WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Acne Vulgaris: A Comprehensive Review of Emerging Therapeutic Strategies

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ABSTRACT:

Acne Vulgaris (*Busoore Labaniya*) is a chronic inflammatory skin disease that targets the skin's pilosebaceous units.It can have serious psychological implications and leave the patient with significant skin scarring. Acne is caused by four well-known pathogenic causes, all of which are potential targets.This review critically examines diverse therapeutic modalities employed in the management of acne vulgaris, encompassing topicaltreatments like retinoids and antibiotics, as well as systemic strategies like hormonal therapies, oral retinoids, and systemic antibiotics. The disease mechanism and available treatments for acne have been thoroughly studied. However, as Propionibacterium acnes becomes more resistant to available antibiotics, new treatment methods are required. There has been a marked increase in public preference for natural and perceived safer therapeutic alternatives.Accordingly, this review further explores the role of Unani medicine as a complementary approach in the management of acne vulgaris.The purpose of this review is to give an informative overview of Acne vulgaris (Busoore Labaniya), including its introduction, etiology, classification, clinical features, investigation, differential diagnosis, diagnosis, and management in Unani and modern medical care. Additionally, this review aims to assess the effectiveness and safety of acne vulgaris treatments as described in traditional Unani medical literature.

Keywords: *Busoore Labaniya*,Unani Medicine, Antibiotic Resistance, Herbal Therapies, Acne vulgaris

INTRODUCTION

Acne vulgaris, traditionally known as *Basoore Labaniya*, is a chronic inflammatory disorder of the pilosebaceous units that affects individuals worldwide. It ranks among the most prevalent dermatological conditions, with an estimated global prevalence of 9.4%. Although this pleomorphic skin disease can manifest at any stage of life, it predominantly affects individuals between the ages of 12 and 24, with over 85% of adolescents experiencing clinically significant acne during this period.[4]Acne is a dermatological disorder that affects the pilosebaceous units, primarily manifesting on the face, neck, and shoulders and upper back, as outlined by the World Health Organization (WHO).Acne is not life-or detrimental to the body, Acne may negatively impact a patient's quality of life (QOL) by impacting their social and psychological functioning, even while it is not physically harmful or life-threatening. [4]

Busoore Labaniya in Unani derives its name from two Arabic terms—"*Busoor,"* meaning "boil," and "*Labaniya,*" meaning "milk". In classical Unani texts, it is characterized as a Mutaddi (Infectious) condition marked by tiny white papules on the face, particularly the nose and cheeks, which release a cheesy discharge when compressed.[7]. Ibn Sina, in his book*Al-Qanun fit Tib*, similarly describes these lesions as resembling drops of condensed milk on the nose and cheeks.[5,8] Hakim Ajmal Khan further notes that, upon maturation, these bright red, firm papules on the face, neck, cheeks, and nose expel comedones and purulent material.[9]

Synonym

- **Arabic** - *Busoore Labaniya*[7, 10, 11, 12]
- **Urdu** - Muhase, Dane,Funsi[10, 13, 14]
- **Hindi** - Kil, Muhase[13, 15,17]
- **English** - Acne [16, 18], Pimples [19]
- **Ayurveda** - *Yuvana Pidaka*[20]

- **Persian** - *Ru'khara*[14]
- **Sanskrit** - *Mukhadushika*[18]

HISTORICAL REVIEW

Skin diseases have existed since antiquity and have been referred to by various names around the world. *Busoore Labaniya*has a very long history. *Busoore Labaniya* is a severe skin disorder, described since ancient times in classical Unani literature. It predominantly affects adolescents and young adults, who are especially vulnerable to the psychological and the most vulnerable to any effects of facial disfigurement. Acne has been recognized as a condition since ancient times, with documented cases among early civilizations such as the Greeks, Romans, and Egyptians.

The History of Acne in Egypt:

It has been noted that pharaohs in ancient Egypt suffered from it and attempted to find a solution. It is known that a number of pharaohs suffered from acne. Ebers' papyrus describes how it is treated using honey and some preparations of animal origin.[20]

Greece's History of Acne:

The term *acne*, derived from the Greek word meaning "point" or "peak," has its origins in ancient Greece,the earliest documented description is attributed to the physician Aetius Amidenus From the historical background.Renowned Greek scholars such as Hippocrates and Aristotle were also aware of the condition, with Aristotle providing a detailed explanation of its features.[20]

Acne in Rome History:

In ancient Rome, acne was reportedly treated with a basic sulphur preparation used in mineral baths, as documented by Aulus Cornelius Celsus (25 BC–50 AD) in his surviving medical text *De Medicina*.In the 4th century AD, Theodosius' physician recommended that individuals with acne wipe their lesions using a cloth while observing a shooting star, and the acne would *'fall from the body'*. The term 'acne' was introduced by Aetius, the physician of Emperor Justinian. Prior to this, Galen had used the term 'ionthoi' to describe what may have been multiple distinct conditions. He also recommended different treatments based on the texture and characteristics of the lesions, indicating an early attempt to differentiate between types of skin. [20]

Acne in Unani Medicine:

Unani scholars have identified a skin disorder called *Basoore Labaniya*, which closely resembles the modern condition known as acne vulgaris.

- In his book *'Firdous al-Hikmat'* (paradise of wisdom), Rabban Tabri provided a detailed explanation of sebaceous glands.[21]
- Thabit ibn Qurrah al-Ḥarranidescribed various Unani compound formulations for treating funsi(acne) on the face.[22]
- In his authoritative compendium *Al-Hawi* (*The Virtuous Life*), by Zakariyya' al-Razi systematically outlined the therapeutic approaches for *BasooreLabaniya*, closely resembling acne vulgaris,thereby contributing significantly to early understandings of acne management in Unani medicine.[23]
- *Ibn-Sina* described in his book *Al-Qanun fi'l Tib* (The Canon of Medicine), the clinical presentation and etiopathogenesis of Busoore Labaniya(Acne vulgaris).He described *Busoore Labaniya* as resulting from *Madda Sadidiyah* (suppurative matter) being expelled through the skin, in association with *Ghaleez Bukharat* (thick, morbid vapours).[5]
- *Ibn Hubal Baghdadi*describes in his book *'Kitab al-Mukhtarat fil tib'*, the cause and clinical presentation of *Basoore Labaniya*.[24]
- According to *Abu Al-Hassan Jurjani's* in his compendium *Zakhira Khawarizm Shahi* (*Thesaurus of the Shah of Khawarizm*), morbid substances (*Madda Ba'd*) may become mixed with healthy humors to mitigate their harmful effects. However, when the healthy humors are eliminated from the body through the process of Istafragh(evacuation), the remaining morbid humors (Maddah Ba'd) are directed toward the skin, leading to localized heat, swelling, or the development of *Busoor* (cutaneous eruptions).[25]
- *Daud Ibn Umar al-Antaki* explained in his famous book '*Tadhkirah-Ul-Albab*' about the filthy Madda Balghamiya cause of *Basoore Labaniya*.[26]
- *Muhammad Akbar Arzani's* treatise "*Mizan al Tib*" identified Khilt Balgham as the primary cause of *Basoore Labaniya*.[27]
- According to *Mohammad Azam Khan* and *Ḥakim Azam Khan* explains that *Madda Sadeedi* (purulent matter) is generally identified as the primary etiological factor responsible for the development of *Busoore Labaniya* (milky pustules) [28].
- According *to Hakim Ajmal Khan's* book "*Haziq*," the causes of this condition include poor personal hygiene, menstrual disorders, and unhealthy eating habits. He also stated that acne varies in size, with small hard tumors on the skin of the face curdling up with a hard, thick fluid. They affect children and are around the size of a hemp seed.[9,18]

Acne in the Elizabethan Era:

The appearance of a woman was given great attention during the Elizabethan era (1558-1603 AD).In historical Europe, women used layers of Venetian Ceruse—a thick white lead-based cosmetic—to achieve a pale complexion was symbol of the elite., inadvertently worsening acne. Mercury-based preparations were also applied to treat *Busoore Labaniya*(acne vulgaris).[20]

Riolanus (1638) and Johnston (1648) linked acne to menstrual disorders, with Johnston further associating it with heterosexual behaviour, reflecting early psychosomatic views.He also quoted that acne are different in size, little hard tumours on the skin of the face curdled up of a hard-thick fluid.Acne primarily affects young individuals and is typically the size of a hemp seed.[28-31]

In 1840, Fuchs introduced the term "Acne vulgaris" and categorized acne into three types: Acne vulgaris, Acne mentagra, and Acne rosacea.

