helps fight infections by directly killing or inhibiting microbes (anthraquinones, saponins) and by boosting the body's defense mechanisms (acemannan, antioxidants). This dual action makes it an effective natural antimicrobial and anti-infective agent in dermatology.[40]

Chamomile

Contains anti-inflammatory and antioxidant compounds, helpful in soothing irritated skin and reducing redness. El-salamouni et al conducted a study and formulated nanoemulgel containing Chamomile oil to determine its effectiveness in the treatment of atopic dermatitis. They developed various formulations using a mix of chamomile oil and olive oil (1:1), along with different combinations of surfactants, propylene glycol, water, and a gelling agent. The developed formulation was tested for its physical and chemical properties, and anti-inflammatory effect and identified effectiveness in the treatment of atopic dermatitis-induced skin lesions in rats. The result concluded that The nanoemulgel containing Chamomile oil was non-irritating, had a skin-friendly pH, spread easily, and remained stable through temperature changes, speeding up healing and reducing inflammation in rats with atopic dermatitis.[41] Similarly, Moradkhani et al conducted a randomised and controlled clinical trial in Hamadan city. They involved 120 parturient women and divided into three groups 1% essential oil of myrtle or chamomile, or placebo were applied topically for 10 days. The redness, oedema, Ecchymosis, Discharge, and Approximation (REEDA) scale and the Visual Analogue Scale were utilized to determine pain intensity and healing capacity. The result showed that there was no major significant difference between the group with respect to pain intensity, Improvement in wound healing was shown on 10^{th} day in chamomile-using group. So, it concluded that chamomile oil contains various healing compounds and might help speed up episiotomy recovery. Chamomile acts as a broad-spectrum antimicrobial and anti-infective agent through its flavonoids, terpenoids, and essential oils that damage microbial membranes, inhibit enzymes, block viral replication, and reduce inflammation—making it an effective herbal ingredient for dermatological formulations.[42]

Calendula

Often used for its wound-healing properties and as an anti-inflammatory agent to treat minor burns, cuts, and skin irritations. Alsaraf et al conducted a clinical study to evaluate the cream of marigold flower extract containing 9 chemical constituents, these include Vitexin (11.40%), Rutin (12.29%), Quercetin-3-galactoside (12.64%), Luteolin-7-glucose (9.27%), Quercetin-3-glucoside (7.38%), Quercitrin (9.83%), Myricetin (10%), Luteolin (10.72%), Apigenin (7.08%), and Kaempferol (9.37%). According to a clinical investigation, a cream containing extract from marigold flowers has antioxidant properties to protect the skin from sunburn-induced oxidative damage and minimize the signs of ageing on the skin., it concluded by Comparing the 10% and 15% cream concentrations to the control group confirmed this effect. Following two weeks of therapy, the control cohort exhibited a 76% enhancement, but the 10% and 15% creams yielded 85% and 92% improvement, respectively.[43] In another study, Buzzi et al conducted a pilot study in Brazil to examine the effectiveness of Calendula officinalis hydroglycolic extract in the treatment of diabetic foot ulcers (DFUs). Out of 84 enrolled patients, 41 completed the study. The result concluded that 78% of patients obtained full closure of the wound after 30 weeks, with an average healing time of 15.5 weeks. There were no reported side effects, and the treatment significantly reduced necrotic tissue, infection, and wound odour. These results imply that calendula extract might be a helpful and safe treatment for DFUs. Calendula (*Calendula officinalis*) exhibits strong antimicrobial and anti-infective activity primarily due to its rich content of flavonoids, triterpenoids, saponins, and essential oils, which disrupt microbial cell membranes, increase permeability, and cause leakage of vital intracellular components. These phytochemicals also inhibit bacterial enzymes while the triterpenoid saponins enhance immune response and accelerate wound healing by promoting leukocyte activity and cytokine release. Additionally, calendula extracts generate oxidative stress in microbial cells, leading to protein and DNA damage, thereby exerting a broad-spectrum antimicrobial effect against bacteria, fungi, and some viruses.[44]

Tea Tree Oil

Known for its antimicrobial and anti-inflammatory effects, commonly used for acne and fungal infections. Zhou et al formulated a photocurable hydrogel based on laponite and polyacrylamide (PAAG/LAP) loaded with tea tree oil nano-emulsion (nanoTTO) to treat MRSA-infected skin wounds. In-vitro and *In-vivo* studies of hydrogel showed significant antibacterial activity against MRSA and showed excellent compressive resistance (~85 kPa), and biocompatibility (over 90%). Additionally, its eradicating ability of bacteria and promoting angiogenesis enhances its wound healing property. In a rat model, the hydrogel significantly reduced wound area within 12 days compared to controls. The result concluded that Drug-resistant bacterial infections in wounds may be treated using this hydrogel's containing tea tree oil provides an alternative to antibiotics. Tea tree oil (*Melaleuca alternifolia*) exhibits potent antimicrobial and anti-infective effects mainly due to its high content of terpinen-4-ol and related monoterpenes, which disrupt microbial cell membranes by increasing permeability and causing leakage of ions and essential metabolites. This membrane damage leads to loss of structural integrity, impaired respiration, and cell death. Additionally, tea tree oil inhibits biofilm formation, interferes with microbial quorum sensing, and induces oxidative stress within bacterial and fungal cells, resulting in protein and DNA damage. These mechanisms make it effective against a wide range of bacteria, fungi, and some viruses.[45]

Turmeric

Contains curcumin, which has anti-inflammatory and antioxidant properties, used in creams to brighten skin and reduce hyperpigmentation. Lahare et al formulated and evaluated a herbal ointment of Turmeric and Neem extract, recognized for its antifungal, antibacterial and anti-inflammatory actions. A levigation method was utilized to make the ointment, which ensured consistent mixing with a stable base. Extrudability, spreadability, and stability tests were done at various temperatures and showed good results for physicochemical parameters. The formulation ensured that skin problems can be treated without creating irritation. Turmeric demonstrates strong antimicrobial and anti-infective activity mainly through its bioactive compound curcumin, which disrupts microbial cell membranes, alters surface structures, and increases permeability, leading to leakage of intracellular contents. Curcumin also inhibits microbial enzymes, interferes

with nucleic acid synthesis, and suppresses quorum sensing, thereby preventing biofilm formation and microbial communication. Furthermore, its antioxidant and anti-inflammatory properties enhance host immune defence, creating an unfavourable environment for microbial survival, making turmeric effective against bacteria, fungi, and certain viruses.[46]

