



ACNE VULGARIS: A COMPREHENSIVE REVIEW OF MEDICINAL PLANTS AND THEIR THERAPEUTIC POTENTIAL

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Article Received on 12/11/2023

Article Revised on 01/12/2023

Article Accepted on 22/12/2023

ABSTRACT

This review article explores the therapeutic potential of medicinal plants in the treatment of Acne Vulgaris, a prevalent skin condition. The discussion encompasses the grading and types of acne, elucidating its etiology, hormonal influences, and the role of specific bacteria. Epidemiological insights into the prevalence of acne are provided, followed by a comprehensive overview of conventional treatments. The latter part of the review delves into the profiles of select medicinal plants known for their efficacy in acne treatment, offering a holistic perspective on natural remedies in dermatological care.

KEYWORDS: Acne Vulgaris, Medicinal Plants, Therapeutic Potential, Acne Grading, Etiology.

INTRODUCTION

Acne vulgaris (AV) is a chronic inflammatory disorder that primarily affects adolescents and young adults, and it can present as comedones, papules, pustules, nodules, and erythema. It is a multifactorial disease resulting from the interplay of genetics and environmental factors. Increased sebum excretion, the proliferation of the pilosebaceous unit, bacterial growth, and inflammation are the four pathogenesis of AV.^[1] It is a chronic inflammatory disease of the pilosebaceous unit, affecting more than 85% of adolescents and young adults, particularly males. Although uncommon in adulthood, recent epidemiological data point to an increasing prevalence, around 40%, predominantly in females. The main clinical manifestations of acne are non-inflammatory and inflammatory lesions, which occur primarily on the face, neck, trunk, and back.

Hippocrates (c. 460–370 BC) a Greek researcher Known as the "Father of Medicine wrote about acne and a variety of skin conditions, including "phyma," a term he used to describe various facial eruptions or pimples.^[2]

Acne is generally a mild and self-limiting condition, but in its most severe form, it can result in scarring and hyperpigmentation of the skin. Sequelae have a strong impact on the quality of life of individuals and Acne vulgaris is commonly observed in adolescents and young adults. Its prevalence rates are estimated to range from 35% to over 90% among adolescents. The natural course of this disease can commence as early as ages 7-12

(preadolescent acne) and resolve by the third decade of an individual's life. However, there are instances where acne can persist into adulthood or even develop for the first time during adulthood.^[5] Acne vulgaris tends to be more severe in males while its frequency increases in females after the age of twenty. Although previous reviews have reported that acne is more common in females than males, a systematic epidemiologic review suggested that this is a controversial issue. In a cross-sectional epidemiologic study, the presence of adolescent acne has been reported among 27.9% of boys and 20.8% of girls. On the other hand, adult acne is preferentially observed in women. In a study with 280 patients, 82.1% of the patients with adult acne were women. In another study, late-onset acne was found in 97.3% of women.^[8]

ACNE GRADING

Acne may be classified as mild moderate and severe. Comedones and inflammatory lesions are usually considered separately.

MILD ACNE

- <20 Comedones.
- <15 inflammatory lesions.
- Or, total lesion count <30.

MODERATE ACNE

- 20-100 comedones.
- 15-50 inflammatory lesions.
- Or, total lesion counts 30-125.

Severe acne

- >50 pseudocysts
- Total comedo count >100
- Total inflammatory count >50
- Or, total lesion count >125^[3]

TYPES OF ACNE

There are several types of acne.

- Fungal acne (pityrosporum folliculitis): fungal acne occurs when yeast builds up in your hair follicles. These can be itchy and inflamed.
- Cystic acne: cystic acne causes deep, pus-filled pimples and nodules that can cause scars.
- Hormonal acne: hormonal acne affects adults who have an overproduction of sebum that clogs their pores.
- Nodular acne: Nodular acne is a severe form of acne that causes pimples on the surface of your skin, and tender, nodular lumps under your skin.^[4]

ETIOLOGY

Acne develops as a result of hypersensitivity of the sebaceous glands to normal levels of circulating androgens. This process is further exacerbated by the presence of *Cutibacterium acnes* (*C. acnes*), a bacterial species, and subsequent inflammation.^[5]

Hormones Responsible

During puberty, male sex hormones called androgens increase, triggering changes in the teenage body. Among the changes, oil-producing glands called sebaceous glands will secrete large amounts of sebum. These oils can capture dead skin cells on the surface of the skin and clog pores. The more sebum that is produced, the greater the risk of acne.

