

**ACNE VULGARIS: REVIEW ON PATHOPHYSIOLOGY AND
HERBAL REMEDIES**

Vandana Yadav^{1*}, Pratima Katiyar², Kalpana Kushwaha², Ruchi Verma³ and Manish Kumar³

^{1,3}Research Scholar, University Institute of Pharmacy, C.S.J.M.U Kanpur, UP India.

²Assistant Professor University, Institute of Pharmacy, C.S.J.M.U Kanpur, UP India.

Article Received on
26 May 2022,

Revised on 16 June 2022,
Accepted on 06 July 2022

DOI: 10.20959/wjpr202210-24889

***Corresponding Author**

Vandana Yadav

Research Scholar, University
Institute of Pharmacy,
C.S.J.M.U Kanpur, UP
India.

ABSTRACT

Acne poses a major challenge to dermatologists due to its prevalence, complexity, and range of clinical symptoms. This is the most common skin condition, affecting Indian 85% of teenage boys and 80% of teenage girls, and can last into adulthood. Treatment of acne with topical and systemic symptomatic medications has mild to severe side effects. Therefore, herbs and herbal preparations play an important role as alternative therapies. This article describes herbs commonly used to treat acne. Acne is a polymorphic skin disorder of the sebaceous gland unit with abnormal sebum production, characterized by both inflammatory (papules, pustules, and

nodules) and non-inflammatory (acne, open, and closed) lesions. *Propionibacterium acnes* and *Staphylococcus epidermidis* are common purulent microorganisms involved in the development of various types of acne treatment including long-term use of acne lysing agents, antibiotics, and anti-inflammatory agents. These are known to cause various side effects. Moreover, the long-term widespread use of antibiotics is, unfortunately, resistant to hypersensitivity reactions affecting the liver, lungs, and side effects such as dryness, scales, erythema, burning, and itching. To avoid such adversity, traditional or herbal formulations are preferred. Herbs are safe, effective, and multifunctional. The use of bioactive phytochemicals from a variety of plants not only cares for the body and its parts, but the components it contains also affect the biological function of the skin and are the nutrients needed for healthy skin provides. In general, plants provide a variety of vitamins, antioxidants, a variety of oils, essential oils, hydrocolloids, proteins, terpenoids, and other bioactive molecules that help treat acne. Ayurveda is a traditional Indian medical system.

Siddha; Unani and the Tibetan system of medicine are very helpful in identifying phytochemicals in skin and body care formulation.

KEYWORDS: Medicinal herbs, Acne, Skin diseases, Acne vulgaris, Propionibacterium acnes, essential oil, terpenoids, inflammatory, hypersensitivity.

INTRODUCTION

Acne is a multifactorial disease that affects the sebum unit of the skin. Blockage of the sebum unit can lead to the development of acne lesions. The medical term for common acne is Acne Vulgaris.^[1] In some people, this problem is so severe that they have pus-filled inflammatory rashes that are very painful. Sometimes acne leaves black spots and scars on the face. The sebaceous glands secrete an oil that turns into a solid white substance called sebum. Sebum migrates to the opening of a hair follicle and bursts into the surface of the skin. This process may be due to infection of these glands or excessive levels of male hormones called androgens.^[2] Blackheads occur when sebum mixes with skin pigment in clogged pores. Acne is an anachronic inflammatory disease of the sebaceous unit.^[3] It usually occurs during puberty but can also be observed in adults.^[4] Its pathophysiology involves three factors, hypersecretion sebum, abnormal follicular keratinization, and proliferation of propionibacterium acnes in the sebaceous unit., the skin's microenvironment changes and leads to an inflammatory host response that promotes the progression of acne lesions pathophysiology of acne.

Acne is a skin condition that suppresses a person's self-esteem about physical appearance and has a clinical onset during puberty and adolescence.^[5] A high incidence of acne is found in 4,444 girls aged 14 to 17 years and in boys aged 16 to 19.^[6] The pathogenesis of acne is regulated by excess sebum in deformed follicles leading to microcomedones, and follicular hyperproliferation of microcomedones causes inflammation^[7] and comedones^[8] in both open and closed types (Black and White comedones) in papules, pustules, nodules, and cysts.^[9] The resulting sebum-enriched skin condition is susceptible to anaerobic growth of Propionibacterium acnes, the main acne microorganism. In addition, Staphylococcus epidermidis and Pitryosporum ovale are present in acne lesions.^[10] The multiplication of these microorganisms, mainly P. acnes, produces inflammatory lesions and severe acne.

Acne is the most common skin problem, three of which are the main forms, pruritus Vulgaris, scabs, and acne. Steroid rosacea acne is rosacea chronic acne, such as the rash in the face of adult adults middle-aged and higher associated with Facial Rinse (Murray and Joseph, 1998).

Acne affects both men and women, although, with the onset of puberty, men tend to more. It looks like a male hormone-like testosterone stimulates the cells that line the hair ducts to produce keratin, which enlarges the sebaceous glands and produces more sebum. This leads to particle formation and channel clogging. when the block is completed, a white head is formed, and when the block is not completed, a darkening is formed. Tube obstruction also causes the overgrowth of p.acnes (*Corynebacterium acnes*), releasing enzymes that break down sebum and promote inflammation. The inflammation causes the acne to turn red. Another cause of acne is low levels of 5 α -reductase, which converts testosterone into a more potent form of dihydrotestosterone (DHT) (Takayasu et al, 1980). Intestines poisoning, where toxins are absorbed from the intestines, which leads to elevated levels of toxins in the blood, is another cause of acne (Juhlin and Michaelson, 1983).



Fig. 1: Herbal medicine.

Clinical classification of acne

- Grade 1 (mild): comedones, occasionally papules. (Comedones or blackheads are worm-like collections of hardened sebum.
- Grade 2 (medium): comedones, papules, few pustules.
- Grade 3 (severe): pustules, nodules, abscesses.
- Grade 4 (cysts).



Fig. 2: Degrees of acne.

The degrees of acne

- **White spikes (Closed comedones):** White spikes are enclosed inflammations of the sebaceous glands with dead cells on the surface of the skin that prevent their exposure to the atmosphere and therefore remain white.

Multiple closed comedones (White heads)

- **Blackheads (open comedones):** Blackheads appear the same in, but exfoliating the skin removes dead debris, exposing the upper part of the white spike, which oxidizes and turns black on contact with the atmosphere. that is why it is called a blackhead. A simple cleansing of the skin will not remove black and white pimples.^[11] When bacteria, oil, and dead cells become trapped in sebum, they can swell and eventually burst, creating an inflamed, tender and painful area that we call a pimple.



Fig. 3: Multiple closed comedones (Whiteheads).

Multiple open comedones (Black heads)

- **Pimples:** pus-filled spots (Pustules).
- **Red pimples or bumps under the skin (Papules)** that contain inflamed tissue.

- Hard knots: under the skin, which can be very painful, penetrate deep into the skin and often cause scarring.



Fig. 4: Multiple open comedones (Black heads).

Papular and Cystic Acne and Post-inflammatory hyperpigmentation

- 1 Open wounds or pimples with scraped ends.
- 2 Marks (spots) and scars.

• **Non-inflammatory acne**

This looks like a few black or whiteheads and occasional pimples. Pimples generally do not leave scars unless they are pinched or pinched, which can lead to infection. It can damage the skin and underlying tissue.