Witch Hazel

An astringent with anti-inflammatory and antioxidant properties, used to treat acne, eczema, and skin irritations. Veronese et al conducted a study to assess the effectiveness of two dermo-cosmetic products containing witch hazel extract to a generic cream in treating dermatitis of the eyelids. A single-blind, controlled, randomised, parallel-group trial was conducted to evaluate this study. Results of the study showed that patients treated with witch hazel products exhibited a higher degree of improvement in their dermatitis symptoms over a four-week period, as compared to the controlled group that was determined by various dermatological markers like (DLQI, OSDI, NRS–itch, EDSI). So, the study concluded that this formulation may be used as a first line and supportive treatment for eyelid dermatitis. Witch hazel (*Hamamelis virginiana*) exerts antimicrobial and anti-infective activity mainly through its abundant tannins and polyphenols, which precipitate microbial proteins, disrupt cell wall integrity, and inactivate key enzymes, leading to growth inhibition and cell death. These compounds also reduce microbial adhesion and biofilm formation, thereby limiting colonization. Additionally, witch hazel's astringent and anti-inflammatory properties create an unfavorable environment for microbial survival while soothing infected tissues, making it effective against bacteria, fungi, and certain viral pathogens.[47]

Lavender

Helps in soothing and calming skin, with mild antibacterial and antifungal effects, used in creams for relaxation and skin repair. Archi D et al formulated an herbal anti-fungal gel by utilizing essential oil from *Calendula officinalis and Lavandula angustifolia* to treat Candida albicans which is responsible for 90% of skin infections. The gel was formulated with carbopol 940 and another excipient. After that evaluation of antifungal activity is determined through various tests including stability, spreadability, Ph, viscosity and in-vitro drug diffusion. The result indicated that All of the formulations had good physicochemical characteristics, according to the data, with batch 4 presenting the best antifungal activity and drug release (98%) among the others. Positive results were obtained from this study, which is the first to assess these essential oils in gel form for antifungal functions. Lavender (*Lavandula angustifolia*) exhibits notable antimicrobial and anti-infective activity primarily due to its essential oil constituents such as linalool and linalyl acetate, which disrupt microbial cell membranes, increase permeability, and cause leakage of vital ions and metabolites. These compounds also interfere with energy metabolism and enzymatic activity, impairing microbial growth and survival. Additionally, lavender oil inhibits biofilm formation, induces oxidative stress leading to protein and DNA damage, and exerts anti-inflammatory effects that support host defenses, making it effective against a broad spectrum of bacteria, fungi, and some viruses.[47,48]

Neem

Known for its antimicrobial properties, used to treat acne, eczema, and other skin infections. Raweh et al formulated a Carbopol 940-based gel that contained leaf extract from Azadirachta indica (neem) and evaluated its anti-acne properties. Three gel formulations with different concentrations of Neem extract (1%, 2%, and 3% w/w) were formulated and evaluated for characteristics such as pH, viscosity, spreadability, skin irritation, and antibacterial activity. The result showed that the gels had good physicochemical properties, were skin-safe, and were stable The 3% extract gel (Gel-III) showed excellent results, with the highest antimicrobial activity against Propionibacterium acnes (zone of inhibition 16.2 mm) and rapid acne healing within 15 days. This concluded that gel containing 3% neem extract is a potentially effective acne treatment. Neem (*Azadirachta indica*) demonstrates strong antimicrobial and anti-infective activity owing to its bioactive compounds such as azadirachtin, nimbidin, nimbolide and flavonoids, which disrupt microbial cell membranes, increase permeability, and cause leakage of cellular contents. Additionally, neem enhances host immune responses and reduces inflammation at infection sites, making it effective against a wide range of bacteria, fungi, parasites, and certain viruses.[49]

Green Tea Extract

Rich in antioxidants, it helps in reducing inflammation and soothing sun-damaged skin. Alkufeidy et al evaluated the antimicrobial properties of green tea extract, catechin, and their combination with antibiotics against acne-causing bacteria (*Staphylococcus epidermidis, Staphylococcus aureus*, and *Propionibacterium acnes*). Green tea extract showed significant antibacterial activity, which was improved when combined with antibiotics like tetracycline and erythromycin. Along with this Catechin, a chemical found in green tea, has the property to damage the structure of bacteria cells by rupturing their membranes. It was found that the green tea extract's minimum inhibitory concentration (MIC) was less than 2.5 µg/mL. The study also demonstrated the correlation between wearing face masks and having more acne, as indicated by the 57% of participants who thought that wearing masks might increase acne. Overall, results concluded that catechin and green tea extract appear promising in the treatment of acne caused by bacterial infections. Green tea extract, rich in catechins such as epigallocatechin-3-gallate (EGCG), exhibits potent antimicrobial and anti-infective activity by disrupting microbial cell membranes, causing increased permeability and leakage of essential metabolites. EGCG also binds to bacterial proteins and enzymes. Additionally, green tea catechins generate oxidative stress in microbial cells, leading to protein and nucleic acid damage, while simultaneously inhibiting quorum sensing and biofilm formation. These mechanisms collectively make green tea extract effective against a wide range of bacteria, fungi, and certain viruses.[50]

Liquorice Root

Liquorice root is used for its anti-inflammatory and skin-brightening properties. It can help reduce hyperpigmentation and soothe irritated skin. Xu et al conducted a study to evaluate the safety and efficacy of oral component glycyrrhizin (OCG) in combination with topical corticosteroid (TCS) for treatment of chronic eczema. A randomized, double-blind, placebo-controlled trial was conducted in a multicentre, for 28 days, 199 individuals received TCS combined with either OCG or a placebo. Results indicated that OCG group had a significantly greater reduction in eczema severity, itching, and recurrence compared to placebo. The study concluded that OCG may be a helpful supplement to eczema treatment, as the drug was well-tolerated and the incidence of adverse events was similar in both groups.[51] MM et al conducted a study to assess the efficacy of mesotherapy for treating acne by injecting the chemical glycyrrhizin into the skin. A total of 108 patients were divided into two groups: one group received clindamycin gel and other group was treated with clindamycin gel plus mesotherapy and glycyrrhizin injection. The outcomes of study showed that the mesotherapy approach was more effective in minimizing moisture loss and inflammation, maintaining the skin barrier, and lessening the severity of acne as compared to clindamycin gel alone. Thus, study concluded that mesotherapy with glycyrrhizin offers a more effective treatment for moderate to severe acne (Figure 2).

