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ANTI-ACNE HERBS: A REVIEW

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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 noninflammatory (comedones, open and closed) lesions. Propionibacterium acnes and Staphylococcus epidermidis are common pus-forming microbes responsible for the development of various forms of acne. Acne therapy includes prolonged use of comedolytic agents, antibiotics and anti-inflammatory agents that are known to cause various side effects. Moreover, the widespread and long-term use of antibiotics over the years has unfortunately led to emergence of resistant strains as well as adverse effects such as dryness, scaling, erythema, burning and itching and even the hyper sensitivity reactions affecting the liver, lungs and kidneys. To avoid such adversities, traditional or herbal formulations are preferred. Herbs are safe, efficacious and multifunctional. The use of bioactive phytochemicals from a variety of botanicals function not only as care taker of body and its parts but also the ingredients present therein influence biological functions of skin and provide nutrients necessary for the healthy skin. In general, botanicals provide different vitramins, antioxidants, various oils, essential oils, hydrocolloids, proteins, terpenoids and other bioactive molecules that can aid in the treatment of acne. Indian traditional systems of medicines, Ayurveda; Siddha; Unani and Tibetan system of medicine are of great help to identify the phytochemicals for skin and body care preparations.

KEYWORDS: Acne Vulgaris, *Propionibacterium acnes*, Herbal Drugs.

INTRODUCTION

The term acne is derived from Greek word “acme” which means “prime of life”. Acne is a skin disorder that leads to an outbreak of lesions called piples or “Zits”. Propionibacterium acnes and Staphylococcus epidermidis are common pus-forming microbes responsible for the development of various forms of acne. The most common form of the disease in adolescents in is called acne vulgaris. Patients experience psychological burdens like depression, anxiety, and low self-esteem because of acne.[2] On the word of statistics, globally around 85% of young adults aged 12–25 years old, approximately 8% of adults aged 25–34 years old, and 3% of adults aged 35–44 years old experience certain degree of acne. On an average 42.5% of men and 50.9% of women continue to suffer from the disease in their twenties. Recent findings concluded that, in 30% of women, acne can persist during their entire fertile period. Affecting 40 to 50 million people in USA per year, a significant number of adults continue to struggle with acne even after their teenage years. One population study in Germany found that 64% of individuals 20 to 29 years old and 43% of individuals 30 to 39 years old had visible acne. Another study from Germany of more than 2000 adults showed that 3% of men and 5% of women still had definite mild acne at the age of 40 to 49 years.[3] In a study of 309 subjects in southern India a total of 186 patients (60.2%) had grade I acne vulgaris and 85 (27.5%), 8 (2.6%), and 30 (9.7%) patients had grades II, III, and IV, respectively, where acne vulgaris was graded using a simple grading system as follows: Grade 1 - comedones, occasional papules; Grade 2 - papules, comedones, few pustules; Grade 3 - predominant pustules, nodules, abscesses; Grade 4 - mainly cysts, abscesses, widespread scarring.[2] Antiacne drugs are the medicines that help clear up the pimples, blackheads, whiteheads, and more severe forms of lesions that occur when a teen has acne. Acne is not a life-threatening condition, it can have detrimental effects on the quality of life of affected individuals. Fortunately, acne is readily responsive to the wide-range of available medications, with the goals of therapy being to clear the lesions, prevent scarring, and limit any treatment-related side-effects and psychosocial sequelae. Newer fixed-dose combination products target multiple acne pathogenic factors and offer simplified dosing regimens, which may potentially enhance both efficacy and patient adherence when compared with single agent therapy. Though the synthetic drugs are effective in the treatment of acne, they suffer from many adverse effects as well.[4] Therefore the herbal treatment has come into the focus of researchers now a days, as being from natural source they are free from side effects.[1]