• **Inflammatory acne**

This inflamed white head develops pimples and pustules and a constant rash occurs that covers the face and sometimes the neck, back, chest and groin. These pus-filled pimples can cause disfiguring cysts.

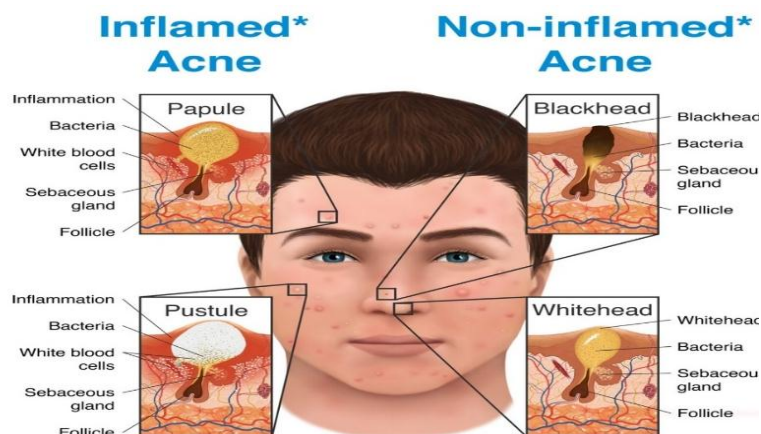


Fig. 5: Image of Inflamed Acne & Non - Inflamed Acne.

What makes acne worse

Acne is generally associated with an increase in hormones during puberty. Hormones increase the production of oil in the skin. Germs that grow in the oil can contribute to redness and inflammation, and acne worsens. Acne is not caused by dirt, poor hygiene, diet, sexual activity, fatty foods, or chocolate. Acne worsens with soap and excessive scrubbing or the use of harsh abrasives and detergents and pimples or bruises from pimples and blackheads (which can delay healing, spread infection deep into the skin, and cause scarring).

Acne is also caused by

- Anabolic steroids.
- Long-term use of oral corticosteroids or antiepileptic drugs such as phenytoin.
- Hormonal treatments.
- Some diseases such as polycystic ovary syndrome.
- Occupational exposure to hazardous chemicals known as dioxins. Sebaceous Gland in acne formation- Acne is more pronounced during puberty and adolescence^[12] and is positively related to sebum function, particularly in adolescents,^[13] which androgenically stimulates increased sebum secretion.^[14] Secreted sebum generally contains a mixture of lipids, squalene, wax, and cholesterol in both free and ester forms, and triglycerides, which naturally provide a barrier function to the skin.^[15] The resulting abnormalities of the sebaceous glands, as the hormonal effects change the composition of the sebum and the linoleic acid content is significantly reduced.^[16] This affects the skin barrier and promotes the colonization of normal flora.

Propionibacterium acnes for acne formation- Abnormalities in sebum function, particularly water-soluble lipids, primarily facial triglycerides in sebum, are pro-inflammatory factors that promote the metabolism of normal flora, such as *P. acne*. *P. acne* has a mitogenic effect on T cells^[17] via heat shock proteins (HSP),^[18] contributes to canopy-like receptors (TLRs),^[19] and activates CD4 +, expressed in keratinocytes and sebocytes and neutrophil function.^[20] Colonization of this anaerobic consequently produces cytokines and other pro-inflammatory compounds, including interleukins (IL), tumor necrosis factors (TNF), interferon (IFN) gamma, and granulocyte-macrophage colony-stimulating factor (GMCSF).^[21,22] In, the induction of IL, in addition to follicular keratinocytes, leads to the formation of microcomedones, and the bacterium activates TLRs that induce the attraction of lymphocytes, neutrophils, and macrophages. Abnormal keratinization and lack of linoleic

acid in follicles also promote the growth of *P. acnes*.^[20] which in turn stimulates the production of pro-inflammatory cytokines/chemokines in sebocytes^[23] and causes chronic inflammatory lesions.

Reactive oxygen species in acne formation - Reactive oxygen species (ROS) are generated from the hypercolonization of *P. acnes*,^[24,25] in addition to metabolism in living organisms and by exposure to UV rays. Although ROS plays a useful role in the skin's barrier against acne microbes,^[26,27] the excess formation influences the condition of the skin by activating the infiltration of neutrophils. ROS including singlet oxygen, superoxide anion, hydroxyl radical, hydrogen peroxide, lipid peroxide, and nitric oxide (NO) play an important role in inflammatory acne and tissue damage. ROS stimulate the formation of the central factor κ B (NF κ B)^[28], promote the formation of TNF,^[29] and, consequently, activate T lymphocytes and keratinocytes. The cytokines IL, TNF, IFN, lipopolysaccharide (LPS), transforming growth factor (TGF), and prostaglandin (PG) are produced and released.^[30-31]

In summary, inflammation of the skin is triggered by CD4 + in T lymphocytes, which is regulated by TLRs after infiltration of neutrophils, which creates ROS, and by protease enzymes, which break down the follicular wall of the glands. sebaceous. This changes the composition of the sebum, especially linoleic acid. Hyperkeratinization begins as well as a reduction in desquamation. The pro-inflammatory cytokines NF κ B, IL, TNF, IFN, LPS, TGF, PG, and GM-CSF are then released and cause microcomedones. The resulting microcomedones develop into comedones and inflammatory lesions.

Topical agents used in the treatment of acne have been grouped, especially naturally occurring compounds, as they are considered safer than synthetic compounds.^[32] Furthermore, the resistance of *P. acne* to some antibiotics used in the treatment of acne has been observed.^[33,34]

Active ingredients for the topical treatment of acne

1. Retinoic Acid and Derivatives: Keratolytic agents such as cis retinoic acid, retinol, and retinyl esters are widely used to normalize keratinization as they have a suppressive effect on sebum function.^[35,36,37] These vitamin A derivatives suppress TLR expression and inhibit IL and IFN production. Cell migration of CD4 + and CD8 + T lymphocytes and macrophages is inhibited.^[38,39] Tretinoin, or trans-retinoic acid, is also used as a comedolytic agent. Normalizes the desquamation of the follicular epithelium by

eliminating the follicle. This reduces the growth of *P. acnes*. The topical application of anti-inflammatory retinoids^[40] produces irritation, which is dose-dependent.^[41] Therefore, in addition to structural modification, appropriate vehicles must be used to reduce this effect. Adapalene, a retinoid-like agent with comedolytic and anti-inflammatory effects, was synthesized. It was formulated mainly in a gel and a cream that was found to be more effective than tretinoin.^[42] Another retinoid-like agent was introduced, tazarotene, which is rapidly converted to its active form, tazarotene acid. However, it had a stronger effect in non-inflammatory than in inflammatory lesions, which was dose-dependent,^[43] as verified^[44] with the other retinoid derivatives such as motretinide, retinol-glucuronide, and retinaldehyde. Unfortunately, there is no comparative study with tretinoin.