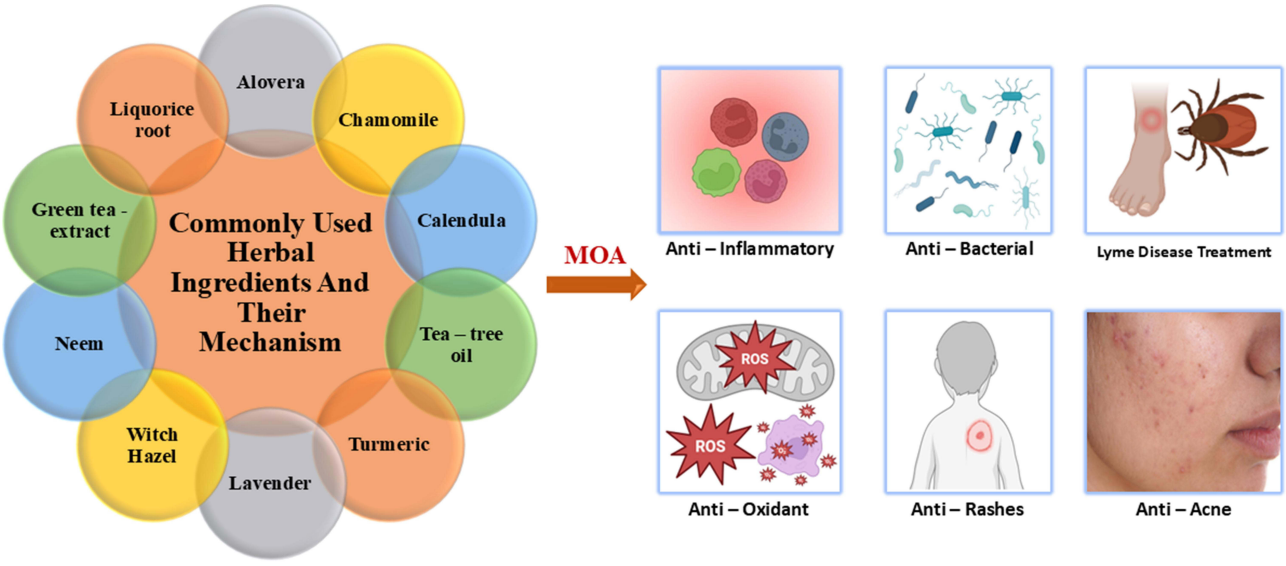

Figure 2 Figure showcasing herbal plants and their unique mechanisms in promoting skin health.

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Liquorice root (*Glycyrrhiza glabra*) exhibits antimicrobial and anti-infective activity through its key bioactive compounds such as glycyrrhizin, glabridin and liquiritin, which disrupt microbial cell membranes, increase permeability, and lead to leakage of cellular contents. These phytochemicals inhibit microbial enzymes, interfere with nucleic acid and protein synthesis, and suppress quorum sensing, thereby preventing biofilm formation and colonization. Additionally, liquorice root enhances host immune response and reduces inflammation at infection sites, making it effective against a broad spectrum of bacteria, fungi, and certain viruses.[52] There are several nano formulations in which herbal drugs have been used for the treatment of skin problems have been discussed in Table 1.

Skin Penetration and Absorption Mechanism

The skin's barrier function presents challenges for drug delivery, but there are four primary pathways that drugs can take to penetrate it.[64] The transcellular route involves the drug crossing directly through the skin cells (keratinocytes). Here, the drug must pass through both lipid-rich cell membranes and the hydrophilic cytoplasm, requiring the drug to have properties that allow it to navigate both environments.[65] On the other hand, the intercellular route allows the drug to pass between the skin cells, moving through the lipid matrix that fills the gaps between keratinocytes. This route is more suitable for hydrophobic (lipophilic) drugs, as the matrix consists mainly of fatty acids, ceramides, and cholesterol, which create a lipid-rich environment.[66] Furthermore, the follicular route uses hair follicles as entry points, bypassing the outermost layer of the skin (stratum corneum), making it easier for larger molecules to penetrate. Since the follicle extends deeper into the skin, this route allows drugs to reach lower layers more effectively. Lastly, the eccrine route involves absorption through sweat glands. Like the follicular route, it provides an alternative to passing through the stratum corneum, particularly for hydrophilic drugs. Sweat glands offer an aqueous pathway, which can be useful for water-soluble drugs.[67,68] While less commonly used, it's a viable option for certain types of drug delivery. These different pathways are chosen based on the drug's properties, such as molecular size and solubility, as well as the desired depth of penetration (Figure 3).

Safety Considerations

Herbal drugs, though natural, offer significant therapeutic advantages due to the active compounds they contain. Many of these compounds have been used for centuries in traditional medicine. They have been applied to treat a variety of conditions, demonstrating their effectiveness over time. The historical use of these remedies, such as turmeric and neem in skin treatments, provides some assurance of their safety and efficacy.[69] These natural compounds often work synergistically, providing holistic benefits to the body with fewer side effects compared to synthetic drugs. Many herbal remedies support the body's natural healing processes, boosting immunity or improving skin health.[70] However, while their natural origin is a key advantage, it's important to remember that active compounds in herbs can still interact with the body in powerful ways, and proper knowledge of their use is essential to maximise benefits while minimising risks. However, some herbs have a narrow therapeutic window, meaning the difference between a beneficial dose and a toxic one is small.[71] Despite their benefits, herbal drugs must be used cautiously, as improper use can lead to harmful outcomes, especially for individuals with specific health conditions or those on other medications. Various adverse effects that may arise due to use of herbal drugs are discussed in the next section.[72]

Adverse Effects and Allergic Reactions

Although herbal medicines offer numerous therapeutic benefits, their safety remains a significant concern for public health. Traditional preparation techniques employed by healers are not scientifically validated, which increases the risk of contamination with microbes and heavy metals in herbal products, potentially posing serious health risks. Regulatory authorities must establish clear guidelines to protect the public from adverse outcomes, including severe health complications or fatalities, that may result from the improper use or overuse of these products. Microbial contamination is particularly common in herbal formulations, and traditional practitioners often lack the necessary resources or methods to prevent or control such contamination.[73] Additionally, it is crucial to implement standardized quality control protocols and enhance awareness regarding the health risks associated with the use or misuse of herbal medicines. Various adverse effects and allergic reactions that have been reported are discussed below.[74]

