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A SYSTEMIC REVIEW: ON DERMATOLOGICAL DISORDER ACNE AND REPORTED HERB FOR ITS TREATMENT

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ABSTRACT
Dermatological disorders are related to the dysfunction of skin's components or layers defects of human skin. It has targeted all kinds of people regardless of age, gender, race, as well as social and economic status. Majority of the global population is affected by skin disorders to some extent this includes the majorly acne causing worldwide 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. 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. 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. 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.

INTRODUCTION
Dermatologic diseases are the fourth most common cause of all human illnesses, with approximately one-third of the world population being affected by at least one skin condition. Skin is the most extensive and diverse organ of the human body. General skin condition is important not only for the aesthetic reasons, but also because of health. The word acne comes from the word acme meaning "the highest point," which comes from the Greek akme meaning "point or spot". In the entire world 650 million people with acne have been suffering, which is about 9.4 % of the world population out of which females are 9.8 % men amounting to 9.0 % which indicates females are more prone to this acne disease .It attracts nearly 40 to 50 million population in the United States (16 %) and more or less 3 to 5 million people in Australia (23 %). Acne is most common skin disease. Acne effects all races and ages and became the most common skin disease, especially in teenagers and young adults. It is estimated approximately 90 % out of age group between 11 and 30 are being attacked by acne outbreaks and during puberty in both sexes, acne can born owing to an increase in androgens such as testosterone and 90 % are suffering from acne at puberty stage all over the globe. Nearly 80 % out of age group of 11 to 30 year-olds are the sufferers with acne at any time of this stage basing on their physiological condition of their body and some people in their age at 40s and 50s still get acne disease. Acne is one of the greatest skin problems faced by adults. As many as 25 percent of all adult men and 50 percent of adult women suffer from acne disease at some point in their life. But adult acne can be particularly frustrating. Research shows 35 % of women in their 30s, 26 % in their 40s, and 15 % age 50 + are the sufferers from acne disease. Women over the age of 33 are more likely to get premenstrual pimples than younger women. The chief ground for this disease is the bad environment, eating an inflammatory diet or living a sedentary lifestyle or both can contribute to the underlying cause of acne.[1] *Acne vulgaris* is a common chronic inflammatory disease of the skin. It is found in about 80% of young adults and adolescents. It is a disease that affects the pilosebaceous units of the skin and may result in inflammatory or non-inflammatory lesions.[2] Although acne lacks the urgency of a life-threatening condition without impairing the overall fitness, it produces long term ramifications that can bemomentous coming up with cutaneous and emotional scars lasting lifetime.[3] It hampers an individual's confidence causing physical, social, and psychological sufferings andreduces self-esteem and emotional distress caused by perceived disfigurement.[4,5] It is almost a

universal disease occurring in all races and affecting 95% of boys and 83% of girls. Acne vulgaris is generally characterized by formation of seborrhea, comedone, inflammatory lesions and presence of bacteria *Propionibacterium acnes Staphylococcus epidermidis* and *Staphylococcus aureus* in the follicular canal and Sebum production. *P.acnes* have been described as an obligate anaerobic microorganism. It is implicated in the development of inflammatory acne by its capability to activate complements and by its ability to metabolize sebaceous triglycerides into fatty acids, which chemotactically attract neutrophils. On the contrary *S. epidermids*, an aerobic organism, usually involves in superficial infections within the sebaceous unit. When the chemicals produced by P. acnes destroy the cellular structure of skin cells, *Staphylococcus aureus* grows causing acne lesions. These factors provide a potential target for treatment. *P. acnes, S. epidermidis and S. aureus* are the target sites of anti acne drugs.[6] The clinical manifestations of acne include seborrhea (excess grease), non-inflammatory lesions (open and closed comedones), inflammatory lesions (papules and pustules), and various degrees of scarring due to cyst formation[7]

- Comedonal (non- inflammatory) – mild
- Papular (inflammatory) – mild-to- moderate
- Pustular (inflammatory) – moderate
- Nodulocystic– severe

This order also follows increasing severity, with cutaneous scarring as the ultimate result.[8]

