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A Review on Herbal Drugs Acting Against Acne Vulgaris

S. D Patel^{1*}, Dr. S Shah², Dr. N Shah³

1. - M.pharm semester 4, L.j institute of pharmacy, Ahmedabad, India

2. - Head of the department and professor at L.j institute of pharmacy, Ahmedabad, India

3. - Assistant professor at L.j institute of pharmacy, Ahmedabad, India

ABSTRACT:

Acne is a cutaneous pleomorphic disorder of the pilosebaceous unit involving abnormalities in sebum production and is characterized by both inflammatory (papules, pustules and nodules) and non-inflammatory (comedones, open and closed) lesions. *Propionibacterium acnes* and *Staphylococcus epidermidis* are common pus-forming microbes responsible for the development of various forms of acne vulgaris. Common therapies that are used for the treatment of acne include topical, systemic, hormonal, herbal and combination therapy. It is the sequelae of the disease that are the distinguishing characteristics of acne in skin of color, namely postinflammatory hyperpigmentation and keloidal or hypertrophic scarring. Although the medical and surgical treatment options are the same, it is these features that should be kept in mind when designing a treatment regimen for acne. This review focuses on the treatment of acne using various drug delivery systems. Many herbal drugs are used for the treatment of acne vulgaris. Though they have very few number of clinical trials, many successful results have been recorded. There are many types of herbal drugs which act against acne vulgaris and some of those are:- Aloe Vera, Amaranth, Arnica, Asparagus, Barberry, Basil, Birch, Bittersweet nightshade, Brewer's yeast, Burdock, Calendula, Celandine, Chaste tree, Chaste berry, Coriander, Cur cumin, Green Tea, Guggul, Jojoba oil, Kali bromatum, Labrador tea, Lavender, Liquorice, Mint, Neem, Orange peel, Pine, Poplar, Rhubarb, Rose, Saw palmetto, Soapwort, Stinging nettle, Tea tree oil, Thyme, Turmeric, Usnea Barbara, Viola, Walnut, Willow bark.

KEY WORDS: Herbal Drugs, Acne Vulgaris, *Propionibacterium acnes*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, stages of acne, causes of acne.

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INTRODUCTION:

Acne vulgaris is a most common chronic inflammatory skin disorder of pilosebaceous unit that affect areas containing the largest oil glands, including the face, back, and trunk.^[1,2,3]

It is almost a universal disease occurring in all races and affecting 95% of boys and 83% of girls.

Acne vulgaris is generally characterized by formation of seborrhea, comedone, inflammatory lesions and presence of bacteria *Propionibacterium acnes*, *Staphylococcus epidermidis* and *Staphylococcus aureus* in the follicular canal and sebum production.^[4] *P. acnes* have been described as an obligate anaerobic microorganism. It is implicated in the development of inflammatory acne by its capability to activate complements and by its ability to metabolize sebaceous triglycerides into fatty acids, which chemotactically attract neutrophils. On the contrary, *S. epidermidis*, an aerobic organism, usually involves in superficial infections within the sebaceous unit. When the chemicals produced by *P. acnes*

For Correspondence:

Ms. S. D Patel

M.pharm semester 4, L j institute of pharmacy, Ahmedabad, India

Email: shalvipatel9@gmail.com

(www.jpsbr.org)

destroy the cellular structure of skin cells, *Staphylococcus aureus*, grows causing acne lesions. These factors provide a potential target for treatment. *P. acnes*, *S. epidermidis* and *S. aureus* are the target sites of antiacnedrugs.^[5] With the excessive use of antibiotics for long periods has led to the increased resistance in acne causing bacteria i.e. *P. acnes*, *S. epidermidis* and *S. aureus*. The development of antibiotic resistance is multifactorial, including the specific nature of the relationship of bacteria to antibiotics, how the antibacterial is used, host characteristics, and environmental factors. To overcome the problem of antibiotic resistance, medicinal plants have been extensively studied as alternative treatments for diseases.^[6] The incidence of women exposed to oral tretinoin, a known teratogen, during pregnancy has been increasing, possibly the result of direct-to-consumer drug advertising. These and other concerns, including cost, underscore the need for safer, effective, more-inexpensive approaches, including those offered by herbal medicine

All forms of acne involve one or more of these pathophysiologic factors

- Hyperkeratinization of the follicular epithelium with comedone formation
- Increased sebum production
- Bacterial proliferation of *Propionibacterium acnes* (*P. acnes*)
- Local immune hypersensitivity causing inflammation.^[7]

Acne may be classified according to predominance of specific skin lesions^[8]

- **Comedonal**(non-inflammatory) – mild
- **Papular**(inflammatory) – mild-to-moderate
- **Pustular** (inflammatory) – moderate
- **Nodulocystic**– severe
- This order also follows increasing severity, with cutaneous scarring as the ultimate result.