In 1842, Erasmus Wilson distinguished between acne simplex (Acne vulgaris) and acne rosacea. That same year, Gustav Simon proposed that acne primarily affects hair follicles and was among the first to identify *Demodex folliculorum* (acarus), suggesting its potential role in the condition's development. [20]

In 1930, laxatives were commonly used to treat acne. By 1950, tetracyclines were introduced after bacteria were identified as a cause. Retin-A, a topical treatment, was developed in the 1960s. criticized the FDA's 1975 endorsement of sulfur-based products. In 1980, isotretinoin was launched but caused serious side effects. Laser therapy, introduced in 1990, effectively treats both acne lesions and scars. In 2000, laser and blue/red light therapies emerged. Dermaroller micro-needling gained popularity for scar treatment. In 1995, Orentreich introduced subcision for scars, and Fernandes developed collagen induction therapy in 2006. In 2007, a vaccine showed promise in mice, but human trials are still needed [20].

EPIDEMIOLOGY

Acne is a common skin disorder, affecting over 80% of adolescents [32, 33], with approximately 681.2 million cases globally in 2016—an increase from 612 million in 2006. It ranked as the eighth most common disease worldwide in 2010, with 645 million cases [35].Acne affects 80% of people aged 12-18, 5% of adult females, and 1% of males.

Halvorson et al. found that males with severe acne were three times more likely to experience suicidal thoughts than those with mild acne [36]. A study in Saudi Arabia showed that acne is more prevalent in higher socioeconomic groups [37]. The U.S. spends around three billion dollars annually on treatment and lost productivity [38]. Acne, while often seen as a normal part of adolescence, causes significant emotional, psychological, and physical distress. Around 60% of teens have mild acne and use over-the-counter treatments, while 40% seek medical help, with 20% of them suffering from severe acne and scarring [40, 41, 42]. The increased adult prevalence is likely due to greater healthcare reporting and awareness.

Etiopathogenesis

According to Unani physicians, *Busoore Labaniya*(Acne vulgaris) is a chronic inflammatory disorder involving the Ghudud-e-Duhaniya (sebaceous glands) of the skin,it is primarily caused by the hyperactivity of these sebaceous glands, leading to an increased secretion of oily substance (*sebum*), which obstructs the glandular apertures. This blockage causes the glands to become inflamed, resulting in suppuration and the formation of pus *Madda Sadidiya* (purulent matter).[42]

Another classical viewpoint is that the condition is caused by a yellow, pus-like substance called Madda-e-Sadidi, which penetrates the skin as the outcome of Ifrat-e-Hararat (abnormal heat). This pathological heat draws up Bukharat-e-Badan (internally vapours) towards the surface of the skin. Where they condense into a thick, whitish discharge. Due to the density of this accumulated material, it becomes more difficult to expel out from the clogged pores, thereby exacerbating the lesion formation [6,7,17,24,5,43].

Adolescents are particularly susceptible to *Busoor Labaniya*, which manifests clinically as whitish pustules or spots on the face. These lesions are the result of the body's attempt to expel the *Madda Sadidiya* via the skin, influenced by the increased internal heat and vapour accumulation at the surface level [43,24,44,45,9,13].

Pathology of Acne

Acne damages the skin's pilosebaceous units, resulting in a range of lesions at different stages of inflammation, such as hyperpigmentation and scars from acne. [46, 47] The face, chest, upper back, and upper arms are known to have a high concentration of sebaceous glands, which is the reason acne lesions are most frequently found there. [48] The four primary pathological elements that contribute to acne development are (i) Hyperkeratinization of the hair follicles, (ii) excessive sebum production by the sebaceous glands, (iii) colonization of Propionibacterium acnes in the pilosebaceous ducts, and (iv) skin inflammation resulting from the release of inflammatory mediators.

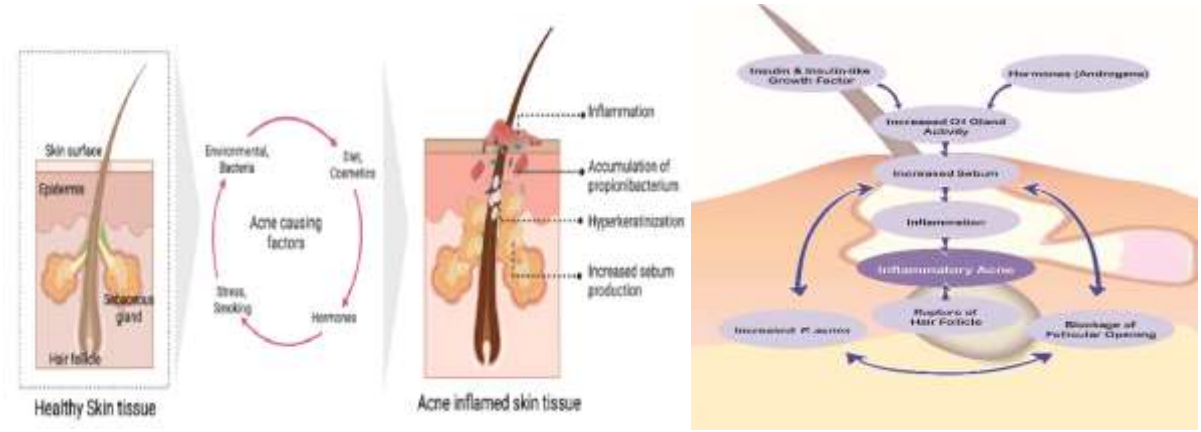

Fig. 1.Diagrammatic representation comparing healthy/normal skin tissue with acne-inflamed skin tissue, highlighting multiple contributing factors involved in the onset and progression of acne.

Acne vulgaris causes aberrant desquamation of epithelial cells and follicular blockage due to androgen production, which results in the formation of microcomedones. Microcomedones cannot be seen with the naked eye, but they gradually turn into noticeable lesions. Increased sebum production during puberty is linked to higher levels of androgens in the blood. Consequently, lipid-rich material is loaded into follicles, producing open and closed comedones that are visible. Because sebum is a great environment for bacteria to thrive, P. acnes spreads quickly. The chemical mediators generated by P. acnes are primarily responsible for generating inflammation, which plays an important role in acne development. Moreover, the constant production of sebum and keratin causes comedones to rupture and enter the dermis, resulting in inflammation. This dermal irritation causes papules, pustules, nodules, and cysts. Furthermore, extreme inflammation causes scarring. [49,50,51]

Physical and Environmental Factors that Influence Acne

Diet :A study suggested nutrition as a cause of acne.[52] Another study examined students' awareness of acne causation and concluded that oily diet was the primary factor.[53]The study revealed a link between milk consumption during adolescence and a past occurrence of teenage acne. This association could be explained by the presence of hormones and bioactive compounds in milk. [54] Milk contains placental-derived progesterone and DHT precursors, including 5α-pregnenedione and 5α-androstenedione. These molecules represent only a few biochemical steps removed from DHT, the primary acne stimulant, and the enzymes needed to mediate the shift are found in the human pilosebaceous unit.[55] An alternate hypothesis explaining the link between milk and acne proposed that milk's iodine content may also play a role in acne development.[56]It is thought that high glycemic indices cause hyperinsulinemia and a subsequent cascade of endocrine effects, including increased androgens, elevated IGF-1, and altered retinoid signalling pathways, which affect acne.[57]

Premenstrual flare: Acne can also be caused by puberty and menstruation. As androgen levels rise during puberty, follicular glands enlarge and sebum production rises as well. The effects of anabolic steroids are comparable. Acne pathogenesis has been linked to androgens, including insulin-like growth factor-1 (IGF-1), dehydrotestosterone sulphate (DHEA-S), testosterone, and dihydrotestosterone (DHT). [58]

Environmental elements: It is made up of several components, including high humidity, constant sweating, increased skin hydration, exposure to filth or vaporized frying oil, and particular substances like petroleum derivatives. Up to 20% of acne patients report that sweating exacerbates their acne, particularly if they live or work in a hot, humid environment, inadequate hydration may be the cause for a cook. [59]

Occupation: Acne can be caused by ductal stratum corneum hydration in occupations like catering and steam cleaning. Patients with oil may develop acneiform oil folliculitis, particularly on their trunks and limbs; however, their entire body must be highly contaminated.[59]

Psychosocial repercussions of acne: According to older literature, stress alone is unlikely to cause the creation of new acne lesions.[60] Acne itself causes tension, and picking at the patches will increase the appearance.[61] Acne excorie was more common in adolescent girls who were under emotional stress and picked at their adolescent acne vulgaris. The disorder is frequent and typically self-limiting.[62]

Table 1: Acne Myths/Misconception Vs Study Result.