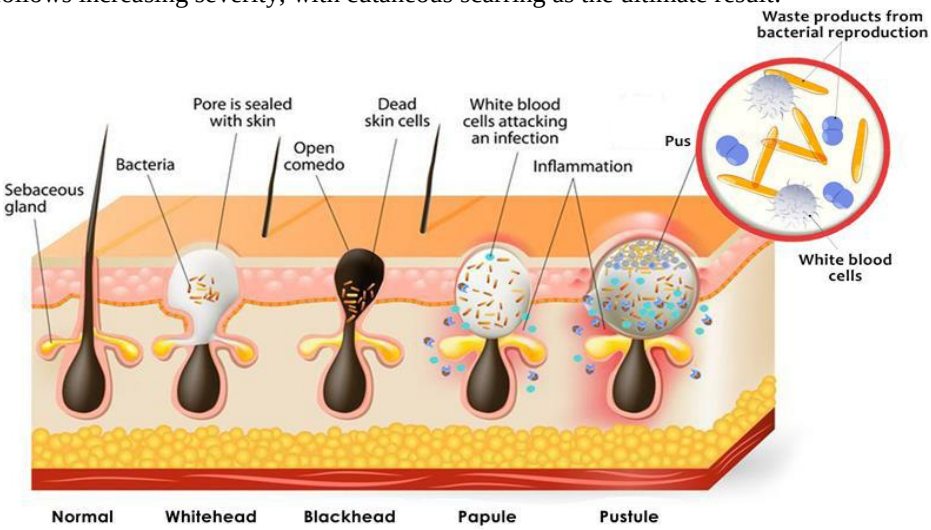


Fig. 1:- Classification of acne.

Classification of Acne

Acne vulgaris is also the haunted disease for India. Acne vulgaris was graded by Indian tradition using a simple grading system, which classifies acne vulgaris into four grades as follows:[9,10]

1. Mild (Grade I): -The mildest form of acne with symptoms of balckheads or whiteheads, milia and minor pimples has no inflammation and can be treated with over the counter products.
2. Moderate (Grade II): -There are more blackheads, whiteheads. Papules and pustules are frequently found. Grade II can also be treated with over the counter medications.
3. Severe (Grade III): -This is moderate to severe acne with widespread papules and pustules. Grade III acne displays the characteristics redness and inflammation.
4. Very severe (Grade IV): -This is also known as cystic acne. Grade IV is the most severe category of acne. The skin will exhibit numerous pustules, nodules, cysts, blackheads and whiteheads. The inflammation and breakouts tend to bodily areas in addition to the face.

