PERINATAL JOURNAL

Original Article

Perinatal Journal 2026; 34(1):1319-1332

https://doi.org/10.57239/prn.26.034100131

Herbal therapies for acne vulgaris: A systematic review of clinical evidence

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Abstract

Acne Vulgaris (AV) is a common chronic inflammatory skin disorder with multifactorial pathogenesis. Comprehensive approach and long-term treatment are required to prevent AV complications such as scarring, and psychosocial distress. Limitations in conventional therapy, including irritation and antibiotic resistance, have encouraged interest in the use of herbal agents. This systematic review evaluates the efficacy, safety, and mechanisms of action of topical herbal agents for the management of AV. A comprehensive search was conducted in PubMed, Scopus, and Cochrane for clinical trials published from 2015 to 2025 evaluating herbal preparations in AV. Eligible studies included randomized controlled trials (RCTs) and open-label studies assessing clinical outcomes such as lesion counts, Investigator's Global Assessment (IGA), Dermatology Life Quality Index (DLQI), and adverse events. Data extraction was performed for study design, intervention, comparator, outcomes, duration, and adverse effects. Twenty-six clinical studies were included, investigating both single-herb (e.g., Curcuma longa, Garcinia mangostana, Melaleuca alternifolia, Camellia sinensis, Nigella sativa, Rhodomyrtus tomentosa) and multi-herbal formulations. Most interventions demonstrated significant reductions in inflammatory and non-inflammatory lesion counts, with some achieving efficacy comparable to benzoyl peroxide or clindamycin. Mechanisms of action included anti-inflammatory, antibacterial, antioxidant, and sebum-regulating effects. Adverse events were minimal and transient, with better tolerability than conventional agents. Evidence quality was moderate due to heterogeneity in formulations, small sample sizes, and short follow-up periods. Conclusion: Herbal agents offer multifaceted therapeutic action and are potentially effective, safe, and well tolerated for mild to moderate AV. They were potentially as alternatives or adjuncts to standard treatments. Standardized formulations, larger RCTs with rigorous methodologies, and longer-term follow-up are needed to confirm sustained benefits.

Keywords: Acne vulgaris, Acne management, Clinical trial, Herbal therapy, Systematic review.

Introduction

Acne Vulgaris (AV) is one of the most prevalent chronic inflammatory skin disorders, affecting up to 85% of adolescents and a significant proportion of adults worldwide (Rathi, 2011). It manifests through a range of lesions including comedones, papules, pustules, and nodules, and often leads to physical discomfort, psychosocial distress, and long-term sequelae such as scarring and post-inflammatory hyperpigmentation (Batista & Ana, 2016). Effective and long-term treatment is crucial to prevent those complications and minimize long-term impact on skin appearance and quality of life (Huang et al., 2023; Lee et al., 2019; Li et al., 2024).

Conventional treatments—including topical retinoids, benzoyl peroxide, antibiotics, and systemic agents such as isotretinoin and hormonal therapy—are effective but are often associated with side effects, limited patient compliance, and growing concerns about antibiotic resistance (Karadag et al., 2021). These challenges have led to a rising interest in complementary and alternative therapies, particularly herbal-based treatments, which are perceived as safer, more natural, and culturally acceptable (Jayronia et al., 2024).

According to the World Health Organization (WHO), herbal medicine refers to plant-derived materials or preparations containing, as active ingredients, parts of plants, other plant materials, or combinations thereof, used for therapeutic purposes (Organization, 2007). In dermatology, herbal agents have attracted interest as potential adjuncts or alternatives to conventional treatments, particularly for chronic inflammatory conditions such as acne vulgaris (AV) (Shree et al., 2022).

Acne vulgaris is a chronic inflammatory skin disease with a multifactorial pathogenesis involving follicular hyperkeratinization, increased sebum production, colonization by *Cutibacterium acnes*, and activation of

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inflammatory immune pathways (Dreno et al., 2015). Numerous plants and plant-derived compounds have demonstrated anti-inflammatory, antimicrobial, sebum-regulating, and keratolytic properties, making them promising candidates in acne management. Extracts from *Melaleuca alternifolia* (tea tree), *Glycyrrhiza glabra*, *Camellia sinensis* (green tea), *Nigella sativa*, and *Rhodomyrtus tomentosa* are among the most studied for their dermatologic benefits (Cristani & Micale, 2024; Draelos, 2015). However, the clinical efficacy, safety, and consistency of these herbal therapies remain under-investigated and scattered across heterogeneous studies.

A systematic evaluation of the current clinical trial information is crucial given the growing use of herbal medicines in acne treatment. This systematic review aims to evaluate and consolidate the clinical outcomes, safety profiles, and methodological quality of herbal interventions used in the treatment of acne vulgaris, thereby supporting evidence-based recommendations for their use in dermatologic practice.

Material and Methods

We conducted a systematic review of the literature according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to study herbal therapies for AV (Figure 1).

This systematic review is not registered in PROSPERO because this study is a retrospective literature review and the protocol was not registered prior to implementation. Nevertheless, the PRISMA procedure was still applied to ensure transparency and methodological reliability.

A. Literature Search Strategies

1. Electronic database

We searched for all relevant studies from July 2015 until June 2025 in the following electronic databases: Pubmed, Scopus, and Cochrane databases, without language or type of publication limitations. The following search criteria were used: ("Acne vulgaris" OR "acne") AND ("Herbal medicine" OR "Plant Extracts" OR "Phytotherapy") AND ("Randomized Controlled Trial" OR "Clinical Trial").

