Exploring Herbal Approaches to Acne Vulgaris: A Review and Clinical Evaluation

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ABSTRACT:

Acne vulgaris is a widespread skin condition affecting nearly everyone at some point. The term "acne" comes from the Greek word "akme," meaning "point" or "spot." Globally, about 650 million people suffer from acne, with women (9.8%) slightly more affected than men (9.0%). In the U.S., 40–50 million people (16% of the population) are affected, while 3–5 million suffer in Australia. Acne is most common among teenagers and young adults, with 90% of individuals aged 11–30 experiencing it, primarily due to hormonal changes during puberty. Adult acne affects 25% of men and 50% of women, with 35% of women in their 30s, 26% in their 40s, and 15% over 50 still experiencing breakouts. Due to concerns over synthetic treatments, natural remedies are gaining popularity. This study aims to formulate a herbal anti-acne face gel using neem, liquorice root, orange peel, and palash flower extracts to offer an effective and safer alternative.

KEYWORDS: Acne vulgaris, akme, Herbal Medication

INTRODUCTION:

Acne (also known as acne vulgaris) is a persistent, chronic skin inflammatory condition of the pilosebaceous follicles that affects people worldwide. It is estimated to affect 9.4 % of the world's population, ranking it eighth among skin diseases. More than 85% of children suffer from acne, which can last until adulthood. It is more common in women and is the reason for two-thirds of dermatologist visits. The distinct lesions can be classified as either inflammatory (papules, pustules, nodules, and cysts) or noninflammatory (open/black and closed/white comedones), which results in skin pigmentation and scarring and calls for ongoing, consistent treatment. [1]. Typically, lesions are observed on the face, neck, upper

back, and chest Acne can take many different forms, including neonatal and infantile acne, acne at work, acne conglobate, acne fulminans, acne mechanica, excoriated acne, chloracne, drug-induced acne (from anabolic steroids, corticosteroids, isoniazid, lithium, and phenytoin, for example).

Clinically and histologically, these variations are similar to acne vulgaris; nevertheless, they can be distinguished by their severity and clinical context, as well as by the symptoms that accompany them [2]. Although acne cannot be prevented or cured, it can be effectively treated.



Fig. 1: Acne rosacea

Cystic acne

Nodular acne

Factors Contributing to Acne vulgaris:

In the classical etiology of acne vulgaris, the following factors are believed to be significant. Acne may be caused, aggravated, or made worse by genetics, environmental factors (such as temperature, pollution, humidity, sun exposure, mineral oils/halogenated hydrocarbons), nutrition, hormonal state, stress, smoking, comedogenic medications like androgens [12], halogens, corticosteroids, bacteria, and cosmetics. Common symptoms of acne vulgaris (AV) include discomfort, mental anguish, deformity, and potentially irreversible scarring. Furthermore, patients may experience feelings of humiliation and worry, both of which exacerbate mental depression.



Fig. 2: Overview of factor contributing to acne vulgaris

Causative factors and pathogenesis of acne vulgaris:

Several causative elements are thought to be important in the conventional etiology of acne vulgaris. As was previously said, higher rates of sebum excretion, endocrinological [4] variables such as androgens, abnormal keratinization of the follicular infundibulum, bacterial infection growth, and the resulting inflammation are the causes of chronic acne skin illnesses.

- **Increased Sebum Production:** One of the main factors contributing to the development of acne is an increase in sebum production in the hair follicles. Gollnick Anonymous claim that androgen hormones—specifically, insulin growth hormone (IGH-1) and testosterone—increase the production and release of sebum. Increased sebum production is a crucial factor that should be taken into consideration in individuals suffering from acne vulgaris because it is correlated with the severity and frequency of acne lesions.
- Anomalies related to hyperkeratinization of the pilosebaceous follicles: Single-cell keratinocytes are frequently released into the lumen by healthy follicles before being eventually removed. Irregular desquamated corneocytes, lipids, and monofilaments accumulate in the pilosebaceous follicles of acne sufferers due to hyperproliferative keratinocytes that are not expelled into the lumen.
- **Hyperproliferation of Propionibacterium acne (P. acne):** Propionibacterium is another acne-causing agent that plays a significant role in the pathophysiology of inflammatory acne. Previously known as Propionibacterium acnes, Cutibacterium acnes is a gram-positive, lipophilic, anaerobic pathogen that prefers to settle in sebaceous follicles due to the high sebum production and the favorable anaerobic environment it offers for bacterial growth. P. acnes produce a lipase enzyme that breaks down sebum triglycerides into glycerol and fatty acids, which can cause skin irritation and comedone production.
- **Inflammation acne:** Continuing from the P. acne process described above, the inflammatory process starts when the immune system comes into contact with P. acnes. P. acnes have a potent inflammatory effect that can produce chemostatic agents such as neutrophils, macrophages, and lymphocytes. Along with follicular damage and rupture, these situations also release lipids, fatty acids, and germs into the dermis layer.