Myth/Misconception	**Study Result**
	Dark chocolate consumption appears to affect the facial skin of Young men by enhancing corneocyte desquamation and promoting bacterialcolonization of the residual skin surface components.[64].

In particular, no conclusive effect has been established between the consumption of chocolate, dairy products, shellfish, or fatty foods and the development of acne vulgaris [63].	Several dietary factors have been explored for their potential role in the pathogenesis of acne vulgaris. Dairy products such as milk, yogurt, and cheese have been associated with an increased odds ratio for acne in individuals aged 7–30 years.[65].
	A four-ounce serving of shrimp contains approximately 325–375 milligrams of omega-3 fatty acids.[66] Notably, supplementation with omega-3 fatty acids for a duration of 10 weeks has been associated with a significant reduction in both inflammatory and non-inflammatory acne lesions.[67]
	Isotretinoin, Retinol (Vitamin A), carotenoids (provitamin A) and retinoids(Vitamin A metabolites) are absorbed better with Parallel intake of vegetable oils.[68]
Both weight loss and the use of metformin have been associated with lower plasma insulin levels and decreased androgen levels, which in turn may contribute to a reduction in acne severity.[70]	Low glycaemic loads, with or without metformin, has been associatedwith greater reduction in acne lesion counts compared with high loads.[69].
There were no significant correlations between IGF-1and acne severity[70].	Plasma levels of insulin-like growth factor 1 (IGF-1) have been shown to positively correlate with the severity of acne.[71]
Too much sex or masturbation may worsen acne. When females begin having a regular sex life their acne will be improved [72] [63]. It has been suggested that masturbation may lead to general weakness, pale eyes, and acne on the forehead [73]. though these claims lack strong scientific support	Despite popular myth, diet, lack of exercise, lack of hygiene, greasyhair hanging over the face, and masturbation do not have any effect. After adjustment for sex and age, the presence of acne remainedhighly associated with less sexual activity [74].
open comedones or blackheads are full of dirt.[75]	The dark color of blackheads is not caused by dirt; instead, it results from the oxidation of melanin in the skin when exposed to oxygen, as blackheads of this type are 'open' Comedone.[76]
One should pop pimples at first sight.	Although squeezing pimples may provide temporary improvement in appearance, it can push the pus deeper into the skin, potentially leading to increased inflammation and a higher likelihood of the area becoming discolored during the healing process [76].
Sitting in the sun exposure helps clear pimples	Sunlight exacerbates acne vulgaris (AV), causing acne solaris, which relapses after sun exposure; clinicians should offer individualized advice on diet, hygiene, face-washing, and sunlight rather than being overly prescriptive [77].

Clinical Presentation : Classical Unani physicians have documented that this condition predominantly affects adolescents, with a higher incidence observed in males [6]. It is characterized by lesions resembling milk droplets, commonly distributed over the face, forehead, nose, and arms. Additionally, it may be accompanied by *Ihtibas Tams* (amenorrhea) in some cases [14, 24, 45].

SITES: Acne is a polymorphic disease that primarily affects the face (99%) but also affects the back (60%) and chest (to a lesser extent) (15%). Acne affects 8% of 25-34 years old and 3% of 30-44 years old, despite the fact that it is typically an adolescent condition. Acne may appear on any hair-bearing skin, but some areas are more vulnerable than others.The affected areas have larger sebaceous glands and hair follicles with short terminal hairs. The face, especially the cheeks, jawline, chin, nose, and forehead, is most commonly involved. Back of neck, front of chest, back, and shoulders are other 'favoured areas.[78]

Acne lesions are polymorphic comprising comedones, papules, pustules, nodules, cysts, and scars. Post-inflammatory pigmentation and pyogenic granulomas may also become apparent..[79,80]

1. **Non-inflammatory lesion lesion:** Closed comedones(Whitehead) and Open comedones (Blackhead)

2. **Inflammatory lesion:** Papules, Pustule, Cysts and, Scars

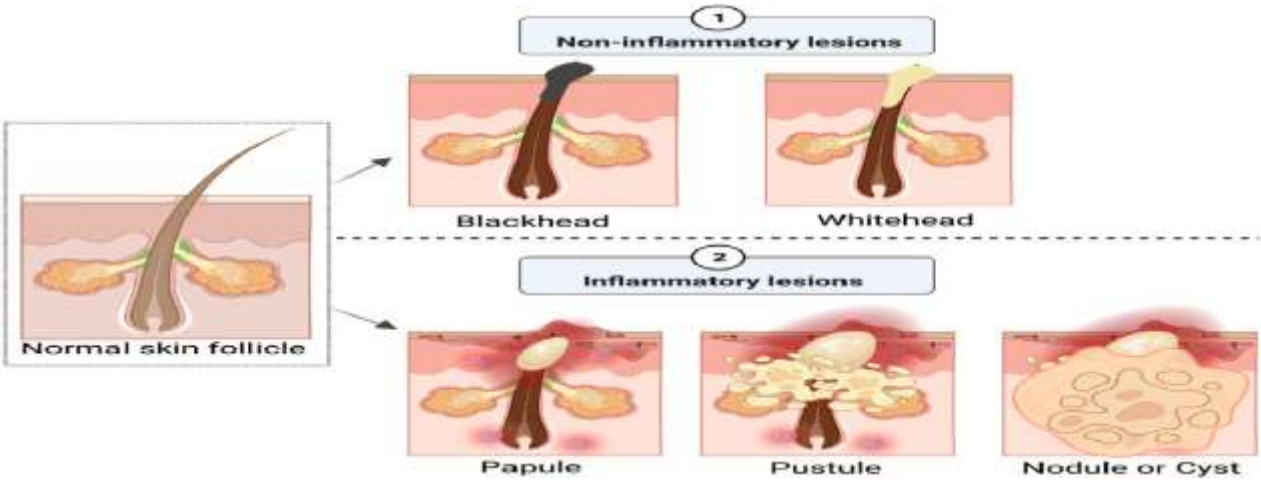

Fig. 2. A schematic illustration highlights the key differences between the two main types of acne lesions—non-inflammatory and inflammatory—along with their respective pathogenesis.

Microcomedone: A comedo is a plug of sebaceous and keratinous material lodged in the hair follicle opening. Initially, obstruction within the follicle is microscopic and cannot be perceived clinically; such lesions are termed as microcomedones..[81,82]

I. **Non-inflammatory lesions (Comedones):** Comedones are characteristic early non inflammatory lesions of acne. typically emerging 1 to 2 years before the onset of puberty.

Types of comedones: Comedones are pathognomonic lesions of acne vulgaris.

a) Closed comedones:

The closed comedones (Whitehead) are generally small (~1 mm), skin-coloured papules with no apparent follicular opening or associated erythema. These lesions may be subtle and better appreciated upon palpation, stretching, or side-lighting of the skin. [79,80]

b) Open comedones:

The open comedones (Blackheads) are have a conspicuous dilated follicular opening that is filled with an inspissated core of shed keratin. [82] Melanin deposition and lipid oxidation within the debris may be responsible for the black colour,it is not covered by the epidermis. [83,84]

c) Macrocomedones:larger than 1 mm

d) Sandpaper comedones:small but large number of closed comedones especially on the forehead.

e) Submarine comedones:large and deep.

f) Secondary comedones: Exposure to pomade(pomade acne), thick oils, chemicals (chloracne), topical steroids, and other drugs causes secondary comedones.