Table 1 List of Herbal Drugs Containing Nano Formulation for the Treatment of Skin Disease

Herbal Drug	Nano Formulations	Disease	Outcomes	Ref.
Citrus sinensis L. fruit peels ethanolic peel extract rich in flavonoids (hesperidin ~610 Da, naringin ~580 Da)	LNPs	Ageing	Topical CSPE-NLC cream for 5 weeks significantly improved UV-induced photoaging in mice, increasing collagen and SOD levels while decreasing PGE2, COX2, JNK, MDA, and elastin.	[53]
Achyrocline satureioides aerial parts; flavonoid-rich extract (notably 3-O-methylquercetin ~316 Da)	Nanoemulsions hydrogel	Skin damage	Under optimized conditions, approximately 2 μg/cm^2 of flavonoids were retained in skin, with 3MQ at 1.0 μg/cm^2, demonstrating protective effects against UVA/UVB-induced oxidative stress.	[54]
Phenytoin synthetic reference drug incorporated into chitosan-based hydrogel matrix	Chitosan hydrogels	Wound	Hydrogels with nanocapsules and nanoemulsions enhanced phenytoin release and skin adhesion, reducing systemic absorption risk while maintaining effective wound healing in rats.	[55]
Dihydromyricetin (DMY) – pure flavonoid isolated from Ampelopsis species (molecular weight ~320 Da)	Cationic nonocapsules	Cytotoxicity and genotoxicity	Eudragit RS100® nanocapsules increased cytotoxicity and DNA damage, but nanoencapsulated DMY showed high antioxidant capacity, preventing free radical formation and associated toxicity.	[56]
3,3′-diindolmethane (DIM) – pure indole metabolite derived from Brassica spp. glucobrassicin breakdown (~246 Da)	Polymeric nanocapsules	Skin inflammation	Nano-based hydrogels retained DIM's anti-inflammatory effects, reducing edema and leukocyte infiltration, and extended DIM's action in UVB-induced inflammation for 48 hours.	[57]
Carrot Extract and Marigold Extract β-carotene rich; Calendula officinalis flavonoid/terpenoid rich	NLCs	Skin inflammation	Formulation showed superior anti-inflammatory effects, reducing IL-1β and TNF-α expression, and significantly decreasing rat paw edema within 3 hours.	[58]
Silibinin (pure flavonolignan ~482 Da) + Pomegranate seed oil (rich in punicic acid)	Nanocapsules suspension	Skin damage	All formulations reduced UVB-induced ear edema in mice, but only hydrogels with nanocapsules or silibinin-pomegranate oil sustained effects beyond 48 hours.	[59]
Bromelain –proteolytic enzyme blend from Ananas comosus stem (approx. 24–32 kDa range)	Liposomes	Wound	Membranes with bromelain-loaded NPs and LIPs showed higher water content, lower permeability, greater strength, and enhanced healing, with no edema observed after 14 days in vivo.	[60]
Smilax china and *Salix alba* – root/rhizome extracts and bark extracts (rich in saponins, salicin)	NLCs	Psoriasis	The dermatokinetic study showed improved skin penetration and non-irritancy of drug-loaded NLC gel, demonstrating better efficacy and safety than the marketed formulation in a psoriatic model.	[61]
Silybum marianum – seed extract enriched in silymarin complex (silibinin major component)	Hydrogel	Irritant contact dermatitis	HP-NC SB showed the strongest anti-inflammatory effect, reducing ear edema and inflammation without affecting normal skin conditions, suggesting potential as an alternative treatment for irritant contact dermatitis.	[62]
Ilex paraguariensis – leaf extract containing chlorogenic acid (~354 Da)	Polymeric nanoparticles	-	Incorporating Ilex extract in nanoparticles delayed chlorogenic acid skin permeation, extending its topical antioxidant effect for over 12 hours.	[63]

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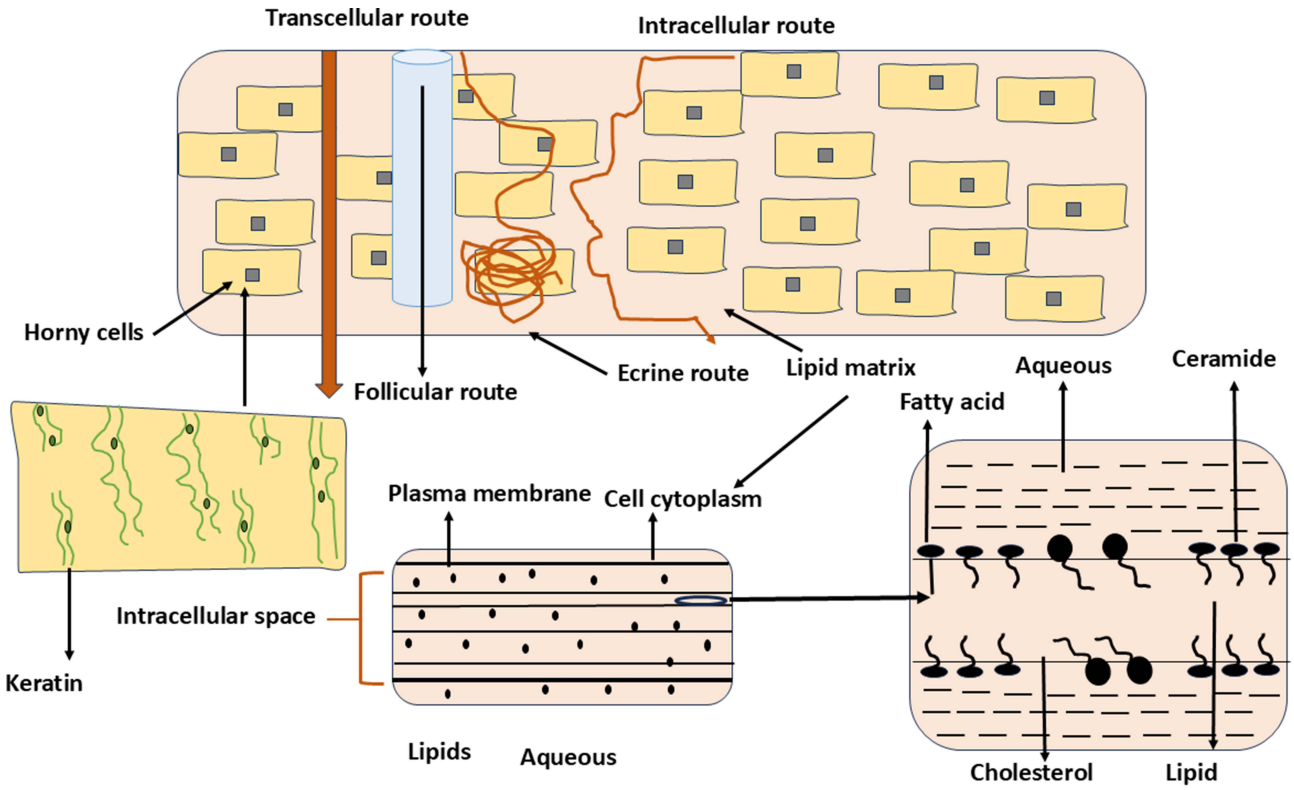