Types of acne lesions:

"Different forms of acne include conglobata, rosacea, fulminans, cosmetica, excoriated (also known as picker's acne), medicamentosa, chloracne, and mechanica.". Acne vulgaris, however, is the most common type of acne, making up 99 percent of all occurrences. Non-inflammatory, open, and closed comedones, together with inflammatory papules, pustules, nodules, and cysts, are the two types of lesions that distinguish it. Comedones can be classified into two types: closed comedones, or whiteheads, and open comedones, or blackheads.



Fig. 3: types of acne lesion

- 1. Blackheads: Obstructing hair shafts with dead skin cells and excess oil causes blackheads, which are non-inflammatory acne lesions. Blackheads are referred to as open comedones because the surface of the pore remains open, allowing the contents to oxidize and appear dark—usually brown or black. They are a mild form of acne that commonly appears on areas such as the face, chest, back, neck, shoulders, and arms.
- 2. Whiteheads: Whiteheads are a type of non-inflammatory acne characterized by small, white bumps on the skin. They form when pores—specifically those connected to hair follicles—become clogged with bacteria, oil, and dead skin cells. Because the pores remain closed, these blemishes are also referred to as closed comedones. While whiteheads can develop on various parts of the body, they are most frequently found in the T-zone, which includes the nose, chin, and forehead.
- **3. Papules:** Inflammation is the body's response to factors like bacteria, excess oil, and androgen activity, and is characterized by swelling, warmth, redness, and pain. Papules represent a transitional stage between noninflammatory and inflammatory skin lesions. These are small, pink, pus-free bumps typically measuring less than 5 mm in diameter.
- 4. **Pustules:** These small pimples are a type of inflammatory lesion that forms when pores become clogged with excess oil and dead skin cells. Pustules are inflamed lesions containing pus or fluid at their center, often appearing as white bumps surrounded by red, irritated skin. They can develop anywhere on the body but are most commonly found on the face, back, chest, shoulders, neck, underarms, pubic region, and along the hairline. Nodules, a more severe form of inflammatory acne, form when a buildup of bacteria, oil, and dead skin leads to deeply clogged pores. This same buildup can also result in comedones such as whiteheads or blackheads.
- 5. Cysts: A severe form of inflammatory acne, cystic acne develops beneath the skin after oil, dry skin cells, and bacteria build up and clog pores. People of all ages who have oily skin are most impacted. Cysts usually manifest as big, painful, pus-filled lesions that are white or red and can occasionally leave scars. While cystic acne can develop anywhere on the body, the face, arms, shoulders, back, chest, and neck are the areas most commonly affected. The majority of individuals with cystic acne have both inflammatory and non-inflammatory acne symptoms.

Recent advancements and commercial products:

New avenues for research and development, such as blocking the mechanistic pathway or process that causes acne, have been made possible by recent scientific advancements in the author's understanding of the complexity of acne. Recent research has focused on controlling these pathways by targeting receptors, cytokines, chemokines, and other proinflammatory mediators. Furthermore, follicle-dwelling bacteria, the patient's genetics, the skin microbiome, and the therapeutic aspects of diet are all important in acne treatment. Using medications that produce nitric oxide (NO) is one of the innovative approaches that may prove beneficial for treating acne. A powerful vitamin A derivative used to treat acne is isotretinoin (ISO). Acne may be permanently remitted with its help. Nevertheless, teratogenicity, skin and eye responses, blood indicator abnormalities, and sporadic acne fulminans are among its reported adverse effects. It's critical to concentrate on reducing these adverse effects by modifying the dosage and taking into account combo medications. Patients' experience receiving therapy will be enhanced as a result. Even though the author's understanding of the causes of acne has grown significantly over the past 20 years, several attempts have been made to create innovative treatment plans that are especially targeted at curing acne. Some of the ongoing or latest clinical trial data is shown in Table 1 (the data obtained from the clinicaltrials.gov)

NCT Number	Interventions	Clinical Trial Phase/Stage	Outcome Measures	Sponsor/Collaborators
NCT01936324	Drug: Olumacostat Glasaretil Gel, 7.5 % Other: Olumacostat Glasaretil Gel, Vehicle	Phase 1,2	Mean absolute change in acne lesion counts (inflammatory &no inflammatory)	Eli Lilly and Company
NCT03761784	Drug: S6G5T-3 Drug: S6G5T-8	Phase 3	Change from baseline in inflammatory, no inflammatory lesion counts	Sol-Gel Technologies, Ltd

 Table 1. Recent or ongoing clinical trial investigations for the treatment of Acne vulgaris:

NCT04594759	Drug: Isotretinoin	Phase 1,2	The number of participants that showed improvement in their visible acne	Medical University of South Carolina
NCT02656485	Drug: B244 &Placebo	Phase 1,2	Safety, Efficacy	AOBiome LLC
NCT01694433	Drug: Calcipotriene	Phase 2,3	Acne severity as assessed	University of California, Los Angeles
			With the investigator's global assessment (IGA)	
NCT02566369	Drug: CD5789 (trifarotene) 50 μg/g cream Drug: Placebo cream	Phase 3	Investigator global assessment (IGA) success rate at week 12	Galderma R&D
NCT04943159	Drug: Afamelanotide	Phase 2	The change in the number of facial inflammatory acne- related lesions	Clinical Pharmaceuticals Limited

Much research has been done on acne, but only a few therapies have made it through clinical testing and are currently on the market. While most acne treatments on the market may be used topically or systemically, very few of them mix the two. Listed below are some commercial goods that are accessible globally (refer to Table 2)

Brand name	Drug class	Acne type	Route of administration	Marketed by
Benzamycin	erythromycin, benzoyl peroxide Macrolide/antiseptic combination	Mild to moderate acne	Topical-Gel form	Dermik Laboratories

Differin	Adapalene-Retinoids	Mild to moderate acne	Topical-Gel form	Nestle pharmaceuticals
Solodyn	Minocycline-tetracycline antibiotics	acne	oral	Teva pharmaceuticals
Absorica	Isotretinoin-retinoids	Severe acne	oral	Hoffmann-Roche pharmaceuticals
Winlevi	Androgen Receptor inhibitors	acne	Topical cream	Cassiopea pharmaceuticals
Vibramycin	Tetracyclines, antimalarials	acne	oral	Pfizer pharmaceuticals
Accutane	Isotretinoin-systemic	Severe acne	oral	Hoffmann-La Roche

Prevalence of acne:

Acne vulgaris is the eighth most prevalent skin condition globally, with an estimated prevalence of 9.38% across all age groups, according to the Global Burden of Disease Study. With estimates ranging from 35% to almost 100% of teenagers having acne at some time, the prevalence of acne varies by nation and age group. In their study on the clinic epidemiological pattern of acne vulgaris in adult patients, Shah Anonymous reported that the prevalence of adult acne was 0.74 percent. Improved awareness and more people reporting to medical institutions may be the reasons for the increasing prevalence of acne in adults.

PATHOPHYSIOLOGY

It is hypothesised that diets and smoking alter insulin/IGF-1 signalling, which in turn alters acne, which is an IGF-1-mediated illness [3]. Insulin, insulin-like growth factor-1, and androgens are the primary hormones that cause AV to form. This process also involves substance P, α melanocyte-stimulating hormone, and corticotrophin-releasing hormone.

Inflammation and the development of various acne lesions are caused by changes in the sebum lipid profile, dysmenorrhea, stress, irritation, cosmetics, and possible nutritional variables throughout puberty [4]. Inflammation is triggered when enlarged follicles burst and

release pro-inflammatory substances into the dermis—Malassezia furfur, P. acnes, and Staphylococcus epidermis cause follicular epidermal proliferation and inflammation.

The skin's barrier function is similarly impacted by androgens, and disruptions in this function may trigger the creation of DNA in the epidermis. Epidermal hyperplasia results from this and it may also be a factor in acne's follicular hyperkeratosis. Atherosclerosis' clinical characteristic, foam cells—lipid-loaded neutrophils and macrophages produced by a large absorption of oxidised lipids—have also been observed in acne lesions.

Ceramide (Cer) and more complicated substances like sphingomyelin (SM) and glycosphingolipids are produced by modifying the backbone of sphingoid bases, which make up the family of lipids known as sphingolipids [7]. In the human epidermis, these lipids serve both biological and structural purposes. The main component of the sphingolipid pathway is ceramide [8]. They contribute to the prevention of trans-epidermal water loss and are among the most significant epidermal sphingolipids, making up almost 50% of the lipids by mass in the intercellular stratum corneum.

Acne vulgaris is a complex and multifaceted skin condition that affects a significant portion of the population, with considerable impacts on quality of life. Its pathophysiology involves a series of interconnected processes that provide insight into potential therapeutic targets. Genetic predisposition, hormonal changes, and environmental factors serve as key contributors to its development, creating a foundation for understanding this condition. The primary mechanisms include excessive sebum production by sebaceous glands, regulated by hormones like androgens and influenced by conditions such as puberty, menstrual cycles, and polycystic ovary syndrome (PCOS). An imbalance in sebum composition also fosters an ideal environment for microbial overgrowth. Dysregulated keratinization further contributes, as excessive keratinocyte production and retention within hair follicles block their openings, resulting in microcomedones, the precursors to visible acne lesions.

