Jundishapur J Microbiol. 2015 November; 8(11): e25580. doi: 10.5812/jjm.25580
Published online 2015 November 21. **Review Article**

# Medicinal Plants for the Treatment of Acne Vulgaris: A Review of Recent Evidences

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**Received** 2015 February 10; **Revised** 2015 July 1; **Accepted** 2015 August 8.

**Abstract**

**Context:** Acne vulgaris affects about 85% of teenagers and may continue to adulthood. There are about two million visits to physicians per year for teenagers and the direct cost of acne treatment in the US exceeds $1 billion per year.

**Evidence Acquisition:** A wide variety of treatment regimens exist for acne vulgaris including benzoil peroxide, retinoids, isotretinoids, keratolytic soaps, alpha hydroxy acids, azelaic acid, salicilic acid as well as hormonal, anti-androgen or antiseborrheic treatments. However, none of these methods is free of side effects and their exact role in therapy is not clear. In this paper apart from presenting the possible causes of acne vulgaris and its available drugs, recently published papers about medicinal plants used in the treatment of acne vulgaris were reviewed.

**Results:** Consumption of alternative and complementary medicine, including medicinal plants, is increasing and is common amongst patients affected by acne and infectious skin diseases. Medicinal plants have a long history of use and have been shown to possess low side effects. These plants are a reliable source for preparation of new drugs.

**Conclusions:** Many plants seem to have inhibitory effects on the growth of bacteria, fungi and viruses in vitro. However, there are a few clinical evidences about the effectiveness and safety of these plants in the treatment of acne and other skin infections.

*Keywords:* Acne Vulgaris, Medicinal Plants, Herbal Medicines, Infectious Disease, Skin Diseases

## 1. Context

Acne vulgaris (or simply acne) is an infectious disease and one of the most prevalent human diseases. It is characterized by different areas of scaly red skin (seborrhea), pinheads (papules), blackheads and whiteheads (comedones), large papules (nodules), and sometimes scarring (piples). Severe acne is usually inflammatory, however it may also be non-inflammatory. In acne, the skin changes, due to changes in pilosebaceous unit skin structures including hair follicles and their associated sebaceous glands. These changes usually require androgen stimulation (1). Acne vulgaris is usually due to an increase in body androgens, and occurs more often in adolescence during puberty, regardless of sex. Acne is usually seen on the face, upper part of the chest, and the back of subjects who possess greater numbers of oil glands (2).

Acne infection affects about 85% of teenagers and may continue to adulthood. There are about two million visits to physicians per year for teenagers and 0.2 million visits are by patients aged over 35 years. The direct cost of acne treatment in the US exceeds $1 billion per year. Furthermore, these patients spend more than $100 million on none-prescription acne products (1). Psychological, social, and emotional impairment that result from acne have been estimated to be equal and in some instances higher than that of diabetes, arthritis, epilepsy and asthma. Acne vulgaris may cause scarring, leading to lifelong problems regarding self-esteem. These patients are prone to depression and are more likely to be unemployed (3). It has been estimated that acne affects 650 million people globally and is the eitgth most common diseases in the world. Most people believe that acne vulgaris tends to disappear and diminishes or decreases over time by age. However, there is no method to estimate how long it would take to start to decrease or disappear entirely (4).

The acne treatment strategy depends on its severity. For patients with large distributed pustules and papules (severe acne) both topical and oral therapies are usually prescribed. Then, after six to eight weeks, the efficacy, compliance and the adverse effects are assessed and again the regimen is adjusted, accordingly (2). A wide variety

of treatment regimens exist for acne vulgaris including benzoil peroxide, retinoids, isotretinoids, keratolytic soaps, alpha hydroxy acids, azelaic acid, salicilic acid as well as hormonal, anti-androgen or antiseborrheic treatments (2). The direct injection of steroids into inflamed cysts, microdermabrasion, chemical peels, radiofrequencies, light or lasers have been shown to result in the relief of acne, however, none of these regimens is free of side effects. Furthermore, more investigations are needed to clarify the exact role of these methods in therapy (2, 5). Using alternative and complementary medicine, including medicinal plants, is also common within patients affected by acne and infectious skin diseases (6).