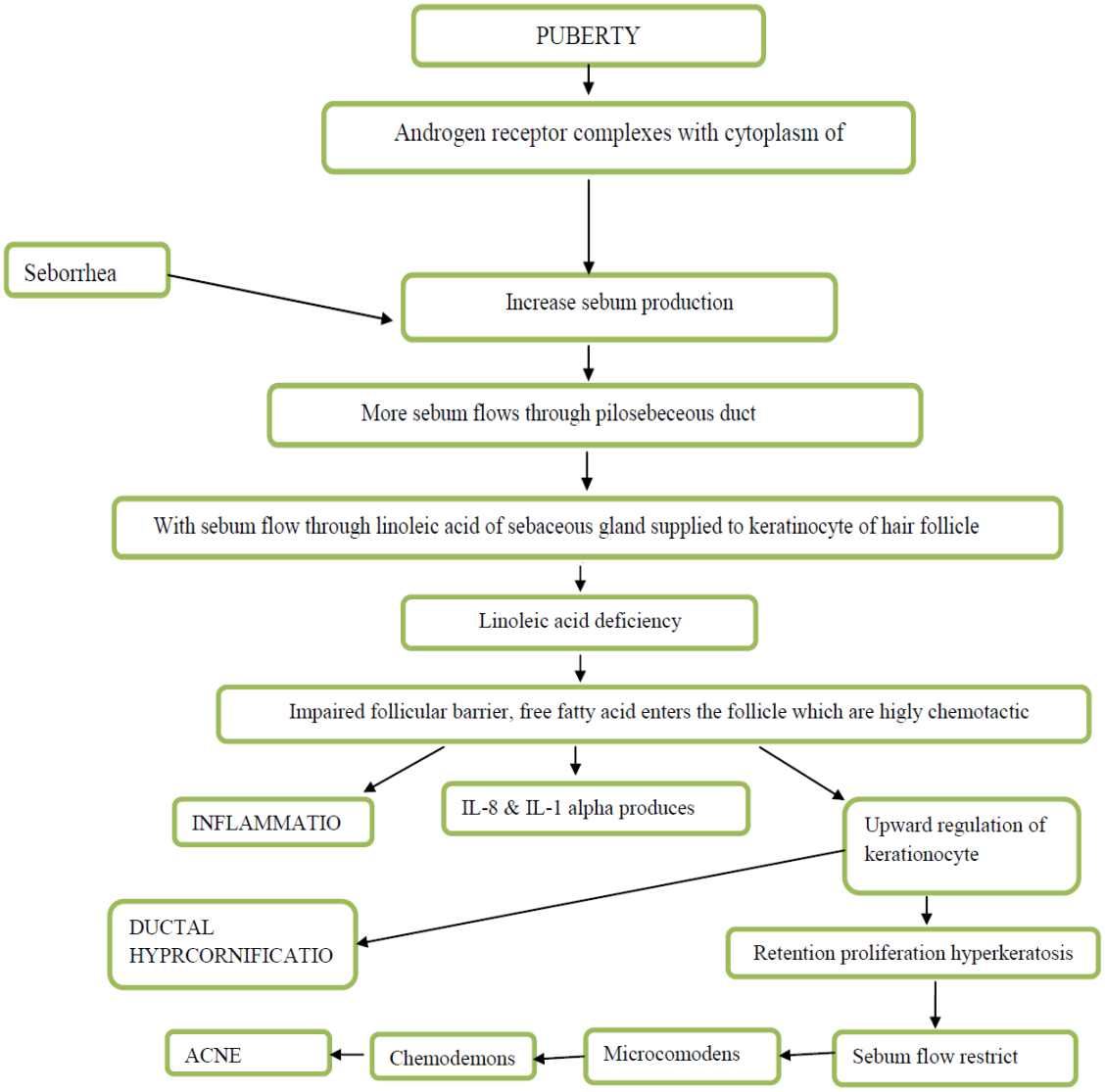
Causes of Acne

1. Infectious Contribution:- Microorganism like *Propionibacterium acnes* and *Staphylococcus* aureus are one of the causative agents for acne. They have ability to adapt the abnormal oil production, inflammation and inadequate sloughing of acne pores. A parasitic mite, Demodex has also been shown to be associated with the development of acne development.[11,12]
2. Dietary Involvement:- Acne vulgaris is seen to be associated with foods with having high glycemic index like milk, salt, chocolates etc. studies has also shown the relation of obesity with acne.[13]
3. Genetic Contribution:- In some peoples, the cause of acne could be genetic rate of acne is seen among first degree relatives and in twin studies as well. The genes, which attributed to acne, are polymorphisms in IL-1α, TNF-α and CYP1A1.[14]
4. Hormonal Changes:- Puberty and menstrual cycles, cause hormonal changes, that contributes to Acne vulgaris. Androgen is the sex hormones that increase during puberty and pregnancy, could cause the more sebum production in follicular glands. Anabolic

steroids can also lead to development of Acne vulgaris in adult women.[15]

5. Psychological Contribution:- Several researchers have suggested the correlation between stress and acne severity. An increase in stress level can result in acne flare. Although, some researchers debate about his correlation between acne and stress.