Colonization by Cutibacterium acnes (C. acnes), a commensal skin bacterium, plays a pivotal role in acne pathogenesis. When the balance of skin microbes is disturbed (dysbiosis), harmful bacteria can grow too much and activate inflammation by producing substances like lipases, porphyrins, and biofilms. These trigger the body's immune system to release chemicals called cytokines and antimicrobial peptides, which worsen inflammation and cause acne lesions. Hormonal issues, like increased sensitivity to androgens or the effects of IGF-1, can also boost oil production and skin cell growth. Other factors—such as genetics, diet, stress, and climate—can influence these processes. Inflammation is made worse by oxidative stress and damage to skin fats, which further harm skin cells and increase immune activity. All these elements form a cycle where too much oil leads to more bacteria and inflammation, upsetting the skin's balance. New research is exploring better treatments, including those that target the microbiome, reduce hormone effects, or calm inflammation. Tailored treatments based on a deep understanding of acne's causes offer hope for more effective care.

TREATMENT OF ACNE VULGARIS

The primary objective of acne treatment is to prevent scarring and shorten the duration of the condition. It also seeks to ease the psychological burden, which affects at least half of those with acne. As such, robust clinical trial data supporting the efficacy of medications is essential for successful management.

Acne therapies function by lowering oil production, minimizing inflammation, or combating bacterial infections. Most prescription treatments require fthe author's to eight weeks to show noticeable results, and full resolution may take several months to years.

Topical Retinol

Retinoids are vitamin derivatives that were first discovered to be successful in treating acne in the 1970s. Vitamin A derivatives have advantages for treating acne as they stop comedone production. Adapalene, tazarotene, and tretinoin are the three primary topical retinoids. For a long time, tretinoin has been the gold standard by which new products are evaluated. Based on a meta-analysis of multicenter random investigator-blinded trials with 900 patients, tretinoin 0.05% gel and adapalene 0.1% gel reduced lesion counts by 53% and 57%, respectively. Compared to tretinoin 0.05% gel, 0.1% microspere gel, or 0.05% cream, adapalene gel is less irritating. In an RCT, 6-9 Tazarotene 0.1% gel demonstrated 52% overall acne reduction of total lesions, compared to 33% with vehicle. In a 12-week RCT and including 169 individuals. tazarotene retinoin were evaluated. 11 Acne severity was decreased by 36% with Tazarotene 0.1% gel and 26% with Tretinoin 0.1% gel (P=.02). In a different comparison trial, tazarotene 0.1% gel was equally efficient in lowering inflammatory lesions and more successful than tretinoin 0.025% gel in reducing the number of noninflammatory lesions (55% vs. 42%; P=.042). Adapalene 0.1% cream showed a 38% decrease in total lesion counts in a multicenter RCT compared to a 20% reduction with vehicle. 13. In a 12-week randomised controlled trial including 145 patients, tazarotene 0.1% gel outperformed adapalene 0.1% gel in terms of mean reductions in the number of noninflammatory lesions (71% vs. 48%; P.0001), inflammatory lesions (70% vs. 55%; P=.0002), and overall disease severity (44% vs. 24%; P.001). 14 In a 15-week RCT15, tazarotene 0.1% gel applied alternately was just as effective as adapalene 0.1% gel applied daily.). Tretinoin is offered as a liquid (0.05%), gel (0.01% and 0.025%), and cream (0.025%, 0.05%, and 0.1%). Adverse effects of tretinoin include oedema, peeling, and cutaneous erythema. With comparable effectiveness, Adapalene 0.1% is offered as a cream, gel, and solution.

In conclusion, all topical retinoids successfully decrease between 40% and 70% of comedones and inflammatory lesions (Table 1). While tazarotene seems to be the most effective, adapalene is better tolerated and less prone to irritate the skin than either tretinoin or tazarotene.

Topical Antimicrobials

Benzoyl peroxide, tetracycline, erythromycin, and clindamycin are among the topically applied antibiotics now on the market. Since azelaic acid has shown antibacterial efficacy against intrafollicular P acnes, it may also be included in this group. 17 Five carefully planned, randomised, double-blind trials evaluating the efficacy of topical antibiotics for acne are the main theme of the author's discussion. The most thorough research has been done on more recent formulations. Clindamycin and erythromycin in initial placebo-controlled RCTs reduced inflammatory lesions by 46% to 70%. 18–21. of topical antibiotics containing retinoids or benzoyl peroxide. A randomised, 10-week, multi-center, single-blind study that included 492 patients and found that treatment with the combination products taken twice daily was more effective than benzoyl peroxide alone provides support for the use of erythromycin or clindamycin in conjunction with benzoyl peroxide. The combination of clindamycin 1% and benzoyl peroxide 5% was also found to be more effective than either medication alone in decreasing lesions and suppressing P acnes, according to a review of three clinical studies involving 1259 participants.