Figure 3 Figure illustrating the primary routes of drug delivery through the skin layers, including transcellular, intercellular, and follicular pathways.

A study was conducted to investigate immediate allergy-like adverse drug reactions (ADRs) associated with herbal medicines using data from VigiBase®, the WHO international pharmacovigilance database. The analysis included reports from 1969 to August 2014, focusing on cases where suspected ADRs had a documented causality assessment and occurred within one day of herbal exposure. Among 1039 ADRs, 757 reports were identified, with mixed herbal products (36%) and oral administration (63.2%) being the most common. The primary reactions were urticaria and rash (49.2%), while anaphylactic reactions were reported in 9.5% of cases. Notably, *Phleum pretense* was linked to a disproportionately high occurrence of mouth edema (IC = 1.81) and anaphylactic reactions (IC = 1.24). The findings highlight that oral herbal medicines can pose risks of immediate allergic reactions, and healthcare providers should be vigilant in recognizing and reporting such events to enhance patient safety.[75] In another study, analysis of the WHO global individual case safety report database, VigiBase®, reveals a rising trend in herbal medicine use among children, with acute hypersensitivity reactions occurring, albeit rarely. The study examined reports from 1968 to 2014, focusing on adverse drug reactions linked to herbal medicines in children. Out of 2646 individual case safety reports, 79 cases with 107 allergy-like reactions were identified, predominantly involving urticaria and allergic reactions. Notably, mixed herbal products, Hedera helix, and Echinacea purpurea were frequently implicated. Most reactions were due to oral administration, and a significant portion was reported in children aged 7 to 12 years, primarily from Germany, Thailand, and Australia. The findings underscore the critical need for stringent quality control and monitoring of herbal products to prevent severe allergic reactions, including life-threatening anaphylactic shock in children.[76] Cliff-Eribo et al performed a retrospective analysis of adverse drug reactions (ADRs) in Nigerian children, based on reports submitted to the Nigerian Pharmacovigilance Centre between 2005 and 2012, in children aged 0–17 years. The most commonly reported ADRs involved antiretrovirals, antibiotics, and anti-malarial. Reactions frequently included rash, fever, and pruritus, with anti-infective agents being responsible for over half of the cases. Tragically, 21 children died, eight from acute renal failure, linked to contaminated paracetamol/diphenhydramine hydrochloride and herbal teething medicines, often tainted with diethylene glycol. Stevens-Johnson syndrome was also prevalent, with 14 cases, three of which were fatal. The study emphasizes the critical need for stringent regulations to prevent ADRs, particularly those from sub-standard and

herbal medications.[77] The Taiwan Adverse Drug Reaction Reporting System for Herbal Medicine (TADRRS-HM) collected 2,079 reports of adverse drug reactions (ADRs) related to herbal medicines from 1998 to 2016. Of these, 941 involved single herbs and 87 were linked to folk herbal products, with 842 reports from clinical trials. Most ADRs were mild (72.4%), while 6.5% were severe, primarily affecting the gastrointestinal system (33.4%) and skin (21.2%). *Aconiti Radix, Xiao-Qing-Long-Tang*, and *Datura suaveolens* were the most frequently reported herbs. This system plays a key role in monitoring the safety of herbal medicines in Taiwan.[78]

Regulatory and Quality Issues

Current Regulatory Standards

It identifies that the regulatory standards of using herbal creams in dermatology still have confusion and disparity in how the products are classified and regulated.[79] For most states, the major use or classification of herbal creams is as cosmetics or traditional medicines, implying that they are more liberalized than actual medicine. For example, in the United States, the Federal Food and Drug Administration (FDA) controls herbal creams mainly as cosmetic products if they do not bear certain therapeutic claims, in which case they are OTC drugs.[80] Nonetheless, cosmetic products do not need permission from their production to be put on the market, and the manufacturers of such cosmetic products lack the consent to prove the safety and efficiency of their products.[81] Likewise, the use of herbal creams is still regulated under Cosmetics Regulation (EC) No. 1223/2009 in the European Union (EU); however, while safety testing is required, the regulation does not demand the efficiency of the product to be tested if it does not contain any medicinal advertisements.[82]

However, in countries like China and India, herbal and traditional medicine products need to follow different regulatory measures. For example, in India, Ministry of Ayush regulates the production of creams that are also classified as medicines dealing with Ayurveda Yoga Unani Siddha and Homeopathy and has laid down GMP and safety standards on the products.[83] However, the enforcement is not regular. Some Kampo medicines are classed as pharmaceuticals in Japan, so the laws require them to be produced and tested like ordinary pharmaceutical drugs before they are marketed. Worldwide, there is an emerging understanding of the importance of heightened and standardized regulatory requirements for the further protection, quality, and efficacy of products containing herbal creams. Some regions are pressing for the inclusion of GACP and standardized methods of testing, such as HPLC, in order to have constant percentages of active ingredients.[84,85] However, there is still no consensus on the regulatory norms. If there is no global consensus, then the customer may face risks associated with contamination, misidentification of products, and their unproven therapeutic effect. It is gradually changing, with noticeable gaps existing, to see that herbal creams meet the same standards as other pharmaceutical products.[85]

