

Acne Vulgaris: An Organised Literature Review

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ABSTRACT: Acne vulgaris, which significantly affects a large number of people during puberty and is distinguished by adolescence, lowers a person's self-confidence by generating anguish with regard to physical appearance. The current study focuses on pathophysiology, differential diagnosis and a number of therapies have been developed to lessen the acne. Benzoyl peroxide, antibiotics, antiandrogen drugs, salicylic acid, alpha hydroxy acid, retinoids, azelaic acid, and other treatments are among the many ones used to treat acne. Because they have fewer negative effects than synthetic drugs, the chemicals in topical acne treatments, particularly herbs and organically derived substances, have received a lot of attention.

KEYWORDS: Acne vulgaris, pathophysiology, diagnosis, treatments etc.

I. INTRODUCTION

Acne vulgaris is a condition of the pilosebaceous unit that results in non-inflammatory lesions, such as open and closed comedones, inflammatory lesions, such as papules, pustules, and nodules, as well as scarring of varied degrees. Acne vulgaris is a disorder that affects a lot of people and is most prevalent throughout adolescence, with a lifetime frequency of about 85%.^[1] It affects the face, neck, upper chest, upper back, and other areas. Both psychologically and psychosocially, it has an impact on the patient.^[3] Four major pathogenesis are involved in the development of androgen-induced increased sebum hyperproduction, altered follicular keratinization, inflammation and Bacterial colonization. It is also impacted by environmental pollution, societal factors, dietary and lifestyle changes, such as worsening air pollution, eating sweets, staying up late, etc.^[2] About 85% of the population suffers from acne, which is more common in people between the ages of 12 and 24.^[3]

➤ Types of Acne:

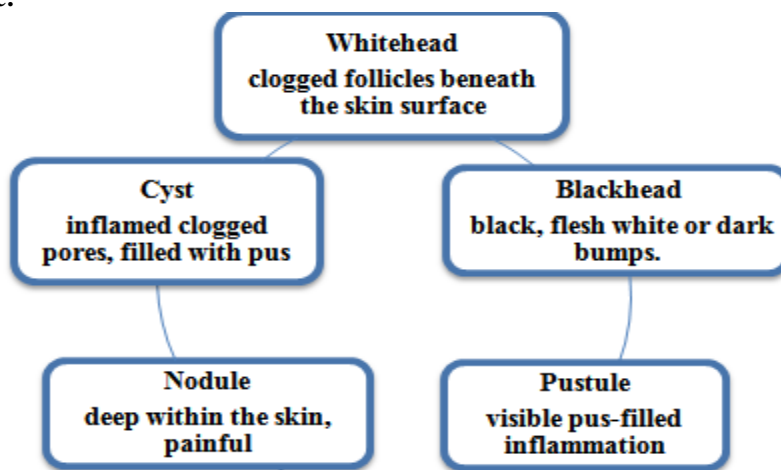


Fig1. Types of acne

➤ **Pathophysiology:**

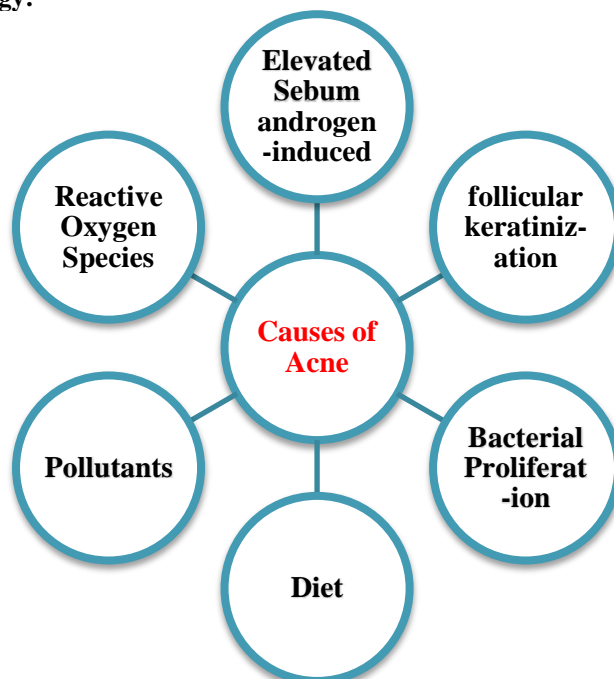


Fig2. Causes of acne

1. Elevated Sebum Production:

Holocrine glands called sebaceous glands are present throughout the body's surface, with the exception of the palms, soles, and dorsum of the feet. They are most abundant on the face and scalp, which are where acne first appears. Sebum is a complex mixture of oils that includes triglycerides and products of fatty acid breakdown, wax esters, squalene, cholesterol esters, and cholesterol. The typical function of sebaceous glands is to create and secrete sebum. Sebum lubricates the skin to prevent abrasion and increases its moisture resistance. Moreover, the sebaceous gland has a natural light protection action and transfers antioxidants into and onto the skin. The development of acne is strongly correlated with increased sebum secretion, altered lipid composition, and the oxidant/antioxidant ratio typical of the lipids on the skin's surface. Pore blockage may occur as a result of sebum interfering with the follicular keratinization process in the pilosebaceous unit, which can lead to the development of lesions and acne. Sebocytes' biological function is further influenced by a number of substances, such as histamines, retinoids, and vitamin D, as well as the ligands of receptors expressed in sebocytes, such as androgens and oestrogens, PPAR ligands,

neuropeptides, and liver-X receptor ligands (LXR).^[4]

Sebaceous gland function is intricately regulated by hormones. The pilosebaceous units are managed by a hormonal interaction. The most significant androgen is testosterone, which is transformed into dihydrotestosterone by the isoenzyme type 1 5-reductase. The primary nuclear androgen, DHT, is ultimately in charge of the sebaceous gland's enhanced sebum production.^[5]

2. Follicular keratinization

An important element in the emergence of acne is follicular hyperkeratinization. It goes by a number of names, such as ductal hypercolonisation and retention hyperkeratosis. Acne's pathophysiology depends heavily on follicular hyperkeratinization, which is also where retinoids are most active. The follicle's cells become cohesive and stop shedding properly onto the skin's surface, leading to retention keratosis. Microcomedones, which are acne's precursors, are the end outcome. Early ductal hyperconicitation is followed by follicular enlargement, which allows keratinized cells, sebum, and Propionibacterium acnes to occupy the space.^[6]

For the precise reason why, follicular plugging and follicular hyperkeratinization occur, a number of views have been put forth. According to

one hypothesis, the follicle has a deficiency in linoleic acid, an important fatty acid. Linoleic acid levels and sebum secretion have been demonstrated to be inversely correlated. Because of these lowered linoleic acid levels, follicular hyperkeratosis and impaired epithelial barrier function may be brought on.^[6]

One such hypothesis is that the follicle is lacking in epidermal lipids. The epidermal lipids are essential for increasing water binding and performing as a barrier. Corneocyte desquamation appears to depend heavily on the conversion of cholesterol sulphate to cholesterol. The enzyme steroid sulphates, which is necessary for this process but may be genetically reduced and cause retention hyperkeratosis, is necessary but insufficient.^[6]

3. Bacterial Proliferation

The largest organ of the body, the human skin, is made up of several important microbial genera linked to healthy skin, including *Staphylococcus*, *Propionibacterium*, *Streptococcus*, *Corynebacterium*, and *Malassezia*. In particular, the Gram-positive anaerobic bacterium *Propionibacterium acnes* is a major resident of the normal human skin microbiota and dominates pilosebaceous units.^[7] The skin of the face, chest, and back has sebum-rich follicles that *P. acnes* colonises. Propionic and acetic acids are produced by the exclusively anaerobic gram-positive fine rod *P. acnes*.^[5] The bacterium *Propionibacterium*, also known as *Cutibacterium*, is what causes skin irritation. *P. acnes* breaks down the triglycerides in sebum to liberate free fatty acids, which in turn triggers an inflammatory response and causes acne to develop. TLR2 is activated by *P. acnes*. Toll-like receptors (TLR2) are a part of the body's inherent defence mechanism.^[8]