2. Inclusion criteria

We included all studies that described herbal therapies for AV and met the following criteria:

- Study type: Randomized Clinical Trials (RCT), quasi-RCT, non-RCT.
- Population: Patients with acne vulgaris (without age and gender restrictions).
- Intervention: Natural herbal-based products, both topical and oral, with details of ingredients and dosage.
- Comparators: Placebo, no comparator, or with standard therapy.
- Outcomes: Report at least one of: Change in number of lesions, Improvement in clinical score, Adverse events.
- Year of publication: 2015 to 2025

3. Exclusion criteria

Studies were excluded if the full text or abstract was unavailable, duplicated, involved animals as subjects, or was published in a language other than English.

B. Outcome measure

The outcome of interest was the identification of the clinical trial of herbal therapies for AV. The following data were extracted from the studies and collected in an electronic database: title, author (year), country, study design, sample size, inclusion criteria, herbal type and dose, dosage form, duration of intervention, comparator/control, main outcome, side effects, conclusion. Descriptive statistics were obtained using Microsoft Excel for Office Home and Students®, 2021.

C. Risk assessment bias

Risk of bias was assessed using the Cochrane Risk of Bias tool, covering randomization, allocation, blinding, incomplete outcome data, reporting of results, and other biases. Each study was categorized as low risk, some concerns, or high risk. Studies with clear randomization and masking (double- or triple-blind) were considered low risk, studies with unclear randomization or masking procedures were considered to have some concerns, and open-label, single-arm, or non-randomized/unmasked studies were categorized as high risk.

Result

A. Study selection

The selection process is illustrated in the PRISMA flow chart (Figure 1). The initial database searches and reference list searches resulted in a total of 156 articles. A total of 71 articles were chosen for full-text reading following the elimination of duplicates and the screening of titles and abstracts. Studies were removed from the 71 total articles for the following reasons: the articles were irrelevant (n = 35), and the full text was not accessible (*n* = 10). Finally, this systematic review examined the 26 remaining articles. In total, 26 relevant patient cases were included for data collection.

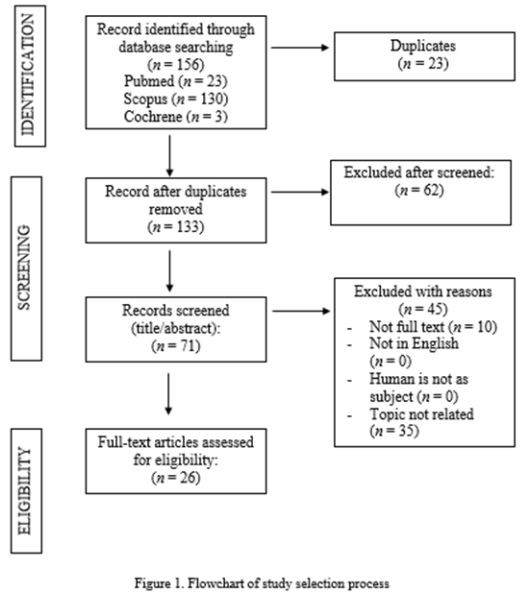

Figure 1. Flowchart of study selection process

B. General comparison result

A total of 26 studies were included in this review, comprising various clinical trial designs such as double-blind RCTs, split-face RCTs, open-label studies, and single-arm clinical trials. Most of the included trials investigated mild-to-moderate acne vulgaris, with only a few focusing on moderate-to-severe cases. The duration of intervention ranged from 10 days to 12 months, with the majority lasting between 4 and 12 weeks.

The included studies evaluated a diverse range of herbal interventions, either as single extracts or in combination, with tea tree oil, green tea, *Aloe vera*, mangosteen extract, and multi-herbal formulations being the most frequently investigated. Comparators varied across trials, including placebo, standard topical agents such as clindamycin or benzoyl peroxide, or no treatment in open-label studies.

Overall, most trials reported improvements in acne lesion counts and severity indices, particularly in inflammatory lesions, with several studies demonstrating comparable efficacy to standard treatments. Additionally, herbal interventions were generally well-tolerated, with the most common adverse effects being mild irritation, dryness, or transient peeling. Serious adverse events were not reported in any study.

C. Assessment of risk of bias

The methodological quality of the included studies varied. Among the 26 studies assessed, 16 trials (61.5%) were judged as low risk of bias, primarily due to their randomized controlled trial design with adequate blinding (double-blind or triple-blind). Four studies (15.4%) were classified as having some concerns, often due to unclear reporting of randomization procedures or the use of split-face designs without clear blinding details. The remaining six studies (23.1%) were rated as high risk of bias, predominantly open-label or single-arm trials, which lack randomization and blinding, increasing the likelihood of performance and detection bias.

A summary of the risk of bias distribution is presented in Figure 2, showing the predominance of low-risk trials but also highlighting the existence of studies with moderate to high risk that may influence the overall certainty of evidence.