Challenges in Herbal Cream Manufacturing

When it comes to the manufacturing of herbal creams, several issues are distinctive from other sorts of creams and arise from the character and variability of plant materials. One of the biggest problems is maintaining the stability of active compounds during the final preparation. The quality of plants used may differ with the region of origin, soil type, climate, time of harvesting, and how the material was prepared.[86] The variability in the extracts means that the creams produced in different batches may have different potencies and different levels of purity and may not possess the same levels of therapeutic efficacy. For example, turmeric contains curcumin, and Aloe vera contains aloin; the concentration of these active compounds can vary, and thus, the quality control of the product is very important.[25] Another major challenge is contamination. The fourth major challenge is statistical testing, which aims at the comparison of proportions or means. Medicinal plant ingredients used in preparing and making these products are often contaminated by heavy metals, pesticide residues, or microbial pathogens at the time of cultivation or processing. This becomes difficult, especially if the raw materials are produced in areas that have poor agricultural measures. These components may be inherently contaminated and guaranteeing that they are clean involves following GACP and GMP, which are still lax in all producers.[87]

Problems related to the stability of herbal creams. The components used are plant-based materials that lose their effectiveness due to decomposition in a relatively short time [66]. This means that the formulation of a stable product often includes the use of preservatives or stabilizing agents. However, getting natural alternatives that are effective and acceptable to the "organic" consumer is always challenging. Also, the combination of some of these extracts with other components may cause problems of oxidation, changes in colouring, or reductions in effectiveness.[88] Also, the challenge arises over the standardization of the procedure used in extracting most herbal ingredients. The solvents used to extract cannabinoids may vary to be water soluble, alcohol soluble, or even carbon dioxide under supercritical fluid extraction to get different concentrations of active ingredients.[89] There are several extraction techniques for obtaining bioactive components, and because the integrity of these constituents is fragile, implementing an appropriate extraction process that would ensure that the active molecules remain active in the finished cream can be challenging, especially during large-scale production.[90] Lastly, the risk considerations also affect the production line through the toll that regulations have on it. Evaluating regulations poses challenges to manufacturers since firms have to deal with different standards depending on the country in which they will be operating, and compliance with international standards is expensive. Some of these factors include time consumption in compounding, stringent process control, rigorous testing, and a reliable supply of raw materials. Amidst all these challenges, making herbal creams a reality fully requires a lot of effort.[90]

Approaches to Ensuring Product Safety

Safeguarding these creams is complex and should involve quality control measures, rigorous testing, and compliance with all regulatory standard rules from the time of manufacturing. One of the main strategies includes undertaking Good Manufacturing Practices (GMP) that offer guidelines on hygiene, supply of raw materials, production equipment, and documentation to guarantee and standardize the production of products under a certain quality standard.[91] Another is the Good Agricultural as well as Collection Practices (GACP), which are the measures that aim at preventing contamination of medicinal plants by pesticide residue or heavy metals or microbial contaminants at the Agricultural and Collection level.[92] Elimination of dangerous impurities in materials that are used in production is another way of minimizing the rate of possible disastrous incidents that may affect the community.[93] Other safe practices include the following: Also, there should be significant testing done on safety issues. This involves a bacteriological examination to determine the existence and type of pathogenic bacteria, fungi, yeast, and other microorganisms, amongst others, and check-ups for poisonous substances such as toxins, pesticides, and heavy metals. Besides, stability testing is also carried out in order to evaluate the stabilities of the cream under different environmental conditions like temperature and humidity so as to confirm that the cream will work effectively in appropriate conditions throughout the shelf life.[94]

Furthermore, the standardized extracts in which the active components of the herbal ingredients are accurately indicated are another strategy Robert Ahrens used to ensure product safety. This makes it possible to avoid cases of variability of the effect required or toxic effects being experienced due to changes in the manufacturing process. Moreover, stabilization may also be done with preservative systems, for instance, for microbial control in herbal creams.[95] Still, milder or natural preservatives should be utilized since a substantial portion of the products market has a corresponding preference for "natural" products. Another important process is patch testing, most especially when the products are to be used for sensitive skin. This requires exposure of the product on less sensitive regions of the human skin or with skin models for assessment of irritating or sensitizing agents. Also, manufacturers should use an open-label declaration of the ingredients, the concentrations thereof, and all the precautions concerning potential allergens and side effects to enable consumers to avoid any possible adverse impacts of the products.[96] Additionally, there must be post-market surveillance to observe for any unfavourable results given by the consumers after letting go of the product into the market. It can help manufacturers get feedback on how to formulate their products better and make them last longer before they pose risks to consumers. When integrated, these two approaches can help manufacturers prove that these herbal creams are safe for use by consumers and, at the same time, have the same effectiveness as the natural products required in the manufacture of the creams.[96]

Clinical Trials

In recent years, numerous clinical trials have been conducted to evaluate the effectiveness of herbal drugs in the management of various skin problems. A summary of these reported trials is presented in Table 2.

Table 2 Various Clinical Trials Reported for the Treatment of Skin Problems by Using Herbal Drug