2. **Benzoyl peroxide:** The application of benzoyl peroxide, a high-affinity antimicrobial agent that inhibits *P. acnes* and *S. aureus*,^[45] has been incorporated into various formulations, mainly gels.^[46] Benzoyl peroxide ameliorates inflammatory and non-inflammatory lesions^[47] by forming ROS in sebum-inhibiting microorganisms^[48,49] with a reduction in free fatty acids, which triggers the formation of microcomedones.^[50] However, its irritant effect limits its application.^[51] Therefore, combination products were formulated to overcome this disadvantage with an additional benefit in terms of the synergistic effect in combination with adapalene.^[52]
3. **Salicylic acid:** Salicylic acid, a mild anti-inflammatory and keratolytic agent^[53,54] that inhibits PG synthesis has been used to clear follicular congestion^[55] in various formulations, particularly in an alcoholic cleansing solution. This formulation showed better efficacy than benzoyl peroxide^[56] Salicylic acid is a milder agent compared to retinoids. A combination of salicylic acid and benzoyl peroxide would increase the efficacy of the treatment because their mechanisms are different^[57] It was found that exfoliating the skin with salicylic acid is not only a cleansing product, but also significantly reduces comedones.^[58]
4. **Azelaic acid:** Natural azelaic acids have comedolytic activity,^[59] antibacterial properties against *P. acnes*,^[60] including the normalization of keratinization^[61] and anti-inflammatory effects on neutrophil function,^[62] as well as clearing properties of the skin.^[63] In, in addition to single azelaic acid treatment, combined treatments with other anti-acne drugs, especially benzoyl peroxide, increased efficacy.^[65] Additionally, azelaic

acid is safer with less irritation and less phototoxic reaction.^[66] Furthermore, P. Acne's resistance to azelaic acid has not been reported.^[67]

5. Vitamin B: Similar to vitamin A, which is widely used in acne, vitamin B3 or nicotinamide is useful because it inhibits the production of IL8 in keratinocytes by P. acnes-induced NFjB in the early stage of inflammation.^[68,69] As a result, melanosomes that are transferred to keratinocytes are reduced.^[70] Additionally, nicotinamide was thought to suppress leukocyte peroxidase, which impairs skin barrier function, including increasing sebum synthesis and consequently reducing transepidermal water loss. Therefore, it is considered the newest vitamin for treating inflammatory lesions.

6. Vitamin C: Ascorbic acid, or vitamin C, the most popular antioxidant, has anti-inflammatory properties valued in the treatment of acne.^[71] It intercepts the generated radicals and stops inflammation accordingly. However, it is unstable in free form. Therefore, a structural modification, eg, sodium ascorbyl phosphate, was made to achieve stability. This more stable derivative was used in addition to Retinol to treat inflammatory lesions. Combination treatment significantly reduced injuries.^[72]

A low level of serum zinc was found in acne patients.^[73] Thus, zinc treatment has been shown to improve inflammatory acne.^[74]

7. Macrolides: In addition to the above agents, the topical administration of antibiotics, particularly macrolides, is used in the treatment of acne. Oral administration is used for severe acne and acne that is resistant to topical treatment.^[75] The macrolides erythromycin and clindamycin are used because of their antioxidant and anti-inflammatory effects.^[76,77] However, after the application of macrolides P. acne resistance^[78] as well as gastrointestinal irritation and vaginal candidiasis in particular photosensitivity including drug interactions.^[79] Although a structural modification was made in a drug with fewer gastrointestinal side effects, azithromycin. An accumulation was found in breast milk.^[80]

8. Tetracyclines: Another class of antibiotics that are widely used in the treatment of acne is tetracyclines. Tetracyclines show anti-inflammatory activity that inhibits PG synthesis and suppresses NO synthase.^[81,82] However, the side effects of tetracyclines are similar to those of macrolides. The most common side effects are drowsiness, dizziness, and

tinnitus^[83] including yellowing of the teeth, and nail disorders such as photoonycholysis, although these side effects are not common with doxycycline and minocycline. Photosensitivity was demonstrated after the administration of doxycycline.^[84]

Combination therapy with systemic treatment should be used to overcome the side effects of antibiotics. Gradual treatment should be used to minimize exposure to antibiotics, reducing microbial resistance.

In addition to the treatments listed above, hormone therapy with antiandrogens such as spironolactone, glutamine, and cyproterone acetate has been used to treat acne. However, adverse reactions were found.^[85,86] laser and light therapy can clear acne with improvements in acne scars and skin texture. However, these methods are expensive and painful.^[87]

A natural therapy without side effects is therefore highly desirable because of the conceivable safety^[88] and the rare resistance to acne. Natural compounds, especially those made from herbs, are discussed in this article. The herbs included are the well-known and candidate herbs to be used in future anti-acne products.^[88]

Treatment of acne: Acne treatment aims to correct altered patterns of keratinization of hair follicles, reduce sebum activity, reduce the number of *Propionibacterium acnes*, and provide anti-inflammatory effects. Treating acne with broad-spectrum antibiotics often causes intestinal overgrowth caused by the yeast *Candida Albicans*. this chronic yeast infection can exacerbate acne and should be treated if present (Murray and Joseph, 1998; Lucinda and Wallace, 1998).^[89]

Ayurvedic perspective: According to Ayurveda, acne is generally an excess of pitta. Therefore, Ayurveda can treat acne from the level of symptoms and causes to the elimination of symptoms and can use herbs and herbal preparation. At the same time, it is necessary to eliminate excess pitta and toxins in the body. If ignored, pitta toxin can cause acne to recur elsewhere in the body or manifest itself as a disease. For causal compensation and healing, 4,444 people need to follow a fire-reducing diet. 4,444 people reduce pitta (Uniyal et al, 1998).^[90]

Herbal treatment

Various botanical and herbal supplements are used to treat acne. Some of these are described below:

1. **Amaranth:** *Amaranthus hypochondriacus* Linn. and *A. cruentus* Linn. (Family: **Amaranthaceae**) are from China and Mexico. Amaranth seeds and leaves are effectively used as astringents and are also good cleansers from skin conditions ranging from acne and eczema to psoriasis (Heinerman, 1996).^[91] The main ingredients are saponins.



Fig. 6: Amaranth.

2. **Arnica:** Arnica is a perennial plant that grows naturally in southern Russia in the mountainous regions of Europe (Bisset, 1994).^[93] Arnica Montanarin dried flower head and several other related types of Arnica are useful in the treatment of acne, bruises, sprains, myalgia, and as a general topical stimulant (James & Tyler, 1999).^[94] Plants contain a variety of sesquiterpene lactones (helenalin, dihydrohelenalin, arnifoline, and Nicolaides), flavonoid glycosides, and about 0.3% essential oils (Newall et al., 1996). The primary energetic substances are helenalin and dihydrohelenaline ester, (Dermarderosian, 2001; Newall et al, 1996; Bisset, 1994), which have been proven to have sturdy antimicrobial effects, anti-edema, and anti-inflammatory properties (James and Tyler,1999).^[95]



Fig. 7: Arnica.

3. **Birch: *Betula alba* Linn. (Family: Betulaceae)** are found primarily in the northern US, Canada, and northern Europe. Tree bark has been used successfully to treat psoriasis, eczema, acne, and similar chronic skin conditions (Heinerman, 1996).^[96] The main compound is phenolic compounds, salicylic acid, and guaiac. terpenoids, betulin, dirges, ethnocide; and flavones, sakuranetin (Jeffery et al., 1999).^[97]



Fig. 8: Birch.