## 2. Evidence Acquisition

Medicinal plants have a long history of use (7) and have been shown to possess low side effects (8, 9). Other than diseases such as common cold and infectious diseases, they have been useful in prevention (10, 11) and treatment (12, 13) of a wide variety of diseases that are difficult to cure, such as cancer (14), cardiovascular diseases (15, 16), diabetes (17, 18) hypertension (19, 20) and atherosclerosis (21, 22). Medicinal plants also possess the capacity to diminish drug-induced adverse effects (23, 24) and even heavy metal or other toxicities, such as the protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rats (25). Acne vulgaris drugs mostly possess adverse effects and therefore, medicinal plants might be considered as reliable sources for development of new drugs.

In this paper other than presenting the possible causes of acne vulgaris and its available drugs, recently published papers about medicinal plants used in the treatment of acne vulgaris are reviewed. In this study, we attempted to present information from studies published since early 1980, which were present in databases such as Google scholar, PubMed and Scopus related to medicinal plants effective in the treatment of acne vulgaris. The included key words were phytomedicine, botanicals, herbs, medicinal plants, herbal medicines, herbal therapy or phytotherapy, and acne vulgaris.

## 3. Results

Generally, 1176 articles were obtained as the result of the research. Overall, 58 articles including clinical and non-clinical studies were found to be useful and were included in this review.

### 3.1. Causes of Acne Vulgaris

#### 3.1.1. Infectious Contribution

*Staphylococcus aureus* and *Propionibacterium acnes* have been attributed to acne vulgaris. However, their exact contributions in the acne process are not entirely clear. There are sub-strains of *P. acnes* in normal skin and some others in long-term acne complications. Therefore, it is unclear whether these strains are involved in this condition or they are pathogenically acquired. Resistance of *P. acnes* to commonly used drugs has been shown to be increasing (1). These strains are able to change, perpetuate, or adapt to the abnormal oil production, inflammation and inadequate sloughing of acne pores. Infection with Demodex, which is a parasitic mite has been shown to be associated with the development of acne. However, eradication of the mites has not improved acnes (26).

#### 3.1.2. Dietary Contribution

The relationship between diet and acne is unclear as there is no good quality evidence. However, a high level of glycemic diet has been shown to be associated with worsening of acne vulgaris. A positive correlation between the use of milk, chocolates or salt, and increase in the severity of acne vulgaris has also been suggested. However, the contribution of chocolates is disputable, as they can be made with different amounts of sugar, with or without milk. A relationship between obesity and acne has also been reported (27).

#### 3.1.3. Genetic Contribution

For specific subjects, the predisposition to acne might be explained by a genetic component. This suggestion has been supported by some studies that have evaluated the rate of acne among first degree relatives, as well as twin studies. There are varieties of genes, which have been attributed to acne, such as polymorphisms in *IL-1α*, *TNF-α*, and *CYP1A1* amongst others (28).

#### 3.1.4. Hormonal Changes

Hormonal changes, such as puberty and menstrual cycles, seem to contribute to formation of acne vulgaris. An increase in some sex hormones, especially in androgens during puberty and pregnancy, cause the follicular glands to produce more sebum. The use of anabolic steroids usually has similar effects. The hormones, which have been attributed to acne vulgaris consist of testosterone, dehydroepiandrosterone and dihydrotestosterone, as well as insulin-like growth factor 1. Development of acne vulgaris in adult women might be due to an underlying condition such as Cushing syndrome, polycystic ovary syndrome or hirsutism (29).

#### 3.1.5. Psychological Contribution

Some scientific researchers have indicated that acne severity is correlated with an increase in stress level and stress has been listed as a factor attributed to acne flare. However, the connection between stress and acne vulgaris has been debated by some other studies (30).

### 3.2. Medical Treatments

Topical or/and systematic treatments are used to treat acne. The response of patients to treatment is consider-

ably different. Usually more than one treatment modality is employed to treat acne and best results are achieved when treatments are individualized on the basis of clinical evaluations. Retinoids are the mainstay of therapy in patients who only have comedones. They are capable of reducing inflammatory lesions and the number of comedones (40% - 70%). Other agents, including isotretinoin, oral antibiotics, topical antimicrobials, and hormonal therapy, have been shown to yield high response rates. Patients with mild to moderate severity, inflammatory acne with papules and pustules are recommended to be treated with topical antibiotics combined with retinoids. For patients with moderate to severe inflammatory acne, oral antibiotics are the first-line therapy. However, oral isotretinoin is recommended for severe nodular acne, frequent relapses, treatment failures or severe psychological distress. Isotretinoin is the most effective drug and to avoid long-term topical or oral antibiotic therapy, which may cause bacterial resistance, this drug may be recommended. However, isotretinoin is a powerful teratogen, needing strict precaution for use among women of the childbearing age. Medicinal plants are also used for the treatment of acne and are discussed below (1, 31).