Pathogenesis of Acne vulgaris



Herbal-Treatment

1. *Barberis aristata* {Barberry}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Berberdiaceae	Root, Leaves	Alkaloid, Berberine, Jatrorrhizinerine	Europe, Africa, Asia, India		Antiacne, Antimicrobial, Antioxidant, Antiinflammatory

Mechanism of action:- It can inhibit the skin cell processes that form comedones in acne, and in animal model research, berberine suppressed sebum production by over 60%. Laboratory studies show that two other barberry alkaloids, berine and jatrorrhizine, exert antibacterial effects against a number of different bacteria, including *Propionibacterium acnes*.[16]

2. *Sereno arepens* { Saw palmetto}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Arecaceae	Fruit	Lauric, Caprylic, Caproicacid	America, Florida, Georgia		Antiacne, Antimicrobial, Antiinflammatory,

Mechanism of action:- Saw palmetto is considered an anti-androgenic substance because it inhibits the enzyme necessary to convert testosterone to dihydrotestosterone (DHT). DHT influences sebum production by the sebaceous glands, and lowering DHT levels may help reduce the excess oils that contribute to the development of acne.[17]

3 *Commiphora wightii* {Guggul}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Burseraceae	Gumm Resin	Terpenoids, Steroids	India, Pakistan, Arabi		Antiacne, Antimicrobial, Antiinflammatory

Mechanism of action:- Guggul extracts appear to have antiinflammatory and antibacterial properties that may benefit acne patients. Guggulipid reduces sebum secretion and blocks bacterial metabolism of triglycerides that promote the development of acne. Those patients with oily skin responded much better to the guggulsterone treatment.[18]

4. *Maleluca alternefolia* {Tea Tree Oil}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Myrtaceae	Leaves plant	Terpinen-4-ol	Queensland, New south, wales, Australia		Anti acne, Antimicrobial, Antiinflammatory

Mechanism of action:- Extracted from the leaves of the tea tree, This includes inhibiting growth of the gram positive bacteria associated with acne Propionibacterium acnes. In laboratory experiments it's even been shown to kill Staphylococcus aureus and methicillin-resistant Staphylococcus aureus (MRSA) and actively inhibits herpes simplex virus. Tea tree oil constituents also have anti-inflammatory properties. Clinical studies have demonstrated the effectiveness of tea tree oil in the fight against acne.[19]

5. *Curcuma longa* {Turmeric}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Zingiberaceae	Rhizome	curcuminoids (curcumin)	Asia, Vietnam, China, India,		Anti acne, Antimicrobial, Antioxidant, Antifungal,

Mechanism of action:- It may prove to be therapeutic against acne. 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.[20]

6. *Rosa Damascena* {Rose}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
	Rosaceae	Flower leaves	Rose water, Rose oil	Africa, Southasia		Anti acne, Antimicrobial, Astringent, Antioxidant, Toner

Mechanism of action:- Rose oil can be utilized as an astringent to tone and clean the skin.[21] It's extract has shown antioxidant activity and inhibits lipid peroxidation similar to α-tocopherol.[22] The hydroalcoholic extract showed analgesic and antiinflammatoryactivity.[23] An extract of R. damascena petals showed antibacterial activity against Pseudomonas aeruginosa, S. epidermidis and Bacillus cereus.[24]

7. *Macrocystis pyrifera* {Seaweed}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Phaeophyceae	Stem, Roots, Leaves	Flavonoids, Alkaloids, Tannins	Shore water		Anti acne, Antimicrobial, Antioxidant, Nutritional

Mechanism of action:- Mild acne was significantly improved when treated topically with a complex of seaweed-derived oligosaccharide and 0.1% zinc pyrrolidone. Even though both the treatments reduced the amount of comedones & papules/pustules on the facial area. The sebum production was also reduced by both treatments.[25]

8. *Copaifera officinalis* {Copaiba Oil}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Fabaceae	Oil Fruit	Oleoresin, Clorechinic, Kaurenoic, kolavenicacid	America, Bolivia, Brazil, Peru		Antiacne, Antimicrobial, Antiastringent,

Mechanism of action:- Copaiba oil-resin has traditionally been used as an antiseptic, anti-inflammatory and healing agent. conducted a double-blind placebo controlled clinical trial in which copaiba oil was prepared into a topical gel to determine its activity against Acne vulgaris. After 21 days of treatment, the copaiba oil gel stopped the outbreak of new pustules, healed pre-existent pustules and reduced the area of erythema.[26]

9.*Ocimum basilicum*{Basil oil}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Lamiaceae (labiatae)	Leaves Oil	Essential oil	India, Iran, Thailand		Anti acne, Antimicrobial, Antioxidant, Anti fungal

Mechanism of action:- Topical application of a preparation containing basil oil in acetomacrogol blend base were more efficient and reduced lesion counts faster than a 10% benzoyl peroxide lotion.[27] A study on Thai basil oils showed that O. basilicum and O. sanctum showed promise to be used for acne treatment as they exhibited antimicrobial activity against P. acnes.