As you enter early adulthood, androgen levels tend to decrease enough that acne breakouts will occur less frequently and eventually start to disappear.

For around 40% of women, however, acne may continue well into their 40s because of hormonal changes influenced by conditions like.

- Menstrual periods
- Pregnancy
- Thyroid medications
- Birth control pills
- Polycystic ovary syndrome (PCOS)

For most people, recurrent acne will usually stop by the time they reach their 30s. However, some adults continue to have acne in their 40s or 50s.^[6]

The genus *Cutibacterium acnes* (*C. acnes*, formerly known as *Propionibacterium acnes* or *P. acnes*, see below) is a commensal lipophilic Gram-positive bacterium. *C. acnes* is described as a diphtheroid or coryneform because it is rod-shaped and slightly curved with a width of 0.4 to 0.7 μm and a length of 3 to 5 μm .

Anaerobic bacteria are characterized by their inability to grow on solid media in the presence of atmospheric oxygen. However, *C. acnes* is considered an aerotolerant anaerobe because it possesses enzymatic systems able to detoxify oxygen, allowing it to be sustained.

Bacteria causing Acne

On the surface of the skin. *C. acnes* was first included in the genus *Bacillus* as *Bacillus acnes*, and then in the genus *Corynebacterium* as *Corynebacterium acnes* or “anaerobic corynebacteria” because of its morphology. Based on its ability to produce propionic acid via its anaerobic catabolism, it was then assigned to the genus *Propionibacterium*, subsequently

renamed *Cutibacterium*. Genus *Cutibacterium* belongs to a branch of *Actinobacteria* and can be split into two groups, one containing the so-called “classic or dairy” species, bringing together saprophytic species isolated from non-human pathogenic dairy products, and the other containing commensal “skin” species, most found on the surface of human skin. Classic species, such as *Propionibacterium freundenreichii*, which is essential for the ripening of Swiss cheeses, or *Propionibacterium acidipropionici*, known for its beneficial effects in the bovine rumen, have been studied in considerable detail due to their importance to the agri-food industry. By contrast, the pathophysiology of cutaneous species is less well understood.

Phylogenetic and genome analyses of classic and cutaneous species have highlighted differences in the 16S RNA gene sequences and the core genome between species. This finding led to proposals to reclassify many species into four different genera.

- The genus *Propionibacterium*, comprising the species *P. freundenreichii*, *P. cyclohexanicum*, *P. acidifies*, and *P. Australians*.
- The new genus *Acidipropionibacterium*, comprising the species *A. jensenii*, *A. thoenii*, *A. acidipropionici*, *A. microaerophilum*, *A. damnosum*, and *A. olivae*.
- The new genus *Pseudopropionibacterium*, containing a single species: *P. propionicum*.
- The new genus *Cutibacterium*, comprising cutaneous *Propionibacterium* bacteria belonging to the species *C. avidum*, *C. granulosum*, and *C. humerusii*. *P. Acnes* has thus been renamed *C. acnes*.^[7]

EPIDEMIOLOGY

Acne vulgaris is commonly observed in adolescents and young adults. Its prevalence rates are estimated to range from 35% to over 90% among adolescents. The natural course of this disease can commence as early as ages 7-12 (preadolescent acne) and resolve by the third decade of an individual's life. However, there are instances where acne can persist into adulthood or even develop for the first time during adulthood.^[5]

Acne vulgaris tends to be more severe in males while its frequency increases in females after the age of twenty. Although previous reviews have reported that acne is more common in females than males, a systematic epidemiologic review suggested that this is a controversial issue.

In a cross-sectional epidemiologic study, the presence of adolescent acne has been reported among 27.9% of boys and 20.8% of girls. On the other hand, adult acne is preferentially observed in women. In a study with 280 patients, 82.1% of the patients with adult acne were women. In another study, late-onset acne was found in 97.3% of women.^[8]

Treatment:

Acne is treated with topical monotherapy and polytherapy with

- Retinoid – There are 4 generations of retinoid.
First generation: Retinol, retinaldehyde, tretinoin.
Second generation: Etretinate, acitretin.
Third generation: Adapalene, tazarotene.
Fourth generation (PYRANONES): Seletinoid – G^[9]
- From these 4 generations of retinoid, only 1 (tretinoin, retinaldehyde) & 3 (adapalene, tazarotene) generations are used
- Anti keratolytic: benzyl peroxide, salicylic acid.
 - Anti-biotics: clindamycin, doxycycline.^[10]
 - Androgen receptor inhibitor: cyproterone, spironolactone.^[11]

Himalayan herbs in the treatment of acne vulgaris: due to the benefits of Himalayan herbs, such as increased tolerance, a long history of widespread use, fewer side effects, and lower costs herbal remedies are gaining popularity.^[11]

Gotu kola, calendula officinalis, Himalayan cedar, and *Bergenia ligulate* herbal medicines have anti-inflammatory and anti-bacterial properties that can be utilized in the treatment of acne vulgaris.