### 3.3. Medicinal Plants with Anti-Acne Activity

Herbal medicines are gaining increased popularity due to their advantages, such as better patient tolerance, long history of use, fewer side-effects and being relatively less expensive (8). Furthermore, they have provided good evidence for the treatment of a wide variety of difficult to cure diseases (7, 32-41). These plants are used alone or in combination with synthetic drugs to treat diseases (42-47). More importantly, other than consumption as preventive or treatment remedy, they might be accompanied with synthetic drugs to reduce their side effects (7, 47-54). With no exception, botanical drugs are also used accompanied by other methods or alone to treat acne vulgaris. Many medicinal plants with anti-inflammation and antibacterial activities are used in different ways in the treatment of acne and other infective diseases (54-60).

*Matricaria recutita*, *Calendula officinalis* and *Triticum aestivum* are commonly used species of these plants (61). Creams or aqueous infusions made from plants including astringents and composites such as tannins are used topically on skin after cleansing or a steam bath. *Hamamelis virginiana* has tannins and extraction of epidermis is commonly used to treat acne because it is very safe for topical prescription. Other plants containing tannins are white oak's bark (*Quercus alba*), walnut's leaf (*Juglans regia*), *Agrimonia eupatoria*, *Syzygium cuminum*, *Syzygium cuminum*, *Ledum latifolium*, *Alchemilla mollis*, *Lavandula angustifolia*, *Verbascum thapsus*, *Krameria triandra*, *Rheum palmatum*, *Hypericum perforatum* and *Rumex crispus* (62). Other plants that are traditionally used topically or as a depurative include *Bellis perennis*, *Viola tricolor*, *Elymus repens* and *Taraxacum officinale*. Topical use of horsetail depurative (*Equisetum* species) is recommended due to the high amount of silicic acid and yellow milk of *Aloe ferox* fresh leaves because of anthranoids (61).

*Vitex agnus-castus* is used for acne before menstruation. The whole fruit extract acting on follicle stimulating and luteinizing hormone levels in the pituitary gland led to an increase in progesterone and decrease in estrogen levels through the dopaminergic mechanism, declining the level of premenstrual prolactin. German Commission E has recommended daily intake of 40 mg *Vitex agnus-castus* extract for the treatment of acne. Pregnant and nursing women should not use this plant. Adverse side effects such as gastrointestinal disturbances and skin rashes have been reported (63, 64). In addition to the traditional use of herbal medicines as anti-acne, antibacterial activities of some plants in order to determine their potential as acne herbal treatment have been investigated (65). An anaerobic pathogen, *P. acnes*, plays an important role in acne pathogenesis and seems to begin the inflammatory process through stimulating the production of reactive oxygen species (ROS) and release of inflammatory and proinflammatory cytokines (66). Interestingly, the inhibitory effect of licorice (*Glycyrrhiza glabra*) is not associated with bacterial resistance induction of the growth of *P. acnes* in vitro (67).

Screening of plant extracts for anti-bacterial and yeast activity has shown that usnic acid, an effective substance of *Usnea barbata*, has strong inhibition effect on the growth of *P. acnes*. The growth of bacteria was inhibited at $\geq 1\mu g/mL$ concentrations. In addition, *U. barbat*a was found to have a wide range of anti-oxidative and antibacterial properties suggesting that it may be a promising substance in acne treatment (68). A four-week clinical trial compared the essence of *Ocimum gratissimum* at four different levels (0.5-5%) and four different bases by placebo and standard treatment (benzoyl peroxide, 10%). Two percent essence of *O. gratissimum* in a hydrophilic base (alcohol or cetomacrogol) reduced skin lesions faster than standard therapy, without any side effects, while 5% concentration was effective but with skin irritation (65). A study reported that topical application of *O. gratissimum* essence was superior to placebo and clindamycin 1%. In this study, topical yellow *Aloe vera* was not solely effective in acne treatment, however, showed a synergistic interaction with *O. gratissimum* (69).

Topical use of 50% *Aloe vera* gel with tretinoin cream was well tolerated during eight weeks in a randomized double-blind clinical trial with 60 patients suffering from mild-moderate acne and was significantly more effective than tretinoin and vehicle (70). German Commission E has confirmed the topical use of *Solanum dulcamara* and edible use of *Saccharomyces cerevisiae* because of their antibacterial effect as an acne remedy (71). In China, *Lemna minor* has been used topically to treat acne. A clinical trial noted that consumption of gugulipid, standardized extraction of oleoresin of an Indian herbal plant named *Commiphora mukul*, for three months, was effective in treating acne. Interestingly, the patients with oily skin respond remarkably to gugulipid. It should be

noted that the aforementioned studies had a number of methodological limitations, for instance, there were only 10 individuals in each group (and without placebo), thus there was not enough power to determine significant differences between the medicines (63).