10 *Camellia sinensis* {Green tea}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Theaceae	Leaves Buds	epigallocatechin-3-gallate,epigallocatechin, epicatechin-3-gallate, epicatechin (EC) Polyphenon-60	China, East asia		Anti acne, Antimicrobial, Antiinflammatory, Antioxidant, Antimutagenic

Mechanism of action :- Polyphenon-60 from green tea is a mixture of polyphenolic compounds. Topical application of polyphenon-60 in patients with mild-to-moderate acne decreased the average amount of open-comedos and pustules. However, polyphenon-60 showed no improvement on closed-comedos. In vitro studies to determine the underlying mechanism by which polyphenon-60 has this therapeutic effect on acne showed that this compound suppresses the inflammation process.[28] It has sebo-suppressive effects, it inhibits the growth of P. acnes and it has antiinflammatory effects. They also found that EGCG may reverse modified keratinization of follicular keratinocytes associated with acne.

11. *Punicagranatum* {Pomegranate}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Puniaceae	Fruit Leaves	Ellagic acid	Middle east, South asia, California, Arizona		Anti acne, Antiallergic, Bacteriostatic

Mechanism of action:- It's rind extract containing13% ellagic acid exhibited potent bacteriostatic effect against P. acnes S. aureus, and S. epidermidis. It also inhibits nitric oxide production by murine macrophage cells and the release of b-hexosaminidase from antigen stimulated rat basophilic leukemia cells revealing its antiallergic properties.[29]

12. *Selaginella involvens* {starry spikemoss}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Selaginellaceae	Leaves	Flavonoids	Mexico, Central America, Hawaii		Anti acne, Antimicrobial, Wound healing

Mechanism of action:- It's extract inhibited nitric oxide production,[30] suppression of PGE2 production by Clerodendron mtrichotomum enables their use against inflammatory acne,[31] The atomic force microscopy and phase images confirmed that at lower concentration rosemary essential oil attached to the surface of bacterial cell and with increase concentration the bacterial bodies were severely damaged.[32]

13. *Rhodomyrtus tomentosa* {Rose Myrtle}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Mytraceae	Flower Fruit	Myricetin, Quercetin, Catechin	U.S.A, Florida, Reston		Anti acne, Antimicrobial, Antibacterical

Mechanism of action:- It's leaves, was tested against P. acnes (MIC 0.5 μg/mL)using broth macrodilution method and was reported to be significantly effective by reducing 99% of the bacterial cells within 24 hours. Cytotoxicity test performed on human normal fibroblast indicated very low cytotoxicity favouring its use as topical therapeutic antiacne agent.[33]

14 *Psoralea corylifolia* {Babchi}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Fabaceae	Seed	Bakuchinol	India, Srilanka, Arabia		Anti acne, Antimicrobial, Antiinflammatory, Antioxidant

Mechanism of action:- It has broad spectrum antioxidant activity, effectively quenches superoxide, hydroxy, peroxy, peroxynitrile radicals, and singlet oxygennon radicals in addition to inhibiting lipid peroxidation. Apilot clinical study showed that 1% bakuchiol reduced acne by a score of about 57%, whereas 2% salicylic acid only reduced acne by about 48%, but when used in combination it reduced acne lesions and inflammation upto 70%.[34]

15. *Artocarpus* {Bread fruit}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Moraceae	Fruit	Artocarpin, Cudraflavone, Artocarpanone	Asia Africa		Anti acne, Antimicrobial