Pathophysiology^[10]

The pathogenesis of acne vulgaris is multifactorial. The key factor is genetics. Acne develops as a result of an interplay of the following 4 factors:

- 1) Follicular epidermal hyperproliferation with subsequent plugging of the follicle.
- 2) Excess sebum production.
- 3) The presence and activity of the commensal bacteria *Propionibacterium acnes*.
- 4) Inflammation

Stages of Acne^[9]



Causes of acne^[11]

- **Menstrual cycle** - Girls and women with acne tend to get it worse one or two weeks before their menstrual period arrives. This is probably due to hormonal changes that take place. Some people say they eat more chocolate during this time and wonder whether there may be a connection. However, experts believe the worsening acne is not due to chocolate, but rather to hormonal changes.
- **Anxiety and stress** - mental stress can affect your levels of some hormones, such as cortisol and adrenaline, which in turn can make acne worse. Again, stress can make some people binge-eat. Experts believe the culprits are most likely the hormone levels, rather than the binge-eating.
- **Hot and humid climates** - when it is hot and humid we sweat more. This can make the acne worse.
- **Oil based makeups** - moisturizing creams, lubricating lotions, and all makeup that contains oil can speed up the blocking of your pores.
- **Greasy hair** - some hair products are very greasy and might have the same effect as oil based makeup. Hair products with cocoa butter or coconut butter are examples
- **Squeezing the pimples** - if you try to squeeze pimples your acne is more likely to get worse, plus you risk scarring.
- **Make-up and hair care products** -can clog pores. When shopping, look for the following acne-friendly terms on product labels: —oil-free, —non-comedogenic, or —non-acnegenic.
- **Physical pressure** -Pressure due to a chin strap, phone receiver, sports helmet, headband, guitar strap, bra strap and other tight clothing can lead to localized acne that develops at the point of skin contact. Sweating
- **Sweating**-can worsen acne in some people. Most likely, it is because sweating helps to clog pores, especially if trapped under clothing.
- **Over washing**-Washing your face twice a day with a mild cleanser is recommended for acne-prone skin. Cleaning it more often, scrubbing/exfoliating, or using strong cleansers or astringent products (i.e. toners with alcohol)

- can actually strip the skin and irritate it, which can lead to more acne.
- **Medications-** Certain medications can cause acne to flare up, such as oral corticosteroids, some contraceptive pills (progestin only), and anti-convulsives, to name a few. Menstrual cycle Many girls and women may notice that their acne flares up as they are nearing their monthly period.
- **Picking or squeezing-**Touching acne lesions can make them worse and raise the risk of permanent scarring. Squeezing or popping pimples can cause an eruption of sebum and bacteria into surrounding skin tissues leading to more swelling and redness and possibly infection

- **Food-**Actually, no study has yet proven that any specific foods or dietary habits can cause or worsen acne. However, if you find that a certain kind of food seems to aggravate your acne, try removing it from your diet. Removing entire food groups from your diet, though, is not healthy so is not recommended.

DRUGS USED AGAINST ACNE VULGARIS^[12]

- Many Allopathic drugs and their combination therapies are used in the treatment of acne vulgaris like Adapalene, Retinoic acid containing drugs, Clindamycin, Benzoyl peroxide and many more are used in suitable formulations. But the problem with these drugs and their combination therapies is that they have recorded side effects.