4. **Burdock: *Arctium lappa* Linn (Family: Asteraceae)** roots and leaves are used for most chronic skin problems, including acne (Foster & Tyler, 1999; Bradley, 1992).^[101] It grows in Europe and North America. The main ingredients are chloropicrin (sesquiterpene lactone), alktigenin (lignan), inulin (fructosan), and mucus (xylocaine) (Jeffery et al, 1999).^[98]



Fig. 9: Burdock.

5. **Calendula: *Calendula officinalis* Linn. (Family: Asteraceae)** phosphorus flower head. Has long been used to treat a variety of skin conditions and is thought to help cure and reduce inflammation (James & Tyler, 1999).^[103] Herbs contain flavonoids (quercetin),

triterpenoid saponins (arvennoside A), essential oils, and polysaccharides (Evans, 2002).^[99]



Fig. 10: Calendula.

6. **Celandine: *Chelidonium majus* Linn. (Family: *Papaveraceae*)** is a perennial herb. It grows in temperate and subarctic regions of Europe and Asia. Any part of the breakdown. the herbs exude a sticky orange juice in a tart with an unpleasant odor. Sticky juice is used to treat grains (Heinerman, 1996).^[100] The main chemical constituents are the isoquinoline alkaloids of the types probberine, benzophenanthrene, and protopine.



Fig. 10: Celandine.

7. **Chaste tree(*Vitex*):** The extract of the fruit of ***Vitex Agnus castus* linn. (Family; *Verbenaceae*)** has been used to treat acne (Amann, 1975, 1984). The Barb is native to the Mediterranean. It contains the alkaloid vitamin; diterpene rotundifuranand vitexilactone (Hoberg et al, 2000), and flavonoid casting (Wollenweter and Mann, 1983).^[101]



Fig. 12: Chaste tree (Vitex).

8. **Neem:** The bark, leaves, twigs, seeds, and latex of *Azadirachta indica* A. Juss. (Family; Meliaceae) are used for their medicinal properties. The plant is native to the wood of India and Sri Lanka. The most important chemical components are the triterpenoids and the tetranortriterpenes (protolimonoides of the Gedunin group) in the seed oil; Nimbolin and B, Nimbin, Gedunin, Tannin and essential oil in the bark and leaves and Bhatt, 1988). Grind some leaves to form a paste; apply to the areas of the face affected by acne. Leave the for 5-10 minutes and then wash it off.^[102]



Fig. 13: Neem.

9. **Orange peel:** The medicinal parts of *Citrus aurantium* Linn. (Family; Rutaceae) are the peels of fresh or dried fruits, flowers, seeds, and essential oil. The plant is native to tropical Asia. The main ingredients are linalool, linalyl acetate, limonene, nerol, geraniol, methyl anthranilate, limonoids (triterpenoid bitter substances), flavonoids (Tatum et al., 1977).^[103] Powdered peel juice and milk paste have been reported to treat acne (Supreeja, 2001).^[104] Take some orange peel and dry in the shade. Sprinkle on dry skin and sift. Take a teaspoon of this powder and mix it with fresh milk to make a paste. Apply this

paste to your face. Hold them for 10-15 minutes and rinse. Take the enthusiasm of an orange or blender. Apply the juice to the affected area of acne several times a day for 5 to 10 minutes and rinse it off.



Fig. 14: Orange peel.

10. Rose: The aqueous extract of petals of the species *Rosa* (family: **Rosaceae**) is used for daily skincare. Rosewater also works against acne and pimples (Heinerman, 1996) The main ingredients are eugenic tannin, pentagalloyl, pyrogallol; monoterpenoid eugenol, geraniol; and rough and phenyl ethyl alcohol (Jeffery et al, 1999). Place a handful of dried rose petals in a little boiling water. Cover and let cool. Drink or use 2 glasses daily externally as a wash pack or wet pack (Heinerman, 1996).^[105]



Fig. 15: Rose.

11. Soapwort: *Saponaria Officinalis* Linn. (Family: **Caryophyllaceae**) is a perennial herbaceous plant native to northern Europe? Soapworts are applied topically to treat acne, psoriasis, eczema, and boil (Dermarderosian, 2001). It contains water-soluble steroidal saponins (saponoside D) which are found in all parts of the plant (Meyer, 1934)^[106], and acts as a surfactant to facilitate cleaning.



Fig. 16: Soapwort.

12. Barberry: *Berberis* (Family- **Berberidaceae**) The main bioactive ingredient of barberry is alkaloid berberine. Berberine has anti-inflammatory, antibacterial, and androgen inhibitory properties. 18 Preliminary studies have shown that it can inhibit the process of skin cells that form acne in acne, and in animal studies, wolverine suppressed sebum production by more than 60%. According to laboratory studies, the other two barberry alkaloids, verin, and matrilysin have antibacterial effects against many different bacteria, including *P. acnes*. If the is used as recommended, the berberine alkaloids of the barberry are considered non-toxic. However, high doses can cause severe and even fatal poisoning. Pregnant or lactating women and newborns should not take herbs containing berberine. These can cause severe, potentially fatal jaundice. Other herbs, including berberine, are turmeric and turmeric. The topical application of barberry can cause skin irritation, but cream containing berberine has been used for 20 days without the side effects.^[107]



Fig. 17: Barberry.

13. Basil: Some studies suggest that certain types of basil may be effective in treating acne. In laboratory experiments, both sweet basil oil and sacred basil oil (*Ocimum basilicum* and *sanctum*) were active against Gram-positive *Propionibacterium acnes* (*P. acnes*), associated with acne seed development. It has been shown that the bacteria that are

present have anti-inflammatory properties. Property. Linolenic acid in St. Basil Seed Oil is thought to inhibit certain pro-inflammatory mechanisms. Low levels of linoleic acid in sebum and inflammatory proteins are thought to be factors leading to acne formation, Randomized placebo-controlled clinical study results show that topical application of linoleic acid determines acne size. It has shrunk. It increases by 25% in one month. Due to the high levels of linolenic acid (52%) and linolenic acid (17%) in seed oil, Holy Basil may help get rid of acne. Sweet basil is generally considered safe when consumed as a spice. Oral administration of the pharmaceutical product made from the aerial portion of sweet basil is considered to be potentially safe for short-term medicinal use, but may not be safe for long-term use. Air part and sweet basil oil contain carcinogenic and mutagenic estragole. Holy Basil is considered potentially safe when taken orally for short-term medicated purposes (up to 4 weeks). The use by pregnant or lactating women is not recommended due to insufficient information on the safety of this group.^[108]



Fig. 18: Basil.

14. Bittersweet nightshade (*Solanum dulcamara*): Traditionally, it was given as an oral antidote for 4,444 skin conditions, including acne. Bittersweet Solanaceae-derived steroid Alkaloid components (Such as solasodine and solasodine) have anti-inflammatory, astringent, and antibacterial properties. Due to these properties, it has been approved by the German Chinese Pharmacy as a topical acne treatment. German Commission E. Proper oral and topical application of the bittersweet Solanaceae (without leaves or fruits) is considered likely to be safe for non-pregnant adults. Oral intake of the bittersweet Nightshade is not recommended for children and pregnant or lactating women. In animal studies, oral administration of bittersweet Solanaceae alkaloids is associated with a birth defect, and there are insufficient data available for topical use during pregnancy.^[109]



Fig. 19: Bittersweet nightshade.