4. Diet

In the study of acne epidemiology, the link between nutrition and acne has been a hot topic. Dairy products and a high-sugar diet are currently recognized as acne risk factors by numerous research. Consuming more sugar (>100 g/d soft drinks (such as carbonated sodas, sweetened tea drinks, and fruit-flavored drinks), and daily dark chocolate consumption were all significantly positively linked with acne. High glycemic load diets can cause blood glucose levels to rise, which causes islets to secrete large amounts of insulin to lower blood sugar. Elevated insulin levels then cause an increase in the secretion of insulin-like

growth factors (IGF-1), which can affect lipid excretion by increasing androgen levels, promoting sebum secretion, and promoting hyperkeratosis of hair follicle sebaceous glands. This can cause acne to develop or worse.^[2]

The health of your skin depends on vitamin A. Dry skin, dry hair, and broken fingernails are some of the earliest signs of vitamin A insufficiency. Vitamin A deficiency also results in incorrect visual adaptation to darkness and has a significant impact on cutaneous biology. Minerals like zinc, copper, and iron, which are known to affect anti-inflammatory enzymes like desaturases and lipoxygenases, are a different category of nutrients that come from diet.^[9]

5. Pollutants

Living things are subject to air contaminants, which have a significant impact on human skin. Particulate matter, liquids, gases, and solids can all be contaminants of the air. They are either taken up directly via the skin into the subcutaneous tissue or by sweat/sebaceous glands and hair follicles. Solar UV rays, polycyclic aromatic hydrocarbons, volatile organic compounds, nitrogen oxides, particulate matter, cigarette smoke, heavy metals, and arsenic are the main air pollutants that have an adverse effect on skin.^[10]

Chloracne is a type of acne that can be brought on by environmental toxins. Chloracne is caused by systemic exposure to certain halogenated aromatic hydrocarbons 'chloracnogens'.^[11]

By causing more oxidative stress, which undermines the skin's antioxidant defences, air pollutants have a negative impact on the skin. The lipid peroxidation reaction cascade is started when free radicals and reactive oxygen species contact with the plasma membrane, which is rich in lipids. Reactive oxygen species also promote the release of pro-inflammatory mediators, which in turn leads to the buildup of neutrophils and other phagocytic cells, which then produce more free radicals, creating a vicious cycle.^[10]

6. Reactive oxygen species




The hypercolonization of *P. acnes*, as well as metabolism in living things and exposure to UV light, produce reactive oxygen species (ROS). The skin barrier protects against acne-causing bacteria attributed in part to ROS, but overproduction worsens skin condition by triggering neutrophil infiltration. Inflammatory acne as well as tissue damage are both caused by ROS, which include





singlet oxygen, superoxide anion, hydroxyl radical, hydrogen peroxide, lipid peroxide, and nitric oxide (NO). ROS encourage the production of TNF, NF- κ B, and NF-k β , which in turn activates keratinocytes and T lymphocytes. Then, transforming growth factor (TGF), prostaglandin (PG), lipopolysaccharide (LPS), interleukin (IL), tumour necrosis factor (TNF), and interferon (IFN) are created. In conclusion, CD4+ in T cells trigger skin inflammation, TLRs control it after neutrophil infiltration produces ROS, and protease enzymes






cause the follicular wall of sebaceous glands to burst. As a result, linoleic acid and other components of sebum are altered. Desquamation is decreased and hyperkeratinization is started. Microcomedones are then produced as a result of the production of the pro-inflammatory cytokines NF- κ B, IL, TNF, IFN, LPS, TGF, PG, and GM-CSF. Microcomedones that occur from this process grow into comedones and inflammatory lesions.