Table 1: Acne type, Treatment and Adverse effects

Acne type	Treatment	Drugs used	Adverse effects
(Mild acne) Comedonal	Topical retinoid and other agent	Isotretinoin Tretinoin Adapalene Azelaic acid	Skin irritation, Local irritation Skin irritation, Skin irritation and low tolerability
(Mild acne) Papulopostular	Topical retinoid and/or benzoyl peroxide	Benzoyl peroxide	Cutaneous irritation, dryness, bleaching of hair and clothes
(Moderate acne) Papulopostular	Oral antibiotics and topical retinoids/ benzoyl peroxide or oral isotretinoin	Oxytetracycline Minocycline Doxycycline Erythromycin Azithromycin	Gastrointestinal upset and vaginal candidiasis vertigo and hyperpigmentation Gastrointestinal upset and photosensitive Gastrointestinal upset and vaginal candidiasis Gastrointestinal upset
Nodular	Oral antibiotic and a topical retinoids/ benzoyl peroxide or oral isotretinoin	Oral isotretinoin	Teratogenicity
Severe acne	Oral isotretinoin or hormonal or high-dose oral antibiotics and topical retinoids and benzoyl peroxide	Spironolactone Oral contraceptive Corticosteroids	Menstrual irregularities Vascular thrombosis, melasma and weight gain Adrenal suppression

- Due to the above reasons herbal approach has also been considered for the treatment of acne vulgaris.

Herbal drugs against acne vulgaris^[13]

Herbal therapies, which have been in use from ancient times for the treatment of acne, include various herbal extracts, oil and their ayurvedic formulation. The introduction of novel herbal formulations for the treatment of acne may produce many advantages over previously used therapies. These herbal drugs are effective against a variety of Gram-positive and Gram-negative Bacteria. Sunder Vati, which is an ayurvedic formulation, was found to be orally effective and well tolerated for the treatment of acne vulgaris. Purintablets and klarina cream formulations, which contain many herbal extracts and have negligible adverse effects compared with modern medicine, are commonly indicated for moderate and severe forms of acne. There are certain herbal extracts, such as *A. dahurica*, *R. coptidis* and *Psidiumquajava*, that are more effective than antibiotics and retinoids. The efficacy of these herbal agents in acne treatment is not only based on antimicrobial activity but on their possessed antioxidant and antiinflammatory

properties by which they inhibit neutrophil migration and generation of ROS. Herbal extracts or oil may be used as monotherapy or in combination therapy. When 2% ocimum oil is used with

aloevera gel, the activity against acne increases due to synergistic effect of these agents. The concerned side effects of herbal drugs are much less compared with modern drugs. Thus, natural substances, which are obtained from the medicinal plant, having antibacterial and anti-inflammatory activity, are commonly employed for the treatment of acne.

SOME HERBAL DRUGS^[14]

Latin binomials Common names

- I. *Achillea millefolium* flowering top Yarrow
- II. *Aloe barbadensis* gel Aloe vera
- III. *Arctium lappa* root Burdock
- IV. *Artemisia absinthium* leaf Wormwood
- V. *Azadirachta indica* leaf Neem
- VI. *Berberis vulgaris* root Barberrry
- VII. *Chamaelirium luteum* root False unicorn
- VIII. *Coptis chinensis* root Goldthread
- IX. *Commiphora mukul* resin Guggul
- X. *Embelia ribes* fruit Vidanga
- XI. *Curcuma longa* rhizome Turmeric
- XII. *Emblica officinalis* fruit Amalaki

- XIII. *Eucalyptus globulus* leaf Eucalyptus
- XIV. *Eucalyptus maculata* leaf Eucalyptus
- XV. *Eucalyptus viminalis* leaf Eucalyptus
- XVI. *Gentiana lutea* root Gentian
- XVII. *Hemidesmus indicus* root Indian sarsaparilla
- XVIII. *Holarrhena antidysenterica* stem bark Kutaj
- XIX. *Hydrastis canadensis* root Goldenseal
- XX. *Mahonia aquifolium* root Oregon grape
- XXI. *Medicago sativa* flowering top Alfalfa
- XXII. *Melaleuca alternifolia* leaf Teatree
- XXIII. *Mitchella repens* leaf Partridge berry
- XXIV. *Ocimum basilicum* leaf Basil
- XXV. *Piper longum* fruit Long pepper
- XXVI. *Scutellaria baicalensis* root Asian skullcap, scute
- XXVII. *Serenoa repens* fruit Saw palmetto
- XXVIII. *Taraxacum officinale* leaf and root Dandelion
- XXIX. *Terminalia chebula* fruit Chebulic myrobalan
- XXX. *Terminalia arjuna* stem bark Arjun
- XXXI. *Verbena* spp. flowering top Vervain
- XXXII. *Vitex agnus-castus* fruit Chaste tree, vitex
- XXXIII. *Xanthorrhiza simplicissima* root Yellowroot
- XXXIV. *Zingiber officinale* rhizome Ginger
- XXXV. *Withania somnifera* root Ashwagandha