PATHOGENESIS OF ACNE

The cells of skin that line hair follicle are continuously replaced. Sebum secreted by the sebaceous glands carries dead skin cells to the surface of the skin. A change in sex hormones occurs during puberty, results in increased sebum production and the shedding of skin cells in the hair follicle. Hair follicle gets plugged due to the increased amount of sebum and cells which then swells as more sebum is produced. The plugged follicle is called a 'comedo'. In this clogged follicles bacteria multiplies and inflammation occurs. A comedo can be of two types- A 'closed' comedo is known as white head. The plug is under the skin. It appears as a creamy white or skin colored bump. Another type is 'open' comedo or Black head, when enough sebum builds up behind the plug to push it to the skin surface. It darkens when exposed to light due to the presence of skin pigment called melanin. Pimples or 'zits' are inflamed acne lesions and may be painful. They include small papules (red bumps) and pustules (bumps with pus) and larger, deeper nodules and cysts. These inflamed lesions develop when bacteria and oil irritate the blocked hair follicle and when blocked hair follicles burst and release bacteria, oil and irritants into surrounding skin. Bacteria that multiplies in clogged follicles i.e. P. acne is an member of normal flora on skin, this bacteria is responsible of release of lipase that degrades triglycerides present in sebum into free fatty acids and also releases inflammatory molecules.[5,6]

TYPES OF ACNE

i. Acne Vulgaris

Acne Vulgaris is the most common form of acne. According to a study in The Journal of the American Academy of Dermatology, acne vulgaris usually begins during puberty, but often extends into the twenties, thirties, and beyond. It can appear all over the body, but is most common on the face, neck and back. Eg: Papules, Whiteheads, Blackheads, Pustules, Nodules.[7]

ii. Acne Conglobata

Acne conglobata is a very severe form of acne vulgaris. It usually presents itself as large lesions that may be interconnected. Blackheads may also be present in patients with acne conglobata. It is most common in males between 18 and 30 years old and can cause permanent damage to the skin. Acne Conglobata may be found on the face, back, chest, back, upper arms, and thighs. It is best treated with strong medication such as Accutane. Anyone with this condition should seek treatment from a dermatologist.[8]

iii. Acne Fulminans

Acne fulminans, also known as acne maligna is a rare and severe disease, a form of nodular and ulcerative necrotic acne vulgaris. The onset is acute and systemic involvement is always present, the severity of symptoms and signs varying from case to case. This type of acne often becomes ulcerated and severe scarring is common. Acne fulminans may be accompanied by aching joints and a fever. It usually doesn't respond to standard acne treatments such as antibiotics, but may respond to oral steroids and /or Accutane.[9]

iv. Gram-Negative Folliculitis

Gram-Negative Folliculitis is a rare bacterial infection that is characterized by cysts and pustules. Some dermatologists believe that Gram-Negative Folliculitis is a complication of taking antibiotics long term to treat acne vulgaris. Little is known about this condition, but Accutane seems to be an effective treatment.[10]

v. Acne Rosacea

Acne Rosacea is often confused with acne vulgaris because they are similar in appearance. Rosacea is a skin condition that affects millions of people around the world. It is usually present as a red rash that is confined to the nose, cheeks, chin, and forehead and the rash may be accompanied by pimples, bumps, and blemishes. Blackheads aren't usually present in acne rosacea. If acne rosacea is not properly treated it is known to cause facial swelling. People with rosacea should be treated by a dermatologist because many traditional acne treatments aggravate this condition.[11]

vi. Pyoderma Faciale (Rosacea Fulminans)

Pyoderma faciale is a severe form of acne that is only found in females. It is usually presents itself as large nodules that may be painful, sores, and pustules. Pyoderma faciale may start suddenly and only presents itself on the face. It can affect women who have not had any previous acne issues. The treatment for pyderma facial may include corticosteroid injections and Accutane. This condition may cause severe scarring, especially if left untreated.[11]

ALLOPATHIC TREATMENT FOR ACNE AND ITS SIDE EFFECTS

Since *Propionibacterium acnes* is a common resident of the pilosebaceous glands of the human skin and acne is caused in part from an infection, it was suppressed with topical and oral antibiotics. Antibiotics were primarily used in treatment against acne for more than 40 years. Normally used topical and oral antibiotics are Clindamycin, Erythromycin, Triclosan,