Gotu Kola



Image 1: Gotu kola^[40]

Centella Asiatica, commonly known as **Indian pennywort** and **Asiatic pennywort**, is a herbaceous, perennial plant in the flowering plant family Apiaceae. It is native to tropical regions of Africa, Asia, Australia, and islands in the western Pacific Ocean. It is consumed as a culinary vegetable and is used in traditional medicine.

Synonyms: brahmi, Gotu kola Indian pennywort, English pennywort

Kingdom: Plantae
Clade: Tracheophytes
Clade: Angiosperms
Clade: Eudicots
Clade: Asterids
Order: Apiales
Family: Apiaceae
Genus: *Centella*
Species: *C. asiatica*^[12]

Morphological characters

It is a perennial plant with leaves and stems that can be consumed as a green leafy vegetable. It is used as a folk remedy to cure various mild and chronic diseases due to its anti-rheumatic, antipyretic, antibacterial, antiviral, and anti-inflammatory effects, and as a mental rejuvenator.^[13] *C. asiatica* prefers relatively shady and damp habitats such as wetlands, riversides, ponds, wet meadows, and forests from a 300-to 1,800-m altitude. The species is characterized as a perennial, flowering, faintly aromatic, low-growing, creeping herbaceous plant, with prostrate or semi-erect-stems-and-rooting-at-the-nodes, with a height varying between 10.0 and 45.0 cm.^[14]

Chemical Composition

Appreciable quantity of phytochemicals. The phytochemical composition of *C. asiatica* leaf contains 2.75% phenolic, saponin 8.2%, flavonoids 12.85%, phytate 0.76%, and 0.00% tannin. dry matter to be 95.76, 2.77 12.40% crude protein, 2.80 and 2.40% crude fibre, and 75.44% carbohydrate.

The composition of vitamins in *Centella asiatica* leaf contains vitamin A, vitamin E, vitamin C, vitamin B6, B12.^[15]

Centella asiatica leaves contain a considerable amount of fatty acids with 78.48% saturated and 21.53% unsaturated. The predominant fatty acids are palmitic acid (55.70%), linoleic acid (17.50%), and lauric acid (13.73%).^[16]

Centella asiatica contains asiatic acid, asiaticoside, madecassic acid, madecassoside.^[17]

Use: some traditional uses of gotu kola include.

- healing wounds^[18]
- relieving diarrhea
- boosting energy levels
- reducing anxiety
- enhancing sexual potency
- treating venereal diseases
- treating skin diseases
- treating menstrual disorders
- slowing Hansen's disease (leprosy) progression
- prolonging life^[19]
- acne & sebum reduction.

- scar reduction.
- collagen production.^[20]

Marigold (*calendula officinalis* L.)



Image 2: Marigold (*calendula officinalis* L.)^[41]

Calendula officinalis is a flowering plant in the daisy family Asteraceae, native to southern Europe. The Latin-specific *officinalis* refers to the plant's medicinal and herbal uses.

Kingdom—Plantae
 Subkingdom-Tracheobionta
 Division-Magnoliophyta
 Class-Magnoliopsida
 Subclass-Asterieae
 Order-Asterales
 Family-Asteraceae
 Tribe-Calenduleae
 Genus-Calendula
 Species-officinalis

Synonyms: Genda, pot marigold, butterwort.

