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Phytotherapy for Acne Vulgaris: A Review

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ABSTRACT

Introduction and Purpose: Acne vulgaris, a chronic inflammatory skin condition, primarily affects adolescents and young adults, causing non-inflammatory and inflammatory lesions. Conventional treatments, including topical retinoids and systemic antibiotics, are effective but may lead to adverse effects, antimicrobial resistance, and high costs. These challenges have spurred interest in plant-derived compounds as potential safer alternatives. This review explores the efficacy and safety of these natural treatments.

State of Knowledge: Research highlights the promise of plant-derived compounds such as polyphenols, essential oils, and herbal extracts in addressing acne pathogenesis.

Epigallocatechin gallate from green tea inhibits sebum production, reduces inflammation, and shows antibacterial activity. Quercetin and essential oils like tea tree and lavender oils effectively reduce lesion counts and inflammation with minimal side effects. Extracts like *Berberis vulgaris*, mangosteen, and red ginseng show significant anti-acne effects. Despite these benefits, studies often feature small sample sizes and limited durations, necessitating further research.

Summary: Plant-based treatments for acne vulgaris present effective, safer alternatives to conventional therapies, particularly for mild to moderate cases. These compounds reduce key factors like inflammation and bacterial colonization while improving patient adherence. However, larger, long-term trials are essential to confirm efficacy, optimize formulations, and establish their role in acne management.

Keywords: acne vulgaris; phytotherapy; polyphenols; essential oils; plant extracts

INTRODUCTION

Acne vulgaris is a common chronic inflammatory skin disorder that primarily affects adolescents and young adults. It is characterized by the formation of various types of lesions, such as comedones, papules, pustules, nodules, and cysts, most often on the face, neck, chest, and back. Acne vulgaris can significantly impact an individual's quality of life, with clinical presentations ranging from mild to severe. Non-inflammatory lesions include open and closed comedones, while inflammatory lesions may progress to papules, pustules, nodules, and cysts, which can lead to scarring and psychological distress if left untreated (Żmuda et al., 2024).

The pathogenesis of acne vulgaris involves several interrelated factors. Increased sebum production, stimulated by androgens such as dihydrotestosterone (DHT), promotes sebaceous gland activity. This, combined with abnormal keratinocyte proliferation and differentiation, leads to hyperkeratinization of the follicular duct. This process results in the formation of keratin plugs, obstructing hair follicles and contributing to acne development. Every acne lesion begins as a microcomedone, formed by the accumulation of sebum and cellular debris (Cong et. al., 2019). As this microcomedone evolves into a visible lesion, Propionibacterium acnes (*P. acnes*) colonization triggers inflammation by activating immune cells, keratinocytes, and sebocytes, which release pro-inflammatory cytokines such as IL-1β, IL-6, IL-8, and TNF-α. P. acnes-induced dermatitis also stimulates the release of cytokines and chemokines via toll-like receptors (TLR2 and TLR4), which are central to the innate immune response. The activation of pathways like NF-κB and MAPK, particularly ERKs, JNKs, and p38, contributes to immune cell activation and the synthesis of inflammatory mediators. Elevated levels of matrix metalloproteinases (MMPs) such as MMP-1, MMP-3, and MMP-9 are also associated with acne lesions, exacerbating the inflammatory response (Hazarika et al., 2021). The combined effect of increased sebum production, follicular hyperkeratinization, and bacterial colonization ultimately triggers the inflammatory cascade, leading to the development of more severe acne lesions.

Treatment of acne vulgaris is typically guided by the severity and type of acne. Topical treatments such as retinoids, benzoyl peroxide, and azelaic acid are commonly used for mild to moderate comedogenic acne. In cases of mild to moderate papulopustular acne, combination therapies using benzoyl peroxide with either adapalene or clindamycin are often recommended. For more severe cases, systemic antibiotics are combined with topical retinoids, such as adapalene, and in cases of severe acne, oral isotretinoin is considered the treatment of choice (Ak et al., 2019). Anti-androgenic hormonal therapy may also be considered for female patients. Despite the effectiveness of these treatments, concerns about adverse effects, treatment resistance, and high costs have spurred interest in alternative therapies, especially those derived from natural sources.

