



AN OVERVIEW OF HERBAL PLANT USE IN THE TREATMENT OF ACNE & ITS USE IN VARIOUS DOSAGE FORMS

Minakshi S. Warghane*, Pravin B. Suruse and Sneha N. Wankhede

Department of Pharmaceutics, Kamla Nehru College of Pharmacy, Butibori, Nagpur Maharashtra, India. 441108.

***Corresponding Author: Minakshi S. Warghane**

Department of Pharmaceutics, Kamla Nehru College of Pharmacy, Butibori, Nagpur Maharashtra, India. 441108.

Article Received on 10/05/2022

Article Revised on 02/06/2022

Article Accepted on 22/06/2022

ABSTRACT

Acne is a common but serious skin condition, affecting approximately 80 patients and young adults between the ages of 11 and 30. 42.5% of men and 50.9% of women continue to have the condition in their twenties. Bacterial drug resistance has now reached an alarming stage due to the inappropriate use of antibiotics. Therefore, the search for a major novel bioactive molecule and the appropriate use of an existing drug (for better therapeutic effect) at the site of action is a daily need. Plants and herbal products have been an integral part of the health care system since time immemorial. So, the herbs that are currently being used to treat acne and those with high potential are summarized in this review. Certain botanicals, especially mountain vine root, tea tree oil, *Saccharomyces* yeast, and possibly *Ocimum basilicum* because their efficacy and safety can be compared with alternative medical treatments. Composite for mild to moderate acne. Further validated clinical studies with controls are needed to use plants. New drug delivery strategies of important botanical clues in the treatment of acne. The consumption of alternative and complementary medicines, including herbal medicines, is increasing and common among patients with acne and infectious skin diseases. Herbal remedies have a long history of use and are proven to have a low curative effect.

KEYWORDS: *Ocimum basilicum*, *Cannabis sativus*, acne, Extract.

INTRODUCTION

Acne (or simply acne) is a contagious disease and one of the most common diseases in humans. It is characterized by various areas of scaly red skin (seborrhoea), pinheads (papules), blackheads and whiteheads (acne), large papules (nodules), and sometimes scarring (pipeline). Severe acne is often inflamed, but it may also be non-inflammatory. In acne, the skin changes due to changes in the skin structure of the sebaceous units including hair follicles and their associated sebum lines. These changes usually require androgen stimulation.^[1]

Acne is usually caused by an increase in androgens in the body, and occurs more often during adolescence during puberty, regardless of sex. Acne commonly found on the subject's face, upper chest, and back have more sebaceous glands. Acne affects about 85% of adolescents and can continue into adulthood. There are about two million hits visits to the doctor each year for adolescents and 0.2 million visits involving patients over 35 years of age. The direct cost of Acne treatment in the United States exceeds \$1 billion per year. In addition, these patients spend more than \$100 million on over-the-counter acne products.^[2]

Mentality, emotional and social impairment due to acne are considered equal and, in some cases, higher than diabetes, arthritis, epilepsy, and asthma. Acne can cause scarring, leading to self-esteem issues. These patients are prone to depression and are more likely to be unemployed. It is estimated that acne affects 650 million people worldwide and is the eighth most common disease in France world. Most people think that acne has a tendency to disappear and decrease or decrease over time age. However, there is no method to estimate how long it will last and will begin to decrease or disappear completely.^[3]

Acne treatment strategies depend on its severity. Because in patients with large pustules and papules (severe acne), topical and oral treatments are usually indicated. Then, after six to eight weeks, efficacy, compliance, and side effects were assessed and again the diet has adjusted accordingly. There are many acne treatment regimens including Benzene Peroxide, Retinoids, Isotretinoids, Keratolytic Soap, Alpha Hydroxy Acid, Azelaic Acid, Salicylic Acids such as as well as hormonal, anti-androgen or anti seborrheic.^[4]

Direct injection of steroids into inflammatory foci cysts, microdermabrasion, chemical peels, radiofrequency,

light or laser have been shown to be effective in alleviating the pain of acne, although However, none of these regimens are free of side effects. In addition, further investigation is needed to elucidate the exact role

of these methods in therapy. The use of alternative and complementary medicines, including herbal medicines, is also common in patients with acne and infectious skin diseases.^[5]

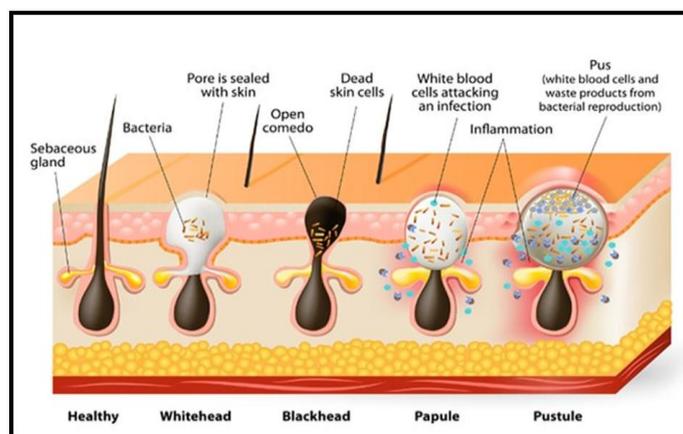


Fig. no. 1: Diagrammatic view of acne vagaries.^[6]