Clindamycin–benzoyl peroxide gel, benzoyl peroxide alone, clindamycin alone, or vehicle25 were administered once overnight to 334 participants in two randomized controlled trials (RCTs). Compared to 41% in the benzoyl peroxide group, 36% in the clindamycin group, and 10% in the vehicle group, 66% of patients in the clindamycin and benzoyl peroxide group had an outstanding response after 11 weeks. Clindamycin 1% benzoyl peroxide 5% reduced lesions by 53% compared to 28% with clindamycin alone in a comparable 16-week experiment (P=.013). Topical retinoids work well in combination with topical antibiotics. 249 participants with mild to moderate acne participated in a 12-week randomised controlled trial (RCT) that examined adapalene gel 0.1% + clindamycin 1%.

Oral Antibiotics

Systemic antibiotics used to treat acne vulgaris share antimicrobial and anti-inflammatory qualities. By lowering P acnes inside follicles, they prevent the synthesis of inflammatory cytokines brought on by bacteria. While minocycline and doxycycline inhibit cytokines and matrix metalloproteinases believed to be involved in inflammation and tissue degradation, tetracycline and erythromycin reduce leukocyte chemotaxis and bacterial lipase activity. Tetracycline, doxycycline, minocycline, and erythromycin are the primary systemic antibiotics used to treat acne vulgaris.

The use of oral antibiotics to treat acne has been the subject of very few RCTs. 200 patients participated in a 12-week RCT40, which revealed that tetracycline reduced the number of inflammatory lesions by 64% compared to 67% with erythromycin and that tetracycline reduced the number of noninflammatory lesions by 34% compared to 22% with erythromycin.

In another comparable study, topical clindamycin 1% resulted in a 72% reduction, whereas oral tetracycline produced a 57% reduction, and a placebo produced a 12% reduction. 41 Doxycycline was recently investigated in a randomised controlled trial (RCT) where 51 patients were given a placebo or a submicrobicidal dose (20 mg twice daily) for six months. Doxycycline reduced total lesions by 52% on average, while a placebo reduced them by 18% 42 Doxycycline may work even at low dosages by inhibiting collagenases, including matrix metalloproteinases. 39 Although the greatest evidence for those dosages comes from small studies, doxycycline is commonly dosed at 100 mg/ to treat acne. Minocycline is an effective treatment for mild acne, according to a Cochrane review43. However, methodological issues in the comparative studies made it impossible to evaluate how effective minocycline is in comparison to other acne treatments. Minocycline was somewhat more successful than zinc gluconate in lowering the number of inflammatory lesions in a three-month double-blind RCT (67% vs. 50%; P.001). 44 Minocycline has stronger antimicrobial activity against P. acnes than either doxycycline or tetracycline45, and its bioavailability in pilosebaceous units is favthe author'sed by its higher lipid solubility. The typical dosage for oral tetracycline is 500 mg twice daily. Tetracycline must be taken on an empty stomach because food and dairy products decrease its absorption. Dyspepsia of the gastrointestinal tract, female vaginal candidiasis, and a slight chance of photosensitivity are among the side effects. Tetracycline can induce enamel hypoplasia and yellowish discolthe author'sation of the developing teeth in children under the age of ten. 46 Traditionally, 50-100 mg of doxycycline should be taken twice a day. Over time, clinical practice may change as a result of success with 20 mg/d. compared to tetracycline, doxycycline is more likely to cause photosensitivity and disturb the gastrointestinal tract. 46 You can take doxycycline with food. Tetracyclines should not be taken right before bed since they can cause ulceration if they get stuck in the esophagus.

The recommended dosage range for minocycline is 50–100 mg twice a day. Vertigo, lightheadedness, ataxia, and, infrequently, a bluish discolthe author'sation of the skin are side effects. 46 Additionally, autoimmune hepatitis, drug-induced lupus, and hypersensitivity syndrome have all been linked to minocycline. Minocycline is associated with an 8.5 (95% CI, 2.1-35.0) relative risk of getting a lupus-like illness, while other tetracyclines have a 1.7 (95% CI, 0.4-8.1) risk. 48 Since the 1970s, the prevalence of antibiotic-resistant P acnes strains has progressively increased, and over 50% of cases in Europe and the UK currently contain these strains. 49 Treatment failures are linked to P. acnes's resistance to oral antibiotics. It's unknown how topical antibiotic use affects P. acnes resistance. 51 Compared to erythromycin49, tetracycline resistance is less frequent, and minocycline resistance is the least likely. 52 The use of combined topical therapy, such as retinoids, benzoyl peroxide, or both when using topical antibiotics, and avoiding long-term use of topical or oral antibiotics where possible are among the recently published recommendations for minimising antibiotic resistance in acne.