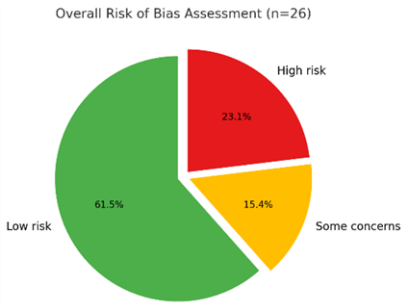

Figure 2. Distribution of risk of bias (26 studies)

Discussion

General summary of findings

Overall effectiveness of topical herbal treatments for acne vulgaris

Topical herbal agents have emerged as promising alternatives or adjuncts in the management of mild to moderate AV (Jayronia et al., 2024). Analysis of the 26 clinical studies included in this systematic review reveals that the majority of herbal interventions demonstrated significant clinical improvement, particularly in reducing both inflammatory (papules, pustules) and non-inflammatory (comedones) acne lesions.

Across RCTs and open-label studies, the primary outcome measure was typically a reduction in total lesion count, often supported by secondary outcomes such as Investigator's Global Assessment (IGA) scores and improvement in dermatologic quality of life indices (e.g., DLQI, CADI). Herbal treatments produced measurable improvement in as early as 4 weeks, with more consistent results seen in studies extending 8 to 12 weeks. Notably, several studies (Lubtikulthum et al., 2019; Lueangarun et al., 2019a; Mazzarello et al., 2018) demonstrated that herbal formulations achieved efficacy comparable to standard treatments such as clindamycin 1% or benzoyl peroxide 2.5%, particularly when addressing inflammatory lesions.

The therapeutic effects observed are attributable to a variety of mechanisms of action present in the botanical constituents, including anti-inflammatory activity (e.g., through inhibition of proinflammatory cytokines like IL-1β and TNF-α), antimicrobial properties targeting *Cutibacterium acnes* (*C. acnes*) and *Staphylococcus epidermidis*, sebum-regulating effects through antioxidant pathways and hormonal modulation (Lueangarun et al., 2019b). Importantly, most herbal preparations exhibited minimal adverse effects, primarily limited to mild local irritation or transient dryness, and in many studies, the tolerability profile was superior to that of conventional topical agents (Lubtikulthum et al., 2019). This makes topical herbal therapies particularly suitable for patients with sensitive skin, those who experience irritation from retinoids or benzoyl peroxide, or those seeking natural or integrative treatment options. Overall, the collective evidence supports the clinical utility of topical herbal therapies as a viable, evidence-based option for mild to moderate AV, either as monotherapy in early or mild cases or as adjunctive treatment in combination with conventional agents.

Predominant herbal agents used

Among the 26 clinical studies included in this review, a wide range of botanical agents was evaluated for their potential in managing AV. While some studies investigated single-herb formulations, many others utilized multi-herbal combinations, reflecting traditional and integrative medicine practices aimed at achieving synergistic therapeutic effects. The most frequently studied and clinically relevant herbal agents can be categorized based on their frequency of use and biological plausibility:

1. Mangosteen (*Garcinia mangostana*)

Featured in multiple trials (Lubtikulthum et al., 2019; Lueangarun et al., 2019b; Mazzarello et al., 2018), mangosteen extract emerged as one of the most prominent herbs. Its active compound, α-mangostin, exhibits strong anti-inflammatory, antioxidant, and antibacterial properties against Cutibacterium acnes. Formulated in both nanoparticle gels and herbal blends, mangosteen consistently demonstrated a reduction in inflammatory lesions with minimal irritation (Lueangarun et al., 2019b; Pan-In et al., 2015; Yang et al., 2021).

2. Tea Tree Oil (*Melaleuca alternifolia*)

Tea tree oil was evaluated in both monotherapy (Draelos ZD, 2006) and combination therapies (Mazzarello et al., 2018). It is known for its broad-spectrum antimicrobial activity and has been shown to reduce *C. acnes* colonization, suppress sebaceous gland activity, and decrease inflammation. Studies reported a clinically significant reduction in lesion counts, although mild side effects such as dryness or peeling were occasionally noted (Draelos ZD, 2006; Mazzarello et al., 2018).

3. Green Tea (*Camellia sinensis*)

Used both topically and orally, green tea extract (Chularojanamontri et al., 2014; Fox et al., 2011)

contains polyphenols such as epigallocatechin gallate (EGCG), which possess anti-inflammatory and sebum-suppressive effects. Results showed not only lesion reduction but also improvement in skin hydration and wound healing, making it beneficial for post-acne recovery. Oral supplementation was generally well tolerated but occasionally associated with gastrointestinal discomfort.

4. *Aloe Vera*

Often included in combination formulas (e.g., Mazzarello et al.[40], Iraji et al.[47]), *Aloe vera* contributes via its soothing, anti-inflammatory, and antimicrobial actions. It enhances skin repair and reduces erythema and irritation. Aloe-based formulations were particularly well tolerated, with few reports of adverse reactions, making them suitable for sensitive or irritated skin types (Camargo Jr et al., 2011; Mazzarello et al., 2018).

5. *Nigella sativa* (Black Seed)

Investigated in a double-blind RCT (Soleymani et al.[48]), *Nigella sativa* showed significant lesion count reduction, presumably due to thymoquinone, its primary active compound. It has potent antioxidant and antimicrobial activity, with an excellent safety profile (Melough MM et al., 2018).

6. *Rhodomyrtus tomentosa*

Tested both alone (Wunnoo et al.[49]) and in combination (Zhang et al.[50]), rhodomyrtone, the main bioactive compound, exhibits anti-*C. acnes* activity, reduces inflammation, and may enhance the skin barrier. It showed non-inferiority to clindamycin, suggesting it could be a candidate for antibiotic-sparing strategies (Lin et al., 2018; Vaughn et al., 2018).