Tetracycline, Minocycline and Metronidazole. The most frequently used topical antibiotic for acne was Clindamycin which is available as a solution, lotion or gel at 1% strength. Salicylic acid are also used in treatment of acne as it was found to be one of the good cleansers that has both anti-inflammatory and mild comedolytic effects. It is used in treatment of mild acne or as an adjunctive agent. Physical treatment in the form of lesion removal, photo-therapy is also helpful in few of them. Now a day's new therapeutic modalities and various permutation and combinations have been designed in topical agents; that include Benzoyl Peroxide, Antibiotics, Retinoids etc. These combinations when tried on patients increase the frequency and severity of dryness, scaling, erythema, burning, stinging and itching. Minocycline has an increased risk of severe adverse effects compared to other tetracyclines. It may induce hypersensitivity reactions affecting the liver, lungs, kidneys or multiple organs (Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS] syndrome) in the first weeks of treatment and with long-term treatment, may cause autoimmune reactions (Systemic Lupus Erythematosus, autoimmune Hepatitis). In addition, Central Nervous System (CNS) symptoms such as dizziness are more frequent compared to other tetracyclines. Long-term treatment may also induce hyperpigmentation of the skin. Therapy with these medications generally lasts from several weeks to months, but may sometimes even continue for years. In particular, this long-term exposure to oral antibiotics creates tremendous selective pressures for the emergence of resistant strains of *P. acnes*. In fact, resistance to *P. acnes* develops in 50% of individuals following treatment with both topical and oral antibiotics. The rate of *P. acnes* resistance corresponds to the length of treatment. In a prospective study of 151 patients, the rate of resistance in patients who had never been on antibiotics was 0, compared to 6.25% in patients on short-term (6-18 weeks) antibiotics and 21.6% in patients on longer periods of antibiotics. Since the use of antibiotics has resulted in resistant strains of *Propionibacterium acnes* and also the many side effects associated with its prolonged use resulted in people opting for holistic treatment. Medicinal plants are known to have enormous therapeutic capabilities that modern medicine is searching for. Thus it became an alternative therapy for consumers, which is cost effective when compared to modern treatment involving antibiotics.[4,9,12]

HERBAL TREATMENT

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 anti-inflammator 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.[13]

Anti-Acne Potential of Medicinal Plants Against Propionibacterium Acnes

Several Plants are used for the treatment of acne. Some of them are discussed below:

Green Tea

Tea, from the plant *Camellia sinensis*, is consumed in different parts of the world as green, black or Oolong tea. Green tea is a rich source of antioxidants called catechins. As such, its antioxidants may be able to combat the oxidative activities of free radicals that appear to be involved in development and progression of acne. Green tea may be able to prevent and treat acne via multiple mechanisms. There is no solid evidence that drinking green tea in any amount can help cure acne, but this may be because not much clinical research has been done in this area. Scientists at the Tang Center for Herbal Medicine Research at the University of Chicago identified a specific green tea catechin called (-) epigallocatechin-3-gallate (EGCG) as the main hormone-regulating catechin. Multiple animal studies show that injections of EGCG modulate androgens and other hormones which contribute to acne development.[14,15]

Fig. 1: Green Tea Leaves.

Aloe Vera

The botanical name of Aloe vera is *Aloe barbadensis miller* belonging to Asphodelaceae (Liliaceae) family. It is generally known as miraculous herb as it is packed with excellent therapeutic properties. Basically it is known for its anti-bacterial and astringent properties. It contains vitamins A (beta-carotene), C and E, which are antioxidants. It also contains vitamin B12, folic acid, and choline. Antioxidant neutralizes free radicals. Aloe vera contains 6 antiseptic agents: Lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulfur. They all have inhibitory action on fungi, bacteria and viruses. Raw aloe gel can be applied directly on the affected area. It provides anthraquinones, which are phenolic compounds traditionally known as laxatives. Aloin and emodin act as analgesics, antibacterials and antivirals. It provides 4 plant steroids; cholesterol, campesterol, β-sisosterol and lupeol. All these have anti-inflammatory action and lupeol also possesses antiseptic and analgesic properties. Hormones present in Aloe vera, Auxins and gibberellins that help in wound healing and have anti-inflammatory action.[16,17,18]

Fig. 2: Aloe Vera.

Tea Tree Oil

Melaleuca alternifolia acts as a powerful anti-bacterial, anti-fungal and anti-viral medicine. It is being used as first aid medicine against various skin ailments like acne, blackheads and topical infections. Considerable attention has been paid to which components of tea tree oil

(TTO) are responsible for the antimicrobial activity. Early indications from RW coefficients were that much of the activity could be attributed to terpinen-4-ol and -terpineol.[19] The few reports of the antibacterial activity of TTO appearing in the literature from the 1940s to the 1980s.[20,21] have been reviewed elsewhere previously.[22] From the early 1990s onwards, many reports describing the antimicrobial activity of TTO appeared in the scientific literature. A broad range of bacteria have now been tested for their susceptibilities to TTO. While most bacteria are susceptible to TTO at concentrations of 1.0% or less, MICs in excess of 2% have been reported for organisms such as commensal skin staphylococci and micrococci, Enterococcus faecalis, and Pseudomonas aeruginosa.[23,24] TTO is bactericidal in nature, although it may be bacteriostatic at lower concentrations. The activity of TTO against antibiotic-resistant bacteria has attracted considerable interest, with methicillin-resistant Staphylococcus aureus receiving the most attention thus far. Additionally, it contains anti-fungal, anti-bacterial and anti-viral agents and works as an expectorant to reduce inflammation.[25,26]

Fig. 3: Tea Tree.