Hormonal Therapy

Only women can withstand hormonal acne treatments. Because androgens are necessary for the pathophysiologic development of acne, these treatments, which reduce androgen expression, are based on this fact. 53–54 although previous research indicates that women with acne may have some degree of hyperandrogenism; there is no proof that the severity of acne is directly correlated with levels of circulating androgens. 55–57 Oral contraceptives (OCs) and androgen-receptor blockers like flutamide, spironolactone, and cyproterone acetate are examples of antiandrogenic substances. Nowadays, some OCs are authorised to treat acne. Each one has less than 35µg of oestrogen. The US Food and Drug Administration has not authorised the use of any androgen-receptor blockers to treat acne. Through an increase in steroid hormone-binding globulin mediated by oestrogen, oral contraceptives decrease bioavailable testosterone and inhibit ovarian androgens. Triphasic norgestimate and ethinyl oestradiol (EE, Orthotri-cyclin [Ortho-McNeil Pharmaceutical Inc, Raritan, NJ]) reduced inflammatory lesions by around 50% after six months, compared to a 30% reduction with a placebo, according to two multicenter RCTs comprising 507 women with moderate acne. 58,59 Compared to 9% to 23% with a placebo, two RCTs examining the effectiveness of 20 μ g of EE + 100 μ g of levonorgestrel (Alesse [Wyeth, Madison, NJ]) demonstrated a 23% to 40% improvement in overall acne.

MEDICINAL PLANTS WITH ANTI-ACNE ACTIVITY:

Herbal medicines are increasingly favored for their numerous benefits, longer duration of usage, and reduced frequency of adverse effects, improved patient tolerance, and relative affordability [27]. These remedies have demonstrated efficacy in treating various challenging diseases, and they can be employed alone or in conjunction with synthetic medications for therapeutic purposes. Importantly, herbal treatments not only serve as preventive or curative measures but can also work alongside synthetic drugs to mitigate their side effects.

In the context of acne vulgaris, botanical therapies are often used either independently or alongside other treatment modalities. Numerous medicinal plants exhibit anti-inflammatory [28] and antibacterial properties that are utilized for treating acne and other infectious conditions. Some widely used species include Matricaria recutita (chamomile), Calendula officinalis (calendula), and Triticum aestivum (wheat)[29]. Preparations such as creams or aqueous infusions made from these plants, which may contain astringents and compounds like tannins, are applied topically to the skin after cleansing or steaming to enhance efficacy.

One such botanical, Hamamelis virginiana (witch hazel), contains tannins and is commonly recommended for topical application in acne treatment due to its safety profile. Other tannin rich plants include the bark of Quercus alba (white oak) and the leaves of Juglans regia(walnut), along with Agrimonia eupatoria, Syzygium cumini, Ledum latifolium, Alchemilla mollis, Lavandula angustifolia (lavender), Verbascum Thapsus, Krameria triandra, Rheum palmatum, Hypericum perforatum (St. John's wort), and Rumex crispus (dock). Some plants have traditionally been used on the skin or for their cleansing effects to help with acne. These include daisy, heartsease, quack grass, and dandelion. Horsetail, which is rich in silicic acid, and the juice of bitter aloe, which contains a compound called anthracoid, are also recommended for topical use.

Chaste tree (*Vitex agnus-castus*) is especially helpful for acne related to the menstrual cycle. Its fruit extract affects hormone levels by increasing progesterone and lowering estrogen, which reduces prolactin levels. A daily dose of 40 mg is recommended by the German Commission E, but it should be avoided by pregnant or breastfeeding women due to possible side effects like stomach upset or skin rashes.

Besides traditional uses, some plants have been studied for their ability to fight bacteria that cause acne. One such bacterium, Propionibacterium acnes, contributes to inflammation by producing harmful molecules and triggering the immune system.

Notably, liquorice (*Glycyrrhiza glabra*) [31] has been found to inhibit P. acnes without inducing bacterial resistance.

Research into plant extracts for their antibacterial and antifungal activity has identified usnic acid from Usnea barbata, which demonstrates strong inhibition of P. acnes growth at concentrations of 1 μ g/mL and possesses a range of antioxidant and antibacterial properties, making it a promising candidate for acne treatment. A clinical trial assessed the effects of extracts from Ocimum gratissimum at varying concentrations, with a 2% concentration shown to reduce skin lesions more rapidly than the standard benzoyl peroxide therapy without adverse effects, while a 5% concentration caused some skin irritation[18], [32]. In another study, topical application of O. gratissimum essence proved superior to both a placebo and clindamycin 1%.