15. Green tea: Green tea is a rich source of antioxidants called catechins. So that antioxidant can counteract the oxidizing effects of free radicals that may be involved in many aspects of acne formation and progression. 5 green tea has the potential to prevent and treat acne through multiple mechanisms. There is no solid evidence that drinking as much green tea can help treat acne, but may be due to the lack of clinical research in the area. Animal studies have shown that the anxiety-reducing and insulin-regulating effects of EGCG help prevent acne or treat acne lesions.^[110]



Fig. 20: Green tea.

16. Saw palmetto (*Serenoa repens*): Saw palmetto is considered an antiandrogen substance because it inhibits the enzyme required to convert testosterone to dihydrotestosterone (DHT). DHT affects the production of sebum by the sebaceous glands, and lowering DHT levels helps reduce excess oil that contributes to the development of acne. If excess androgen hormone is suspected in acne cases (eg, women with polycystic ovary syndrome), herbalists often use saw palmetto as a first-line treatment. Saw palmetto is generally considered to be safe to use orally. Based on 's reports of excessive bleeding during surgery in patients using saw palmetto, there is concern that may have anticoagulant properties. People undergoing elective surgery should be discontinued

weeks before surgery. Also, people taking anticoagulants (Such as aspirin and warfarin) should be careful when using the Palmetto Saw.^[111]



Fig. 21: Saw palmetto.

17. Tea tree oil: A study extracted from tea tree leaves confirmed the antibacterial activity of tea tree oil against harmful microorganisms without harming normal healthy skin microorganisms. This includes inhibiting the growth of 4,444 Gram-positive bacteria associated with acne and *Propionibacterium acnes*. Laboratory tests have even shown that kills *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA), and actively inhibits herpes simplex virus. The ingredients of tea tree oil also have anti-inflammatory properties. clinical studies show the effectiveness of tea tree oil in the fight against acne. The topical application of tea tree oil is generally well-tolerated but can cause skin irritation, such as dry, itchy red skin. There is some clinical evidence that suggests that pregnant or lactating women can safely use topical tea tree oil, but there are reports of estrogen-like hormonal activity. For safety reasons, Tea Tree Oil is not recommended for pregnant and lactating women.^[112]



Fig. 22: Tea tree oil.

18. MINT (*Calamintha graveolens*): Lemon balm essential oil, a perennial herbal member of the mint family, is commonly used in aromatherapy, topical creams, natural homeopathic remedies, and foods. Studies have shown that the bioactive ingredient exerts an antibacterial and sedative effect. The vapor of lemon balm oil in aromatherapy allows these active polyphenols to be absorbed by the lungs and suppress the neurotransmitters (such as GABA) that cross the blood-brain barrier and create fear. Lemon balm also helps to systematically relieve acne symptoms when taken orally. Laboratory experiments have shown antioxidant properties, while animal studies have shown that oral administration of lemon balm reduces oxidative damage to the skin associated with a high-fat diet. increase. Studies in rats have confirmed that lemon balm relieves symptoms of depression and anxiety, These results suggest that lemon balm may help prevent diet-related oxidative damage associated with acne and concomitant mood disorders (eg, depression).

Dermatologists are careful not to use peppermint essential oil topically. This is because it can irritate already inflamed or sensitive skin. Lemon balm should not be used in pregnant women or patients with hypothyroidism. It may have a mild sedative effect. For this reason, caution should be exercised when using a lemon balm with other sedatives or alcohol. Also, do not use lemon balm for more than 2- weeks before anesthetizing for surgery.^[113]



Fig. 23: Mint.

19. Willow bark: Willow bark contains salicin, which is metabolized by the liver to salicylic acid. The acetylated form of salicylic acid is aspirin. Willow bark contains salicin, which is metabolized in the liver to salicylic acid. The acetylated form of salicylic acid is aspirin. However, unlike aspirin, salicin does not irritate the stomach. Salicylic acid is involved in the antiseptic and anti-inflammatory properties of willow bark, which is important in the treatment of acne. Salicylic acid in willow bark not only has strong anti-inflammatory properties but also divides pimples. Salicylic acid is superior to the water-soluble treatment in this respect because it dissolves in fat and can penetrate the sebum

unit. When taken orally, willow bark is safely used for -12 weeks. However, there is insufficient information to recommend its use for pregnant women. Breastfeeding women should avoid the use of willow bark as it contains salicylates, which are associated with unwanted side effects of breast-fed babies.^[114,115]



Fig. 24: Willow bark.

20. Viola or wild pansy (*Viola tricolor*): Viola has traditionally been used as a topical treatment for skin conditions such as eczema and acne. In the Ayurvedic sense, Viola is a blood purifying herb. The dry above-ground portion of the viola is used to prepare natural remedies. They contain beneficial polyphenols, including salicylic acid, a known antibacterial agent used in many homeopathic and over-the-counter acne treatment products. Laboratory experiments have confirmed that Viola extract has antibacterial activity against Gram-positive and Gram-negative bacteria.^[116,117,118]



Fig. 25: Viola or wild pansy.

CONCLUSION

There are many important aspects to be considered in the treatment of Acne. A comprehensive treatment approach is required to achieve the desired results. There are many drugs to choose from, but plants are it is a natural medicine that plays an important role in the

treatment of acne without side effects. Therefore they are widely used as an alternative to synthetic acne medication.

REFERENCES

1. Garner, S. E.; Common acne. In: Williams, H.; Bigby, M.; Diepgen, T.; Herxheimer, A; Naldi, L .; Rzany, B. Ed., Evidence Based Dermatology. London: BMJ Books, 2003; 3: 87-114.
2. Shanmuganathan, S.; Ramasubramanian, P.; Seenivasan, P.; Gopinath, S .; Umamaheshwara Reddy; Satyanarayana, D.; Narendranath, K.A. Preparation and Evaluation of Herbal Acne Formulation. *Suppl. Antiseptic*, 2006; 2: 55-57.
3. Taylor M, González M, Eur J Dermatol, Porter R. Pathways to inflammation; Acne pathophysiology, May-Jun, 2011; 21(3): 323-33.
4. Jeremy AH, Holland DB, Roberts SG, Thomson KF, Cunliffe WJ. Inflammatory events are involved in the development of acne lesions. *J Invest Dermatol*, 2003; 121(1): 20-7.
5. Brown, S.K. and Shalita, A.R. Acne vulgaris; *Lancet*, 1998; 20, 351(9119): 1871-6.
6. Rivera, A.E. Acne Scars: Overview and Current Treatments modalities. *J. Am. Acad. Dermatol*, 2008; 59: 659–676.
7. Cunliffe, W. J., Holland, D. B. and Jeramy, A. Comedo formation: etiology, clinical presentation, and treatment. *Clin. Dermatol*, 2004; 22(5): 367-74.
8. Do, T. T., Zarkhin, S., Orringer, J.S. et al. Computerized alignment and tracking of acne lesions shows that the majority of inflammatory lesions originate from comedones and de Novo. *J. Am . Acad. Dermatol*, 2008; 58, 4: P603-608, 01.
9. Leyden , J. J. The evolving role of *Propionibacterium acnes* in acne. *Semin. Cutan. Med. Surg*, 2001; 20(3): 139-43.
10. Shehadeh, N. H., and Kligman, A. M. The Bacteriology of Acne. *Arch. Dermatol*, 1963; 88: 829-31.
11. Juhlin L. and Michaelson G, Fibrin microclot formation in acne patients with Acne , *Acta Dermatol Venerol*, 1983; 63(6): 538-40.
12. Murry Michael ND and Joseph Pizzorno ND, *Encyclopedia of Natural Medicine*, Prima Health Publishing, UK, 1998; 191-197.
13. Jacob, C. I.; Dover, J. S.; Kaminer, M. S. Acne scarring: a classification system and review of treatment options. *J. Am. Acad. Dermatol*, 2001; 45(1): 109-17.
14. Lehmann, H.P. Acne management: evidence report and appendixes. *Agan. Health. Res. Qual*, 2001; 01, (17): 1-3.