For instance, isotretinoin, although highly effective, can cause significant side effects such as skin dryness, sun sensitivity, liver damage, and birth defects, making it unsuitable for pregnant women.

In light of these concerns, there has been growing interest in exploring the therapeutic potential of medicinal plants for treating acne vulgaris (Eichenfield et al., 2021). This surge in interest is driven by the need to address challenges such as antimicrobial resistance, minimize adverse effects, improve patient adherence, and overcome treatment resistance. This review aims to synthesize the available clinical evidence on the efficacy of herbal medicines in the treatment of acne vulgaris, evaluating their potential as safe and effective alternatives to conventional therapies.

METHODS

For this review, a comprehensive search was conducted across academic databases such as PubMed and Google Scholar to identify original research articles on herbal treatments for acne vulgaris. The search strategy incorporated the MeSH term "acne vulgaris" in combination with related terms such as "phytotherapy," "plants, medicinal," "plant extracts," and "herbal medicine." Only original studies, including clinical trials, were considered for inclusion, while in vitro investigations, review articles, meta-analyses, and case reports were excluded.

Studies were selected based on their methodological rigor, and the relevance of their outcomes to acne treatment, specifically focusing on lesion counts, acne severity, and treatment efficacy. Emphasis was placed on studies that evaluated the safety and therapeutic potential of herbal interventions, detailing the plant species, preparation methods, active constituents, and any reported adverse effects. The final selection of studies offers a comprehensive overview of the efficacy and safety of herbal treatments for acne vulgaris, contributing valuable insights into their clinical applicability.

RESULTS

1. **Polyphenols**

Polyphenols are naturally occurring compounds abundant in plant-based foods and beverages. These compounds are absorbed across the intestinal epithelium and enter systemic circulation, offering significant antioxidant benefits by neutralizing reactive oxygen species (ROS). Additionally, polyphenols exert anti-inflammatory effects and have been shown to protect the skin from UV radiation-induced damage (Rana et al., 2022). These properties make polyphenols potential candidates for treating various dermatological conditions, including acne.

1.1. Epigallocatechin Gallate (EGCG)

Green tea, one of the world's most consumed beverages, is rich in polyphenols, especially catechins. Among these, epigallocatechin-3-gallate (EGCG) is the most abundant and has been associated with various health benefits, including apoptotic, sebum-suppressing, and anti-inflammatory effects on human sebocytes, as well as antibacterial activity against *P. acnes*. Research on EGCG has demonstrated its ability to reduce sebum production by modulating the AMPK–SREBP-1 signaling pathway.

Additionally, EGCG decreases inflammation by suppressing the NF-κB and AP-1 pathways. It induces apoptosis in sebocytes, leading to cytotoxicity, and reduces *P. acnes* viability, addressing key pathogenic features of acne (Yoon et al., 2013).

A randomized, single-blind controlled trial conducted by Sharquie et al. examined the efficacy of a 2% tea lotion in reducing acne lesions compared to a placebo. This study involved 60 adolescents aged 14-22, who applied the lotion twice daily for two months. The results demonstrated a significant reduction in both papules and pustules in the treatment group, with 88% of participants expressing satisfaction with the treatment. In contrast, the placebo group showed no significant improvement. The study confirmed the efficacy of green tea in treating acne without any adverse events (Sharquie et al., 2006). Further supporting these findings, a 2008 study by Sharquie et al. compared the effects of a 2% tea lotion with a 5% zinc sulfate solution for acne treatment. In this trial, 47 participants applied their assigned treatments twice daily for two months. The tea lotion group showed a significant reduction in inflammatory lesions, with 85% of participants reporting a good or moderate response. On the other hand, the zinc sulfate group demonstrated no significant improvement, reinforcing the potential of green tea as an effective acne treatment (Sharquie et al., 2008).

Yoon et al. in 2013 conducted a randomized, split-face trial to compare 1% and 5% EGCG formulations with a control. Both concentrations significantly reduced both non-inflammatory and inflammatory lesions compared to baseline, with minimal side effects.

Specifically, the 1% EGCG group showed a 79% reduction in non-inflammatory lesions and an 89% reduction in inflammatory lesions after eight weeks, highlighting the efficacy of EGCG in acne management (Yoon et al., 2013).