Morphological Character

Calendula officinalis L. is an annual herbaceous plant that can grow up to 80cm tall.^[21] It has a deep taproot and thick, weak stems that form a shrubby, well-branched, mounded habit.^[22] The leaves are oblong or spatulate in shape with a hairy surface, and have either an entire margin or few teeth.^[21] From spring to summer, the plant produces daisy-like flowers that are yellow to orange in color and appear above the foliage.^[22]

Chemical constituent: The Marigold flowers contain lutein esters of palmitate, mono myristate, and dimyristate. The whole plant also contains essential oils such as limonene, ocimene, linalool, linalyl acetate, tagetone, and n-nonyl aldehyde. its petal contains tagetin and hydroxyflavons.^[23] Various chemical constituents including thiophenes, flavonoids, carotenoids, and triterpenoids have been isolated through berphytochemical studies of its different parts.^[24]

Use: The extract of *C.officinalis* showed significant healing activity by increasing hexosamine and collagen hydroxyproline content with a significant decrease in the level of tissue damage marker enzymes (aspartate transaminase and alkaline phosphatase) and acute phase proteins (orosomycid and haptoglobin), *C. officinalis* polysaccharide (PS) fraction exhibits immuno-stimulant

activity. PS-I and PS-II showed 40- 57% and 20-30% phagocytosis, respectively, while PS-III exhibited the highest (54-100%) phagocytosis.^[25] Immunostimulant activity was also observed in shrimp (*Fenneropenaeus chinensis*) against *Vibrio harveyi* when injected with SFPSE i.e., a *Sargassum fusiforme* polysaccharide extract. Moreover, the polysaccharides from *Salicornia herbacea* show immuno-modulatory activity and are efficiently used against various types of cancers. The aqueous/ethanolic plant extract showed spasmogenic activity. The aqueous/ethanolic extract of *Calendula* flowers caused relaxation of spontaneous contraction and K⁺-induced contraction of muscles. *Calendula* flower hydro-alcoholic extract caused a 28.5% reduction in hepatocytolysis of CCl₄-intoxicated rat liver due to a reduction in glutamic-pyruvate transaminase and glutamic-oxalate-transaminase. *C. officinalis* inflorescence extract shows anti-inflammatory activity against dextran and carrageenan-induced acute paw edema in mice. Also, a significant increase in the level of pro-inflammatory cytokines like IL-1 β , IL6, and TNF- α in the sera of LPS (lipopolysaccharide) 780 Nelofer Jan et al. induced animals has been observed.^[26]

Bergenia Ligulata



Image 3: Bergenia ligulate^[42]

Bergenia ligulata (*Paashaanbhed*, *Prashanbheda*, and other spellings in Ayurveda traditional Indian medicine) is a plant belonging to the family Saxifragaceae and the genus *Bergenia*. It is a plant that is sometimes treated as a form of *Bergenia ciliata*.

Classification

Kingdom: Plantae
 Clade: tracheophytes
 Clade: angiosperms
 Clade: eudicots
 Order: saxifragales
 Family: Saxifragaceae
 Species: *B.ligulata*

Synonyms: Paashaanbhed, prasanbheda.^[27]

Morphological characters: It is a perennial herb with thick rootstock. Leaves simple, orbicular to broadly obovate, fleshy, entire, strongly ciliate, inflorescence corymbose scapes, fruit Globose. The rhizome is solid, barrel-shaped, cylindrical, 1.5-3 cm long, and 1-2 cm in diameter. With ridges, furrows, and root scars distinct, odor-aromatic, and taste-astringent.

Chemical Composition

The most potent bioactive component of *Bergenia ligulata* is Bergenin. Bergenin is a trihydroxybenzoic acid glycoside and is the C-glycoside of 4-O-methyl gallic acid. It possesses an o-demethylated derivative called norbergenin.^[28] and other major bioactive compounds are (+)-catechin, gallic acid, ferulic acid, β -sitosterol, catechin-7-O- β -D-glucoside, (+)-afzelechin, *arbutin*, 4-O-galloylbergenin, 11-O-galloylbergenin, caffeoylquinic acid, pashaanolactone, 3,11-di-O-galloylbergenin, bergapten, kaempferol-3-O-rutinoside, quercetin-3-O-rutinoside, (+)-catechin-3-O-gallate, 2-O-caffeoyl arbutin, leucocyanidin, methyl gallate (allicin), sitoinoside I, β -sitosterol-D-glucoside, avicularia, reynoutrin, procyanidin B1, afzelin, and aloemodin.

The constituents have been categorized into polyphenols, flavonoids, quinones, sterols, terpenes, tannins, lactones, and others.