1. **Barberrry:** Barberrry's main bioactive constituent is the alkaloid berberine. Berberine exhibits anti-inflammatory, antibacterial, and androgen-inhibiting properties.¹⁸ Preliminary studies show that it can inhibit the skin cell processes that form comedones in acne, and in animal model research, berberine suppressed sebum production by over 60%. Laboratory studies show that two other barberrry alkaloids, berine and jatrorrhizine, exert antibacterial effects against a number of different bacteria, including *Propionibacterium acnes* (*P. acnes*). When used as recommended, berberine alkaloids from barberrry are considered nontoxic. However, if consumed in large quantities they can cause severe, even fatal, poisoning. Pregnant or nursing women and newborn infants should not consume any herb that contains berberine because it can cause a severe, potentially fatal form of jaundice. Other herbs that contain berberine are goldenseal and yellowroot. Topical use of barberrry can cause skin irritation, but creams containing berberine have been used for 20 days without adverse side effects.^[15]

2. **Guggul (Commiphoramukul):** Guggul extracts appear to have anti-inflammatory and antibacterial properties that may benefit acne patients. Research suggests guggulipid reduces sebum secretion and blocks bacterial metabolism of triglycerides that promote the development of acne. The cholesterol-lowering effects of guggul appear to work best when combined with a non-Western, Indian diet. Those patients with oily skin responded much better to the guggulsterone treatment.^[16]
3. **Tea Tree Oil:** Extracted from the leaves of the tea tree, studies have confirmed tea tree oil's antibacterial activity against harmful microbes without damaging normal, healthy skin microbes. This includes inhibiting growth of the gram positive bacteria associated with acne *Propionibacterium acnes*. In laboratory experiments it's even been shown to kill *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) and actively inhibits herpes simplex virus. Tea tree oil constituents also have anti-inflammatory properties. Clinical studies have demonstrated the effectiveness of tea tree oil in the fight against acne.^[17]
4. **Turmeric (Curcuma longa):** Turmeric's primary biologically active component is curcumin. Research has shown that curcumin has potent antioxidant, wound-healing, and anti-inflammatory properties, which may prove to be therapeutic against acne. Turmeric is considered safe in amounts found in foods and when taken orally and topically in medicinal quantities. It may cause atopic dermatitis in some people. However, pregnant women should not take medicinal amounts of turmeric because it could stimulate the uterus. Topically turmeric may cause the skin to temporarily stain yellow—especially in people with light skin tones. When used as a topical remedy, it is typically mixed with water or honey to a pasty consistency and applied directly to the skin. Orally, dried turmeric can be mixed into liquid and consumed.^[18]
5. **Saw palmetto (Serenorepens):** Saw palmetto is considered an anti-androgenic substance because it inhibits the enzyme necessary to convert testosterone to dihydrotestosterone (DHT). DHT influences sebum production by the sebaceous glands, and lowering DHT levels may help reduce the excess oils that contribute to the development of acne. In fact, when excessive androgen hormones are suspected in acne cases (e.g., in females with polycystic ovary syndrome) herbal clinicians often look to saw palmetto as a first-line regimen. Oral use of saw palmetto is generally considered safe.^[19]

Case study and clinical trials^[20]

Purim has hepatoprotective herbs, which help to eliminate various toxins present in the blood and improve digestion and blood circulation. It has also anti-inflammatory and antibacterial properties.

Clarina cream acts topically as an astringent, anti-inflammatory and antibacterial agent. In an experimental trial Aloe barbadensis exhibited topical anti-inflammatory activity equivalent to hydrocortisone⁵. Alternanthera sessilis contains very high amounts of carotene, which is a potent antioxidant. Clinical trials conducted using acne gels containing zinc showed that at the end of the test period there was a significant difference in the reduction of inflammatory and non-inflammatory lesions. The extract of Rubiacordifolia has been shown to possess significant inhibitory properties in experimentally induced lipid peroxidation⁸. Borax, which is present in Clarina cream, acts as an astringent.