15. Frequently asked questions: Acne www.womenshealth.gov, 2009; 3.
16. Thiboutot, D. Acne: Hormonal Concepts and Therapy. *Clin. Dermatol.* Sep-Oct, 2004; 22(5): 419-28.
17. White, G. M. Latest findings in the epidemiologic evidence, classification and subtypes of acne vulgaris. *J. Am. Acad. Dermatol.* 1998; 39(2 Pt 3): S34-7.
18. Henderson, C. A., Taylor, J. and Cunliffe, W. J. sebum excretion rates in mother and neonates. *Br. J. Dermatol.* 2000; 142(1): 110-1.
19. Pilgram, G. S., van der Meulen, J., Gooris, G. S. et al. The influence of two zones and sebaceous lipids on the lateral organization of isolated lipids from the human stratum corneum. *Biochim. Biophys. Acta*, 2001; 1511, 2, 2: 244-254.
20. Downing, D.T., Stewart, M.E., Wertz, P.W. et al. Essential fatty acids for acne. *J. Am. Acad. Dermatol.* 1986; 14(2 Pt 1): 221-5.
21. Jappe, U., Ingham, E., Henwood, J., et al. Propionibacterium acnes and inflammation in acne: P. acnes has mitogenic T cell activity. *Br. J. Dermatol.* 2002; 146: 202-209, 09.
22. Farrar, M. D. e Ingham, E. Acne: Inflammation. *Clin. Dermatol.* Sep-Oct, 2004; 22(5): 380-4.
23. Kim, J., Ochoa, M.T., Krutzyk, S.R., et al. Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses. *J Immunol*, 2002; 1, 169(3): 1535-41.
24. Layton, A.M., Morris, C., Cunliffe, W.J. et al. Immunohistochemical investigation of evolving inflammation in lesions of acne vulgaris. *Exp. Dermatol.* 1998; 7(4): 191-7.
25. Holland, D. B. and Jeramy, A.H.T. The role of inflammation in the pathogenesis of acne scarring. *Semin. Cutan. Med. Surg.* 2005; 24(2): 79-83.
26. Holland, K.T., Aldana, O., Bojar, R.A. et al. Propionibacterium acnes and acne. *Dermatology*, 1998; 196(1): 67-8.
27. Nagy, I., Pivarsci, A., Kis, K. et al. Propionibacterium acnes and lipopolysaccharide induce the expression of antimicrobial peptides and pro-inflammatory cytokines/chemokines in human sebocytes. *Microbes Infect.* 2006; 8(8): 2195-205.
28. Bojar, R. A. and Holland, K. T. Acne and Propionibacterium acnes. *Clin. Dermatol.* Sep-Oct, 2004; 22(5): 375-9.
29. Leyden, J.J., McGinley, K.J. and Vowels, B. Propionibacterium acnes colonization in Acne and Non-Acne. *Dermatology*, 1998; 196(1): 55-8.
30. Boh, E. E. Role of reactive oxygen species in dermatological diseases. *Clin. Dermatol.* Jul-Aug, 1996; 14(4): 343-52

31. Cals-Grierson, M.M. and Ormerod, A.D. Nitric oxide function in the skin. *Nitric oxide*, 2004; 10(4): 179-93.
32. Gougerot-Pocidalo, M. and Revillard, J .. Oxidative stress, cytokines, and lymphocyte activation. In: Fuchs, J. and Packer, L. (Eds.) *Oxidative stress in dermatology*, Marcel Dekker, New York, 1993; 187- 205.
33. Trefzer, U., Brockhaus, M., Lötscher, H. et al. The 55 kd tumor necrosis factor receptor on human keratinocytes is regulated by tumor necrosis factor-alpha and ultraviolet B radiation. *J. Clin. Invest*, 1993; 92(1).
34. Wilmer, J.L., Burleson, F.G., Kayama, K. et al. Induction of cytokines in human epidermal keratinocytes exposed to contact irritants and its relation to chemical induced inflammation in mouse skin. *J. Invest. Dermatol*, 1994; 102(6): 915-22.
35. Grewe, M., Gyufko, K. y Krutmann, J. Production of interleukin10 by cultured human keratinocytes: regulation by ultraviolet B and ultraviolet A1 radiation. *J. Invest. Dermatol*, 1995; 104(1): 3-6.
36. Kock, A., Schwartz, T., Kirnbauer, R. et al. Human keratinocytes are a source of tumor necrosis factor-alpha: evidence of synthesis and release upon stimulation with endotoxin or ultraviolet light. *J. Exp. Med*, 1990; 1, 172(6): 1609–1614.
37. James, L. C., Moore, A. M., Wheeler, G. M. et al. Transforming growth factor-alpha: in vivo release by normal human skin following UV irradiation and abrasion. *Skin Pharmacol*, 1991; 4(2): 61-4.
38. Pentland, A. P., and Mahoney, M. G. Keratinocyte prostaglandin synthesis is enhanced by IL1. *J. Invest. Dermatol*, 1990; 94(1): 43-6.
39. Cordell, G. A. Natural product in Drug Discovery: Creating a New Vision. *Phytochem. Rev*, 2002; 1: 261–273.
40. Webster, G. F., and Graber, E. M. Antibiotic for the treatment of acne vulgaris. *Semin. Cutan. Med. Surg*, 2008; 27(3): 183-7.
41. Nord, C. E., and Oprica, C. Antibiotic resistance in *Propionibacterium acnes*. Microbiological and clinical aspects. *Anaerobe* Oct-Dec, 2006; 12(5-6): 207-10.
42. Gollnick, C. and Schramm, M. Topical acne therapy. *J. Eur. Acad. Dermatol. Venereol*, 1998; 11, 1: S8-12; discussion S28-9.
43. Kligman, A. M. Treatment of acne with topical retinoids: a man's opinion. *J. Am. Acad. Dermatol*, 1997; 36(6 Pt 2): S92-5.