II. Inflammatory lesions

- **Papule:** The comedone ruptures, forming a persistent, deep papule resembling a small nodule (less than 5 mm in diameter). Superficial papules usually heal within 5–10 days, often leaving mild scarring and post-inflammatory hyperpigmentation. In contrast, deeper papules take longer to resolve and have a higher risk of scarring due to their severity.[80]
- **Pustule**: Pustules are lesions with a visible purulent center [66].They typically begin as solid papules, which then liquefy, marking a partial breakdown of comedones. The roof of the pustule often ruptures, allowing pus to escape. The fragmented comedo is expelled, and healing occurs similarly to that of a typical wound.[79]
- **Nodule**: A nodule in acne is a firm, painful, deep skin lesion larger than 5 mm, often lasting weeks and likely to cause scarring. when a comedo undergoes complete disintegration, often with widespread effects.
- **Cyst:** Acne cysts are soft, fluid-filled lesions caused by repeated rupture and re-encapsulation of comedones. Common on the trunk, they gradually enlarge and may rupture, leading to abscesses that often require surgical removal and may result in scarring. [85]

III. Scars: The final common pathway for the healing of inflammatory lesion of acne is scarring,. Acne scars are the second most common symptom after comedones. [86].

Table 2: Acne Scars[87-89]

Atrophic Scars	Atrophic acne scarring is a permanent complication most likely related to inflammatory mediators and enzymatic degradation of collagen fibers andsubcutaneous fat. Theatrophic acne scars into the following three main types: a) icepick, b) rolling and c) boxcar scars
(a) Ice pick	Ice pick scars are narrow (<2 mm), deep pits, sharply margined epithelial tract.
(b) Rolling	Rolling scars are caused by abnormal fibrous attachment of the dermis to the subcutaneous tissue results in superficial shadowing, giving the skin an undulating or rolling
(c) Boxcar	Boxcar scars can be superficial or deep which are round or oval depressions with well-defined vertical edges, resembling varicella scars.
Hypertrophic scars	Hypertrophic scars, which are less common, can develop on the chest, back, or shoulders, particularly in individuals with severe acne. They form when an overproduction of connective tissue occurs during the healing process.
Keloid Scars	Keloids are a result of abnormal wound healing following skin trauma or inflammation, characterized by an overproduction of connective tissue. Unlike hypertrophic scars, keloids extend beyond the original inflamed area. This type of acne scarring is very rare.

TYPES OF ACNE[90]

There are several subtypes of acne. Some of them occur because pf physiologic changes assoaciated with normal development.

1. **Neonatal and Infantile acne:**Comedones,papules and pustules in newborn are due to adrenal activity and androgen transfer from the mother and are usually transient.

2. **Infantile acne:** It presented with papules, pustules and comedones;starts at 3-6months and is seen usually in boys, such parents often give a history of acne and children are at risk for severe acne later. Infantile acne may heal with pitted scar.

3. **Mid-childhood acne:** It is observed in children aged 18 months to 7years.Acne in this age range is rare and systemic problems such as Cushing syndrome, premature adrenarche, congenital adrenal hyperplasia, gonadal/adrenal tumorsor true precocious puberty. These patients require an extensive endocrinological evaluation.

4. **Preadolescent acne:** This encompasses ages 8 to 12 years.Typically,comedones are evident on the face and neck, but are less common on the torso. This may be an indicator of emerging puberty.

5. **Adolescent acne:** This is acne or persisting >25 years and is seen most commonly in women. Tends to flare in the week prior to menstruation and up to the one-third of these women have hyperandrogenism. Typically, papulonodules on the lower face,jawline,and neck.

6. **Acne conglobata:** Cystic acne is the mildest form of acne conglobata (conglobate means shaped in rounded mass), an unusually severe type of acne. This form is characterized by numerous comedones (many of which are double or triple) and large abscesses with interconnecting sinuses, cysts, and grouped inflammatory nodules. Suppuration is characteristic of acne conglobate Pronounced scars remain after healing. The cysts occur on the back, buttocks, chest, forehead, cheeks, anterior neck, and shoulders.

7. **Acne fulminans or acne maligna:** Acne fulminans is a rare form of extremely severe cystic acne that occurs primarily in teenage boys. It is characterized by highly inflammatory nodules and plaques that undergo swift suppurative degeneration, leaving ragged ulcerations, mostly on the

chest and back. The face is usually less severely involved. Fever and leukocytosis are common. Polyarthralgia and polymyalgia, destructive arthritis, and myopathy have been reported in association with acne fulminans. Focal lytic bone lesions may be seen.

8. **Acne excoriée:** It is also known as picker's acne and acne excoriée des jeunes filles, excoriated acne is seen primarily in young women with a superficial type of acne. The primary lesions are trivial or even non-existent, but the compulsive neurotic habit of picking the face and squeezing minute comedones produces secondary lesions that crust and may leave scars.

Acne vulgaris can be associated with certain rare syndromes, including:

9. **SAPHO syndrome:** The SAPHO syndrome is characterized by synovitis, acne, pustulosis, hyperostosis, and osteitis particularly of the anterior chest wall. Skin findings may include acne fulminans, acne conglobata, pustular psoriasis, hidradenitis suppurativa, dissecting cellulitis of the scalp, Sweet syndrome, Sneddon-Wilkinson disease, and palmoplantar pustulosis.
10. **PAPA syndrome:** An autosomal dominant disorder, occurs due to mutations in CD2 binding protein-1 gene. It is characterized by sterile pyogenic arthritis, pyoderma gangrenosum, and acne.

Diagnosis

Diagnosis of Acne vulgaris (*Basoore Labaniyya*) is based on history and physical examination.It is based on:

- Adolescent patient.
- Background skin of face is greasy with prominent follicular openings.
- Polymorphic eruption of papules, pustules, nodules, and cysts; lesions heal with typical scarring.
- Presence of comedones (essential for diagnosis).
- Typical distribution: face, shoulders, upper part of trunk and chest. Lesions commonly found in the areas with the greatest concentration of sebaceous glands that include the face, neck, upper arms, and back.

Assessment of acne severity

Various ways of measuring the severity of acne include simple grading systems based on clinical examination, lesion counting, and the ones requiring complex instruments such as photography, polarized light photography, fluorescent photography, video microscopy, and measurement of production of sebum. The two commonly used measures are grading and lesion counting.

Table 3: Acne Grading severity [91]

Grade	**Severity**	Clinical Findings
I	**Mild**	Comedones, occasional papules
II	**Moderate**	Small papules with erythema indicate inflammatory lesions. Inflamed pimples are known as "papules" (little bumps) or "pustules" (filled with yellow pus).
III	**Moderately Severe**	On the chest and back, there are numerous papules and pustules, as well as a few inflammatory nodules.
IV	**Severe**	Mainly cysts, or abscesses, widespread scarring.

Acne grading is helpful for documenting severity, prognosis, and treatment choices. The grading system for acne was developed in the 1950 as the number of treatments for the condition increased. [92]

Grading Systems:

In 1990, the American Academy of Dermatology created a classification system for primary acne vulgaris. Three levels of acne were described by this grading system: mild, moderate, and severe..[92]

i. **Cook system :**The assessment of the overall severity of acne on a 0–8 scale based on photographic standards.[93] **Leeds system:** This system serves and categorizes lesions as inflammatory or non-inflammatory lesions. On the scale, zero represents no acne and ten represents the most severe type of acne.[94]

ii. **Cunliffe pictorial method :**This grading scale evaluates facial acne in addition to other trunk areas that are impacted. There are four categories for acne severity: mild, moderate, moderately severe, and severe.[85]

iii. **Marquis grading :** This system divides acne into four grades: I, II, III, and IV. [85]

iv. **The Global Acne Severity Scale (GAGS) :** Every location receives a local score. Ultimately, this is included in the global score. This system's advantages include precision, repeatability, and the removal of lesion counting. [85]

v. **Pillsbury scale:** The Pillsbury scale categorizes acne according to severity, with 1 indicating the least severe and 4 indicating the most severe. [85]

Differential Diagnosis

A. **Acne rosacea**: When papules, pustules, and erythema are prominent on the flush areas of the face and chin. Eye involvement may be seen. However, comedones, cysts, and scarring are not present. It is commonly observed in middle age or later in life. [90]

B. **Folliculitis and boils**: It may appear as pustular lesions similar to acne. [85]

C. **Milia:** It is small keratin cysts that may be confused with whiteheads. They may be whiter thanacne Whiteheads are most commonly seen around the eyes. [85]

D. **Perioral dermatitis.**

E. **Pityrosporum folliculitis**: It predominates on the trunk. [79]

F. **Chloracne:** It is characterised by comedones, pustules, and cysts in the post-auricular area, axillae, and groin. Patients may have a history of exposure to halogenated aromatic hydrocarbons and other systemic manifestations. [79]