Mechanism of action:- Signs of acne are evident as dark spots (hyperpigmentation) and scars on the affected skin surface, which is due to over expression and accumulation of melanin regulated by the enzyme tyrosinase. It was confirmed in a study that Artocarpus integer root extract possessed tyrosinase inhibition potential (90.57%) and antimicrobial activity against S. aureus, S. epidermidis, P. acnes, Compounds isolated from the above plant extract, artocarpin and cudraflavone C, showed the potent antibacterial activity against S. aureus, S. epidermidis, and P. acnes with MIC at 2, 4,and 2 g/mL, respectively, whereas artocarpanone exhibited antityrosinase potential.[35]

16. *Serenoa repens* {saw palmetto}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Arecaceae	Berries	Flavonoids, Sterols, Fatty acids	Florida and America		Anti acne, Antimicrobial, Antiinflammatory

Mechanism of action:- The primary active compounds in saw palmetto are a combination of flavonoids, plant sterols and fatty acids which acts as anti-acne, anti-inflammatory agent and immune system booster. It alters testosterone levels by inhibiting the conversion of testosterone into dihydrotestosterone or DHT.[36]

17. *Soponaria officinalis* {common soapwort}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Caryophyllaceae	Flower	Steroidal, Saponins, (saponoside-D)	Asia, Africa		Anti acne, Antimicrobial

Mechanism of action:- It is a perennial herbaceous plant native to Northern Europe. Soapwort had been administered topically for the treatment of acne, psoriasis, eczema and boils.[37] It contains steroidal saponins (saponoside-D) which acts as surface-active agent to facilitate cleaning.

18.*Carica papaya*{Papaya}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	caricaceae	Fruit Seed Leaves latex	Alkaloids Tannis Flavonoids Phenolic compound	Mexico Central America		Antiacne, Antioxidant, Anti cancer, Wound healing

Mechanism of action:- Its fruit, seeds, peel and leaves of the papaya are all rich in essential enzymes that give outstanding topical medicinal properties for the treatment of skin conditions. Literature data have found that the papaya have the capability to rejuvenate and repair the skin.[38] The fruit contains the enzyme papain which has wonderful exfoliating properties such as removing dead cells and specifically damaged skin.[39] The juice of raw papaya has been shown to be beneficial in the treatment of swollen acne and prevents pus formation.[40]

19. *Arnica montana* {leopard's bane}

Sr. No.	Family	Part used	Phyto-constituents	Geographical sources	Picture	Properties
1.	Asteraceae	Flowers	sesquiterpene lactones, helanalin, 11 α, 13 dihydrohelanalin, chamissonolid	Central Europe Syberia		Antiacne. Antimicrobial

Mechanism of action:- It is a common herb used in many gel and cream for topical treatment to improve inflammatory skin conditions and heal chronic wounds. The major constituents contains sesquiterpene lactones, helanalin, 11 α, 13- dihydrohelanalin, chamissonolid and their ester derivatives.[41] It appears that these components act to reduce inflammation by inhibiting the transcription factor nuclear factor-B and hence, useful in the treatment of acne, bruises and sprains.[42]

CONCLUSION

Dermatological disorder is a big concern which need to be cured. Acne vulgaris is a common skin affliction impacting the lives of millions. It is inflammatory skin disease which causes much distress to patients constantly suffering from it. It has been researched extensively with regards to the disease itself as well as available and potential treatment options. Medicinal plants continue to play an important role in the healthcare system. Much disparate and introductory research exists on the effects of herbs on multiple aspects of acne. A comprehensive approach combining multiple herbs as well as lifestyle and dietary changes has helped people with acne. Herbal medicinal plant are the best source as they do not have potentially harmful side effects on human skin and health and it is the cheapest source as compared to any other therapies.