Using a 50% Aloe vera gel along with tretinoin cream for eight weeks has shown better results and good skin tolerance compared to tretinoin alone. The German Commission E supports the topical use of Solanum dulcamara and recommends the oral use of Saccharomyces cerevisiae because of its antibacterial effects on acne.

Studies have also found that guggulipid, an extract from Commiphora Mukul, helps treat acne—especially in people with oily skin—but many of these studies were small and had some limitations.

Applying a 2% green tea lotion for six weeks was effective for mild to moderate acne, likely due to its antiseptic and anti-inflammatory properties from tannins and flavonoids. Mahonia aquifolium (or Berberis aquifolium) root extracts have been used in traditional medicine for skin problems. They contain alkaloids like jatrorrhizine and berberine, which can reduce acne-causing bacteria and fungi and lower sebum production.

Berberine, a bitter compound, has shown anti-inflammatory effects and helps reduce oil production in the skin, though the exact way it works is not fully known. Tea tree oil is known for its strong antibacterial and anti-inflammatory effects by blocking histamine. A three-month trial found that both 5% tea tree oil and 5% benzoyl peroxide helped reduce acne, although tea tree oil worked more slowly and sometimes caused skin irritation. Another study with 60 people showed that 5% tea tree oil gel worked much better than a placebo. Furthermore, gluconolactone, a polyhydroxy acid derived from Saccharomyces boulardii,

showed promise in a clinical study where a 14% solution significantly reduced inflamed acne lesions compared to placebo and was on par with 5% benzoyl peroxide while causing fewer side effects. These findings suggest that herbal treatments and botanical compounds may serve as effective adjuncts or alternatives to conventional acne therapies.

- Achyranthes Aspera [prickly chaff flower]: Traditionally, this medicinal plant has been used to treat scabies, boils, acne vulgaris, and other skin conditions. The plant's leaves contain saponin, alkaloid, and non-alkaloid fractions that have a significant inhibitory effect on Raji cells' early Epstein-Barr virus antigen activation. The nonalkaloid fraction, which contains non-polar compounds, exhibits the highest inhibitory activity (96.9%; 60% viability). The total methanolic extract demonstrated a strong anticarcinogenic effect in the two-stage in vivo mouse skin carcinogenesis test (76%). The findings showed that the non-alkaloid fractions and the leaf extract were effective antitumor promoters in carcinogenesis. The plant's strong estrogenic activity may be the reason for its contraceptive and abortifacient qualities in rodents [34].
- Allium cepa [Onion]: In patients with seborrhoeic keratosis, onion extract gel has demonstrated the capacity to enhance the look of scars. It has been demonstrated that this extract gel improves the scar's smoothness, softness, and redness at the excision site fthe author's, six, and ten weeks after the extract is used. In different research, the antibacterial and antifungal qualities of A. cepa and A. sativum were demonstrated against dermatophyte strains, Acne vulgaris microorganisms, Malassezia furfur, Candida albicans, and other Candida species. According to the findings, A.cepa and A.sativum may show promise in the management of illnesses linked to bacteria and fungi [35].
- Azadirachta indica [NEEM]: Ethanol extracts of Azadirachta indica, G. glabra, Andrographis paniculata, Ocimum sanctum, and green tea were found to have the ability to suppress acne in a study on an anti-acne formulation made from herbal extracts. Propionibacterium and Staphylococcus epidermis were effectively combatted by the anti-acne solution in this investigation. Additionally, Azadirachta indica leaf aqueous extract has chemopreventive potential against the development of skin cancer in mice. It has been demonstrated that, in contrast to the control group [36], skin tumors increase the expression of the nuclear antigen of proliferating cells. Lipid peroxidation was shown to be elevated in skin tumors in this investigation.
- Cannabis Sativus [Hemp seed]: Psoriasis, dermatitis, eczema, seborrhoeic dermatitis, acne rosacea, and lichen planus can all be treated using Cannabis sativus seed oil. This plant's leaf powder works well as a treatment for cuts and sores [37]. An external application of cannabis sativus extract helps reduce itching skin discomfort. The seed oil fortifies the skin and increases its resistance to viral, bacterial, and fungal diseases.
- Rosmarinus Officinalis [Rosemary]: The domestic plant Rosmarinus officinalis is cultivated all over the world. It is utilized in cosmetics, culinary flavoring, and beverages. There is rosmarinic acid in Rosmarinus officinalis. Chronic UV exposure can cause photoaging and photocancers, among other symptoms. Because R. officinalis has an antioxidant action, its aqueous extract can effectively prevent photodamage caused by UV radiation [16], [38]. Oxidative stress is linked to infections as well.

Consequently, the chemicals may be advantageous in this manner regardless of their antibacterial activity because they have antioxidant qualities. Additionally, rosmarinus officinalis oil has demonstrated efficacy against the acne-causing bacteria P. acnes. According to one study, R's antimicrobial qualities. When officinalis essential oil was tested against P. acnes, notable morphological and size alterations in the bacteria were noted in response to treatment.