G. **Acne keloidalis nuchae:** It is often seen in black patients; Unlike acne vulgaris, acne keloidalis nuchae lacks comedones, localizes to the posterior neck, and progresses to keloid-like scarring, not typical in common acne. [78]

H. **Acneiform eruptions:** This type of acne arises due to systemic drugs, topical steroids, contrast dyes, or cosmetics. It often has a sudden onset linked to exposure and improves once the triggering agent is stopped.[79]

I. **Hidradenitis suppurativa acne inversus:** It is a chronic inflammatory condition marked by deep nodules, abscesses, draining sinuses, and scarring, typically affecting intertriginous areas rich in apocrine glands like the axillae, groin, perianal, perineal, and inframammary regions. [79]

J. **Rosacea:** Rosacea presents with erythema and telangiectasias without comedones and may affect the eyes or cause a bulbous nose. Unlike acne, which is common in teenagers, rosacea develops later and often features blackheads and pimples on the trunk and arms. [79]

K. **Seborrheic dermatitis:** Seborrheic dermatitis appears as greasy scales and yellow-red, merging macules or papules. It typically affects areas like the eyebrows, glabella, nose folds, beard, scalp, and chest with ill-defined, red patches and greasy scaling. [85]

Investigations [18]

- Routine management of acne vulgaris does not require any investigations
- In women, who have late-onset acne associated hirsutism, virilization, and menstrual irregularities,
- investigations to exclude an androgen secreting pathology (*e.g.*, polycystic ovaries) need to be done.
- Some women might need blood tests to check their hormone levels, especially if there are signs of a hormonal imbalance. It's also important to consider the possibility of pregnancy, as that can affect which treatments are safe to use.
- Signs suggesting high levels of male sex hormone, Excessive prolactin, Cushing's syndrome.
- An ultrasound scan can usually rule out ovarian cysts and ovarian and adrenal gland tumors.

Table 4: Laboratory tests in patients with suspected hormonal acne.[96]

TEST	VALUES
Testosterone	Elevated levels below 200 ng/dL typically indicate a benign ovarian or adrenal origin, whereas levels exceeding 200 ng/dL raise concerns about potential neoplasia.
Androstenedione	Secreted by both ovaries and adrenals, with peak levels in the early morning, making morning samples ideal for testing.
Dehydroepiandrosterone (DHEA)	The level of DHEAS >8,000 ng/dL between the range of 4,000–8,000 ng/dL suggest adrenal tumor or benign adrenal hyperplasia.
Sex hormone bining globulin (SHBG)	Decreased SHBG levels increase free testosterone, aggravating androgenic symptoms.
Prolactin	Elevated prolactin may point to hypothalamic or pituitary dysfunction, warranting further investigation.
Luteinizing hormone (LH)	An LH:FSH ratio >2:1 is diagnostic of polycystic ovary syndrome (PCOS).

17-Hydroxy progesterone	Levels >200 ng/dL suggest congenital adrenal hyperplasia or non-classic CAH due to 21α-hydroxylase deficiency.
Serum cortisol	Elevated cortisol levels may indicate adrenal neoplasia or hypercortisolism.
Fasting and Post prandial (PP) Insulin	Insulin testing should be performed in overweight/obese patients to evaluate insulin resistance, commonly linked to hyperandrogenism

Management of *Busoore Labaniya* in Unani medicine

The treatment of acne vulgaris should primarily focus on addressing the underlying causes of the condition. As outlined in Unani medical texts, the following therapeutic measures are recommended:

Usoole Ilaj

▪ The treatment should focus on addressing the primary underlying cause of the disease.[9]

▪ Tanqiya-e-Badan wa Dimagh (evacuation of body and brain) followed by Itfa-e-Dam (To modulate the heat of sanguine)[17,45,97]

▪ Tanqiya of Balgham (phlegm evacuation) from body.[98]

▪ Systemic therapy with MusaffiKhun (blood-purifying) medications. [17]

▪ Tajliya [topical cleansing] by using jaliadvia (Detergent drug). [17]

▪ TahlilwaTajfif(Resolution and Desiccation) [17,45]

▪ Correction of menstrual abnormalities[17]

▪ Islah-e-Hazm (Correction of digestion) [45]

‘Ilaj [Treatment]

The Unani approach to treatment incorporates three main categories:

‘Ilaj bi’l Tadbir (Regimenal Therapy), ‘Ilaj bi’l Ghidha’ (Dieto-therapy), ‘Ilaj bi’l Dawa’ (Pharmacotherapy) [17]

‘Ilaj bi’lGhizha’ (Dieto-therapy)

Diet plays a vital role in the management of acne vulgaris. Specific dietary guidelines are recommended to improve the body's balance:

▪ The use of easily digestible foods, such as soups and chapati, is recommended.

▪ Incorporate vegetables which having *Barid* (cold) properties.

▪ Prefer Sada Ghiza(simple food items) like Turai (ridge gourd), Kaddu (pumkin), Palak (spinach), Shalgham (Turnip), Moong (green gram), Arhar (split red gram), mutton, etc. [18]

▪ Regular intake of Seasonal fruits including oranges, pomegranates, apples and pears.

▪ Avoid Raddi (waste), Fasid (Putrified) and badi (flatulent)Aghziya like mash dāl (black gram), matar (pea), Gobhi (cauliflower),Baingan(Brinjal).

▪ Abstain from Sharab (Alcohal) intake. [9]

***‘Ilaj bi’l Tadbir* (Regimenal Therapy)**

Tanqiya-e-Badan wa Dimagh: Unani scholars recommend a comprehensive approach to the purification (tanqiya) of the body through Fasd (venesection) and Ishaal (purgation). Fasd is performed on specific areas such as the Sararu(head) and the vessels of the nose. For the purpose of purgation (*Ishal*), oral administration of formulations such as *Aftimun*, *Habbe Quqaya*, *Habbe Sibr*, and *Habbe Ayarij* is recommended [17, 9, 45]. These remedies are intended to detoxify the body and assist in the management of conditions like acne vulgaris

‘Ilaj bi’l Dawa’(Pharmacotherapy)

Mussaffī-DamAdviya:

Some single drugs: Shahtra (*Fumaria parviflora*) [99] ,Mundi (*Sphaeranthus indicus*) [99],Siras (*Albizia lebbeck*) [99-102],Neem (*Azadirachta Indica*) [100]

Compound Formulation:

▪ Joshanda for Mussafi-i Khūn advia as: Shahitra 4 g, Chraita 4 g, Sarfhooka 4 g, Gul-e-Mundi 4 g, Unnab 5 adad.

▪ Qurse Mavizi 2 tab in morning and Maghrabi 2 tab in evening with water [9],QurseMuṣaffi (500 mg) 2 tab thrice a day ,HabbeMuṣaffi2 tab twice a day

▪ Itrifal Shahtra7 gm twice a day [102,103],Majun Mundi 5 gm twice a day [103,104],Majun Chobchini5 gm twice a day[103,104],Majun Ushba 12 gm at bed time[9]

Topical therapy

Many preparations are suggested for relieving lesions of *Busoore Labaniyya*s ome of them are:

Ubtan

- Local application of paste prepared with MaghzGhongchi (kernel of Abrus precatorius Linn) mixed with Roghankunjad on affected part overnight and wash in next morning [9]
- Local application of paste prepared with Salikha(*Cinnamomum cassia* Blume) mixed with Honey[45]
- Local application of a paste prepared by mixing Kafe Dariya and Zaranbad with water [45]
- Local application of paste prepared by Murdar Sang(litharge) mixed with Vinegar [45]
- Local application of paste prepared with the powder of Khubkalan (*Sisymbrioirio*Zinn), Sandal Safaid(*Santalum album* Linn.) and Sandal Surkh(*Pterocarpus santalinus* Linn.) mixed with rose water.[45]
- Local application of a paste prepared by mixing the powder of Post-e-Saras (bark of *Albizia lebbeck* L. Benth) and Kunjad Siyah (seed of *Sesamum indicum* L.) with vinegar[105]

Zimad: Irsa, Gunghchi safaid, Barge Neem, Poste Saras and Namak Sambhar in equal proportion[24],Salikha along with Shahed (Honey)[17],Karsana had mixed Shahed (Honey) [17],Shuniz, Boraq, Naushadar long with Sirka[17]

Tila :Tila Muhasa[17,27],Tila Akbar [23],Fine powder of kafe Dariya 1part, Badam talkh 2 part[106]