REFERENCES

1. Ravisankar P, Koushik OS, Himaja V, Ramesh J, Pragna P. Acne-causes and amazing remedial measures for acne. Journal of Pharm Research, 2015; 5(07): 73-8.
2. Bershad SV. The modern age of acne therapy: a review of current treatment options. The Mount Sinai journal of medicine, New York, 2001; 68(4-5): 279-86.
3. Sinha P, Srivastava S, Mishra N, Yadav NP. New perspectives on antiacne plant drugs: contribution to modern therapeutics. BioMed research international, 2014.
4. Nguyen R, Su J. Treatment of acne vulgaris. Paediatrics and Child Health, 2011; 21(3): 119-25.
5. Safizadeh H, Shamsi-Meymandy S, Naeimi A. Quality of life in Iranian patients with acne. Dermatology research and practice. 2012.
6. Y.M. Charde, P.H. Sharma, N.G. Choudhary and J.G. Avari. Development and Evaluation of Herbal Formulation for the Treatment of Acne, International Journal of Pharmaceutical Sciences and Research, 2014; 5(6): 2250-2260.
7. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. The Lancet, 2012; 379(9813): 361-72.
8. http://www.dermatology.ca/skin-hair-nails/skin/acne/ stages-of-acne/. Cited on 21-01-2015.

9. SNEDDON J, SNEDDON I. Acne excoriee: a protective device. Clinical and experimental dermatology, 1983; 1: 65-8.
10. Layton AM, Yip J, Cunliffe WJ. A comparison of intralesional triamcinolone and cryosurgery in the treatment of acne keloids. British Journal of Dermatology, 1994; 130(4): 498-501.
11. Peck GL, Olsen TG, Yoder FW, Strauss JS, Downing DT, Pandya M, Butkus D, Arnaud-Battandier J. Prolonged remissions of cystic and conglobate acne with 13-cis-retinoic acid. New England Journal of Medicine, 1979; 300(7): 329-33.
12. Bek-Thomsen M, Lomholt HB, Kilian M. Acne is not associated with yet-uncultured bacteria. Journal of clinical microbiology, 2008; 46(10): 3355-60.
13. Melnik BC. Evidence for acne-promoting effects of milk and other insulinotropic dairy products. Milk and Milk Products in Human Nutrition, 2011; 67: 131-45.
14. Taylor M, Gonzalez M, Porter R. Pathways to inflammation: acne pathophysiology. European Journal of Dermatology, 2011; 21(3): 323-33.
15. Melnik B, Jansen T, Grabbe S. Abuse of anabolic-androgenic steroids and bodybuilding acne: an underestimated health problem. JDDG: Journal der Deutschen Dermatologischen Gesellschaft, 2007; 5(2): 110-7.
16. Therapeutic Research Faculty. Oregon Grape (Barberry) Full Monograph. Natural MedicinesComprehensivedatabase(http://naturaldatabase.therapeuticresearch.com/nd/Search). Accessed on 26-01-2015.
17. Chanda R, Poornima T, Vikas S. Acne and its Treatment Lines. International Journal of Research in Pharmaceutical and Biosciences, 2013; 3(1): 1-6.
18. Thappa DM, Dogra J. Nodulocystic acne: oral gugulipid versus tetracycline. The journal of Dermatology, 1994; 10: 729-31.
19. Akdogan M, Koyu A, Ciris M, Yildiz K. Anti-hypercholesterolemic activity of Juniperuscommunis Lynn Oil in rats: A biochemical and histopathological investigation.
20. Husain A, Sofi GD, Tajuddin T, Dang R, Kumar N. Unani system of medicine-introduction and challenges. Medical Journal of Islamic World Academy of Sciences, 2010; 1: 27-30.
21. Jain M. PEER REVIEWED Ayurvedic Textiles: A wonderful approach to handle health disorders. Colourage, 2010; 57(10): 45.
22. Shahriari S, Yasa N, Mohammadirad A, Khorasani R, Abdollahi M. In vivo antioxidant potentials of Rosa damascena petal extract from Guilan, Iran, comparable to α-tocopherol. Int J Pharmacol, 2007; 3(2): 187-90.
23. Hajhashemi V, Ghannadi A, Hajiloo M. Analgesic and anti-inflammatory effects of Rosa damascenahydroalcoholic extract and its essential oil in animal models. Iranian journal of pharmaceutical research: IJPR., 2010; 9(2): 163.
24. Tofighi Z, Molazem M, Doostdar B, Taban P, Shahverdi AR, Samadi N, Yassa N. Antimicrobial activities of three medicinal plants and investigation of flavonoids of Tripleurospermumdisciforme. Iranian journal of pharmaceutical research: IJPR, 2015; 14(1): 225.
25. Capitanio B, Sinagra JL, Weller RB, Brown C, Berardesca E. Randomized controlled study of a cosmetic treatment for mild acne. Clinical and Experimental Dermatology: Clinical dermatology, 2012; 4: 346-9.
26. Gomes da Silva A, de Freitas Puziol P, NunesLeitão R, Gomes TR, Scherer R, Lacerda Lopes Martins M, ScárduaSaadeCavalcanti Á, Cavalcanti LC. Application of the Essential Oil from Copaiba (CopaiferalangsdorffiiDesf.) for Acne Vulgaris: a Double-Blind, Placebo Controlled Clinical Trial. Alternative Medicine Review, 2012; 17(1).
27. Hay IC, Jamieson M, Ormerod AD. Randomized trial of aromatherapy: successful treatment for alopecia areata. Archives of dermatology, 1998; 134(11): 1349-52.
28. Jung MK, Ha S, Son JA, Song JH, Houh Y, Cho E, Chun JH, Yoon SR, Yang Y, Bang SI, Kim M. Polyphenon-60 displays a therapeutic effect on acne by suppression of TLR2 and IL-8 expression via down-regulating the ERK1/2 pathway. Archives of dermatological research, 2012; 304(8): 655-63.
29. Panichayupakaranant P, Tewtrakul S, Yuenyongsawad S. Antibacterial, anti-inflammatory and anti-allergic activities of standardised pomegranate rind extract. Food Chemistry, 2010; 123(2): 400-3.
30. Joo SS, Jang SK, Kim SG, Choi JS, Hwang KW, Lee DI. Anti-acne activity of Selaginellainvolvens extract and its non-antibiotic antimicrobial potential on Propionibacterium acnes. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 2008; 3: 335-9.
31. KC SK, Müller K. Medicinal plants from Nepal; II. Evaluation as inhibitors of lipid peroxidation in biological membranes. Journal of Ethnopharmacology, 1999; 64(2): 135-9.
32. Fu Y, Zu Y, Chen L, Efferth T, Liang H, Liu Z, Liu W. Investigation of antibacterial activity of rosemary essential oil against Propionibacterium acnes with atomic force microscopy. Planta medica, 2007; 73(12): 1275.
33. Saising J, Voravuthikunchai SP. Anti Propionibacterium acnes activity of rhodomyrtone, an effective compound from Rhodomyrtustomentosa (Aiton) Hassk. leaves. Anaerobe, 2012; 18(4): 400-4.
34. Chaudhuri RK, Marchio F. Bakuchiol in the management of acne-affected skin. Cosmetics and toiletries, 2011; 126(7): 502.
35. Dej-Adisai S, Meechai I, Puripattanavong J, Kummee S. Antityrosinase and antimicrobial