Calendula

Calendula (marigold) flower is known for its healing property and it is been used since Cleopatra time. It consists of flowers of Calendula officinalis, belonging to family Compositae/ Asteracea. It enhances the healing process of the skin tissues.[27] It contains flavonoids (Quercetin and rutin), carotenoids, essential oils, saponins, carotenes, triterpenes, glycosides, resins, and also contains methone, isomethone, caryophgyllene, pedunculatine. Calendula officinalis flower extract have been proved for possessing significant anti-inflammatory activity against carrageenan and dextran-induced acute paw edema. In recent study conducted on flower extracts to find out mechanism involved in this, it was found that TNF-alpha production by macrophage culture treated with lipopolysaccharide (LPS) was

inhibited by Calendula extract. The flavonoids present in Calendula accounts for its anti-inflammatory impact Different hydro alcoholic extracts of marigold possesses -antimicrobial, antifungal and antiviral properties of against Staphylococcus aureus and Streptococcus fecalis Prophyromonas gingivalis, Fusobacterium nucleatum, Capnocytophaga gingivalis, Veilonella parvula, Eikenella corrodens, Peptostreptococcus micros and Actinomyces odontolyticus, Staphylococcus aureus, Sarcina lutea, Escherichia coli, Klebsiella pneumonia and Candida monosa on one hand, and on the other hand, the etiology of acne.[28]

Fig. 4: Calendula Flower.

Witch Hazel

It is popularly known for its astringent and anti-bacterial properties. It is beneficial in tightening your skin pores and removal of the excess oil. The extract and formulations of witch hazel has a protective effect on fibroblast cells and elicited a significant decrease in the amount of IL-8 produced by fibroblast cells against hydrogen peroxide induced damage.[29] It is used as an ingredient in Dr. Somchai Acne Prevention Moisturizer (SS Manufacturing Co., Ltd.), Blissoma Solutions Natural Skincare (Irie Star), Oriental Princess Acne Control Moisturizing Cream (O.P. Natural products co., LTD) which are the marketed formulations for the treatment of acne.[30]

Fig. 5: Witch Hazel.

Walnut Leaf

Different parts of walnut leaves (Juglans regia) have been shown to have antibacterial activity on many bacteria. Its leaves have antioxidant property and if it shows antibacterial effect on propionibacterium acnes. The antibacterial effects of walnut leaves on propionibacterium acnes in vitro has been determined. Ethanolic extract of walnut leaves was examined for antibacterial activities on propionibacterium acnes using the disk-diffusion minimum inhibitory concentration (MIC), minimum bacterial concentration (MBC) and macrodilution methods. Ethanolic extract of walnut leaves had an inhibitory effect on Propionibacterium acnes using the agar-diffusion and macrodilution methods. The minimum inhibitory concentration was 12.5 mg/ml while the minimum bactericidal concentration was 15 mg/ml. The findings showed that ethanolic extract of walnut leaves had antibacterial effect on Propionibacterium acnes and may be considered as an alternative drug for the treatment of external infections.[31]

Fig. 6: Walnut Leaf.

Rose

The aqueous extract of the petals of the Rosa species (Family: Rosaceae)are used for the daily care of the skin. The rose water is also effective against acne and black heads. The main constituents are tannins, eugeniin, pentagalloyl, pyrogallol;monoterpenoids-eugenol, geraniol; andrugosal and phenylethyl alcohol.[32]

Fig. 7: Rose Flower.