A randomized, double-blind, placebo-controlled trial by Lu et al. in 2016 investigated the effects of systemic green tea supplementation on acne in post-adolescent women. Over four weeks, participants who took 1500 mg of decaffeinated green tea daily showed a significant reduction in inflammatory lesions on the nose, chin, and perioral area compared to the placebo group. While both groups experienced reductions in lesions, the green tea group demonstrated greater improvements, suggesting a possible benefit of systemic supplementation for acne treatment. However, further research with larger sample sizes and longer durations is needed to confirm these findings (Lu et al., 2016).

1.2. Quercetin

Quercetin, a flavonoid polyphenol found in various fruits, vegetables, and leaves, is renowned for its antioxidant properties. In a study by Amer et al., quercetin was encapsulated in vitamin C-based nanovesicles, known as aspasomes, to improve its delivery and efficacy in treating acne vulgaris. Twenty participants (14 females and 6 males) applied the quercetin-loaded formulation once daily for 12 weeks. The results indicated a substantial reduction in inflammatory lesions (77.9%), comedones (11.8%), and overall acne lesions (55.3%). Additionally, an in vitro analysis revealed enhanced antioxidant, anti-inflammatory, and antibacterial effects against *P. acnes* compared to quercetin alone (Amer et al., 2020).

2. Tea Tree Oil and Lavender Oil in Acne Treatment

Tea tree oil (TTO), derived from *Melaleuca alternifolia*, is widely recognized for its antibacterial, anti-inflammatory, and antioxidant properties, making it a popular treatment for acne vulgaris. Numerous clinical studies confirm its effectiveness in reducing inflammatory lesions with minimal adverse effects, supporting its use in topical acne treatments (Nascimento et al., 2023).

Lavender oil, with its diverse compounds such as mono- and sesquiterpenes and phenolic acids, also offers significant antibacterial and anti-inflammatory effects. In a pretest-posttest experimental study, a combination of TTO (3%) and lavender oil (2%) resulted in a marked reduction in inflammatory lesions ($p < 0.001$) and *P. acnes* colonization ($p = 0.005$). Additionally, this combined treatment led to a decrease in sebum production ($p = 0.004$), with the combined oil group showing more significant improvements than the control group. The treatment was well-tolerated, with only one participant reporting mild itching, which resolved without further complications (Kim et al., 2013).

A multicenter, open-label, phase III randomized clinical trial (RCT) compared the efficacy of a 5% TTO topical gel with oral tablets containing neem, turmeric, and piper extract, as well as a combination of the gel and tablets, over a 4-week period in patients with mild to moderate acne. The TTO gel (Group II, $n = 46$) demonstrated a 78.3% reduction in non-inflammatory lesions, consistent with the other treatment groups. However, it showed less improvement in inflammatory lesions such as papules and nodules compared to the other groups. Notably, for deeper inflammatory lesions, such as pustules and cysts, the TTO gel produced significantly greater results-17% more effective than the oral tablet group and over 20% better than the combination treatment. Despite these promising results, the study suggested that further investigation is needed to optimize TTO's role in acne treatment (Yadav et al., 2011).

In another open-label, uncontrolled phase II pilot study, TTO-based facial cleansing and moisturizing products were tested in patients with mild to moderate acne vulgaris over 12 weeks. The two formulations - Face Wash (7 mg/g) and Gel (200 mg/g) - led to a 54% reduction in total acne lesions ($p < 0.001$) and a decrease in the investigator's global acne severity score ($p < 0.05$). Despite twice-daily application, only mild side effects, such as dryness and peeling, were reported (Malhi et al., 2017).

A double-blind, split-face RCT assessed 5% TTO versus Lactobacillus-fermented *Chamaecyparis obtusa* (LFCO) in treating mild to moderate acne over 8 weeks. LFCO demonstrated superior efficacy, with a 65.3% reduction in inflammatory lesions compared to 38.2% for TTO. LFCO also showed greater improvements in non-inflammatory lesions (52.6%, $p < 0.05$) and reductions in sebaceous gland size and sebum production. Additionally, LFCO led to earlier decreases in inflammatory markers and greater patient satisfaction, suggesting its faster and more effective action (Kwon et al., 2014).