Use of 2% lotion of green tea (*Camellia sinensis*) topically, during six weeks among 20 patients suffering from mild to moderate acne, was found to be effective compared with pretreatment. Tannins and flavonoids of green tea may possess an anti-acne effect, since they seem to have an antiseptic effect while tannins also have an anti-inflammatory effect (71). In Western traditional medicine the root of *Mahonia aquifolium* or *Berberis aquifolium* has been used to treat chronic skin rashes (pustule). The main effective substances of *Mahonia* extracts include two alkaloids of Protoberberine, namely Jatrorrhizine and Berberine, which have inhibited the in vitro growth of *Staphylococcus coagulase*, *P. acne* and *Candida* species. Berberine (100 μmol/mL) in an animal model inhibited fat production in Sebaceous by 63% (72).

Berberine alkaloid is a bitter substance with anti-fat production and anti-inflammatory effect on 3T3-L1 fatty cells, and its anti-fat production effect, has been related to down regulation of fat production enzymes and transcription factors. However, the exact mechanism of Berberine and herbs enriched in Berberine is still unknown (73). Tea tree oil (TTO) has a broad spectrum of antibacterial properties and reduces skin inflammation due to inhibition of histamine release. Five percent tea tree oil and 5% benzoyl peroxide improved acne in a three-month single-blind clinical trial on 124 patients, however, the effect of tea tree oil began slowly and a few patients in the tea tree oil group showed skin complications (74). While the mentioned study had no placebo group, a 45-day double-blind, randomized trial with 60 patients showed the efficacy of 5% topical gel of tea tree oil on mild to moderate vulgaris acne. The efficiency of tea tree oil gel for the total numbers of acne lesions and intensity index of acne was found to be 3.55 and 5.75 times higher than the placebo, respectively (75).

Gluconolactone is made of a polyhydroxy acid formed by *S. boulardii*. The results of a double-blind clinical study on 150 patients with topical usage of a 14% gluconolactone solution showed the removal of inflamed acne lesions, which was significantly superior when compared to the placebo and comparable with 5% benzoyl peroxide, however, with less adverse side effects (76). The plants, which have gained more popularity for the treatment or prevention of Acne vulgaris during the past two decades, are presented with more details below.

### 3.3.1. Achyranthes aspera

This medicinal plant is traditionally used for the treatment of Acne vulgaris, eruptions of the skin, boils, scabies and other skin diseases. Saponin, alkaloid and non-alkaloid fractions obtained from the leaves of this plant have enormous inhibitory effect on the Epstein-Barr virus early antigen activation in Raji cells, with the most inhibitory activity (96.9%; 60% viability) observed for the non-alkaloid fraction, which contains non-polar compounds. In the in vivo two-stage mouse skin carcinogenesis test the total methanolic extract possessed a pronounced anti-carcinogenic effect (76%). The results revealed that the leaf extract and the non-alkaloid fractions were valuable antitumor promoters in carcinogenesis. The plant has abortificient properties in rodents and also has contraceptive activity, which might be due to its potent estrogenic activity (76).

### 3.3.2. Allium cepa

Onion extract gel has shown the ability to improve the appearance of scars in patients with seborrheic keratosis. This extract gel has been shown to improve the scar's appearance by improving its redness, softness and texture at excision site four, 6 and 10 weeks after the extract usage (76). In another study, the antimicrobial and antifungal properties of a *A. cepa* and *A. sativum* were revealed against *Malassezia furfur*, *Candida albicans* and some other *Candida* sp, as well as some strains of dermatophytes and Acne vulgaris microbes. The results indicated that *A. cepa* and *A. sativum* might be promising in the treatment of bacterial and fungal-associated infections (77).

### 3.3.3. Azadirachta indica

In a study, conducted on an anti-acne formulation prepared from herbal extracts, it was revealed that ethanol extract of *Azadirachta indica*, *G. glabra*, *Andrographis paniculata*, *Ocimum sanctum*, and green tea possessed the potential for inhibiting acne. In this study the anti-acne formula successfully acted against *Propionibacterium* and *Staphylococcus epidermis* (78). Aqueous extract of *Azadirachta indica* leaves also possess chemopreventive potential against murine skin carcinogenesis. Skin tumors have been shown to enhance the expression of proliferating cell nuclear antigen in comparison to the control group. In this study, skin tumors exhibited high level of lipid peroxidation (40).

