



A Brief Review on Herbal and Synthetic Treatment of Acne Vulgaris: A Review

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ABSTRACT:

Acne vulgaris (acne) is one of the dermatological disorders that affects teenagers and young adults most frequently. It begins to show up after the commencement of puberty and lasts up to 40 to 50 years. A pilosebaceous unit illness called acne vulgaris causes papules, pustules, nodules, and cysts as well as open and closed comedones. Face, chest, and back areas with dense sebaceous follicles are all affected by acne. There are numerous recognized hormonal factors that contribute to acne, including androgens and insulin-like growth factors., linolic acid deficiency, upward regulation of keratinocytes, oxygen stress. Generally, topical treatments of acne vulgaris are made of synthetic substances and first line treatment for acne but typically cause dry, irritate, and itch the skin. As an alternate source of treatment, naturally occurring plant components (phytochemicals), which are usually thought to be harmless, have drawn a lot of attention. In this review, we arrange the various types of medicinal plant and current using synthetic drugs in synchronise way in order to treat acne vulgaris. Therefore, this review paper gives a brief overview of herbal part used, distribution, chemical component, biological activity and pharmacological activity of synthetic drugs and different formulation and adverse event.

KEYWORDS. Acne vulgaris, inflammation, pilosebaceous duct, hyperseborrhea, Propionibacterium acnes, comedone, Sebaceous gland

1. INTRODUCTION

In the United States, acne vulgaris a prevalent condition of the pilosebaceous unit, affects 85% of people between the ages of 12 and 25[1]. In their 40s, 26% of women and 12% of men still have acne, indicating that it typically persists into adulthood [2]. Acne is the eighth most common disease worldwide with Western Europe, "high-income" North America, and southern Latin America having the highest prevalence rates [3]. Neonatal and childhood forms of acne are included in usual age-based categories for acne. The second most common reason for suicide among skin diseases is acne vulgaris. Acne sufferers are found to have higher levels of anxiety, more socio-inhibition, and higher levels of aggression as compared to those without the condition [4]. The skin's surface can be found on the face, upper chest, and back with the highest density of sebaceous follicles that are affected by acne. Although moderate cases of acne can appear without inflammation, severe occurrences are distinguished by inflammation.[5] [6]Whiteheads, blackheads, pustules, papules, and cysts are just a few of the skin eruptions that characterize the condition known as acne vulgaris. Lesions in acne vulgaris can be either inflammatory or non-inflammatory, or they can be both. [7]The high incidence of acne vulgaris is linked to environmental factors, including diet, medicine, occupational factors, pollution, environmental influences, psychosocial issues, and lifestyle factors.[8-11] Exposome variables have an impact on the microbial diversity of the skin, the skin's natural barrier, inflammation, hyperseborrhea, and aberrant keratinization of the pilosebaceous duct.[12]

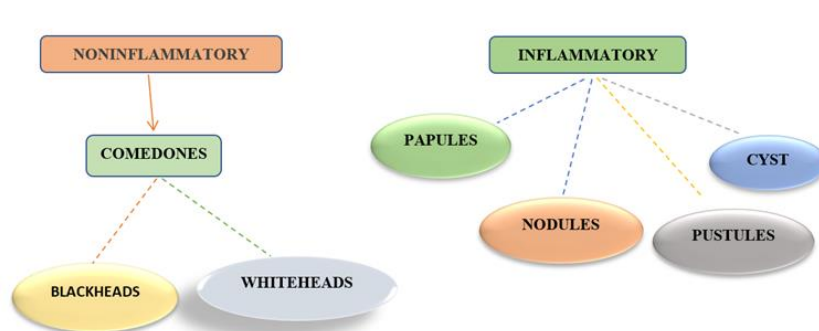


Fig. 1: classification of acne

2. ETIOLOGY OF ACNE

Sebum production, hyperkeratinization, follicular blockage, and keratin plug creation all contribute to acne development (microcomedo). Sebaceous glands swell and sebum production rises in response to increasing androgen production. The microcomedo (microcomedones are the smallest of all acne blemishes as it expands, it might become an open comedone (blackhead) or a closed comedone). Dead skin cells and sebum, a naturally occurring oil, clog sebaceous glands, causing comedones to form.[13]