Rosemary

The inhibitory effect of rosemary (*Rosmarinus officinalis*) extract on *P. acnes*–induced inflammation *in vitro* and *in vivo* has been investigated. The results showed that ethanolic rosemary extract (ERE) significantly suppressed the secretion and mRNA expression of proinflammatory cytokines, including interleukin (IL)-8, IL-1*β*, and tumor necrosis factor-*α* in *P. acnes*–stimulated monocytic THP-1 cells. In an *in vivo* mouse model, concomitant intradermal injection of ERE attenuated the *P. acnes*–induced ear swelling and granulomatous inflammation. Since ERE suppressed the *P. acnes*–induced nuclear factor kappa-B (NF-*κ*B) activation and mRNA expression of Toll-like receptor (TLR) 2, the suppressive effect of ERE might be due, at least partially, to diminished NF-*κ*B activation and TLR2-mediated signaling pathways. Furthermore, three major constituents of ERE, carnosol, carnosic acid, and rosmarinic acid, exerted different immumodulatory activities *in vitro*. In brief, rosmarinic acid significantly suppressed IL-8 production, while the other two compounds inhibited IL-1*β* production. Further study is needed to explore the role of bioactive compounds of rosemary in mitigation of *P. acnes*–induced inflammation.[33]

Fig. 8: Rosemary.

Goldenseal

It is known for its anti-microbial properties and it prevents oozing. Goldenseal (*Hydrastis canadensis* L.) is used to combat inflammation and infection. Its antibacterial activity *in vitro* has been attributed to its alkaloids, the most abundant of which is berberine.[34,35]

Fig. 9: Goldenseal.

Echinacea

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 completely 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. Echinacea has also been used to treat other skin problems such as psoriasis, skin wounds, burns, ulcers, herpes and hemorrhoids.[36]

Fig. 10: Echinacea.

Basil

Some studies suggest that certain species of basil may be effective as acne treatments. Lab experiments show that both sweet and holy basil oils (Ocimum basilicum and sanctum) are active against gram positive Propionibacterium acnes (P. acnes), the bacteria associated with acne development. Holy basil extracts from leaves and oil from the seeds have anti-inflammatory properties. It is believed that the linolenic acid in holy basil seed oil inhibits certain pro-inflammatory mechanisms. Low levels of linoleic acid in sebum and inflammatory proteins are considered to be factors leading to the formation of acne, and results from a randomized, placebo-controlled clinical trial showed that topical application linoleic acid reduced pimple size.[37]

Fig. 11: Basil Leaves.

Guggul

Guggul (Commiphora mukul): 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. When taken orally guggul can cause some digestive side effects (e.g., nausea, diarrhea, and vomiting), headaches, and skin rash. Skin reactions appear to be dosedependent. Guggul can stimulate menstruation and the uterine muscle, so do not use if you are pregnant. Because of guggul's hormonal effects, and lack of sufficient safety information, experts recommend not using if you are nursing.[38]

Fig. 12: Guggul.

Thyme

Thyme, one of the first herbs in history utilized for its powerful healing properties. Thyme contains volatile oils with potent antimicrobial action. The herb's antiseptic, antibiotic, disinfectant and germicidal properties cleanse and prevent acne outbreaks. It was witnessed that thyme essential oil exhibited the best antibacterial activities with MIC of 0.016%.[39]

Fig. 13: Thyme.

Vitex

Vitex agnus-castus has been shown to be effective in the treatment of premenstrual acne. 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.[40,41]

Fig. 14: Vitex.

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.[13,42]

Fig. 15: Turmeric.

CONCLUSION

In recent times, plants are the rich source of drugs in traditional system of medicine, nutraceuticals, food supplements, modern medicines, pharmaceutical intermediates and chemical entities for synthetic drugs. Plants have played a very important role in drug discovery. A majority of drugs being used in modern medicine have been obtained from medicinal plants. Large numbers of herbs are associated with anti-acne, anti-inflammatory, anti-bacterial and wound healing activity. Few of them are discussed in present review paper.