### 3.3.4. Cannabis sativus

The seed oil of *Cannabis sativus* is useful for the treatment of acne rosacea, seborrhoeic dermatitis, eczema, dermatitis, psoriasis and lichen planus. The leaves powder of this plant is very useful as a wound and sore dressing. *Cannabis sativus* extract is externally useful to relieve pain in itchy skin. The seed oil strengthens the skin and makes it more resistant to bacterial, fungal and viral infections (79).

### 3.3.5. Echinacea angustifolia and Echinacea purpurea

The extract of *Echinacea purpurea* has been shown to readily kill *P. acnes*, which is the main cause of acne vulgaris. In cell culture models, *P. acnes* induced substantial secretion of several pro-inflammatory cytokines, such as IL-6 and IL-8. However, the *E. purpurea* was able to com-

pletely reverse this effect to normal leaves. Hence, *E. purpurea* provided a safe two-fold benefit to acne patients by inhibiting bacterial-induced inflammation and inhibiting the proliferation of organism (49). Echinacea has also been used to treat other skin problems such as psoriasis, skin wounds, burns, ulcers, herpes and hemorrhoids (71).

### 3.3.6. Rosmarinus officinalis

*Rosmarinus officinalis* is a household plant, which is grown in many parts of the world. It is used as a beverage drink, flavoring food, as well as in cosmetics. *Rosmarinus officinalis* contains rosmarinic acid. Chronic UV exposure has manifestations such as photo-cancers and photo aging. Aqueous extract of *R. officinalis* is effective in prevention of photo damage induced by UV radiations due to its antioxidant effect (71). Infections are also associated with oxidative stress. Therefore, the compounds, which possess antioxidant properties, might be beneficial in this way, regardless of their antibacterial activity. *Rosmarinus officinalis* oil has also been effective against *P. acnes*, a type of bacteria that causes acne. In a study, the antibacterial properties of *R. officinalis* essential oil was evaluated against *P. acnes* in which significant changes were reported in size and morphology of *P. acnes* in response to treatment (80).

### 3.3.7. Melaleuca alternifolia

*Melaleuca alternifolia* or tea-tree is a tree or tall shrub in the plant genus *Melaleuca*. It is native in Australia, and occurs in north coast and adjacent areas of New South Wales. It also grows on swampy flats and along streams and where it occurs, it is often the dominant species. Tea tree oil is a broad-spectrum agent against Gram-positive and Gram-negative bacteria and even *S. aureus* resistant to methicillin and yeasts such as *C. albicans* in vitro. Its mechanism of action has been attributed to monoterpenes, which cause disruption of the plasma membrane barrier. Other than antimicrobial activity, tea tree oil has monocyte activators and anti-inflammatory activities. Topical use of low concentrations of tea tree oil has anti acne activity with low side effects. It is effective in chronic infectious wounds and osteomyelitis (81).

### 3.3.8. Eucalyptus globulus, E. viminalis and E. maculata

In one study, the leave extractions of 29 *Eucalyptus* species were examined for anti-microbial activities. Extractions of *Eucalyptus globulus*, *E. maculata* and *E. viminalis* were able to inhibit the growth of six gram-positive bacteria including *P. acnes*, *S. aureus*, *Enterococcus faecalis*, *Bacillus cereus* and *Alicyclobacillus acidoterrestris*, and a fungi, *Trichophyton mentagrophytes*, yet they did not show a strong inhibitory activity against gram-negative bacteria. A component of *E. maculate* (8-desmethyl-eucalyptin) also had strong inhibitory activity against the above-mentioned microorganisms. The authors concluded that *Eucalyptus* extracts and some components isolated from this plant had an inhibitory effect on microorganisms causing acne and Athlete's foot infection, as well as some fungal infections (18). Clinical trials with positive effects are summarized in Table 1.