Inflammation and inflammatory lesions, such as infected pustules, nodules, and papules in the dermis around the microcomedone or comedone, can result from the naturally occurring commensal bacterium *Propionibacterium acnes*, which can cause redness, scarring, or hyperpigmentation.[13, 14]

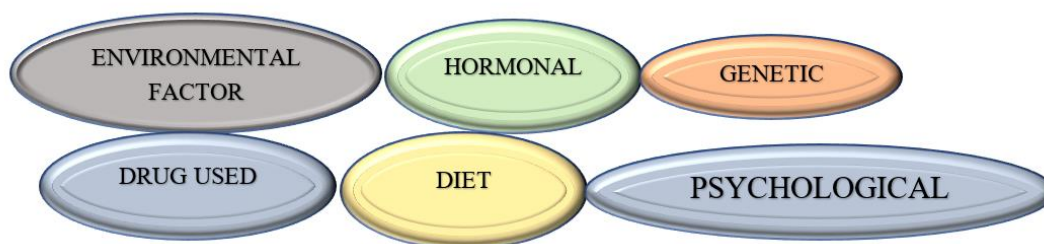


Fig.2: Etiology

2.1.1 Environmental Factors:

It consists of various components, such as high humidity, constant sweating, a rise in skin moisture, exposure to squalor or aerosol frying oil, or certain substances, such as petroleum derivatives.

2.1.2 Drug Use:

Acne can be brought on by medications such as phenytoin, isoniazid, phenobarbital, lithium, ethionamide, steroids, azathioprine, quinine, and rifampin.

2.1.3 Hormonal:

Acne can also be brought on by menstruation plus puberty. Follicular glands swell and sebum production rises throughout puberty due to an increase in androgen levels. [13, 15] Anabolic steroids produce similar effect.[16] The hormones insulin-like growth factor 1 (IGF-I) and the androgens testosterone, dihydrotestosterone, dehydroepiandrosterone sulfate, are among those linked to acne. Acne vulgaris development in older age groups is rare, but the incidence of rosacea, which has symptoms similar to those of acne vulgaris, will rise. The underlying cause of adult female acne vulgaris may be a disorder like pregnancy, polycystic ovary syndrome, Cushing's syndrome, or hirsutism. Acne climacterica, also known as menopause-related acne, develops when the ovarian hormones estradiol and progesterone are produced in excess, which allows the acne-causing hormone testosterone to continue to have an impact.

2.3.4 Psychological:

According to studies, acne severity is correlated with increasing stress levels.[17] According to the National Institutes of Health (USA), stress can make acne worse.[18] Stress levels and acne severity were found to be positively correlated in a study of teenagers in Singapore.[19]

2.3.5 Diet:

Despite being heavy in sugar, is connected to acne deteriorating, the connection between diet and acne is still unclear.[11, 20] Consuming milk is correlated positively with an increase in the prevalence of acne.[21-23] According to reports, eating salt and chocolate is not linked to the emergence of acne.[21] Chocolate has a high sugar content, which might result in a high glycemic load. It's probable that obesity and insulin metabolism are related to acne.[24]

2.3.6 Genetic:

Acne does not have a typical Mendelian inheritance pattern; hence its genetic susceptibility is polygenic. There are a number of potential genes causing acne, including polymorphisms in CYP11A1, Interleukin-1 alpha, and tumor necrosis factor-alpha.[25]

3. PATHOPHYSIOLOGY

Sebum production increases as a result of increasing androgen concentration caused by seborrhea, hereditary factors, reaching puberty, and other causes. At puberty, the body produces more androgen. Androgens are both reabsorbed and produced in the sebocyte. The androgen-receptor complex is then created in the cytoplasm by these androgens. They then reach the nucleus via the nucleopore and change a certain gene's sequence, which affects the reading rate and increases sebocyte sebum production. The pilosebaceous ducts allow the sebum that is so created to pass to the skin's surface. The keratinocytes in the hair follicle receive linoleic acid from this sebum as it flows to them. As a result, the follicular barrier is compromised due to a localized linoleic acid deficiency. This permits *P. acnes*'s (Propionibacterium acnes) free fatty acid to enter the follicle through the action of its triglycerides using the lipase enzyme or through other ways..