REFERENCES

1. Tahir CM. Pathogenesis of acne vulgaris: Simplified. J Pakistan Assoc Dermatologists, 2010; 20(2): 93–7.
2. Sinha P, Srivastava S, Mishra N, Yadav NP. New Perspectives on Antiacne Plant Drugs: Contribution to Modern Therapeutics. Biomed Res Int, 2014; 2014.
3. Durai PC, Nair D. Acne vulgaris and quality of life among young adults in South India. Indian J Dermatol [Internet], 2015; 60(1): 33. Available from: http://www.e-ijd.org/text.asp?2015/60/1/33/147784
4. Fabbrocini G, Annunziata MC, D'Arco V, De Vita V, Lodi G, Mauriello MC. Acne scars: Pathogenesis, classification and treatment. Dermatol Res Pract, 2010; 2010(1): 1-13.
5. Rosso JQ Del, Bhambri A. Journal of Drugs in Dermatology, 2009; 6: 615-8.
6. Keri J, Shiman M. An update on the management of acne vulgaris. Clin Cosmet Investig Dermatol, 2009; 2: 105–10.
7. Moradi Tuchayi S, Makrantonaki E, Ganceviciene R, Dessinioti C, Feldman SR, Zouboulis CC. Acne vulgaris. Nat Rev Dis Prim [Internet], 2015; 1(July 2016): 15029. Available from: http://dx.doi.org/10.1038/nrdp.2015.29
8. Van Pelt HPA, Juhlin L. Acne conglobata after pregnancy [8]. Acta Derm Venereol, 1999; 79(2): 169.
9. Brănişteanu DE, Cotrutz CE, Luca MC, Molodoi DA, Stoica LE, Ianoşi SL, et al. Morphopathological stigmata in acne fulminans. Rom J Morphol Embryol, 2015; 56(3): 1185–90.
10. James J, Richard R, Otto H, Albert M. Gram-negative folliculitis–a complication of antibiotic therapy in acne vulgaris. British Journal of Dermatology, 1973; 88(6): 533-538.
11. Jansen T, Plewig G. Rosacea: classification and treatment. J R Soc Med J R Soc Med., March, 1997; 9090: 144–50.
12. Amrita, G. Greeshma, N. Deepa, M. Poornima EH. a Review on Anti-Acne Potential of

Medicinal Plant Extracts Against Propionibacterium Acnes. Int J Pharma Bio Sci., 2012; 3(3): 987–97.

13. Patel SD, Shah S, Shah N. A Review on Herbal Drugs Acting Against Acne Vulgaris. J Pharm Sci Biosci Res [Internet], 2015; 5(2): 165–71. Available from: http://www.jpsbr.org/volume_5/JPSBR_Vol_5_Issue_1_htm_files/JPSBR15RV2022.pdf
14. Liao S. The medicinal action of androgens and green tea epigallocatechin gallate. Hong Kong Med J., 2001; 7(4): 369–74.
15. Chacko SM, Thambi PT, Kuttan R, Nishigaki I. Beneficial effects of green tea: A literature review. Chin Med., 2010; 5: 1–9.
16. Hutter JA, Salmon M, Stavinoha WB, Satsangi N, Williams RF, Streeper RT. Anti-inflammatory C-glucosyl chromone from Aloe barbadensis. J Nat Prod., 1996; 59: 541-3.
17. Chithra R Sajithlal GB, Chandrakasan G. Influence of aloe vera on collagen characteristics in healing dermal wounds in rats. Mol Cell Biochem, 1998; 181: 71–6.
18. Amar Surjushe, Resham Vasani, and D G Saple, Aloe vera: A short review. Indian jornal of dermatology, 2008; 53(4): 163–166.
19. Penfold, A. R., R. Grant. The germicidal values of some Australian essential oils and their pure constituents, together with those for some essential oil isolates, and synthetics. Part III. J. R. Soc. New South Wales, 1925; 59: 346–349.
20. Atkinson, N., and H. E. Brice. Antibacterial substances produced by flowering plants. Australas. J. Exp. Biol., 1955; 33: 547–554.
21. Walsh, L. J., and J. Longstaff. The antimicrobial effects of an essential oil on selected oral pathogens. Periodontology, 1987; 8: 11–15.
22. Carson, C. F., T. V. Riley. Antimicrobial activity of the essential oil of Melaleuca alternifolia. Lett. Appl. Microbiol, 1993; 16: 49–55.
23. Banes-Marshall, L., P. Cawley, and C. A. Phillips. In vitro activity of Melaleuca alternifolia (tea tree) oil against bacterial and Candida spp. isolates from clinical specimens. Br. J. Biomed. Sci., 2001; 58: 139–145.
24. Hammer, K. A., C. F. Carson, and T. V. Riley. Susceptibility of transient and commensal skin flora to the essential oil of Melaleuca alternifolia (tea tree oil). Am. J. Infect. Control, 1996; 24: 186–189.
25. Bishop, C. D. Antiviral activity of the essential oil of Melaleuca alternifolia (Maiden & Betche) Cheel (tea tree) against tobacco mosaic virus. J. Essent. Oil Res, 1995; 7: 641–644.