Purim tablets contain different herbs. Picrorrhizakurroa has hepatoprotective and hepatic stimulant properties. In a randomised, double-blind placebo controlled trial in patients with acute viral hepatitis, a 375 mg extract was administered three times a day for 2 weeks. Inhibition of bilirubin, SGOT and SGPT was significant. Andrographis paniculata has andrographolide as an active principle, which acts as an anti-inflammatory agent. Studies have shown that Ecliptaalba has potent hepatoprotective activity, the mechanism of action being the regulation of the levels of hepatic microsomal drug metabolising enzymes. Tinosporacordifolia is found to possess immunomodulatory activities. Saussurealappa has many active principals which act as an anti-inflammatory drug, it acts by inhibiting the production of inflammatory mediators and the proliferation of lymphocytes. Embeliaribes was found to be effective as an analgesic by oral, i.m. and i.v. routes and the results are comparable with morphine. In a study on the wound healing properties of Curcuma longa, it was observed that there was faster wound closure of punch wounds in curcumin-treated animals in comparison with untreated controls. Biopsies of the wound showed re-epithelialization of the epidermis and increased migration of various cells including myofibroblasts, fibroblasts, and macrophages in the wound bed. Multiple areas within the dermis showed extensive neovascularization. Azadirachta indica has antibacterial activity against a variety of micro-organisms such as *Staphylococcus*, *Enterococcus*, *Pseudomonas*, *Escherichia*, *Klebsiella*, *Salmonella* and *Mycobacterium*. A study was done to assess various plants for antibacterial properties. Among them *Cassia fistula* showed significant antibacterial activity against various bacteria¹⁷. The growth curve of *Staphylococcus*

aureus in a liquid medium with and without bakuchiol, the main component of *Psoralea corylifolia* also displayed the antibacterial properties of the herbal ingredient in vitro.

significant symptomatic relief was noted with 4 weeks of treatment with Clarina cream and Purim tablets, administered concurrently. The results in this clinical trial show that Clarina cream and Purim tablets can be safely given to patients with acne.

Case Study^[21]

Digestive Herbs for Acne

A 23-year-old male patient with mild-to-moderate papulopustular acne on the face, back, and chest that had not responded to systemic erythromycin treatment sought naturopathic care. He also complained of having claylike stools. He was a vegan (and had been for 7 years) except for occasional dairy-product intake and was in a stressful educational program. He used no medication but was taking a multivitamin and vitamin C. Blood tests revealed that he had low-grade macrocytic anemia. Stool fecal-fat analysis indicated elevated fecal-fat levels. Celiac disease was excluded by a negative serum antiendomysial antibody test. The initial treatment for this patient included:

- Increasing omega-3 fatty acid-rich foods in his diet, particularly (*Linum usitatissimum*) flax oil
- An elimination/challenge diet (which revealed that he had various negative reactions to dairy products, avocados, and chocolate)
- One intramuscular (IM) vitamin B12 shot weekly for 6 weeks.

After 3 months on this protocol, the patient had a moderate reduction in number of acne lesions and his anemia was resolved, but his stools had not improved much. Therefore, a bitter tincture

formula containing 50 percent *Gentiana lutea* (gentian) root, 30 percent *Taraxacum officinale* (dandelion) leaf, and 20 percent *Mahonia aquifolium* (Oregon grape) root was prescribed at a dose of 2 droppers-full before meals. The patient also decided to start eating fish and began taking 6 g of fish oil per day. Three (3) months of this program led to a near-total resolution of all lesions as well as normalization of his stools. The bitters were discontinued after 1 more month, and the acne remained almost entirely resolved. After 1 year that was associated with a severe time of stress, some of his acne lesions recurred, but these were reduced when his stress passed. Reinstating bitters, occasional use of topical tea

tree (*Melaleuca alternifolia*) oil in jojoba (*Simmondsia chinensis*) oil, and stress reduction were sufficient to control these episodes. After 4 years of this treatment, the patient would often go for months with no lesions, and acute outbreaks would consist of no more than 4–5 lesions on his back and face.

a Vitamin B12 has been reported to exacerbate acne in some cases, but this patient was vitamin B12-deficient and, clearly, the vitamin was indicated (and it did not exacerbate his acne). This is an instance that illustrates the value of individualized medicine.

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