The degradation of the follicular wall is also attributed to oxygen stress and the generation of free radicals by phagocytes in response to invasive pathogens. Free fatty acids that are ingested are very chemotactic and cause the production of a number of cytokines, including IL-8 and IL-1, which promote inflammation and increase keratinocyte proliferation. This causes ductal hypercornification, which results in the development of thick horny lamellae. It leads to retention-proliferation hyperkeratosis. Retention-proliferation hyperkeratosis first produces a microcomedone, which then enlarges and transforms into a comedone, which then progresses to produce acne.[26-28]

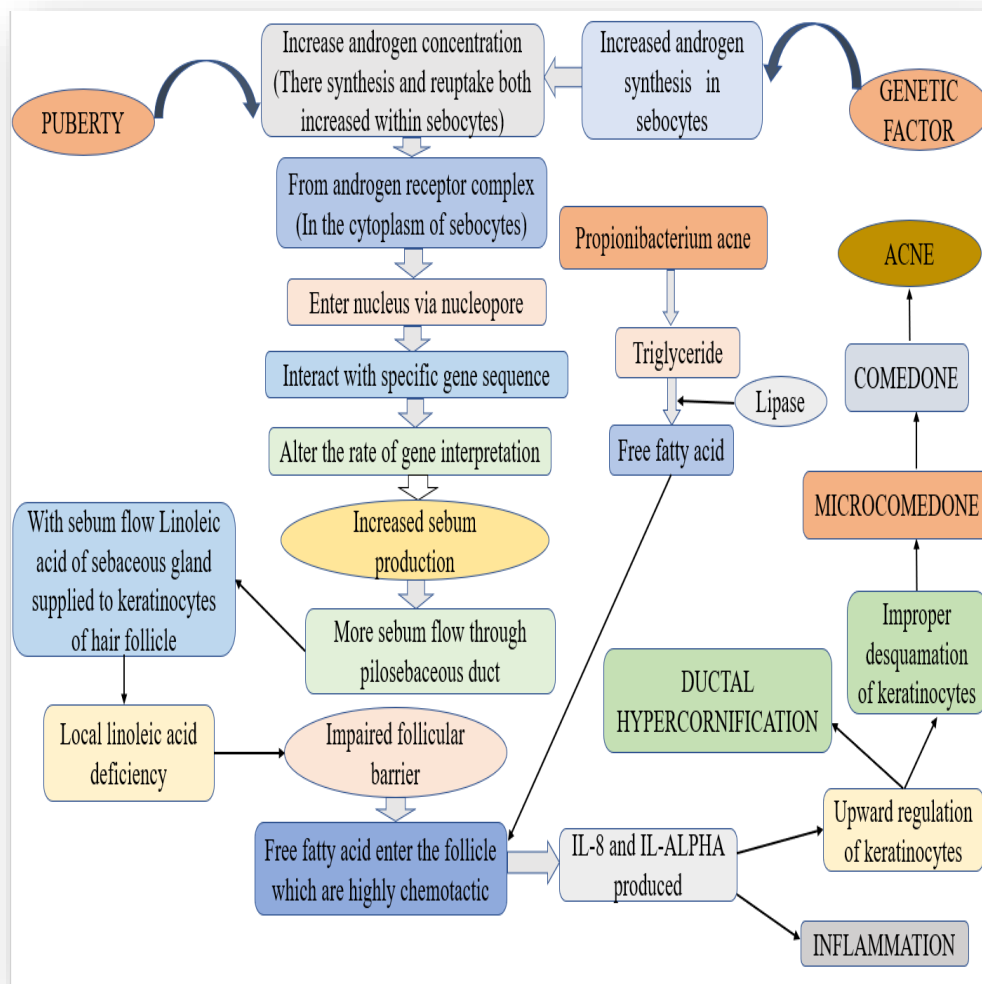


Fig 3: Pathogenesis of acne vulgaris

4. HERBAL TRETMENT

owing to their advantages, which include a greater tolerance, a history of extensive use, fewer adverse effects, and a lower price, herbal medications are becoming more and more popular.[29]To treat illnesses, these herbs are used either alone or in conjunction with synthetic medications.[30, 31] More importantly, they may be combined with synthetic medications to lessen their negative effects in addition to being consumed as a preventive or therapy measure. [32-36]Without fail, herbal medicines are also utilized to treat acne vulgaris, either in conjunction with other techniques or on their own. A lot of medicinal herbs which have anti-inflammatory and antibacterial properties which can be considered in treatment for acne.[37-41]



Fig4: Herbal medicine

4.1.1 *Azadirachta indica* Linn:

Part used: Due to their therapeutic characteristics, bark, leaves, seeds, and latex have been used to treat a variety of skin issues.