Other Topical formulations

- A paste prepared by combining equal parts of *Arad Turmus*, *Arad-e-Baqla*, and *Arad-e-Adas* is applied to the face—using half the quantity of the prepared paste—left on overnight, and washed off the following morning.[17]

❖Kafe Dariya, Tukhm-e-Turb, Zarawand mudharaj all are equal quantity of 36gm , Afsanteen and Beikh-e Sosan6gm, are powdered. mixed with a small amount of water, are placed to the lesions [17]

❖Anjir and Shuniz combined with Sirka [5]

- ZimadMajalli, Dawa-e-Muhasa, and Ubtan Ajeeb[11]

Conventional therapy

Mild acne is best treated with topical therapies, while severe cases require systemic medications. Topical treatments include retinoids (retinoic acid, adapalene, isotretinoin, tazarotene), benzoyl peroxide, clindamycin, erythromycin, and azelaic acid. Systemic options, such as doxycycline, minocycline, erythromycin, and azithromycin, are used for more severe cases. These medications can reduce severity and scarring but may cause side effects like dryness, redness, burns, and acne recurrence. Therefore, careful management is essential for acne treatment. The goal is to alleviate distress, enhance skin appearance, prevent scarring, and improve emotional well-being and self-esteem[107,108]

General Measures:

Patients with acne often experience depression and may require empathetic counselling and emotional support.**[109]**

Proper cleansing

Avoid use of cosmetics

Avoid picking of pimples

Prevent constipation

Maintain a diet rich in salads and fruits

Current Treatment of Acne

The first line of acne treatment is to control existing lesions, helps to prevent permanent scarring, shorten the disorder's duration, and minimize associated morbidity.Patients should be informed that improvements may take 3–6 weeks [110,111]

Treatment regimens must be individualized, considering factors like the patient's medical condition, lesion severity, endocrine history, and preference for oral or topical treatments. As illustrated in Table 5, acne can be managed through both topical and systemic treatment approaches.

Alternative treatments, including natural products or non-drug options like optical therapy, may also be used. Combination therapies targeting multiple acne mechanisms are often most effective. The treatment plan should be adjusted based on the patient's response.[110]

Table 5. Different treatment options for acne.

Treatment Methods	Examples
Topical	**Retinoids:** Tretinoin(0.025%gel),Isotretinoin(0.05% cream,0.05%gel),Adapalene(0.1%),Retinalhyde,Tazarotene,: **Antibiotics**: Clindamycin(1% gel), Erythromycin(2–3% gel),Dapsone(5% gel), Nadifloxacin (1% cream) **Diverse**: Azelaic acid 20%, Benzoyl peroxide(5–10%), chemical peels, corticosteroids, , hydrogen peroxide, niacinamide, salicylic acid (0.5–2%), sodium sulfacetamide, sulphur, triclosan
Systemic	**Retinoids:** Isotretinoin **Antibiotics**: Tetracycline(1g/day), Minocycline azithromycin, clindamycin & Doxycycline,(50–100mg) daily , co-trimoxazole, erythromycin, levofloxacin, lymecycline. **Hormonal**: Spironolactone (50–200mg), Oral glucocorticoids, Gonadotrophin-releasing hormone Inocoterone acetate, Cyproterone acetate,contraceptives **Diverse:** clofazimine, corticosteroids, ibuprofen, zinc sulfate
Physical Treatment	Light chemical peels with α-hydroxy acids (AHA) or other mild agents are sebostatic and help with superficial scars. – Surgical management of scars requires individual adjustment; can include laser ablation, dermabrasion, cryotherapy, collagen injections, comedone extraction, cryolush therapy, electrocauterization, intralesional corticosteroids and optical treatments

Future treatment options

Possibly the most interesting treatment on the perspective is the vaccine therapy for acne. The vaccines are targeted against the *P. acne* bacteria.A recent review discusses the latest research on *Propionibacterium acnes* (P. acnes) vaccines and how they have shown good results and immunity, when used in mice challenged by *P. acnes*.[112]

Psychological Intervention:

Patients with acne often experience anxiety, depression, and symptoms related to the obsessive-compulsive spectrum. Psychological interventions, such as biofeedback-assisted relaxation, can help by monitoring and modifying psychological factors linked to thoughts, emotions, and behaviors. Cognitive-behavioral therapy (CBT) focuses on addressing thoughts, emotions, physical symptoms, and behaviors. A simplified version of CBT can be effectively used in everyday clinical practice, especially for less severe cases.[113]

CONCLUSION

Skin diseases place a considerable financial and emotional strain on both individuals and their families. Acne, one of the most common conditions, affects around 80% of adolescents aged 12 to 18. Globally, acne accounts for approximately 9.4% of the total disease burden and ranks as the eighth most prevalent disease worldwide. It impacts about 85% of young people aged 12 to 25, 8% of adults aged 25 to 34, and 3% of those aged 35 to 44. As a widespread inflammatory skin disorder, acne is often associated with significant psychological distress.

Renowned Unani physicians have described a skin condition called Busoore Labaniya in their classic texts, which bears clinical resemblance to modern-day acne vulgaris.Acne vulgaris, commonly manifested by eruptions resembling milk drops on the face, forehead, nose, and arms, is a prevalent dermatological disorder. While the modern system of medicine provides numerous therapeutic options, many patients continue to experience suboptimal responses or adverse effects. This has led to increased interest in alternative systems of medicine such as Unani, Ayurveda, Yoga, Siddha, and Homeopathy, which are gaining popularity and wider acceptance. The Unani system, in particular, offers holistic and effective treatment strategies for acne vulgaris. These treatments not only address the symptoms of the disease but also aim to eliminate its root causes and prevent the formation of scars. Considering these advantages, there is a strong need to explore Unani therapies through systematic clinical studies to validate their efficacy in the prevention and long-term management of *Busoore Labaniya* (acne vulgaris).

Acknowledgement

The authors gratefully acknowledge the faculty of Hakim Syed Ziaul Hasan Government Unani Medical College, Bhopal (M.P.) for providing the necessary facilities and infrastructure. Special thanks to Mr. Mohd Dilshad Ali and Dr. Mohammad Anzar Husain for their continuous support and assistance.

Conflict of interest

The authors declare no conflicts of interest related to this work.