NCT Number	Intervention	Study Start Date	Enrolments	Phase	Disease Condition	Description[88–91,93–97]
NCT06301997 **– USA**	ZAX.1400.P03	2023-02	104 participants; Male & Female; 18–65 yrs	2	Psoriasis	This clinical trial compares ZAX.1400.P03 and placebo in 104 psoriasis patients, assessing the treatment's effectiveness on skin improvement over three weeks of topical application.
NCT00972062 **– USA**	Bach's Rescue Remedy Cream	2009-06	60 participants; Male & Female; 18–70 yrs	-	Multiple Sclerosis	This study examines the effectiveness of Bach's Rescue Remedy Cream in reducing skin reactions from MS injections. It hypothesizes that the cream will decrease redness and discomfort, while improving quality of life. The research builds on previous success in minimizing injection site reactions.
NCT02138539 **– USA**	Hydroquinone Herbal depigmenting agent (Epionce)	2013-10	28 participants; Male & Female; 20–60 yrs	4	Melasma	This study evaluates the effectiveness and safety of an herbal de-pigmenting regimen for hyperpigmentation and melasma, comparing it to Hydroquinone. Efficacy is measured via visual grading, devices, and photography, while safety is assessed by tracking irritation and adverse events.
NCT04841239 **– Iran**	Herbal topical formulation	2012-01-01	78 participants; Male & Female; ~12–60 yrs	-	Leishmaniasis	This study aimed to develop an alternative treatment for cutaneous leishmaniasis (CL) by formulating two herbal topical creams, Gyburene and Thuscare, containing 5% *Casuarina equisetifolia* L. and *Thespesia populnea* L. extracts. Preclinical tests on BALB/c mice and a six-week randomized, single-blind, placebo-controlled trial with 78 patients infected by *Leishmania major* were conducted to evaluate the creams' leishmanicidal potential.
NCT01715740 **– Taiwan**	Chinese Herbal Medicine (CHM)	2012-11	74 participants (planned 100); Male & Female; 18–65 yrs	III	Chronic Urticaria	This study evaluates the effectiveness of traditional Chinese medicine (Xiao-feng-san and Qing-shang-fang-fen-tang) for chronic urticaria in a double-blind, placebo-controlled trial. One hundred patients will be treated for one month, with symptom severity as the primary outcome and sleep improvement and serologic markers as secondary outcomes.
NCT03753113 **– Iran**	Topical Herbal Solution Topical Minoxidil 5%	2018-11-28	24 **male-only** participants; 18–45 yrs	III	Androgenetic Alopecia	This study focuses on male subjects with androgenetic alopecia (AGA) recruited from the Dermatology department of Sina Hospital. Participants will be randomized to use either a topical herbal solution or 5% minoxidil for 36 weeks. The herbal solution uniquely targets all four major causes of AGA through a quadruple mechanism, making it a promising treatment option.

(*Continued*)

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Table 2 (Continued).

NCT Number	Intervention	Study Start Date	Enrolments	Phase	Disease Condition	Description[88–91,93–97]
NCT03941431 – **China**	Jueyin granules	2019-06-01	378 participants; Male & Female; 18–75 yrs	II	Plaque Psoriasis	This study investigates the optimal combination of cupping, phototherapy, and Chinese medicine for treating plaque psoriasis, which affects patients' quality of life. A multicenter, randomized, single-blind, controlled trial will be conducted to enhance treatment efficacy while ensuring safety. The research builds on existing literature confirming the effectiveness of these treatments.
NCT04949932 – **Pakistan**	Mixed powder of Lens culinaris, Curcuma longa, Mentha arvensis, Azadirachta indica, and Trigonella foenumgraecum. Cicer arietinum powder	2021-04-03	42 participants; Male & Female; 18–35 yrs	-	Acne Vulgaris	This study evaluates the efficacy of a poly herbal powder (PHP) containing *Azadirachta indica, Curcuma longa, Lens culinaris, Mentha arvensis*, and *Trigonella foenum-graecum* for treating acne vulgaris in adults aged 18 to 35. Forty-two participants will be randomized into treatment and placebo groups over five months, with primary outcomes measured by total lesion count and Global Acne Grading System (GAGS) score. Safety will be assessed through the incidence of adverse events during the study.
NCT04686955 – **Taiwan**	Xiao Xian Gui Fu Tang	2021-01-01	24 participants; Male & Female; 18–65 yrs	-	Atopic Dermatitis	This clinical trial aims to evaluate the effectiveness of integrating traditional Chinese medicine with Western treatments for atopic dermatitis, assessing lesion remission and correlating syndrome differentiation types before and after treatment. The goal is to enhance understanding of treatment efficacy and provide alternative options for patients with atopic dermatitis.
NCT01389362 – **China**	Chinese herbal medicine (Radix Rehmanniae and Radix Astragali	2009-05	16 participants; Male & Female; 40–75 yrs	II and III	Diabetic Foot Ulcer	This study investigates a simplified herbal formula from Traditional Chinese Medicine, consisting of two herbs, to promote healing of early foot ulcers in diabetes patients by enhancing vascularization, granulation, and modulating inflammatory responses. Given the high risk of ulceration and complications in this population, the study aims to provide an effective treatment option for preventing gangrene and limb amputation.
NCT05592041 – **India**	Banaba Leaf Extract	2022-10-20	20 participants; Male & Female; 18–65 yrs	I	Plantar Wart	Moringa, banana, nigella, and Banna coat extracts were formulated into a biogel for transdermal delivery, characterized for organoleptic properties, morphology, and penetration efficacy. The optimized formulation underwent a Phase I clinical study with randomized allocation, targeting patients with plantar warts.

NCT04419584 – **China**	Modified Qing-Ying Decoction	2020-09-10	64 pediatric participants; Male & Female; 3–14 yrs	II and III	Atopic Dermatitis	This randomized, double-blind, placebo-controlled trial aims to evaluate the efficacy and safety of modified Qing-Ying Decoction (mQYD) for treating subacute and chronic atopic dermatitis in children. Clinical symptoms, quality of life, gut microbiome, and Chinese medicine body constitution will be assessed over a 12-week treatment period with a 4-week follow-up.
NCT02085395 – **Taiwan**	SR-T100 ® Gel	2007-11	27 participants; Male & Female; 18–80 yrs	II	Actinic Keratosis	This Phase II open study evaluates the efficacy and safety of topical SR-T100 gel for treating cutaneous cell carcinoma in situ (Actinic Keratosis and Bowen's Disease). Primary efficacy is measured by at least a 75% reduction in lesion size, while secondary endpoints include complete and partial clearance rates, and histological response. Safety is assessed through physical exams, vital signs, lab assessments, and adverse events.
NCT00442091 – **Italy**	Dandelion juice	2010-12	4 participants; Male & Female; 18–65 yrs	-	Vesicular Palmoplantar Eczema, Pompholyx	This study aims to evaluate the potential benefits of dandelion juice in treating vesicular hand eczema, a rare and difficult-to-treat condition, based on a case report suggesting its efficacy. The goal is to determine if this positive effect can be replicated in other patients.
NCT03447925 – **Iran**	Medicinal Plant Salicylate Vaseline	2017-06-01	90 participants; Male & Female; 18–70 yrs	II	Keratosis Plantaris	This randomized, double-blind study aims to evaluate the effectiveness of a medicinal plant compared to salicylate and vaseline in treating keratosis in diabetic patients. Ninety adult patients with type 1 or 2 diabetes will receive daily topical treatment for 30 days, and results will be assessed through numerical scores of keratosis areas. Statistical comparisons will determine the efficacy of each treatment group.