Distribution: The plants belong to India and Sri Lanka.

chemical components: Tri-terpenoids and tetra-nortriterpene are found in seed oil, and nimbolin A and B, nimbin, gedunin, tannin, and volatile oil are found in the barks and leaves.

Biological activity: The substance demonstrates anti-inflammatory, antimicrobial, and antibacterial effect. [42, 43] It has demonstrated that it is successful in treating acne.[44] In a study on acne, *Azadirachta indica*'s shown anti-acne efficacy by preventing *P. acnes* from growing.



Fig 5: *Azadirachta indica* Linn

4.1.2 *Curcuma longa* Linn

Family: Zingiberaceae

Part used: Root, stem

Distribution: It is distributed widely throughout India, Asia.[45-47]

Chemical components: Pale yellow to orange-yellow volatile oil (6%) made up of several monoterpenes and sesquiterpenes, such as zingiberene, curcumene, -, and turmerone, among others. Curcuminoids, which make up five percent of the coloring agents, contain between fifty and sixty percent each of curcumin, monodemethoxycurcumin, and bisdemethoxycurcumin.. [48, 49]

Biological activity: anti-bacterial and anti-inflammatory properties.[50]



Fig6: Curcuma longa Linn

4.1.3 Amaranthus hypochondriacus Linn

Family: Amaranthaceae

Distribution: China and Mexico.

Part used: Amaranth seeds and leaves are effectively used

Chemical components: The main ingredients are saponins.

Biological activity: powerful cleaners and used as astringents for a number of skin conditions, such as psoriasis, eczema, and acne.[51]



Fig7: Amaranthus hypochondriacus Linn

4.1.4 *Carica papaya* Linn

Family: caricaceae

Distribution: A native to Mexico, northern South America and India.

Part used: papaya fruit, papaya leaf

Chemical components: Papaya fruit includes linalool, 4-terpinol, and monoterpenoids, and the seeds of the fruit contain flavonoids, kaemferol, and myricetin.

Biological activity: Since papaya's biological activity and medical applications have substantially improved over the past few decades, it is now considered as a valuable fruit plant for dietary supplements. The benefits of *Carica papaya* include treatment for acne-related issues and widespread antibacterial activity against germs including *Staphylococcus aureus* and *Bacillus cereus*. [52-55]



Fig8: *Carica papaya* Linn

4.1.5 *Melaleuca alternifolia*

Family: Myrtaceae

Distribution: It is indigenous to Australia and can be found along New South Wales' north coast and in nearby places. [55]

Part used: leaves of the tea tree

Chemical components: terpinen-4-ol as its major compound. [56]

Biological activity: Tea tree oil contains anti-inflammatory and monocyte activator properties in addition to its antibacterial properties. [57] Many skin care, personal care, hair preparations, and cosmetic items contain this oil. [58]

Anti-bacterial activity is due to terpinen-4-ol. [59] Tea tree oil has good penetration power and is non-irritating to skin.



Fig9: Melaleuca alternifolia

4.1.6 Rubusideaus

Family: Rosaceae

Distribution: It was believed that they might have come from Asia and traveled the world via Europe.

Part used: - Raspberry fruit and leaves

Chemical components: In addition to anthocyanin pigments, ellagic acid, ellagitannins, quercetin, gallic acid, cyanidins, pelargonidins, catechins, kaempferol, and salicylic acid, raspberries also include cyanidins, pelargonidins, and gallic acid.

Biological activity: Red raspberries' health advantages are thus guaranteed by the anthocyanins' antioxidant properties.[60]



Fig10: Rubusideaus

5. SYNTHETIC TREATMENT OF ACNE VULGARIS

5.1 Topical Retinoids

Retinoids are vitamin A compounds that were initially used to treat acne in the 1970s. They normalize the follicular epithelium's desquamation to prevent comedone development.[61]

The 3 main topical retinoids are:

1. tretinoin
2. adapalene
3. tazarotene

5.1.1 Tretinoin

A kind of vitamin A is called retinoin.[62] It is a common comedolytic drug used to regulate epithelial desquamation, which prevents pilosebaceous units from becoming clogged. Moreover, it appears to have anti-inflammatory qualities. For more than three decades, it has been used as a topical therapy for acne.[63, 64]