Use: The drug is used as a litholytic agent for urinary calculi.^[30] Dichloromethane, a bioactive fraction of *B. ligulata* extract showed high efficiency against kidney stone aggregation when administered orally for 21 days at a dose of 7 mg/kg body weight. *B. ligulata* is considered an antipyretic herbal drug, particularly the dried rhizome is used to prevent such fever, a possible mechanism of anti-diabetic action of *B. ligulata* may be attributed to its bioactive compound (+)-afzelechin, which acts as an inhibitor of α -glucosidase enzyme, as ascertained by enzyme inhibition assay [30] It is widely used in the treatment of dysuria, cystitis, crystalluria and renal failure, vertigo, and headache. The rhizomes and roots of the plant act as astringent, and tonic and have anti-inflammatory effects, and are applied as poultices for stiff joints, boils, abscesses, and skin infections. The root powder is considered to be a mild diuretic, but in higher doses, it exhibited anti-diuretic action.^[35] Ferulic acid's anti-inflammatory properties may prevent pimples and reduce the appearance of discoloration from acne.^[31]

Himalayan cedar



Image 4: Himalayan cedar^[43]

Chemical constituents from different parts of *Cedrus deodara*.

Essential oils from wood	Methylacetophenone, Atantonl ^[37]
The stem bark of the plant	Deodrin, Toxifolin, Flavonodis and Glycosides ^[37]
Other parts of the plant	Wikstromal, Matairesional, Dibenzylbutyrolactol, Bergapent, Isoimpinellin, Benzofuranoid neo lignin, Isohemacholone ^[37]

Cedrus deodara, the **deodar cedar**, **Himalayan cedar**, or **deodar**, is a species of cedar native to the Himalayas.

Kingdom: plantae
Clade: Tracheophytes
Clade: Gymnospermae
Division: Pinophyta
Class: Pinophyta
Order: Pinales
Family: Pinaceae
Genus: *Cedrus*
Species: *C. deodara*

Synonyms.

Deodar, cedar, Himalayan deodar^[32]

Morphological Character

Cedrus deodara is an evergreen coniferous tree that may reach a height of 60 meters with a trunk diameter of up to 3 meters. The tree's crown is conical when it is young and becomes rounded with age. When the bark ages, it changes from being smooth and grey-brown to having narrow furrows with scaly ridge tips. The leaves are needle-like, ranging in length from 2.5 to 5 cm, sometimes reaching 7 cm, and thin (1 millimeter or 1/32 mm thick). They are borne individually on long shoots and in dense clusters of 20 to 30 on short shoots. Their color varies from bright green to glaucous blue-green. As they grow (around 13 cm in length and 5 to 9 cm in width) the female cones, which are barrel-shaped disintegrate when mature (in 12 months) to release the winged seeds.^[39]

Chemical Composition: The major constituents in the *C. deodara* samples were himachalene (23.5-68.5%) and atlantone (15.0-61.6%). The other constituents in the *C. deodara* wood were himachalene oxide, Himachal, oxidohimachalene, dehydro-arhimachalene, and cis- α -bisabolene.^[33]

Use

The plant has been used in Ayurvedic medicine for centuries and is believed to have therapeutic properties.^[34] The essential oil of *Cedrus deodara* has been found to have antifungal properties and can be used to treat fungal infections.^[35] The plant's essential oil is also known to have anthelmintic, carminative, diuretics, diaphoretic, and astringent properties.^[36] The plant has been used to treat a variety of ailments, including arthralgia, traumatic injury, sleeplessness, edema, eczema, acariasis, neurological disorders, asthma, infested wounds, headache, fever, pruritis and arthritis.^[37] Essential oil of *Cedrus deodara* is a strong medicinal remedy which when diluted can be used for massage on the skin.^[38]

CONCLUSION

This review highlights the multifaceted approach to understanding and managing Acne Vulgaris, shedding light on the therapeutic potential of medicinal plants in its treatment. The exploration of acne grading, types, etiology, hormonal imbalances, and bacterial involvement emphasizes the complex interplay of factors contributing to this common dermatological concern. Traditional treatments have been discussed, underlining the need for comprehensive strategies in acne management.

The incorporation of medicinal plants into acne treatment regimens adds a promising dimension to skincare, capitalizing on the diverse bioactive compounds inherent in botanical resources. The epidemiological insights provided contribute to a better understanding of the prevalence of acne, underscoring the need for effective and accessible treatments.

As the search for alternative and complementary therapies gains momentum, the profiles of selected medicinal plants presented here serve as valuable resources for clinicians and researchers alike. The integration of natural remedies into mainstream dermatological care aligns with the growing interest in holistic approaches, paving the way for future studies and innovations in the pursuit of effective, sustainable, and patient-friendly acne management strategies.

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