**Table 1.** Clinical Trials With Positive Effects

| Medicinal Plants | Family | Used Part(s) | Active Compound | Results | Ref. |
|---|---|---|---|---|---|
| ***Aloe vera*** | Xanthorrhoeaceae | extracts | | anti-bacterial and anti-inflammatory properties | (82) |
| ***Azadirachta indica*** | Meliaceae | extracts | | anti-bacterial and anti-inflammatory properties | (82) |
| ***Curcuma longa*** | Zingiberaceae | extracts | | anti-bacterial and anti-inflammatory properties | (82) |
| ***Hemidesmus indicus*** | Apocynaceae | extracts | | anti-bacterial and anti-inflammatory properties | (82) |
| ***Terminalia chebula*** | Combretaceae | extracts | | anti-bacterial and anti-inflammatory properties | (82) |
| ***Withania somnifera*** | Solanaceae | extracts | | anti-bacterial and anti-inflammatory properties | (82) |
| ***Butyrospermum paradoxum*** | Sapotaceae | oil | | anti-bacterial activity | (83) |
| ***Camellia sinensis* L.** | Theaceae | | polyphenol, polyunsaturated fatty acid | anti-inflammatory and 5 α-reductase inhibitory activities | (84) |
| ***Commiphora mukul*** | Burseraceae | gugulipid, a standardized extract of the oleoresin | oleoresin | anti-bacterial activity | (85) |
| ***Hippophae rhamnoides* L.** | Elaeagnaceae | fruit extract | vitamins C and E, organic acids, macronutrients, polyunsaturated fatty acid | type 1-α reductase inhibitory activity | (86) |
| ***Lens culinaris*** | Fabaceae | powder and complex extracts | polyphenol, | anti-oxidant, anti-inflammation, anti-androgen and anti-bacterial activities | (87) |
| ***Aloe barbadensis*** | Asphodelaceae | powder and complex extracts | polysaccharide, | anti-oxidant, anti-inflammation, anti-androgen and anti-bacterial activities | (87) |
| ***Vitex negundo*** | Verbenaceae | | flavonoid | anti-oxidant, anti-inflammation, anti-androgen and anti-bacterial activities | (87) |
| ***Andrographis paniculata*** | Acanthaceae | | | anti-oxidant, anti-inflammation, anti-androgen and anti-bacterial activities | (87) |
| ***Salmalia malabarica*** | Malvaceae | | | anti-oxidant, anti-inflammation, anti-androgen and anti-bacterial activities | (87) |
| ***Melaleuca alternifolia*** | Myrtaceae | oil | | anti-inflammation and Anti-bacterial | (88) |

## 4. Conclusions

Many plants seem to have inhibitory effects on the growth of bacteria, fungi and viruses in vitro. Also, some plants have been shown to have anti-inflammatory and anti-fat properties. However, there are a few clinical evidences about the effectiveness and safety of these plants in the treatment of acne and other skin infections. For this reason, chemical drugs seem to still be the first choice in the treatment of acne and skin infections. However, the efficacy and safety of synthetic drugs are under question in the treatment of acne and other skin infections. Some plants reviewed in this paper have shown promising results. Hence, they might possibly be used alone or as adjuvant with other therapeutic measures or in mild to moderate situations. Possible contact sensitization especially in topical or oral use should be considered. Some plants, especially the roots of mountain grapes, tea tree oil, *Saccharomyces*, and perhaps *Ocimum basilicum* due to their effectiveness and safety can be compared to alternative treatments with synthetic drugs for mild to moderate acne (74-76). Further clinical studies validated with controls are required to use plants particularly the three species of *eucalyptus* (*E. globulus*, *E. maculata*, *E. viminalis*), *G. glabra*, *U. barbata*, *L. minor*, green tea, mountain grape root (*M. aquifolium*) and gluconolactone of *S. bulderi*, and gugulipid to treat acne. Efficacy and clinical safety trials of *H. perforatum*, *C. sativum*, *B. serrata*, *U. barbata*, *R. officinalis* and green tea are also essential in bacterial skin infections.

Mechanism of action of these plants is another important subject, which should be addressed. Phenolic compounds derived from plants have been shown to possess antibacterial activity. Most of the presented plants in this review article possess these compounds. However, in most cases it is not known how much these compounds are responsible for their anti-acne activity. It should be noted that a lot of other plants have phenolic compounds (18, 33, 89-97). Hence, if these compounds are solely responsible for the observed anti-acne activities, all plants with phenolic compounds should have anti-acne properties, which worth examining.

## Acknowledgments

We would like to thank the Research Deputy of Shahrekord University of Medical Sciences, Shahrakord, Iran for their support.

## Footnote

**Authors' Contribution:**All authors contributed in the preparation of the first draft and confirmed the final version. Mahmoud Rafieian-Kopaei edited and confirmed the final version.

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