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Table 3 Various Herbal Marketed Formulations Along with Their Mechanism of Action, Marketed Preparation and Brand Name

Ingredient	Source	Action	Marketed Preparation	Brand Name/ Manufacturer[97–100]
Turmeric (Curcuma longa)	Rhizome of Turmeric Plant	Anti-inflammatory, antioxidant; typically applied to face/neck for pigmentation and acne; once or twice daily	Curcumin Gel	Curcuma Health
Milk Thistle (Silybum marianum)	Milk Thistle Seeds	Antioxidant, anti-inflammatory; used on face and hands for UV/sun damage; daily morning use	Silymarin Cream	Nutraceutical Corporation
Neem (Azadirachta indica)	Neem Tree (Leaves, Bark)	Antimicrobial, anti-inflammatory; used for acne-prone face; twice daily	Neem Cream	Himalaya Wellness
Gotu Kola (Centella asiatica)	Gotu Kola Plant (Leaves)	Wound healing, anti-inflammatory; applied on scars, legs, arms; once daily for 2–4 weeks	Cica-Care Hydrogel	Smith & Nephew
Licorice (Glycyrrhiza glabra)	Licorice Root	Skin brightening, anti-inflammatory; used on face/neck for melasma; daily or night use	Licorice Skin Cream	Himalaya Wellness
Aloe Vera (Aloe vera)	Aloe Plant (Leaves)	Soothing, moisturizing; applied to face/arms/legs; multiple times daily as needed	Aloe Vera Gel	Aloe Farms
Tea Tree Oil (Melaleuca alternifolia)	Tea Tree (Leaves)	Antimicrobial; used on acne lesions on face/chest/back; 1–2 times daily, anti-inflammatory	Tea Tree Oil Gel	Thursday Plantation
Triphala	Amalaki, Bibhitaki, Haritaki	Antioxidant, anti-inflammatory; applied to face for rejuvenation; nightly or daily	Triphala Paste	Himalaya Wellness
Calendula (Calendula officinalis)	Marigold Flowers	Antiseptic, wound healing; used on minor cuts on arms/legs; 2–3 times daily	Calendula Cream	Weleda AG
Indian Frankincense (Boswellia serrata)	Boswellia Tree Resin	Anti-inflammatory, analgesic; applied to joints, hands, legs; twice daily	Boswellia Cream	Ayushakti
Arnica (Arnica montana)	Arnica Flowers	Anti-inflammatory, analgesic; used on bruises on arms/legs; 2–3 times daily	Arnica Gel	Boiron
Rosemary (Rosmarinus officinalis)	Rosemary Leaves	Antioxidant, antimicrobial; applied on scalp or face; daily application	Rosemary Oil	Herb Pharm
Gotu Kola (Hydrocotyle asiatica)	Gotu Kola Plant	Skin regeneration, healing; applied on scars/face; once daily for ≥4 weeks	Gotu Kola Gel	Bioré
Yerba Mate (Ilex paraguariensis)	Yerba Mate Leaves	Antioxidant, anti-inflammatory; used on body/arms/legs; daily use	Yerba Mate Cream	Herbalife
Ginkgo (Ginkgo biloba)	Ginkgo Tree (Leaves)	Antioxidant, promotes circulation -enhancing; applied on face/neck; daily or nightly	Ginkgo Biloba Cream	Nature's Way

Marketed Formulations

Herbal formulations in dermatology provide numerous advantages for treating various skin conditions. For atopic dermatitis, St. John's Wort and liquorice are valued for their anti-inflammatory effects. Treatments for psoriasis often incorporate turmeric and indigo naturalis.[96] Acne vulgaris can be addressed with tea tree oil and green tea extract, both recognized for their antimicrobial and anti-inflammatory properties. To alleviate redness in rosacea, green tea and liquorice are commonly used. For wound healing, birch bark and onion extract are frequently utilized, while aesthetic dermatology benefits from gotu kola and pine bark extract, which enhance skin elasticity and reduce the appearance of wrinkles.[96] These formulations come in various forms, including creams, gels, ointments, and serums, offering diverse therapeutic benefits. Besides these, several herbal formulations available in the market are mentioned in Table 3.[97]

Future Perspective and Conclusion

Herbal creams are poised to play an increasingly significant role in dermatology as the demand for natural and holistic skincare solutions continues to rise. With growing awareness among consumers about the side effects of synthetic products and the need for sustainable alternatives, herbal formulations enriched with plant-derived bioactive compounds offer an attractive, safer option. These creams, known for their antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties, hold considerable promise in combating a wide range of skin infections, while minimizing the risk of adverse effects and resistance often associated with conventional treatments. Advancements in extraction methods and formulation technologies are expected to enhance both the effectiveness and skin absorption of herbal ingredients, making them even more potent and accessible. The potential of herbal creams to target a broad spectrum of pathogens further reinforces their relevance as therapeutic options in skin infection management. However, to translate this potential into widespread clinical use, future research must prioritize large-scale clinical trials, robust standardization of formulations, and in-depth mechanistic studies to establish safety, stability, and bioavailability. Incorporating cutting-edge technologies such as nanotechnology and biopharmaceutical delivery systems can lead to more precise, efficient, and targeted treatment options, maximizing the therapeutic benefits of herbal ingredients.

The future of dermatological care may also see a shift toward personalized skincare solutions, powered by digital tools and data-driven insights. Tailored treatments designed to meet individual skin profiles and sensitivities could make herbal creams even more effective and widely accepted. Yet, to fully realize these advancements, it is imperative to develop a unified regulatory framework that ensures product safety, efficacy, and consistent quality across markets. Alongside this, sustainable sourcing of herbs must become a central concern, promoting ethical harvesting practices and eco-friendly production methods that protect biodiversity and support local communities. In conclusion, herbal creams represent a powerful, nature-inspired approach to skin health—one that bridges traditional wisdom with modern scientific innovation. By embracing rigorous research, technological advancements, and responsible practices, these formulations have the potential to redefine dermatological care. With continued effort and collaboration across disciplines, herbal creams can offer safe, effective, and accessible solutions for managing skin infections while paving the way for a more sustainable and compassionate future in skincare.

Disclosure

The authors report no conflicts of interest in this work.

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