5.1.2 Adapalene

The topical retinoid treatment for acne vulgaris is the most common use of the synthetic retinoid analog adapalene. It regulates the follicular epithelium's cell differentiation and inhibits the growth of comedones. Moreover, it exhibits anti-inflammatory effects on acne lesions.[62, 63, 65]

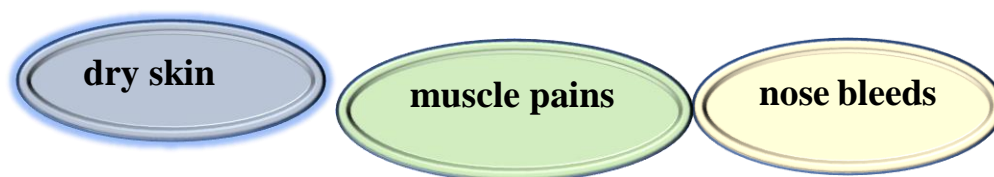
5.1.3 Tazarotene

In keratinocytes, tazarotene, an artificial pro-drug for acetylcholine, is transformed into tazarotenic acid.[63] It is a more recent retinoid that is used to treat acne. It may also possess anti-inflammatory qualities and impacts keratinocyte development and proliferation in the epithelial tissue.[66] Because it may irritate acne patients' skin, it is considered a second-line treatment when there has been no improvement after using tretinoin or adapalene.[63]

5.2 Oral Retinoids

In situations with moderate to severe acne, improvement can be seen after using isotretinoin for one to two months. More than 50% of patients get full remission after a single treatment session in about 80% of instances, whereas 20% of patients require a second round of therapy..

Adverse effects include



Elevated blood lipid levels and elevated liver enzymes. Fetal abnormalities are quite likely to occur throughout pregnancy. There is no proof that taking oral retinoids makes you more likely to experience side effects like sadness or suicidal thoughts.[67]

5.3 Topical antibiotic

For a range of disorders, including mild-to-moderate acne vulgaris, secondary infected dermatitis, rosacea, the treatment and prevention of wound infections, and impetigo, dermatologists routinely use topical antibiotics.[68]

5.3.1 Benzoyl Peroxide

Benzoyl peroxide, which is generated from coal tar, is a topical medication for the treatment of mild-to-moderate acne vulgaris that has been licensed by the FDA.

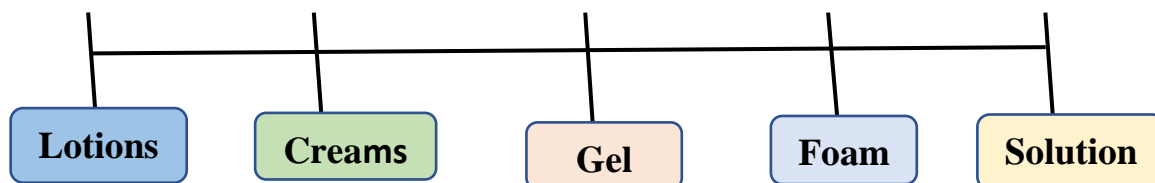
Topical: On the epidermis and in hair follicles, benzoyl peroxide has bactericidal effects on Cutibacterium acnes.

Pharmacological Activity

1. Benzoyl peroxide also possesses antibacterial activity

2. According to the study, benzoyl peroxide had quick and potent bactericidal action against the organisms, but it was ineffective against Gram-negative bacteria.

The preparations that are available include:



Adverse events of benzoyl peroxide are limited:



5.3.2 Clindamycin

Clindamycin has replaced the naturally occurring lincosamide known as lincomycin, which was first isolated from the soil bacteria *Streptomyces lincolnensis* in Lincoln, Nebraska. Lincomycin has been substituted with clindamycin due to Compared to lincomycin, it is more effective and has a larger range of sensitive species.[69]

Function:

Clindamycin inhibits the synthesis of fresh bacterial proteins by binding to the 50S component of the bacterial ribosome's 23S rRNA. By interfering with ribosome assembly and the translation process, this prevents bacterial growth.

Formulation

There are parenteral and oral forms of clindamycin.