7. Others

Additional botanicals studied with promising results include:

- *Curcuma longa* (Turmeric) – anti-inflammatory, used in photodynamic therapy (Palmer & Kitchin, 2010).
- Licorice (*Glycyrrhiza glabra*) – anti-androgenic and antimicrobial (Camargo Jr et al., 2011).
- *Ziziphus spina-christi* (Cedar) – shown to reduce lesion counts in RCTs (Lodén et al., 1999).
- Pomegranate, chamomile, lavender, onion, and berberis – used in complex formulations with various levels of evidence (Callender et al., 2011).

The most dominant herbs—mangosteen, tea tree oil, green tea, aloe vera, and *Nigella sativa*—demonstrated consistent clinical efficacy in reducing acne severity with favorable safety profiles. These herbs act through multiple mechanisms, including antimicrobial, anti-inflammatory, antioxidant, and seboregulatory effects. Their frequent inclusion in trials reflects both traditional use and increasing scientific validation, underscoring their potential as evidence-based alternatives or adjuncts in acne therapy (Callender et al., 2011; Lubtikulthum et al., 2019).

Main clinical effects observed

Across the 26 clinical trials analyzed in this review, the most consistently reported clinical outcomes of topical herbal therapies for AV were reduction in lesion count, improvement in overall acne severity, and enhancement in skin quality. These effects were observed regardless of whether the herbal agents were administered as monotherapy or in combination with other herbs or vehicles, and across various delivery systems, including creams, gels, hydrogels, serums, and nanoparticles.

1. Reduction in acne lesion counts

The primary outcome reported in nearly all studies was a significant reduction in total acne lesion count, including both inflammatory lesions (papules, pustules, nodules) and non-inflammatory lesions (comedones). For instance, studies on tea tree oil, mangosteen extract, green tea, *Nigella sativa*, and rhodomyrtone consistently showed substantial improvement in inflammatory lesion count, often within 4 to 8 weeks of therapy. Notably, studies involving comparators such as clindamycin or benzoyl peroxide (e.g., Wunnoo et al.[49], Lubtikulthum et al.[41], Lueangarun et al.[39]) showed that herbal formulations achieved comparable reductions in lesions with fewer adverse effects (Lin et al., 2018;

Lubtikulthum et al., 2019; Lueangarun et al., 2019b).

2. Improvement in global acne severity

Many trials employed IGA or similar scoring systems to rate the severity of acne before and after treatment. Herbal agents such as Berberis root and spearmint (Saeidi et al.[53]) and *Rhodomyrtus tomentosa* (Wunnoo et al.[49]) demonstrated significant improvements in IGA scores over 4–8 weeks of treatment, indicating a clinically meaningful improvement in disease severity (Callender et al., 2011; Lin et al., 2018).

3. Enhancement in skin barrier and sebum regulation

Some studies explored additional parameters beyond lesion count, such as sebum production: Topical application of green tea, *Eucalyptus extract*, and red ginseng was associated with sebum reduction, likely due to antioxidant and hormonal modulation effects (Chularojanamontri et al., 2014; Palmer & Kitchin, 2010). Transepidermal Water Loss (TEWL) and skin hydration improvements were noted in trials involving *Aloe vera*, chamomile, and calendula, suggesting a supportive role of herbal agents in restoring skin barrier function, particularly beneficial in acne patients with sensitive or compromised skin (Camargo Jr et al., 2011).

4. Quality of life improvements

A number of trials evaluated quality-of-life measures such as the DLQI and CADI. These instruments showed measurable improvement in patient-reported outcomes, indicating that herbal interventions not only improved clinical signs but also had a positive psychosocial impact (Callender et al., 2011; Sarkar et al., 2013; Jam et al., 2025).

5. Safety and tolerability

Across all included studies, adverse effects were minimal. When present, they were typically mild and self-limited, including transient erythema, dryness, or mild irritation. No serious adverse events were reported. This reinforces the notion that topical herbal therapies are well tolerated, and potentially suitable for long-term use or maintenance therapy, especially in populations sensitive to retinoids or conventional antimicrobials (Lueangarun et al., 2019b; Mazzarello et al., 2018).

Topical herbal treatments for acne vulgaris are associated with a multifaceted range of clinical benefits such as consistent and significant reduction in both inflammatory and non-inflammatory acne lesions, improvements in global acne severity and patient satisfaction, favorable effects on sebum regulation and skin barrier function, and enhancements in quality of life with minimal adverse effects. These outcomes underscore the potential role of botanical formulations as safe, effective, and patient-preferred options for managing mild to moderate AV (Callender et al., 2011; Lueangarun et al., 2019b).

Mechanism of action

Anti-Inflammatory effects of herbal agents

Inflammation is a central pathogenic mechanism in AV, contributing not only to lesion formation but also to scarring and post-inflammatory hyperpigmentation. Herbal agents with anti-inflammatory properties target this pathway by modulating cytokine release, inhibiting oxidative stress, and downregulating inflammatory mediators such as TNF-α, IL-1β, IL-6, COX-2, and NF-κB. Among the 26 studies reviewed, many herbal extracts demonstrated clinically and biologically significant anti-inflammatory effects (Lueangarun et al., 2019b; Yang et al., 2021).