activities from Thai medicinal plants. Archives of pharmacal research, 2014; 37(4): 473-83.
36. Melnik BC, Schmitz G. Role of insulin, insulin-like growth factor-1, hyperglycaemic food and milk consumption in the pathogenesis of acne vulgaris. Experimental dermatology, 2009; 18(10): 833-41.
37. Joshi BC, Sundriyal A. Healing acne with medicinal plants: an overview. Inventi Rapid: Planta Activa, 2017; 201: 1-3.
38. Hewitt H, Whittle S, Lopez S, Bailey E, Weaver S. Topical use of papaya in chronic skin ulcer therapy in Jamaica. The west Indian medical journal, 2000; 49(1): 32-3.
39. Laidet B, Letourneur M. Enzymatic debridement of leg ulcers using papain. InAnnales de Dermatologie et de Venereologie, 1993; 120(3): 248-248.
40. Beck WC, Gent D. Enzymatic debridement with topical papain. Guthrie Clinic bulletin, 1953; 23(2): 149-51.
41. Wagner S, Suter A, Merfort I. Skin penetration studies of Arnica preparations and of their sesquiterpene lactones. Planta medica, 2004; 70(10): 897-903.
42. Robbers JE, Tyler VE. Tyler's herbs of choice. The therapeutic use of phytomedicinals. Haworth Press Inc., 1999.