II. SOME TRADITIONALLY USED HERBS FOR TREATING ACNE

Table 1: some traditionally used herbs for treating acne

SR. NO	COMMON NAME	BOTANICAL NAME AND FAMILY	PARTS USED	CHEMICAL CONSTITUENTS
1	Tulsi 	Ocimum sanctum L. Labiatae	Leaves	Eugenol, Ursolic Acid, Carvacrol, Rosmarinic Acid, A & B- Caryophyllene etc. ^[13]
2	Tea tree 	Melaleuca Alternifolia Myrtaceae	Leaves	Terpinen-4-ol, γ -Terpinene, α -Terpinene, ρ -Cymene etc. ^[14]
3	Papaya 	Carica papaya Caricaceae	Fruit	p-hydroxybenzoic acid, salicylic acid, hyperoside, gentsyl alcohol, trigalloyl glucose etc. ^[15]

4	<p>Turmeric</p> 	<p>Curcuma longalinn. Zingiberaceae</p>	<p>Rhizome</p>	<p>Curcumin, 8,9-Dehydro-9-formyl-cycloisolongifolene, dihydrocostunolide, velleral, and germacrone etc.^[16]</p>
5	<p>Neem</p> 	<p>Azardirachta Indica Meliaceae</p>	<p>Leaves</p>	<p>Nimbin, Gedunin, Salannin, and Quercetin, Nimbidol Etc.^[17]</p>
6	<p>Aloevera</p> 	<p>Aloe barbadensis miller Liliaceae</p>	<p>Leaves</p>	<p>Beta-carotene, Anthraquinone, vitamin B12, folic acid, beta-(1,4)-acetylated mannan etc.^[18]</p>
7	<p>Orange lentils (Masur dal)</p> 	<p>Lens culinaris Legumes</p>	<p>Seed</p>	<p>a-galactosides, Niacin, Pantothenic acid, Pyridoxine, α-tocopherol and β and γ-tocopherols etc.^[19]</p>
8	<p>Nutmeg (Jaiphal)</p>	<p>Myristicafragrans Myristicaceae</p>	<p>Seed</p>	<p>Sabinene, 4terpineol, myristicin, safrole, eugenol, Limonene, β-ocimene etc.^[20]</p>

				
9	<p>Indian sandalwood (Chandan)</p> 	<p>Santalum album Santalaceae</p>	Bark, root	<p>α-Santalol, β-santalol, α-bergamotenol, epi-cis-βsantalol, cis-lanceol, β-bisabolol, hydrocarbons like α-santalene, β-santalene, epi-β-santalene, αbergamotene etc.^[21]</p>
10	<p>Orange peel</p> 	<p>Citrus sinensis Rutaceae</p>	Fruit, peel	<p>α-Pinene, Linalool, Citronellal, β-Citral, p-Mentha-1,8-dien-9-ol, α-Farnesene, β-Sinensal, α-Sinensaletc.^[22]</p>
11	<p>Manjishta (Indian Madder)</p> 	<p>Rubiocordifolia Rubiaceae</p>	Bark, root	<p>Cordifoliol, Cordifodiol, Purpurin, Alizarin, Rubiasins A–C (1–3), Rubicoumaric acid and Rubifolic acid etc.^[23]</p>
12	<p>Mint leaves</p> 	<p>Menthapiperita Lamiaceae</p>	Leaves	<p>Menthol, Menthone, Menthofuran, is-carane, 1,8-Cineole, Neomenthol, limonene, trans-caryophyllene, β-Pinene, α-Pinene etc.^[24]</p>