1. Mangosteen (*Garcinia mangostana*)

Mangosteen contains α-mangostin, a xanthone with well-documented anti-inflammatory activity. It inhibits Cyclooxygenase (COX) enzymes and proinflammatory cytokines, contributing to reduced erythema and lesion size. In studies by Lueangarun et al.[39], Yang et al.[42], and Pan-In Porntip et al.[43], topical mangosteen formulations significantly reduced inflammatory lesion counts with minimal irritation, indicating effective local anti-inflammatory action (Lueangarun et al., 2019a; Mazzarello et al., 2018; Yang et al., 2021; Moghavvemi et al., 2025).

2. Green tea (*Camellia sinensis*)

Green tea polyphenols, especially eEGCG, are known to suppress NF-κB activation, reduce toll-like receptor 2 (TLR-2) expression, and inhibit pro-inflammatory cytokines in sebocytes. In studies by Lu et al.[45] and Lin

et al.[46], both oral and topical green tea significantly improved inflammatory acne, suggesting systemic and local modulation of inflammation (Chularojanamontri et al., 2014; Fox et al., 2011).

3. Tea tree oil (*Melaleuca alternifolia*)

Tea tree oil exhibits dual anti-inflammatory and antimicrobial effects. It downregulates histamine release and cytokine expression, resulting in decreased lesion inflammation. Malhi et al.[44] and Mazzarello et al.[40] reported improvement in acne severity along with reduction in erythema, despite some mild irritation, likely related to terpene content (Draelos ZD, 2006; Mazzarello et al., 2018).

4. *Nigella sativa* (Black seed)

The active constituent thymoquinone exerts antioxidant and anti-inflammatory effects by scavenging reactive oxygen species and downregulating inflammatory genes. Soleymani et al.[48] demonstrated a significant reduction in acne lesions with 20% *Nigella sativa* gel, without any reported adverse effects (Melough MM et al., 2018).

5. *Rhodomyrtus tomentosa*

Rhodomyrtone, the bioactive compound of this plant, has been shown to suppress TNF-α and IL-8. Wunnoo et al.[49] showed that topical rhodomyrtone serum reduced inflammatory lesion counts comparably to clindamycin, supporting its anti-inflammatory role (Lin et al., 2018).

6. Licorice (*Glycyrrhiza glabra*) and *aloe vera*

In the study by Iraji et al.[47], a herbal cream combining licorice root, pomegranate peel, zataria, and *Aloe vera* led to significant reduction in acne severity. Licorice's glycyrrhizin and *Aloe vera*'s acemannan contribute to decreased leukocyte infiltration and histamine-induced erythema (Chularojanamontri et al., 2014).

7. *Curcuma longa* (turmeric)

Curcuma longa (turmeric), through its active compound curcumin, exerts potent anti-inflammatory effects by inhibiting key mediators such as NF-κB, TNF-α, IL-1β, and COX-2, thereby reducing erythema and inflammatory lesion formation in acne vulgaris. In the study by Crusca et al.[38] (2025), curcumin combined with blue light photodynamic therapy significantly reduced lesion counts and improved quality of life in patients with moderate to severe acne, with excellent tolerability and no reported adverse effects. These findings support its role as a promising botanical anti-inflammatory agent in acne management (Tirado-Yañez A et al., 2020).

The anti-inflammatory effects of herbal agents in acne therapy are multifactorial, including inhibition of proinflammatory cytokines and enzymes, suppression of oxidative stress and immune cell recruitment, and restoration of skin barrier function. These mechanisms translate into clinically observable outcomes such as: reduced erythema and induration faster resolution of papules and pustules, decreased risk of scarring and hyperpigmentation. The broad spectrum of anti-inflammatory activity across different botanicals supports their inclusion in acne management protocols, particularly for patients with inflammatory-predominant acne, sensitive skin, or inflammatory flare-ups triggered by conventional therapies (Lin et al., 2018; Melough MM et al., 2018).

Antibacterial effects of herbal agents (especially against cutibacterium acnes)

One of the primary drivers of inflammatory AV is proliferation of *C. acnes* (formerly *Propionibacterium acnes*), which contributes to comedone formation, inflammation, and immune activation via TLR-2 stimulation and induction of proinflammatory cytokines. Antibiotics such as clindamycin and erythromycin have long been used to control *C. acnes*, but increasing concerns regarding antibiotic resistance have prompted the exploration of herbal alternatives with antimicrobial activity (Lueangarun et al., 2019a; Mazzarello et al., 2018).

Several herbal agents included in this systematic review demonstrated broad-spectrum antibacterial effects, with specific inhibitory action against *C. acnes*. The mechanisms involve membrane disruption, enzyme inhibition, and interference with microbial replication, offering promising non-antibiotic strategies to control acne flora (Camargo Jr et al., 2011; Lin et al., 2018).

1. Tea tree oil (*Melaleuca alternifolia*)

Tea tree oil contains terpinen-4-ol, its primary

antibacterial compound. It exerts antimicrobial activity by disrupting bacterial cell membranes and increasing permeability. Malhi et al[44]. and Mazzarello et al.[40] found that topical tea tree oil reduced *C. acnes*-related inflammation and lesion counts significantly. Its efficacy is comparable to benzoyl peroxide, though with milder side effects (Draelos ZD, 2006; Mazzarello et al., 2018).

2. *Rhodomyrtus tomentosa*

Rhodomyrtone, extracted from *Rhodomyrtus. tomentosa*, has potent antibacterial effects against *C. acnes* by inhibiting fatty acid biosynthesis and disrupting cell walls. Wunnoo et al[49]. reported that a 1% rhodomyrtone liposomal serum was non-inferior to clindamycin 1% gel, showing equal efficacy in reducing lesion counts and inflammation, without bacterial resistance concerns (Lin et al., 2018).