The combination of adapalene, a retinoid with anti-inflammatory and antiseborrheic effects, and TTO was evaluated in a triple-blind RCT. The TTO + adapalene group exhibited a 71.69% success rate in reducing both inflammatory and non-inflammatory lesions, significantly outperforming adapalene alone (6.38%). This combination addresses the four major acne pathogenesis factors - hyperseborrhea, hyperkeratinization, inflammation, and bacterial colonization - providing a comprehensive treatment approach (Najafi-Taher et al., 2022).

Lastly, a randomized controlled trial testing a topical herbal extract gel containing TTO was compared to 2.5% benzoyl peroxide (BP) cream for mild to moderate acne. Both treatments showed statistically significant reductions in acne lesions, with better patient adherence and satisfaction in the herbal extract gel group (Lubtikulthum et al., 2019).

3. Ocimum gratissimum

There is just one clinical study with humans. Eighty-four individuals with clinically significant Acne vulgaris were randomly assigned to one of seven groups and treated with different test preparations. These included a 2% Ocimum oil lotion containing varying concentrations of aloe gel (ranging from 0 to approximately 100%), as well as placebo or control preparations. The treatments were applied to the face after washing, twice daily, for a period of 4 weeks. Inflammatory lesions were counted before treatment and daily during the study. The efficacy of the preparations was assessed based on product activity (1/D), which represents the reciprocal of the number of days needed to achieve a 50% reduction in lesion count. Results showed that the effectiveness of the Ocimum oil lotion improved as the concentration of aloe gel increased. The products containing either undiluted aloe gel or a 50% aloe gel concentration were the most effective, resolving inflammatory lesions more rapidly than the standard formulation. Aloe gel alone demonstrated minimal activity. The adverse effects observed were mild and well-tolerated by the participants (Orafidiya et al., 2004).

4. Seaweed - derived oligosaccharide complex

An 8-week double-blind, vehicle-controlled study was carried out with 60 age-matched participants diagnosed with mild acne. The participants were split into two groups: 30 individuals received the vehicle control, while the other 30 were treated with the active treatment, which contained a seaweed-derived oligosaccharide complex and 0.1% zinc pyrrolidone. After 8 weeks, both groups experienced a reduction in comedones, papules, and pustules. However, the active treatment group showed a significantly greater reduction in these lesions at 2, 4, and 8 weeks compared to the control group (Capitanio et al., 2012).

5. *Berberis vulgaris L.*

Berberis vulgaris L. (barberry) is widely acknowledged in traditional medicine for its anti-inflammatory and antibacterial properties (Birdsall et al., 1997). Additionally, its antilipogenic effect on sebaceous glands in animal models suggests its potential in acne treatment. In a randomized trial, adolescents aged 12–17 with moderate to severe acne were administered 600 mg of aqueous dried barberry extract daily for 4 weeks. This group exhibited significant reductions in acne lesion counts (non-inflamed, inflamed, and total lesions) and Michaelson's acne severity score, with no significant side effects observed ($p < 0.001$) (Fouladi et al., 2012). Similarly, a separate study evaluated the effectiveness of a topical formulation combining *Berberis integerrima* root extract with spearmint essential oil for treating mild to moderate acne vulgaris. The treatment, applied twice daily for 4 weeks, led to significant reductions in lesion counts (from 27.33 ± 26.17 to 21.58 ± 21.10) and Modified Global Acne Grading Scale (mGAGS) scores (from 18.76 ± 8.61 to 13.87 ± 8.14), comparable to clindamycin 1% solution ($p = 0.906$ and $p = 0.882$ for lesion counts and mGAGS scores, respectively).

These results suggest that this herbal combination offers an effective, antibiotic-free alternative for acne treatment (Saeidi et al., 2024).