44. Kang, B.Y., Chung, S.W., Kim, S.H. et al. Retinoid-mediated inhibition of interleukin 12 production in mouse macrophages suppresses Th1 cytokine profile on CD4 + T cells. *br. J. Pharmacol*, 2000; 130(3): 581–586.
45. Nozaki, Y., Yamagata, T., Sugiyama, M. et al. Anti-inflammatory effects of trans-retinoic acid in inflammatory arthritis. *Clin. Immunol*, 2006; 119(3): 272-9.
46. Gollnick, H. und Krauthei, A. Topical treatment for acne: current status and future aspects. *Dermatologie*, 2003; 206(1): 29-36.
47. Webster, G. F. Topical Tretinoin in Acne Therapy. *J. am. Acad. Dermatol*, 1998; 39(2 Pt 3): S38-44.
48. Irby, C. E., Yentzer, B. A. and Feldman, S. R. A review of adapalene in the treatment of acne vulgaris. *J. Adol. Health*, 2008; 43, 5: 421-424.
49. Chandraratna, R.A.S. Tazarotene - first of a new generation of receptor-selective retinoids. *br. J. Dermatol*, 1996; 135, 49: 18-25.
50. Krautheim, A. and Gollnick, H.P.M. Acne: topical treatment. *Clin. Dermatol. Sep-Oct*, 2004; 22(5): 398-407.
51. Bowe, W. P., and Shalita, A. R. Effective over-the-counter acne treatments. *Semin. Cutan. Med. Surg*, 2008; 27: 170-176.
52. Burke, B., Eady, E.A. and Cunliffe, W. J. Benzoyl peroxide versus topical erythromycin for the treatment of acne vulgaris. *J. Dermatol*, 1983; 108(2): 199-204.
53. Natch, S., Gans, E.H., McGinley, K.J. et al. Comparative activity of benzoyl peroxide and hexachlorophene: in vivo studies against *Propionibacterium acnes* in humans. *Arch . Dermatol*, 1983; 119(7): 577-579.
54. Haustein, U. F., Tegtmeier, L. y Ziegler, V. Allergic and irritant potential of benzoyl peroxide. *Contact dermatitis*, 1985; 13(4): 252-7.
55. Thiboutot, D.M., Weiss, J., Bucko, A. et al. Adapalene-benzoyl peroxide, a fixed-dose combination for the treatment of acne vulgaris: results of a multicenter, randomized, double-blind, controlled study. *J. Am. Acad .Dermacol*, 2007; 57(5): 791-9.
56. Gupta, A.K., Lynde, C.W., Kunyetz, R.A.W., et al. A randomized, double-blind, multicenter, parallel-group study comparing the relative efficacy of topical gels 3% of erythromycin 5% / benzoyl peroxide and 0.025% tretinoin / erythromycin 4% in the treatment of moderate acne vulgaris of face. *J. Cutan. Med. Surg. Jan-Feb*, 2003; 7(1): 31-7.
57. Kaminsky, A. Less common methods of treating acne. *Dermatology*, 2003; 206(1): 68-73.

58. Shalita, A. R. Comparison of a salicylic acid cleanser and a benzoyl peroxide wash in the treatment of acne vulgaris. *Clin. Ther.* Mar-Apr, 1989; 11(2): 264-7.
59. Hashimoto, Y., Suga, Y., Mizuno, Y. et al. Salicylic acid peels on polyethylene glycol Vehicle for the treatment of comedogenic acne in Japanese patients. *Dermatol. Surg.* 2008; 34(2): 276-9, 279.
60. Gibson, J.R. Rationale for the development of new topical treatments for acne vulgaris. *Cutis*, 1996; 57(1): 13-9.
61. Holland, K. T., and Bojar, R. A. The effect of azelaic acid on skin bacteria. *J. Dermatol. Treat*, 1989; 1: 17-19.
62. Usatine, R. P., Quan, M. A. y Strick, R. Acne vulgaris a treatment update. *Hosp. Prak.* (1995), 1998; 15, 33(2): 111-7, 121-4, 127.
63. Akamatsu, H., Komura, J., Asada, Y. et al. Inhibitory effects of azelaic acid on neutrophil functions: a possible cause of its efficacy in the treatment of pathogenetically unrelated diseases. *Bow. Arch. Dermatol. Res*, 1991; 283(3): 162-6.
64. Fitton, A. and Goa, K.L. Azelaic Acid: A Review of Its Pharmacological Properties and Therapeutic Efficacy for Acne and Hyperpigmented Skin Conditions. *Drugs*, 1991; 41(5): 780-98.
65. Webster, G. combination Azelaic acid therapy for acne vulgaris. *J.Am. Acad. Dermatol*, 2000; 43(2 Pt 3): S47-50.
66. Graupe, K., Cunliffe, W. J., Gollnick, H. P. et al. Efficacy and Safety of Topical Azelaic Acid (20% Cream): An Review of the Results of European Clinical Trials and Experimental Report, 1996; 57(1): 20-35.
67. Grange, P. A., Raingeaud, J., Calvez, V., and Dupin, N. Nicotinamide inhibits *Propionibacterium acnes*-induced IL8 production in keratinocytes through the NF- κ B and MAPK pathways. *J. Dermatol. Science*, 2009; 56(2): 106-12.
68. Hakozaki, T., Minwalla, L., Zhuang, J. et al. The effect of niacinamide on reducing cutaneous pigmentation and suppression of melanosome transfer. *br. J. Dermatol*, 2002; 147(1): 20-31.
69. Perricone, N.V. The photoprotective and anti-inflammatory effects of topical ascorbyl palmitate. *J. Geriatr. Dermatol*, 1993; 1: 5-10.
70. Amer, M., Bahgat, M. R., Tosson, Z. et al. Serumzink bei Akne vulgaris. *Int. J. Dermatol*, 1982; 21(8): 481-4.
71. Dreno, B., Moyse, D., Alireza, M. et al. Multicenter, randomized, comparative, double-blind, controlled clinical study of the safety and efficacy of zinc gluconate versus

- minocycline hydrochloride in the treatment of inflammatory acne vulgaris. *Dermatology*, 2001; 203: 135-140.
72. Culic, O., Erakovic, V. and Parnham, M.J. Anti-inflammatory effects of macrolide antibiotics. *Eur. J. Pharmacol*, 2001; 19, 429(1-3): 209-29.
73. Ianaro, A., Ialenti, A., Maffia, P., et al. Anti-inflammatory activity of macrolide antibiotics. *J. Pharmacol. Exp. Ther*, 2000; 292(1): 156-63.
74. Carter, E. L. Antibiotics in der Hautmedizin: ein Update. *Semin. Cutan. Med. Surg*, 2003; 22(3): 196-211.
75. Briggs, G. R., Freeman, R. K. and Yaffe, S. J. Drugs in pregnancy and lactation: a reference guide for fetal and neonatal risk. Lippincott Williams and Wilkins, Baltimore, 2002.
76. Amin, A.R., Attur, M.G., Thakker, G.D. et al. A new mechanism of action of tetracyclines: effects on nitric oxide synthase. *Proc. Natl Akad. Science USA*, 1996; 26, 93(24): 14014-9.
77. Humber, P., Treffel, P., Chapuis, J.F. et al. Las tetraciclinas en dermatología. *J. Am Acad. Dermatol*, 1991; 25(4): 691-7.
78. Shapiro, L. E., Knowles, S. R. and Shear, N.H. Comparative safety of tetracycline, minocycline, and doxycycline. *Bow. Dermatol*, 1997; 133(10): 1224-30.
79. Layton, A. M., and Cunliffe, W. J. Phototoxic eruptions due to doxycycline: a dose-dependent phenomenon. *Clin. Exp. Dermatol*, 1993; 18(5): 425-7.
80. Thiboutot, D. Acne: Hormonal Concepts and Therapy. *Clin. Dermatol. Sep-Oct*, 2004; 22(5): 419-281
81. Strauss, J.S., Krowchuk, D.P., Leyden, J.J. et al. Guidelines of acne vulgaris management. *J. Am. Acad. Dermatol*, 2007; 56(4): 651-63.
82. Mariwalla, K. and Rohrer, T.E. Use of lasers and light-based therapies to treatment of acne vulgaris. *Laser surg Med*, 2005; 37(5): 333-42.
83. Amann W, 1st acne vulgaris ene psychosomatische erkrankung? Versuch einer klärung ; Der psychosomatische aspekt der acne vulgaris, *Art Zliche Kosmetol*, 1984; 14: 162170.
84. Bisset NL, In: *Herbal Drugs and Phytopharmaceuticals*, CRC Press, Stuttgart, Germany, 1994; 83-87, 159, 292-294.
85. Bradley PR, In: *British Herbal Compendium*, British Herbal Medicine Association, Bournemouth, 1992; 1: 48-49.
86. Bruneton J and Seancur NY, en: *Medicinal Plants*, Lavoisier Paris, EE. UU., 1995; 461.