3. *Nigella sativa* (Black Seed)

Thymoquinone, the main bioactive of *Nigella sativa*, has been shown to have direct antimicrobial effects on *C. acnes*, as well as anti-inflammatory and antioxidant properties. In the RCT by Soleymani et al.[48], a 20% *Nigella sativa* hydrogel led to significant reduction in acne lesions with no reported side effects (Melough MM et al., 2018).

4. Mangosteen (*Garcinia mangostana*)

Alpha-mangostin, found in mangosteen pericarp, possesses both antibacterial and anti-inflammatory activity, targeting *C. acnes* and *S. epidermidis*. Lueangarun et al.[39] and Pan-In Porntip et al.[43] showed that topical formulations—especially in nanoparticle forms—enhanced penetration and bactericidal effect, resulting in notable reduction of inflammatory lesions (Lueangarun et al., 2019b; Pan-In et al., 2015).

5. Green Tea (*Camellia sinensis*)

Though primarily known for its antioxidant properties, green tea polyphenols (especially EGCG) also demonstrate bacteriostatic activity against *C. acnes* by inhibiting dihydrofolate reductase and damaging bacterial membranes. Lu et al.[45] reported that both topical and oral green tea led to improvement in inflammatory lesion counts, suggesting antimicrobial action as part of its mechanism (Chularojanamontri et al., 2014).

6. Curcuma longa

Curcuma longa exhibits notable antibacterial activity against *C. acnes*, primarily through the action of curcumin, which disrupts bacterial membranes, inhibits biofilm formation, and interferes with bacterial replication.[55] Although its antimicrobial potency is generally lower than conventional antibiotics or agents like tea tree oil, its efficacy is enhanced when combined with photodynamic therapy (PDT), as shown in Crusca et al.[38] (2025). In this study, curcumin-based PDT resulted in significant acne lesion reduction, suggesting that curcumin may serve as an effective adjunctive antibacterial agent in acne treatment, especially in light of growing antibiotic resistance (Tirado-Yañez A et al., 2020).

7. Other Notable Antibacterial Herbs

Berberis integerrima (with spearmint oil) – as studied by Saeidi et al., showed strong antimicrobial synergy, reducing lesion counts and improving DLQI. Onion, lavandula, and mangosteen combination – reported by Lubtikulthum et al.[41] to have efficacy comparable to BPO, with less irritation. *Ziziphus spina-christi* (Cedar leaf extract) – reported significant antimicrobial effects, particularly in adolescent acne patients (Shakiba et al.) (Lodén et al., 1999).

Topical herbal agents exhibit significant antibacterial activity against *C. acnes*, through mechanisms including: cell membrane disruption (e.g., tea tree oil, rhodomyrtone),[40] inhibition of bacterial replication and metabolism (e.g., EGCG, thymoquinone),[45] and prevention of biofilm formation (e.g., berberine-containing plants).[53] This antibacterial effect not only reduces acne severity but may also limit resistance development, positioning these botanicals as viable alternatives or adjuncts to conventional topical antibiotics. Their use may be especially valuable in long-term maintenance regimens, acne-prone patients with antibiotic intolerance, or in settings with high antibiotic resistance rates (Lin et al., 2018).

Sebum-regulating and antioxidant effects of herbal agents

Sebum overproduction is a key contributor to the pathogenesis of Acne Vulgaris (AV), promoting the

proliferation of *C. acnes* and contributing to follicular occlusion. In parallel, oxidative stress plays a central role in sustaining inflammation, damaging skin cells, and aggravating post-acne sequelae.[10] Several herbal agents investigated in the included studies demonstrated seboregulating and antioxidant properties, either by directly reducing sebum output, modulating hormonal pathways, or scavenging free radicals, contributing to comprehensive acne control (Palmer & Kitchin, 2010).

1. Green Tea (*Camellia sinensis*)

One of the most studied botanicals with both sebum-suppressive and antioxidant effects is green tea, particularly due to its high content of EGCG. As seboregulation, EGCG inhibits 5α-reductase, reducing Dihydrotestosterone (DHT) activity and thereby decreasing sebocyte proliferation and sebum production. As antioxidant activity: EGCG is a potent scavenger of reactive oxygen species (ROS), reducing lipid peroxidation and oxidative stress in the pilosebaceous unit. Studies by Lu et al.[45] and Lin et al.[45] showed significant reductions in sebum levels and acne lesions following topical or oral administration of green tea extract, with additional benefits in skin hydration and barrier repair (Chularojanamontri et al., 2014).

2. Panax Ginseng

In the study by Hou et al.[56], red ginseng extract demonstrated both sebosuppressive and antioxidant activity. Ginsenosides are believed to reduce lipogenesis in sebocytes and enhance intracellular antioxidant enzyme expression. Patients showed improvement in acne severity, lesion counts, and reduction in facial sebum over 4 weeks, without any reported side effects (Mukhtar & Ahmad, 2000).

3. *Aloe vera*

Aloe vera, commonly used in combination therapies (e.g., Mazzarello et al.[40], Iraji et al.[47]), has sebum-modulating effects through polysaccharides and sterols that normalize skin hydration and reduce oiliness. As antioxidant effects via compounds like vitamin C, E, and zinc, which help reduce ROS-mediated damage. Its soothing and hydrating properties also enhance patient comfort, particularly in combination with other actives that may cause dryness (Mazzarello et al., 2018).