6. Ginseng

This study aimed to identify the active ingredients responsible for the antimicrobial effects of red ginseng (*Panax ginseng* C.A. Meyer), compare its activity to that of existing antibacterial agents, and assess its potential as a natural therapeutic product. The hydrophobic fraction of the red ginseng ethanol extract (RGEF) demonstrated antimicrobial activity against *P. acnes* that was comparable to or more potent than benzoyl peroxide or azelaic acid. Nuclear magnetic resonance spectroscopy revealed that panaxynol and panaxydol were the active antimicrobial components. In a small clinical trial, 20 participants with early to moderate acne were treated with a cream containing 3 mg/g of RGEF for 4 weeks. The results showed significant improvements in acne symptoms, including reduced oxidized sebum content and skin redness. However, the small sample size warrants further investigation to confirm these findings. The study design and lack of a placebo or control group limit the generalizability of the results (Hou et al., 2019).

7. Hippophae rhamnoides and Cassia fistula

This study aimed to evaluate the effectiveness of emulsion formulations containing plant extracts from Hippophae rhamnoides and Cassia fistula in treating acne, compared to a placebo. Using a single-blind, randomized, placebo-controlled, split-face design, 50 participants (ages 18-37) with grade I and II acne vulgaris applied the active formulations to one side of their face and the placebo to the other, twice daily for 12 weeks. The antibacterial properties of the extracts were tested in vitro, and sebum production was assessed using a sebumeter® and clinical evaluations. Significant reductions in sebum production were observed in both plant extract groups, with improvements in clinical outcomes and sebumetry, as opposed to the placebo group. These results suggest that emulsion formulations containing 5% plant extracts are effective, safe, and well-tolerated for treating mild to moderate acne vulgaris (Khan et al., 2014).

8. Rose Extract and 0.05% Hexamidine Diisethionate

This study assessed the efficacy and safety of APDDR-0901 (containing 0.03% retinol, 0.7% rose extract, and 0.05% hexamidine diisethionate) compared to 0.1% adapalene gel for treating mild-to-moderate acne. In this 12-week, multicenter, double-blind trial, 97 participants were evaluated based on lesion count, acne severity, global improvement, and patient self-assessment, with safety monitored for cutaneous irritation. Both treatments showed significant improvements, with no major differences observed between the two. However, APDDR-0901 exhibited a better safety profile, particularly during the first two weeks of treatment (Lee et al., 2011).

9. Mangosteen

In this double-blind, split-face, randomized controlled study involving 28 participants (mean age 25.14 ± 5.8 years) with a Global Acne Grading System (GAGS) score of 15.43 ± 5.96, the efficacy of a 0.5% mangosteen extract nanoparticle-loaded gel was compared to 1% clindamycin gel for treating mild-to-moderate acne vulgaris.

Both treatments were applied twice daily for 12 weeks, with participants using 2.5% benzoyl peroxide cream on both sides of their faces for 5 minutes once daily. After 12 weeks, the mangosteen extract significantly reduced comedones by 66.86% and inflammatory lesions by 67.05% ($P < 0.001$), with results similar to clindamycin. Improvements were evident as early as two weeks post-treatment, with no significant difference in lesion count reduction between the two treatments. However, the mangosteen extract demonstrated superior clinical improvement in acne severity, a better safety profile, and no severe side effects. These findings suggest that mangosteen extract could be a promising, well-tolerated alternative to conventional acne treatments (Lueangarun et al., 2019).

10. CBD

Ali et al. conducted a 12-week, single-blind comparative study with 11 participants, applying a 3% cannabis seed extract cream to one side of the face and a control cream to the other. Although results showed a reduction in sebum and erythema, suggesting the potential of cannabis seed extract cream for treating acne and seborrhea, the small sample size (n=11) limits the generalizability of the findings. Furthermore, the absence of statistical significance or detailed numerical data weakens the overall validity of the conclusions. No adverse reactions were observed, but a larger, double-blind study would provide more robust evidence (Ali et al., 2015).

Cohen et al. examined the synergistic effects of CBD combined with Centella asiatica and Silybum marianum extracts for acne treatment in a 30-participant clinical trial. The formulation demonstrated superior anti-inflammatory effects and inhibition of P. acnes growth compared to individual treatments. While the study's findings were promising, further research with larger sample sizes and detailed mechanisms of action would provide more definitive conclusions about its clinical potential (Cohen et al., 2023).