III. CLASSIFICATION OF ANTI-ACNE DRUGS

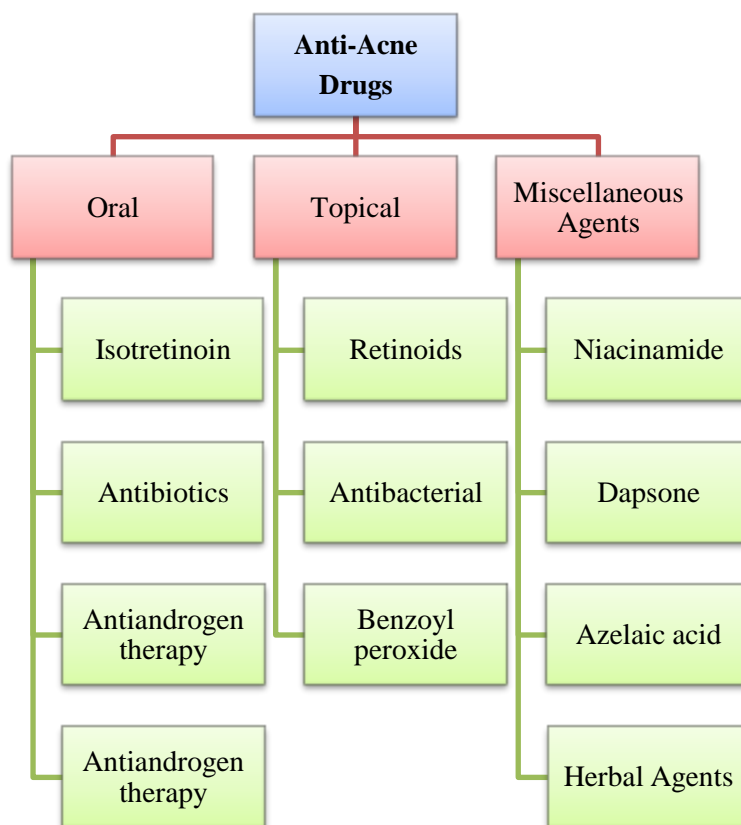


Fig 3. Classification of Anti-Acne Drugs

Over the Counter Acne Treatments:

Many people buy over-the-counter (OTC) products marketed for AV from pharmacies, the internet, retail stores, and skin care/cosmetic centers, which have sizable sections intended to draw customers with skin-related needs, including OTC treatments for AV. These products are often used to seek advice or to self-treat.^[25] However, all treatments for AV are theoretically designed to target one or more of the pathogenic pathways involved in the development of AV lesions. OTC acne treatments, commonly referred to as "cosmeceuticals," come in lotions, creams, washes, kits, scrubs, brushes, and devices. Due to the enormous number of different OTC brands, plus newer products constantly being developed, it is hard for both physicians and patients to keep aware of the numerous products. These processes are often broken down as follows:^[26]

1. Increased sebum production,
2. Aberrant follicular keratinization (microcomedo development),
3. Propionibacterium acnes proliferation, and
4. Inflammation.

Facial cleansers:

Getting rid of undesired debris, germs, and dead skin cells through cleansing is a significant aspect of maintaining personal hygiene and wellness.^[26] A cleanser can be used in association with other dermocosmetics as part of a skin care routine. Lipid-free cleansers, synthetic detergents (syndets), astringents, exfoliants, or mild abrasives are among the cleansers used for acne. They might be in the form of cleaning bars or liquid.^[27] Since the introduction of synthetic detergents (syndets) into both bar and liquid cleansers, genuine soap has developed into much more than a cleaning agent. Soap-free skin cleansers are currently promoted to reduce skin's look of ageing, soften skin, and enhance general skin health.^[26]

Hydroxy acids:

Hydroxy acids can be divided into two major categories: α -hydroxy acids (AHA) and β -hydroxy acids (BHA). α -hydroxy acids (AHA). AHAs are -hydroxy acids. Glycolic, lactic, and citric acids are among the AHAs, a class of hydroxy acids. AHA acts as an exfoliant at lower doses, preventing corneocyte adhesion in the upper SC by interfering with the formation of ionic connections. Therefore, by encouraging individual corneocyte desquamation and minimizing corneocyte clumping, AHAs lead to finer skin texture and less visible scaling and flaking. AHAs that are present in higher quantities (8–10%) can thicken the dermis as well as cause epidermolysis. In patients with many and/or chronic closed comedones, a brief exposure to glycolic acid at concentrations of 30 to 70% is widely utilized in superficial peeling, which may be a useful adjuvant treatment.^[26] β -hydroxy acids. Salicylic acid, the only β -hydroxy acid that is used in dermatological practice, it is a highly frequent active component in a variety of over-the-counter (OTC) acne cleansers, astringents, and lotions. Salicylic acid has mild comedolytic action and induces individual corneocyte desquamation, which mimics natural exfoliation, due to its desmolytic qualities.^[26]

Benzoyl peroxide:

A crucial part of treating acne vulgaris is the organic acid benzoyl peroxide (BP), which belongs to the peroxide family.^[26] For patients with mild to severe acne that is non-inflammatory, tretinoin, and antibiotics are recommended. Based on the anticipated synergistic impact owing to distinct modes of action, BPO has been utilized both alone and in combination with antibiotics or retinoids. Combining BPO with antibiotic therapy may slow the spread of *P. acnes* that is resistant to antibiotics.^[28]

Azelaic acid:

Azelaic acids that are present in nature include comedolytic action, antibacterial capabilities against *P. acnes*, including the ability to restore normal keratinization, anti-inflammatory effects on neutrophil function, and skin-lightening qualities. A combination of azelaic acid and other anti-acne medications, especially benzoyl peroxide, improved results in addition to a single therapy. Azelaic acid is further less irritant and phototoxic, making it a safer substance. Azelaic acid resistance in *P. acne* has also not been documented.^[29]

Salicylic acid:

Salicylic acid was used to clear follicular blockage in a variety of formulations, most notably an alcoholic cleaning solution. Salicylic acid is a moderate keratolytic and anti-inflammatory drug that inhibits PG formation. When compared to benzoyl peroxide, this composition was more effective. Comparing salicylic acid to retinoids, it is a gentler substance. As their processes are different, combining salicylic acid and benzoyl peroxide could lead to better therapy outcomes. Salicylic acid skin peeling, in addition to acting as a purifying agent, was discovered to significantly decrease comedones.^[29]

Sunscreen skin care products:

UV light is one of the key external environments that affects the skin and is linked to the development and aggravating causes of acne. According to certain research, UV exposure can increase sebocyte proliferation, sebum production, and the release of inflammatory cytokines, all of which contribute to the growth and worsening of acne lesions. Skin care products with sunscreen can lessen the impact of UV radiation on the skin's barrier, lessen the negative effects of standard treatment medications, and lessen skin pigmentation following inflammation. Additionally, the moisturizing component included in sunscreen can enhance skin barrier performance.^[30]

Moisturizing skin care products:

The term "moisturizing skin care products" refers to a category of skin care items that can improve the epidermis' moisture content, aid in the skin barrier's recuperation, lessen dryness and desquamation, and smooth the skin. Some moisturizers contain plant-based anti-inflammatory ingredients and acne-specific local medications. The new generation of humectants contain substances that are similar to the human sebum membrane (such as ceramide and squalene), which can replenish the lipids between cells and on the surface of the cuticle. They can also quickly penetrate into the skin's cuticle to combine with water and lock in the water, which enhances the function of the skin barrier. Benzoyl peroxide, topical retinoids, oral isotretinoin, photodynamic therapy, chemical exfoliation therapy, laser therapy, and other acne treatments can create infiltration barriers that harm the stratum corneum, accelerate the rate at which the epidermis loses water, result in dryness and inflammation of the

skin, and increase skin sensitivity. A moisturizer can increase skin hydration, preserve the integrity of the cuticle permeability barrier, and encourage and speed up the physiological cuticle healing process.^[29]

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