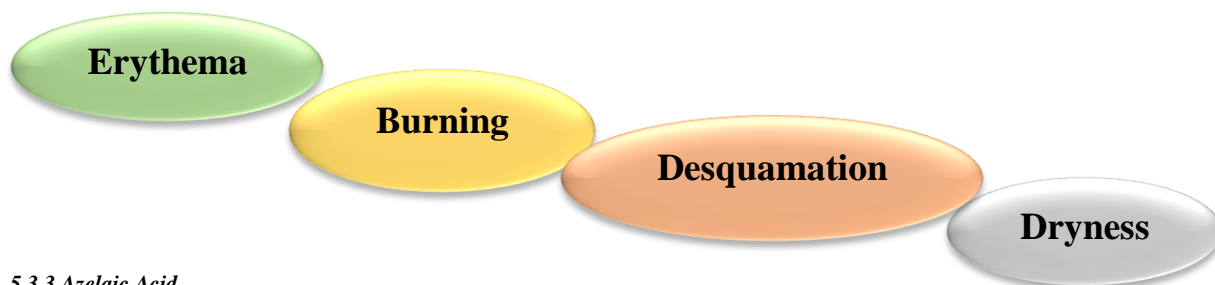
Topical agent

Common formulations include gel, lotion, solution, and foam.



Pharmacological activity

1. Both to non-antimicrobial and antimicrobial effects.

Adverse event**5.3.3 Azelaic Acid**

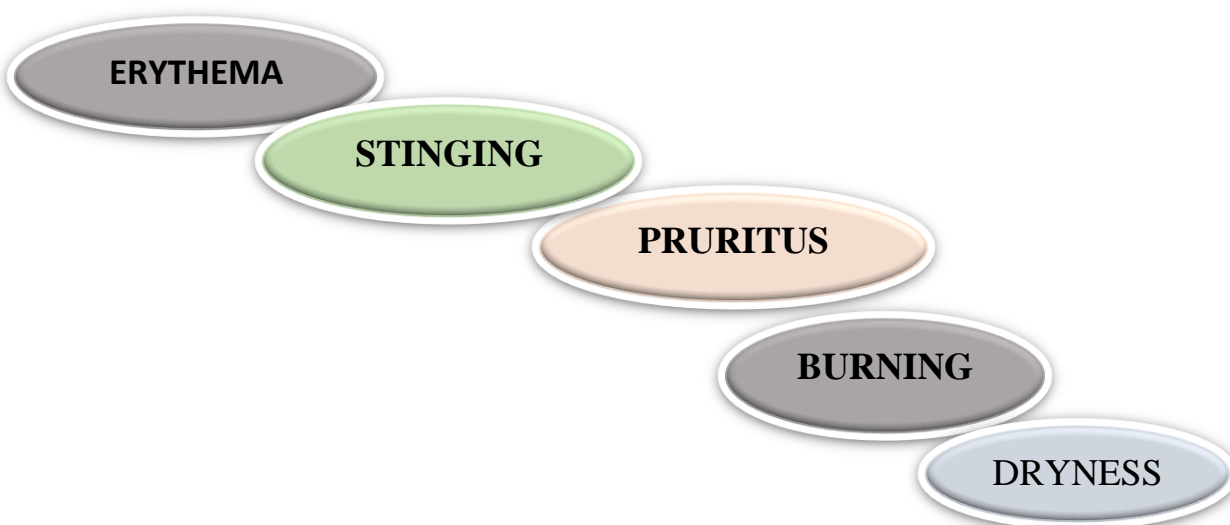
A dicarboxylic acid called azelaic acid is a harmless one that occurs naturally. It provides significant medical advantages. Azelaic acid can successfully cure *Staphylococcus aureus*, *Cutibacterium acnes* (*C. acnes*), and *S. epidermidis*.

Function

Azelaic acid has also been demonstrated to affect human keratinocyte development by lowering the production of keratinocyte precursors. Azelaic acid acts as a modest anti-keratinizing agent due to this decrease, which also changes the stages of epidermal differentiation. This lessens the obstruction of follicular ducts.[70]

Pharmacological activity

1. antimicrobial properties of azelaic acid,
2. anti-inflammatory effects
3. Anti-keratinizing agent.

Adverse events**Conclusion**

By reducing the number of lesions, sebum production, the severity of the pathology, and porphyrin production, as well as by improving participants' quality of life in several studies, the evidence provided by the studies described suggests that herbal and phytochemical formulations can be effective in the treatment of acne vulgaris.