4. *Silybum marianum* (Milk Thistle)

In the 12-month cohort study by Saurat et al.[57], *Silybum marianum* fruit extract (rich in silymarin) contributed to long-term homeostasis in acne-prone skin, by modulating sebaceous gland activity and reducing oxidative stress. Patients reported reduced lesion counts and improved skin texture over time (Yoon et al., 2013).

5. *Nigella sativa* and *Calendula officinalis*

Nigella sativa contains thymoquinone, an established antioxidant that protects against oxidative damage and lipid peroxidation. *Calendula officinalis* (used in the study by Deuschle et al[58].) offers free radical scavenging and skin barrier support, particularly relevant in "maskne" or acne caused by mechanical irritation (Wahyuni et al., 2023).

6. Other Multi-Herbal Combinations

Many formulations included in the reviewed studies combined multiple herbs with synergistic seboregulatory and antioxidant actions. Examples include propolis–tea tree–*Aloe vera* (Mazzarello et al.[40]): combining antimicrobial, antioxidant, and sebum-modulating effects, others: Lavender, mangosteen, onion, paper mulberry (Lubtikulthum et al[41].): botanical synergy with antioxidant-rich profiles (Lubtikulthum et al., 2019).

Herbal agents that exhibit sebum-regulating and antioxidant properties contribute to acne management by normalizing sebum output through hormonal and cellular mechanisms (Chularojanamontri et al., 2014), protecting against oxidative stress, which exacerbates inflammation and follicular damage (Dreno et al., 2015), enhancing skin healing, texture, and post-acne recovery (Yoshida et al., 2004). These mechanisms complement antimicrobial and anti-inflammatory pathways, offering a multi-targeted therapeutic approach. The favorable safety profile and broad skin health benefits make such herbs attractive, especially for patients seeking natural, well-tolerated treatments (Melough MM et al., 2018).

3. Comparative analysis between studies

3.a. Herbal vs. control (placebo, benzoyl peroxide, clindamycin)

Several randomized controlled trials included in this review directly compared topical herbal formulations with standard acne treatments such as clindamycin 1%, benzoyl peroxide (BPO) 2.5%, or inert placebo. Notably, herbal agents demonstrated clinical efficacy that was often comparable to conventional treatments, especially in mild to moderate acne cases. For instance, the study by Lueangarun et al.[39] reported that mangosteen extract in a nanoparticle gel was as effective as 1% clindamycin in reducing inflammatory lesions, with fewer adverse effects. Similarly, Lubtikulthum et al.[41] found that a combination of onion, lavender, mangosteen, aloe vera, and paper mulberry produced results equivalent to 2.5% benzoyl peroxide, but with less irritation and better tolerability. Trials comparing herbal products to placebo also showed a consistent trend in favor of the active treatment groups, with significant reductions in lesion counts and acne severity indices. For example, rhodomyrtone,[49] green tea,[45] and Nigella sativa[48] each outperformed their respective placebo controls, demonstrating both antimicrobial and anti-inflammatory benefits. These findings suggest that certain herbal formulations could serve as viable alternatives to antibiotics or BPO, particularly in patients with sensitive skin or those concerned about long-term antibiotic resistance (Chularojanamontri et al., 2014; Melough MM et al., 2018).

3.b. Combination Herbal Therapies vs. Single-Herb Formulations

An interesting distinction emerged between studies that utilized multi-herb formulations and those that relied on single-herb interventions. Combination therapies appeared to provide broader therapeutic coverage, leveraging the synergistic action of various botanical constituents. For example, the formulation studied by Barak-Shinar and Draelos[60] included a blend of *Rheum palmatum, Portulaca oleracea, Chrysanthemum indicum*, and others, and showed improvements in erythema and induration.[60] In contrast, single-agent studies, such as those involving tea tree oil[44] or Nigella sativa[48], still demonstrated significant clinical benefits but were often limited to specific mechanisms such as antimicrobial or anti-inflammatory action. Multi-herbal formulations may offer enhanced efficacy by simultaneously targeting multiple acne pathomechanisms—such as inflammation, microbial overgrowth, and oxidative stress—though this also introduces complexity in standardization, dosing, and identifying the active components responsible for clinical outcomes (Chularojanamontri et al., 2014; Melough MM et al., 2018)

3.c. Treatment duration, clinical response, and side effects

The duration of treatment across studies ranged from as short as 10 days to as long as 12 months. In general, trials lasting between 4 and 12 weeks reported the most substantial clinical improvements, especially in inflammatory lesion reduction. Shorter studies, such as those lasting under 4 weeks, often showed partial improvement or focused on early changes in skin parameters like sebum level and erythema. Notably, sustained treatment over 8 to 12 weeks with herbal products like green tea,[45] rhodomyrtone,[49] or mangosteen extract[39] often yielded results comparable to conventional therapies. In terms of side effects, herbal treatments were overwhelmingly well tolerated. The most commonly reported adverse effects were mild, including transient erythema, dryness, or a slight burning sensation, with no serious events documented. This contrasts with conventional agents like benzoyl peroxide and topical antibiotics, which are frequently associated with dryness, peeling, and irritation. The favorable safety profile of herbal therapies makes them particularly appealing for patients requiring long-term maintenance treatment or those with reactive or compromised skin (Chularojanamontri et al., 2014; Lueangarun et al., 2019b; Tsai et al., 2005).