87. carsonCF and Rily TV, Antimicrobial activity of the main components of the essential oil of *Melaleuca alternifolia*, *J Appl Bacteriol*, 1995; 160: 236.
88. Chevallier A, In; *Encyclopedia of Medicinal Plants*, DK Publishing, New York, 1996; 81.
89. Defmarderosian A, In; *The Review of Natural Products* Kluver, Germany, 2001.
90. Evans WC, In; *Trease and Evans Pharmacognosy*, Saunders Publishers, UK, 2002; 22: 248.
91. Foster Sand Tyler VF, In; *Tyler Honest Herbal*, Parker Publishing Company, New York, The Haworth Press, London, 1999; 71-72.
92. Hoberg E, Meier B, and Sticher O, Quantitative analysis by high-performance liquid chromatographic analysis of diterpenoids in agni-casti Fructus, *Planta Med*, 2000; 66(4): 352-5.
93. James ER and Tyler VF, In; *Tylers Herbs of choice*, The Herbs of choice The Haworth Press, London, 1999; 219-223.
94. Jeffery BH, Herbert B and Gerard PM, In ; *A Phytochemical Dictionary, A Handbook of Bioactive Plant Compounds*, Tylor and Francis, 1999; 575: 745 - 799.
95. Murray Michael ND and Joseph Pizzorno ND, *Encyclopedia of Natural Medicine*, Prima Health Publishing, UK, 1998; 191-197.
96. Nahrstedt A, Vetter U and Hammerschmidt FJ Zur kenntnis des wasserdampfdestillates der bltter von *Juglans Regia* [composition of the steam distillation product form the leaves of *Juglans regia*], *Planta Med*, 1981; 42 (4): 313-332.
97. Ohshiro Masaaki, Masanori Kuroyanagi and Akira Ueno, structures of Sesquiterpene from *Curcuma longa* , *Phytochemistry*, 1990; 29, 29(7): 22012205.
98. Rao DVK, In Vitro Antibacterial Activity of Neem Oil, *Indian J Mes Res*, 1986; 84: 314-6.
99. Rao TS, Basu and Siddiqui HH, Anti-inflammatory activity of curcumin analogues, *India J Med Res*, 1982; 75: 574-8.
100. Sukhdev SH, Deepak M, Joseph GVR, Shella J, and Gajendra, In; *Indian Herbal pharmacopoeia* ,CSIR and IDMA, New Delhi, 1999.
101. Supreeja A, Helpful tips on Health and Hygiene, *AMRUTH*, December, 2001; 25.
102. Tatum STR and Berry RE, *Phytochem*, 1977; 16: 109.
103. Wollenweber E and Mnn K, Flavonole from fruit of *Vitex agnus – castus* , *Planta Med*, 1983; 48(2): 126-7.

104. Reuter, Juliane, Merfort, Irmgard and Schempp, Christoph M. Am J Clin Dermatol. Botanicals in Dermatology: An Evidence-Based Review.Medscape Today.[Online], 2010; 11(4). [Cited: January 18, 2011.]
105. Therapeutic Research Faculty. Oregon Grape (Barberry) Full Monograph. Natural Medicines Comprehensive Database. [Online], 2011. [Cited: January 22, 2011.]
106. Yarnell, Eric, and Abascal, Kathy. Alternative & Complementary Therapies: Herbal Medicine for Acne Vulgaris. Touro Institute. [Online] December, 2006. [Cited: January 19, 2011.]
107. Viyoch , J., et al. International Journal of Cosmetic Science Evaluation of in vitro antimicrobial activity of Thai basil oils and their micro-emulsion formulas against Propionibacterium acnes. Wiley Online Library. [Online] March, 2006; 28(2). [Cited: January 18, 2011.]
108. Reuter, Juliane, Merfort, Irmgard and Schempp, Christoph M. Am J Clin Dermatol. Botanicals in Dermatology: An Evidence-Based Review.Medscape Today.[Online], 2010; 11(4). [Cited: January 18, 2011.]
109. Thiboutot D, Gilliland K, Light J, Lookingbill D. Androgen metabolism in sebaceous glands from subjects with and without acne. Arch Dermatol. Sep, 1999; 135(9): 1041-5.
110. Liao, S. The medicinal action of androgens and green tea epigallocatechin gallate.Hong Kong Medical Journal, 2001; 7: 4. [Online] December
111. Bose, Mousumi, et al. The Major Green Tea Polyphenol, (-)-Epigallocatechin-3-Gallate, Inhibits Obesity, Metabolic Syndrome, and Fatty Liver Disease in HighFat–Fed Mice. The Journal of Nutrition, 2008; 139: 9. [Online] 1 September
112. Vignes, Michel, et al. Brain Research Anxiolytic properties of green tea polyphenol (–)-epigallocatechin gallate (EGCG). ScienceDirect. [Online] 2006; 1110(1): 19.
113. Melnik, Bodo C. and Schmitz, Gerd. Experimental Dermatology Role of insulin, insulin-like growth factor-1, hyperglycaemic food, and milk consumption in the pathogenesis of acne vulgaris. Wiley Online Library. [Online] 2009; 18(10): 25. [Cited: December 29, 2010.]
114. Martin, K.W., Ernst, E. J. Antimicrob. Chemother. Herbal medicines for the treatment of bacterial infections: a review of controlled clinical trials. Oxford Journals. [Online] 2003; 51(2): 14. [Cited: January 18, 2011.]
115. Naghibi, Farzaneh, et al. Iranian Journal of Pharmaceutical Research 2: Labiatae Family in folk Medicine in Iran: from Ethnobotany to Pharmacology. Shaheed Beheshti

- University of Medical Sciences and Health Services. [Online], 2005. [Cited: January 18, 2011.]
116. Jacobs, M. Amanda and Roenigk, Randall.. Superficial chemical peels. [book auth.] Zoe Diana Draelos. Cosmetic Dermatology Products & Procedures. Oxford: Blackwell Publishing Ltd, 2010; 47. ISBN 978-1-4051-8635-3.
117. Graber, Emmy M. and Thiboutot, Diane.. Over-the-counter acne treatments. [book auth.] Zoe Diana Draelos. Cosmetic Dermatology Products & Procedures. Oxford: Blackwell Publishing Ltd, 2010; 60. ISBN 978-1- 4051-8635-3.
118. European Scientific Cooperative on Phytotherapy. ESCOP Monographs: the Scientific Foundation for Herbal Medicinal Products. Second; Supplement. s.l.: Thieme, 2009. ISBN 1901964086, 9781901964080.