26. Hammer, K. A., C. F. Carson, and T. V. Riley. In vitro activity of Melaleuca alternifolia (tea tree) oil against dermatophytes and other filamentous fungi. J. Antimicrob. Chemother, 2002; 50: 195–199.
27. Kathi JK., MD, MPH; Calendula (Calendula officinalis); Revised July 13, 1999; 1-9.
28. Preethi KC., Kuttan R.; Wound healing activity of flower extract of Calendula inflammatory agents. Studies in Natural Products Chemistry, 2000; 22(3): 93-143.
29. T. S. Thring, P. Hili, and D. P. Naughton, Antioxidant and potential anti-inflammatory activity of extracts and formulations of white tea, rose, and witch hazel on primary human dermal fibroblast cells. Journal of Inflammation; 2011; 8: 1-7.
30. Chularojanamontri L, Tuchinda P, Kulthanan K, Pongparit K. Moisturizers for acne: What are their constituents? J Clin Aesthet Dermatol, 2014; 7(5): 36–44.
31. Sharafati-chaleshtori A, Sharafati-chaleshtori R, Sharafati-chaleshtori F, Rafieian M, Antibacterial effects of ethanolic extract of walnut leaves (Juglans regia) on propionibacterium acnes. Journal of Zanjan University of Medical Sciences and Health Services, 2010; 45-49.
32. Husain, Sofi, Tajuddin, Dang, Kumar. Unani System of Medicine-Introduction and Challenges. Medical Journal of Islamic World Academy of Sciences, 2010; 18(1): 27-30.
33. Tsung-Hsien Tsai, Lu-Te Chuang, Tsung-Jung Lien, Yau-Rong Liing, Wei-Yu Chen, and Po-Jung Tsai. *Rosmarinus officinalis* Extract Suppresses *Propionibacterium acnes*–Induced Inflammatory Responses, Journal of Medicinal Food, April 2013; 16(4): 324-333. https://doi.org/10.1089/jmf.2012.2577
34. Keivan A. Ettefagh, Johnna T. Burns, Hiyas A. Junio, Glenn W. Kaatz, and Nadja B. Cech. Goldenseal (Hydrastis canadensis L.) extracts synergistically enhance the antibacterial activity of berberine via efflux pump inhibition. Planta Med., 2011; 77(8): 835–840. doi:10.1055/s-0030-1250606.
35. Chanda Ray, Poornima Trivedi, Vikas Sharma. Acne and its treatment lines. International Journal of Research in Pharmaceutical and Biosciences, 2013; 3(1): 1-16.
36. Mirhosseini M, Baradaran A, Rafieian-Kopaei M. Anethum graveolens and hyperlipidemia: A randomized clinical trial. J Res Med Sci., 2014; 19(8): 758–61. [PubMed: 25422662].
37. Viyoch, J. Evaluation of in vitro antimicrobial activity of Thai basil oils and their micro-emulsion formulas against Propionibacterium acnes. International Journal of Cosmetic Science, 2006; 28(2): 125-33.

38. Thappa, D.M., Dogra, J. Nodulocystic acne: oral gugulipid versus tetracycline. J Dermatol, 1994; 21(10): 729-31. [Online] October 1994. [Cited: January 18, 2011.] http://www.ncbi.nlm.nih.gov/pubmed. PMID: 7798429
39. Y. Zu, H. Yu, L. Liang. Activities of ten essential oils towards Propionibacterium acnes and PC-3, A-549 and MCF-7 cancer cells. Molecules, 2010; 15(5): 3200–3210.
40. Bedi MK, Shenefelt PD. Herbal therapy in dermatology. Arch Dermatol, 2002; 138(2): 232–42. [PubMed: 11843645]
41. Wuttke W, Jarry H, Christoffel V, Spengler B, Seidlova-Wuttke D. Chaste tree (Vitex agnus-castus)-pharmacology and clinical indications. Phytomedicine, 2003; 10(4): 348–57. doi: 10.1078/094471103322004866. [PubMed: 12809367]
42. Hamid Nasri, Mahmoud Bahmani, Najmeh Shahinfard, Atefeh Moradi Nafchi, Shirin Saberianpour, Mahmoud Rafieian Kopaei. Medicinal Plants for the Treatment of Acne Vulgaris: A Review of Recent Evidences. Jundishapur J Microbiol, 2015; 8(11): e25580.