4. Quality of evidence and clinical implications

The overall quality of evidence derived from the 26 included studies suggests that while many herbal therapies demonstrate clinical promise, substantial variability remains in study design, intervention standardization, and outcome measures. Nevertheless, a number of well-conducted Randomized Controlled Trials (RCTs) support the use of specific botanical agents in the management of mild to moderate acne vulgaris (Lin et al., 2018; Lueangarun et al., 2019b). Studies employing rigorous methodologies—such as triple-blind randomization, placebo control, and objective outcome assessment—

strengthen the credibility of the findings, although the absence of consistent blinding and small sample sizes in several trials limits generalizability (Lin et al., 2018; Sharma S & Wagh S, 2011).

One of the most consistent advantages of herbal interventions across studies is their favorable tolerability profile. Compared to conventional agents like benzoyl peroxide or topical antibiotics, which frequently cause dryness, burning, or peeling (Sharma S & Wagh S, 2011), herbal formulations were associated with minimal and transient side effects (Draelos, 2015). Most participants tolerated the interventions well, and no study reported serious adverse events. This makes herbal therapies especially beneficial for patients with sensitive skin or those experiencing irritation from standard treatments, and also reduces the risk of treatment discontinuation due to adverse reactions (Draelos, 2015; Sharma S & Wagh S, 2011).

Clinically, the findings suggest that herbal products hold substantial potential as adjunctive therapies in mild to moderate acne, either used alongside conventional treatments or as standalone regimens in patients with contraindications to synthetic agents (Chularojanamontri et al., 2014). Their multifactorial mechanisms—ranging from anti-inflammatory and antimicrobial effects to sebum regulation and antioxidant protection—enable them to target various aspects of acne pathogenesis (Draelos ZD, 2006). For instance, combining a botanical with antibiotic therapy may enhance efficacy while potentially reducing the dose and duration of antibiotic use, thereby minimizing the risk of resistance (Dreno et al., 2015).

In terms of long-term use, the safety and tolerability of herbal products support their potential role in maintenance therapy or chronic skin care regimens (Lin et al., 2018). Given the chronic and relapsing nature of acne, treatments that are gentle, effective, and sustainable over time are especially valuable. However, extended use should ideally be supported by longer-duration studies to confirm consistent efficacy and safety beyond the typical 8 to 12-week trial window. Until such data are more widely available, clinicians should consider integrating standardized, evidence-based herbal preparations as complementary components of acne management, particularly in personalized care plans or integrative dermatology settings.

5. Limitations of the review and included studies

While the findings of this systematic review suggest a favorable role for topical herbal agents in the treatment of mild to moderate acne vulgaris, several limitations must be acknowledged when interpreting the results (Draelos ZD, 2006). A key limitation lies in the heterogeneity of formulations, with studies using diverse herbal combinations, concentrations, vehicles (gels, creams, serums, hydrogels), and delivery systems (e.g., photodynamic therapy or nanoparticles) (Lubtikulthum et al., 2019). This variation hinders direct comparison and precludes meta-analysis, as each formulation represents a unique therapeutic profile (Lubtikulthum et al., 2019; Tirado-Yañez A et al., 2020).

Another limitation is the wide variation in sample sizes, ranging from as few as 10 to over 100 participants, with many studies fallings below the threshold typically considered adequate for statistical power. Small-scale studies may inflate effect sizes or fail to detect adverse events that only appear with broader usage. Furthermore, the duration of interventions was relatively short in most trials, typically between 4 to 12 weeks, leaving uncertainty about the long-term efficacy and safety of these treatments (Chularojanamontri et al., 2014; Draelos, 2015; Melough MM et al., 2018).

The methods of clinical evaluation were also inconsistent across studies. While some utilized standardized tools like lesion counts, IGA, DLQI, or CADI, others relied solely on subjective assessments or omitted control groups altogether. Additionally, adverse event reporting was inconsistent; several trials failed to detail side effects explicitly or did not include structured safety monitoring, which may lead to underreporting of tolerability issues.

Finally, this review highlights a current gap in translational evidence for certain promising herbal agents. For example, piperine, the major active compound of *Piper nigrum* (black pepper), has shown strong antimicrobial and anti-inflammatory effects in in vitro studies against *C. acnes*. However, no clinical trials to date have evaluated its efficacy in vivo. Given its low molecular weight, lipophilicity, and pharmacological activity, piperine represents a

compelling candidate for future acne therapies, pending validation through controlled in vivo and human studies (Saric et al., 2016; Tsai et al., 2005).

5. Conclusion

This systematic review supports the clinical potential of several topical herbal agents—such as *Curcuma longa, Aloe vera, Garcinia mangostana, Melaleuca alternifolia, Camellia sinensis, Nigella sativa,* and *Rhodomyrtus tomentosa*—for managing mild to moderate acne vulgaris, demonstrating anti-inflammatory, antibacterial, antioxidant, and sebum-regulating effects with favorable tolerability and, in some cases, efficacy comparable to benzoyl peroxide or topical antibiotics. However, the overall evidence quality is limited by variability in formulations, study design, and follow-up duration. Standardized preparations, robust methodologies, and longer-term trials are needed to confirm sustained safety and efficacy. Notably, emerging botanicals such as piperine (*Piper nigrum*) show promising in vitro activity against *C.acnes* and warrant further in vivo and clinical evaluation to inform integration into personalized, sustainable acne treatment strategies.

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