REFRENCES

1. Maddiboyina B, Jhawat V, Ramesh K, Balaji M. A review on nanoparticle based herbal remedies for the management of alopecia. 2020;12:1–17.
2. Hazarika N. Acne vulgaris: new evidence in pathogenesis and future modalities of treatment. J Dermatol Treat. 2021. https://doi.org/10.1080/09546634.2019.1654075.
3. Heath CR, Usatine RP. Acne vulgaris. J Fam Pract. 2021. https://doi.org/10.12788/jfp.0271.
4. Katare OP, et al. Acne: An Understanding of the Disease and its Impact on Life. Int J Drug Dev Res. 2012;4(2):14-20.
5. Ibn e Sina Abu Ali.Al-*qanoon Fit-Tib*, (Urdu translation by Kantoori Sayed Ghulam Hasnain). Vol-II IV. New Delhi: Idara Kitab-ul-shifa; 2007:145-46,36, 43, 50, 59, 96, 224, 246:1432,1420.
6. Arzānī MA. Mīzān al-Ṭib. Kabiruddin T by M, editor. New Delhi: Idārā Kitāb al-Shifā; 2001 &2002: 249, 256,722.
7. Qarshi Hassan M. "Jami" al-Hikmat' Vol-2. Delhi: Idārā Kitab al- Shifā Daryagunj; 2011. 1005.
8. Anjum S. Concept of Busoor e Labaniya (Acne vulgaris) and its Management In Light of Unani System of Medicine. J Drug Deliv Ther. 2021;11(5-S):159-163.
9. Ajmal khan MH. Haziq. Karachi: Madeena Publication; 1983:550, 590-592.
10. Aqsarai Jamaluddin vol 3. Aqsarai. Lucknow: Munshi Nawal Kishore Publications; 2010:459.
11. Syed JH. "Daqayiq al-Ilaj". (Urdu tran). 478–80, 531.
12. Kabiruddin A. TarjumaSharḥAsbab. Delhi: Ajaz publishing house; 2014:243–244.
13. Ghulam J. Makhzan-ul-Hikmat. Deoband: New Delhi: Ejaz Publishing House; 1996:698–699.
14. Zakariyya A-R. al-ḤawiFi'lTibb (Vol. 23). M Y Siddiqui H, editor. Aligarh: Saba Publishers Aligarh; 1994:36-37.
15. Avicenna. Cannon of Medicine. English T. O, C. Gruner, daruI Shifa, Burleigh press-Lewins, Bristol, 1930:168.
16. Dorland's Illustrated Medical Dictionary. 25th ed. W.B Saunders Company; 1979:732.
17. Khan A. Akseer Azam. Vol-4. Lucknow: Matab Munshi Naval Kishore; 1917:450-1.
18. Sultana et al. Buthur-i-labaniyya (Acne vulgaris) With Special Reference to Unani Medicine: Review. Journal of AYUSH. 2015;4(3):1-6.
19. Grant RNR. The Section of the History of Medicine: The History of Acne. Proceedings of Royal Society of Medicine. 1951;44:649-52.
20. Tabasum H, Ahmad TF, et al. The historical panorama of Acne vulgaris. J Pakistan Association of Dermatologists. 2013;23(3):315-319.
21. Tabari R. Firdaws al-Ḥikmat. New Delhi: CCRUM, Ministry of Health and Family Welfare; 2010:128.
22. Thabit Ibn QurrahTarjuma Zakhira. Litho Colo. Urdu Translation by Hakīm S.A. A, editor. AMU, Aligarh: Litho Colour Printers Aligarh; 1987:33-34.
23. Khan GJ. Makhzanul Ilaj. Vol 2. Lahore: Shaikh Muhammad Basheer and Sons; 1978; 1144-5.
24. Ibn Hubal. Kitab al-Mukhtaratfi'lTibb-Vol-2. CCRUM, Ministry of Health and Family Welfare, India, editors. New Delhi, 2005:188–189, 32.
25. Jurjani I. Zakheera Khwarzam Shahi, Vol-II X. Lucknow: Munshi Nawal Kishor; New Delhi; 1878:6:13-16, 45-49.
26. Antaki D. TadhkiraUl al-Albab. 2001st ed. New Delhi: CCRUM, Ministry of Health and Family Welfare; 2010:87.
27. Azam Khan. Rumuz-iAzam Vol-2. New Delhi: CCRUM; 2006. 382–84.
28. Cunliffe WJ, Holland DB, Jeremy A. Comedone formation etiology, clinical presentation and treatment. Clin Dermatol. 2004:367-374.
29. Raw Materials, Publications & Information Directorate ND. The Wealth of India Vol-11; 1976:89, 99-100.
30. Batemans T. A practical synopsis of cutaneous diseases according to the arrangement of Dr. Willan: exhibiting a concise view of the diagnostic symptoms and the method of treatment. YNM:156, 271.
31. Bloch B. Transmissible Diseases of Skin. Br J Dermatol. 1931;43:67.

32. Romańska-Gocka K, Woźniak M, Kaczmarek-Skamira E, Zegarska B (2016) The possible role of diet in the pathogenesis of adult female acne. Postepy Dermatol Alergol 33: 416-420.

33. Minh PPT, Bich DD, Hai VNT, Van TN, Cam VT, et al. (2019) Microneedling Therapy for Atrophic Acne Scar: Effectiveness and Safety in Vietnamese Patients. Open Access Maced J Med Sci 7: 293-297.

34. Purdy S, Langston J, Tait L (2003) Presentation and management of acne in primary care: a retrospective cohort study. Br J Gen Pract 53: 525-529.

35. Global Acne Market Report for 2016-2026.

36. Magin, P, Adams, J, Heading, G, Pond D. Acne's relationship with psychiatric and psychological morbidity: results of a school-based cohort study of adolescents. J Eur Acad Dermatol Venereol. 2010.

37. Al-Sayeed, Al-Dawud, Bukhari IA, Bahnassy A. Risk factors and co-morbidity of skin disorders among female schoolchildren in Eastern Saudi Arabia. Br J Dermatological Surg. 2007; 48:199–212.

38. Bickers, DR, Lim, HW, Margolis D *et al*. The burden of skin diseases: A joint project of the American Academy of Dermatology Association and the Society for Investigative Dermatology. J Am Acad Dermatol. 2004; 55:490–500

39. Ettel DL, Lamanno LR, Neyra SA, Ettel WJ, Ettel GL III, et al. (2017) Teens and Technology Transforming Acne Treatment. Perm J 21: 16-192.

40. Gollnick HP (2015) From new findings in acne pathogenesis to newapproaches in treatment. J Eur Acad Dermatol Venereol 5: 1-7.

41. Sutaria AH, Schlessinger J. Acne Vulgaris (2018) [Updated 2018 Nov 14].In: StatPearls [Internet]. Treasure Island (FL).

42. Alīm S. Amrāz-i Jild. Alighar: Ajmal Khan Tibbia College; 74.

43. Kabiruddin M. *Tarjuma-e-Kabir*, (Delhi : Idara KItab-ush-Shifa), 2009, pp. 243-244.

44. Tabri M. *Moalejat Buqratiyah.* (Urdu translation). Vol. 2, (New Delhi: Ministry of Health and Family Welfare Government of India, CCRUM), 1997, pp. 144-147.

45. Arzani A. *Tib-e-Akbar* (Urdu translation by Hussain M), (Deoband : Faisal Publications), 2002, pp.256,722.

46. Olutunmbi, Y.; Paley, K.; English, J.C. Adolescent female acne: etiology and management. J. Pediatr.Adolesc. Gynecol. 2008, 21, 171–176. [CrossRef] [PubMed]

47. Webster, G.F. Clinical review: Acne vulgaris. Br. Med. J. 2002, 325, 475–479. [CrossRef]

48. Lavers, I. Diagnosis and management of Acne vulgaris. Nurse Prescr. 2014, 12, 330–336. [CrossRef].

49. Follador I, Rego V. Etiopathogenesis of acne. Future Drugs Ltd. 2006;1(1):153–5. [doi:10.1586/17469872.1.1.153]

50. Dawson AL, Dellavalle RP. Acne vulgaris. BMJ. 2013;346:f2634. [doi:10.1136/bmj.f2634]

51. Bhate K and Williams HC Epidemiology of acne vulgaris. *British Journal of Dermatology*. 2012;168:474–485.

52. Rigopoulos D, Gregoriou S, Ifandi A, et al. Coping with acne: beliefs and perceptions in a sample of secondary school Greek pupils. *J Eur Acad Dermatol Venereol,* 2007; 21: 806-810.

53. Smithard A, Glazebrook C, Willams HC. Acne prevalence, knowledge about acne and psychological morbidity in mid-adolescence: a community based study. *Br J Dermatol*, 2001; 145: 274-279.

54. Lucky AW. Hormonal correlates of acne and hirsutism. *Am J Med*, 1995; 98: 89S-94S.

55. ChenW, Thiboutot D and Zouboulis CC. Cutaneous androgen metabolism: basic research and clinical perspectives. *J Invest Dermatol*, 2002; 119: 992-1007.

56. Arbesman H. Dairy and acne-the iodine connection. *J Am Acad Dermatol*, 2005; 53: 1102.

57. Thiboutot DM, Strauss JS. Diet and acne revisited [comment]. *Arch Dermatol*, 2002; 138: 1591-1592.

58. Stoll S, Shalita AR, Webster GF, et al. The effect of the menstrual cycle on acne. *J Am Acad Dermatol*, 2001; 45: 957-960.

59. Williams M, Cunliffe WJ, Gould D. Pilo-sebaceous duct physiology I. Effect of hydration on pilo-sebaceous duct orifice. *Br J Dermatol*, 1974; 90: 631-635.