DISCUSSION

Plants and their extracts have been valued in traditional medicine for centuries due to their bioactive properties, which are now gaining attention in the context of acne vulgaris treatment. Numerous plant-derived compounds, such as polyphenols (e.g., EGCG and quercetin) and essential oils (e.g., tea tree oil and lavender oil), have demonstrated significant potential in managing acne by addressing inflammation, sebum production, and bacterial growth. Among these, green tea and its active component, EGCG, consistently show efficacy in reducing both non-inflammatory and inflammatory lesions, making them promising candidates for natural therapies (Kwon et al., 2013). Acne vulgaris is a multifactorial condition involving the interplay of excessive sebum production, follicular obstruction, and secondary bacterial infections. While bacterial overgrowth is a contributing factor, it is not the primary cause, which underscores the complexity of therapeutic approaches (Williams et al., 2012).

Current pharmacological treatments, such as oral isotretinoin and antibiotics, are associated with limitations, including adverse effects and the risk of resistance. As a result, the search for safer and more sustainable alternatives, including plant-based therapies, has gained momentum. Extracts such as TTO are widely recognized for their topical application in managing acne lesions.

Mechanistically, these compounds target acne pathogenesis through diverse pathways. Polyphenols are known for their antioxidative and anti-inflammatory effects. They act by scavenging ROS, activating antioxidant enzymes, and reducing oxidative stress (Kim et al., 2016). Furthermore, they influence key inflammatory pathways, such as NF-κB, MAPK, and PI3K/Akt, while also suppressing pro-inflammatory mediators like TNF-α, IL-1β, and IL-6. This dual action of combating oxidative stress and inflammation underscores their multifaceted role in acne management. Essential oils, on the other hand, exert their effects primarily through their bactericidal and anti-biofilm properties. Compounds such as terpenes penetrate bacterial membranes, disrupting their structural integrity and causing cytoplasmic leakage (Carson et al., 2006).

The therapeutic potential of these compounds is complemented by their ability to mitigate antibiotic resistance. TTO has shown synergistic effects with antibiotics, enhancing their antimicrobial action and potentially reducing the required dosages (Dreno et al., 2018). This is particularly valuable given the rising concern over antibiotic resistance in acne treatment. However, challenges such as variability in compound composition and issues with bioavailability persist. Factors like plant source, extraction methods, and storage conditions can affect the consistency and potency of these treatments. One study suggested that the TTO nanoemulsion containing adapalene is more effective than nonnanoemulsion (Najafi-Taher et al., 2022).

CONCLUSION

The reviewed studies underscore the therapeutic promise of plant-based treatments for acne vulgaris, particularly their ability to target inflammation, oxidative stress, and bacterial growth through varied mechanisms. Despite these benefits, challenges such as the lack of standardization, poor bioavailability, and limited long-term data remain. Addressing these gaps through well-designed studies, larger sample sizes, diverse populations, and extended follow-ups will be crucial. Furthermore, advancements in delivery systems and the exploration of combination therapies could significantly enhance the therapeutic profile of these natural compounds. Ultimately, plant-based treatments hold considerable potential as complementary or alternative options to conventional acne therapies, offering a holistic approach to managing this multifaceted skin condition.

Abbreviations:
DHT - dihydrotestosterone
P. acnes - Propionibacterium acnes
IL-1β, IL-6, IL-8 - Interleukin-1 beta, Interleukin-6, Interleukin-8
TNF-α - Tumor Necrosis Factor-alpha
TLR2, TLR4 - Toll-Like Receptors 2 and 4
NF-κB - Nuclear Factor kappa-light-chain-enhancer of activated B cells
MAPK - Mitogen-Activated Protein Kinases
ERKs - Extracellular Signal-Regulated Kinases
JNKs - c-Jun N-terminal Kinases
MMPs - Matrix Metalloproteinases (e.g., MMP-1, MMP-3, MMP-9)
EGCG - Epigallocatechin Gallate
AMPK–SREBP-1 - AMP-activated protein kinase – Sterol Regulatory Element-Binding Protein 1
ROS - Reactive Oxygen Species
TTO - Tea Tree Oil
RCT - Randomized Controlled Trial
LFCO - Lactobacillus-Fermented Chamaecyparis obtusa BP
- Benzoyl Peroxide
mGAGS - Modified Global Acne Grading Scale
RGEF - Red Ginseng Ethanol Extract
CBD - Cannabidiol

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