- Melaleuca alternifolia [Tea tree]: The tea tree, or Melaleuca alternifolia, is a tall shrub or tree that belongs to the genus Melaleuca. It is indigenous to Australia and can be found along the north coast and in the surrounding regions of New South Wales. It is frequently the dominant species where it grows, including along streams and on swampy flats. Tea tree oil is a broad-spectrum agent that works against methicillin-resistant S. aureus, as well as Gram-positive and Gram-negative bacteria and yeasts like Candida albicans in vitro. Monoterpenes, which disrupt the plasma membrane barrier, have been identified as its mechanism of action. Tea tree oil has anti-inflammatory and monocyte-activating properties in addition to its antimicrobial ones. Tea tree oil applied topically in small amounts has anti-acne properties and minimal adverse effects. It works well for osteomyelitis and persistent infected wounds.
- Eucalyptus globulus, E.viminalis and E.maculata [Tasmanian gum]:One study looked at the antimicrobial properties of 29 different species of eucalyptus leaf extracts. Although they did not exhibit strong inhibitory activity against gram-negative bacteria, extracts of Eucalyptus globulus[34], [39], E. maculata, and E. viminalis were able to inhibit the growth of six gram-positive bacteria, including P. acnes, S. aureus, Enterococcus faecalis, Bacillus cereus, and Alicyclobacillus acidoterrestris, as well as a fungus called Trichophyton mentagrophytes. A strong inhibitory effect against the aforementioned bacteria was also demonstrated by 8-desmethyl-eucalyptin, a component of E. maculate. The researchers found that eucalyptus extracts and certain components extracted from this plant inhibited the growth of bacteria that cause fungal infections, acne, and athlete's foot infections.

Laser and Light-Based Therapies:

Studies have demonstrated the successful use of photodynamic therapy, light-emitting diode (LED) therapy, and combinations of pneumatic energy and light in conjunction with conventional acne treatments.

Specifically, the Isolaz system, a device that combines vacuum suction with broad-spectrum light, has shown promising results in treating acne. In a clinical trial with 11 participants, treatments given every three weeks led to a marked decrease in both inflammatory and non-inflammatory acne lesions.

Hormonal Therapy:

Hormonal therapies such as estrogen-containing birth control pills and spironolactone can successfully treat acne in women, even when no clear hormonal imbalance is present.

Birth control pills: These help lower levels of free testosterone in the body. Most types are similarly effective, so the best option depends on individual side effects and how well the patient tolerates them.

Spironolactone: This medication can be taken on its own or with birth control pills. It works by blocking hormone activity that can lead to acne.

Effectiveness: Noticeable results typically take 3 to 6 months.

Side effects: Birth control pills may cause various side effects, while spironolactone can lead to elevated potassium levels and changes in menstrual cycles.

Combination therapy: Using hormonal treatments alongside topical agents or antibiotics often yields the most effective outcomes. Hormonal treatments [38], [39] are a valuable option for women with acne, even without clear hormonal imbalances. However, they often require long-term use and may have side effects.

Oral Medications:

Antibiotics: For individuals with moderate to severe acne, oral antibiotics may be necessary to decrease bacterial presence. Tetracyclines, such as minocycline and doxycycline, or macrolides like erythromycin and azithromycin are typically the first-line treatments [40]. Macrolides may be recommended for those unable to take tetracyclines, such as pregnant women and children under the age of eight.

Oral antibiotics should be prescribed for the shortest duration possible to minimize the risk of developing antibiotic resistance, and they are often best used in conjunction with other medications, such as benzoyl peroxide, to further lower this risk. While severe side effects from antibiotics used to treat acne are rare, these medications can increase ythe author's skin's sensitivity to sunlight.

CONCLUSION

Acne vulgaris is a common skin condition affecting millions worldwide. Traditional medicine offers a wealth of potential solutions with numerous plants possessing antibacterial, antiviral, and antifungal properties. These natural remedies generally have low side-effect profiles, making them attractive alternatives to conventional treatments. Many plants exhibit antibacterial and anti-inflammatory properties, making them promising candidates for acne treatment. Our ancient heritage holds a treasure trove of herbal remedies with proven efficacy against acne.

The pharmaceutical industry is actively seeking innovative solutions to address the acne epidemic, which significantly impacts the lives of teenagers and adults alike. Leveraging cuttingedge technology and conducting rigorous long-term research is crucial to identify and harness the potential of these botanicals in modern skincare products. This research will inspire a collaborative effort among researchers, cosmeticians, academics, chemists, industrialists, and dermatologists to optimize the use of these herbs in effective and safe topical formulations for consumers.

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