60. Kenyon FE. Psychosomatic aspect of acne. *Br J Dermatol*, 1966; 76: 344-351.

61. Chiu A, Chon SY, Kimball AB. The response of skin disease to stress: changes in the severity of acne vulgaris as affected by examination stress. *Arch Dermatol*, 2003; 139: 897-900.
62. Sneddon J and Sneddon I. Acne excoriee: a protective device. *Clinical and Experimental Dermatology*, 1983; 8: 65-68.
63. Goodman G. (2006) Acne--natural history, facts and myths. Aust Fam Physician 35: 613-6.
64. Chalyk N, Klochkov V, Sommereux L, et al. (2018) Continuous Dark Chocolate Consumption Affects Human Facial Skin Surface by Stimulating Corneocyte Desquamation and Promoting Bacterial Colonization. J ClinAesthet Dermatol 11: 37-41.
65. Juhl CR, Bergholdt HKM, Miller IM, Jemec GBE, Kanters JK, et al. (2018) Dairy Intake and Acne Vulgaris: A Systematic Review and Meta-Analysis of 78,529 Children, Adolescents, and Young Adults. Nutrients 10.
66. Web George Mateljan Foundation. Shrimp What's New and Beneficial About Shrimp. Available From: http://www.whfoods.com/genpage.php?pfriendly=1&tname=foodspice&dbid=107
67. Jung JY, Kwon HH, Hong JS, Yoon JY, Park MS, et al. (2014) Effect of acid on acne vulgaris: a randomised, double-blind, controlled trial. Acta Derm Venereol 94: 521-525.
68. Pappas A (2009) The relationship of diet and acne: A review. Dermatoendocrinol 5: 262-267.
69. Kidson W (1998) Polycystic ovary syndrome: a new direction in treatment. Med J Aust 169: 537-40.
70. Aizawa H, Niimura M (1995) Elevated serum insulin-like growth factor-1 (IGF-1) levels in women with postadolescent acne. J Dermatol 22: 249-52.
71. Rahaman SMA, De D, Handa S, Pal A, Sachdeva N, et al (2016) Association of insulin-like growth factor (IGF)-1 gene polymorphisms with plasma levels of IGF-1 and acne severity. J Am Acad Dermatol 75: 768-773.
72. Mahmood NF, Shipman AR (2016) The age-old problem of acne. Int J Womens Dermatol 3: 71-76.
73. Rossner S. John Harvey Kellogg (2006) Masturbation results in general debility, unnatural pale eyes and forehead acne. Obes Rev 7: 227-228.
74. Misery L, Wolkenstein P, Amici JM, et al. (2015) Consequences of acne on stress, fatigue, sleep disorders and sexual activity: a population-based study. Acta Derm Venereol. 95: 485-488.
75. Zelickson AS, Strauss JS, Mottaz J (1985) Ultrastructural changes in open comedones following treatment of cystic acne with isotretinoin. Am J Dermatopathol. 7: 241-244.
76. InformedHealth.org (2013) Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG), Which birth control pills can help reduce acne?, [https://www.ncbi.nlm.nih.gov/books/NBK279209/].Accessed on 2016 Jul 28.
77. Magin P, Pond D, Smith W, et al. (2005) A systematic review of the evidence for 'myths and misconceptions' in acne management: diet,face-washing and sunlight. Fam Pract 22: 62-70.
78. Marks R. Roxburgh's common skin diseases. 17th Edition. London: Arnold publisher; 2003: 149-57. https://doi.org/10.1201/b13512
79. Thomas B. Fitzpatrick, Klaus Wolff, Richard Allen Johnson, Arturo P. Saavedra, Ellen K. Roh. Color Atlas and Synopsis of Clinical Dermatology, United States of America: Mc-Graw Hill Companies; 2001. 51–52.
80. Marks R, Roxburgh AC, Archibald C. Roxburgh’s common skin diseases. Arnold; 2003. 11.
81. Layton AM. Rook’s Textbook of Dermatology.Disorder of Sebaceous gland. 8th ed. Burns T, Breathnch S, Cox N GC, editor. UK; 2009.
82. Feldman S,Careccia RE,Barham KL HJ. Diagnosis and Treatment of Acne. Am Fam Physician. 2004; 69(9):2123–30.
83. Rachel B,Bedars BH. Hand book of Diseases. 2nd ed. Pennsylvania, editor. Spring House Co-orportion; YNM.10–11.
84. Mitchell W, Lynch PJ. Principles and practice of Dermatology. 2nd ed. Churchill livingstone; 1996. 801–2.
85. Ralston S, Penman ID, Strachan MWJ, Hobson RP, Britton R, Davidson S. Davidson’s principles and practice of medicine.2014: 1417.
86. Martin AR, Lookingbill DP, Botek A, Light J, Thiboutot D, Girman CJ. Health-related quality of life among patients with facial acne - Assessment of a new acne-specific questionnaire. Clin Exp Dermatol. 2001; 26(5):380–5.
87. Fabbrocini G, Annunziata MC, D'Arco V, et al. (2010) Acne scars:pathogenesis, classification and treatment. Dermatol Res Pract.
88. Fife D (2011) Practical evaluation and management of atrophic acne scars: tips for the general dermatologist. J Clin Aesthet Dermatol. 4:50-57.
89. Kravvas G, Al-Niaimi F (2017) A systematic review of treatments for acne scarring. Part 1: Non-energy-based techniques. Scars Burn Heal.

90. Sardana K,Agarwal P.Textbook of Dermatology and Sexually Transmitted Diseases with HIV Infections.2nd ed.New Delhi;CBS Publishers & Distributors Pvt.Ltd.;2022.
91. Kraft J, Freiman A Management of acne. CMAJ.2011. 183: E430-E435.
92. Pochi P E, Sthalita AR, Strauss JS, CunliffeWJ *et al*. Report of the Consensus Conference on Acne classification. J Am Acad Dermatol. 1991; 24:495–500.
93. Cook CH, Centner RL MS. An Acne grading method using photographic standards. Arch dermatol. 1979; 115:571–5.
94. Burke BM, WJ C. The Assessment Of Acne vulgaris-The leeds technique. Br J Dermatol. 1984; 111:83–4.
95. Doshi A, Zaheer A SM. Comparison of currect acne grading system and proposal of novel system. Int J Dermatol. 1997; 36:416–8.
96. Elsaie ML (2016) Hormonal treatment of acne vulgaris: an update. Clin Cosmet Investig Dermatol 9: 241-248.
97. Ibn al-Quf. Kitāb al-'Umda Fi'l Jarāhat. Central Council for Research in Unani Medicine; 15.
98. Azahar M *et al*.Therapeutic Evaluation of a Topical Unani Formulation, *Tila-i-Muhāsā*in*BasooreLabaniyya*(Acne vulgaris): A Randomized, Controlled Clinical Study.Cellmed.2020; 10(2)1-9.
99. Khare CP. Indian Medicinal Plants An Illustrated Dictionary. 1st ed. New York: Springer Science + Business Media; 2007. 30,92,275,760.
100. Standard Unani Treatment Guidelines. Central Council for Research in Unani Medicine; 2014. 163–65.
101. Ghani A-N. Qarabadīn-ī Najm al-Ghanī. Delhi: CCRUM; 2010. 42.
102. CCRUM. Qarābādīn-ī Āzam wa Akmal. Translation U, editor. Delhi: CCRUM, Ministry of Health and Family Welfare; 2005: 7.
103. CCRUM. Anonymous. NFUM. Part-1. Delhi: Ministry of Health and Family Welfare, Govt. of India; 2006:96,124.
104. Khan A. Muhīṭ-i Āzam vol-2,vol-4 New Delhi: CCRUM, Ministry of Health and Family Welfare; 2012. 385–388,1920,138.
105. Razi A. Kitāb-al Fākhir Fit Tib,Part-1, Vol-1. CCRUM, editor. New Delhi: Ministry of Health and Family Welfare India; 2005. 37-8.28,46.
106. Hajazi MR. Bayaze Hajazi. Lahore: Bashir and Sons; 1967: 56.
107. Nasri Hamid *et al*. Medicinal Plants for the Treatment of Acne Vulgaris: A Review of Recent Evidences. *Jundishapur J Microbiol*. 2015;2(8):1-9.
108. Larson Siri Knutsen *et al.* Acne Vulgaris: Pathogenesis, Treatment, and Needs Assessment. Vol. 30. *Dermatol Clin.* 2012. pp. 99–106.
109. Behh PN, Aggarwal A, Srivastava G. Practice of Dermatology, 9th Edn. New Delhi: CBS Publishers and Distributors; 2002; 408-09p.
110. Feldman, S.; Careccia, R.E.; Barham, K.L.; Hancox, J. Diagnosis and treatment of acne. Am. Fam Physician 2004, 69, 2123–2130. [PubMed]
111. Webster, G.F. Acne vulgaris and rosacea: Evaluation and management. Clin. Cornerstone 2001, 4, 15 [CrossRef].
112. Keri J, Shiman M. An update on the management of acne vulgaris. *Clinical, Cosmetic and Investigational Dermatology*, 2009; 2: 105-110.
113. Katlein França, Torello Lotti, Advances in Integrative Dermatology, *Wiley online.* 2019, pp. 35-41.