Causes of acne vulgaris

Diet

The relationship between diet and acne is unclear because no good quality evidence. However, a high level of glycemic diet has been shown to be associated with the exacerbation of acne. A positive correlation between the use of milk, chocolate, or salt, and an increase in the severity of acne have also been suggested. However, the contribution of chocolate is still controversial, as it can be made with different amounts of sugar, yes or no milk. There is also a relationship between obesity and acne reported.^[7,8]

Genetic

A hereditary component may explain the tendency to acne in certain individuals. Some research that looked at the rate of acne among first-degree relatives, as well as other sources, back up this theory as well as twin studies. There are many different types of genes. Single nucleotide polymorphisms in IL-1, for example, have been linked to acne. TNF-, and CYP1A1, to name a few.^[9,10]

Hormonal changes

Acne vulgaris appears to be influenced by hormonal changes such as adolescence and menstrual cycles. The follicular glands create more sebum as a result of an increase in several sex hormones, particularly androgens, during puberty and pregnancy. The effects of anabolic steroids are typically comparable. The hormones testosterone, dehydroepiandrosterone, dihydrotestosterone, as well as insulin-like growth factor, have been linked to acne vulgaris. Adult women may develop acne vulgaris as a result of an underlying illness such as Cushing syndrome, polycystic ovarian syndrome, or hirsutism.^[11,12]

Pathophysiology of acne

Multifactorial pathogenesis Acne caused at the level of the hairy unit includes multiple sebaceous glands, one cyst lined with epithelium channel, and a hair. The pathophysiology of acne is thought to be due to various notable factors such as the hyperplasia of the sebaceous glands increased sebum secretion, quality deterioration of sebum lipids, inflammatory processes in addition to the immune response, dysregulation of the hormonal microenvironment, interactions with neuropeptides, and follicular hyperkeratosis, followed by *Propionibacterium acnes* bacteria proliferation in follicles.^[13]

The relationship between androgen levels and sebum production in acne is well established. First element in the origin of acne is androgen-induced hypertrophy Sebaceous glands overproduce sebum. The sebaceous glands have steroid-metabolizing enzymes converts dehydroepiandrosterone (DHEAS) to dihydrotestosterone (DHT). In addition, two subtypes of 5α isoenzyme reductase, i.e. type 1 and type 2, is expressed in the scalp, breasts, sebaceous glands, genital tissues, and skin papillae as well as in hair follicles, converting testosterone to make DHT more active.^[14]

Excess sebum production causes blockage in the cilia unit and increased cell renewal in the cystic duct. Furthermore, in the second factor of pathogenesis, the cilia are surrounded by macrophages and the inflammatory mediators expressed on their surface. Toll-like receptors (TLR2). TLR2 activation leads to transcription of nuclear activating factor and thereby advance the expression of cytokines, such as such as interleukin 1β (IL 1β), IL8, and granulocyte-macrophage colony-stimulating factor (GMCSF), which initiate and propagate an inflammatory response that augments keratinocytes.^[15]

Store dirt the keratinocytes in the ciliary unit initiate follicular formation blockages and blockages leading to obliteration. The normal structure of the cyst and the formation of a thin-walled cystic lesion is acne. Like keratinocytes and sebum continues to accumulate, the wall of microcomedone can rupture causing inflammation.

The development of acne is composed of lipids including a mixture of keratin, sebum, bacteria and surface layers of melanin that can appear as blackheads or whiteheads on the head. Come done when they break out through the surface of the skin have a central black aspect (due to oxidation of tyrosine in melanin by tyrosinase) and is known as "blackhead" or open comedones. However, the compression and bulge of the cyst with poor shedding of keratinocytes and sebum leads to the development of "whiteheads" or closed acne that remain below the surface of the skin as closed cysts.^[16]

Depending on the severity of the medical condition, these Lesions take the form of papules, pustules, nodules, and cysts. Propionibacterium acnes is an anaerobic gram-positive bacteria bacteria produce propionic and acetic acid. Inside radio cysts of the acne, a large number of P. acnes is seen because the acne is filled with lipid

substrates as a source of nutrients suggesting it is the ideal site for anaerobic bacteria. Ultrastructural observations show that P. acnes is 0.4–0.7 μm wide and 3–5 μm long, and possesses a cytoplasm rich in ribosomes and a relatively thick layer The cell wall is composed of peptidoglycan.^[17]

P. acnes is related to the development of inflammatory acne by activating complements and converting sebum triglycerides into fat. The acid irritates the wall of the follicle and the surrounding dermis. It also produces exoenzymes and attracts chemotactic neutrophils. P. acnes produces lipase, protease, and hydrolase, which contribute to inflammation and tissue destruction; express stress proteins responsible for the rupture of the nucleus accumbens, and also cause an inflammatory response by acting on TLR2. It can stimulate the expression of cytokines, such as IL6 and IL8 by hair follicle keratinocytes and IL8 and IL12 in macrophages, thought to be activation of hyperkeratosis, cell adhesion, cystic obstruction, and inflammation. Sequential phenomena lead to vascular and cellular events of the inflammatory response and Folliculitis leads to acne-like lesions in papules, pustules, and nodules.^[18]

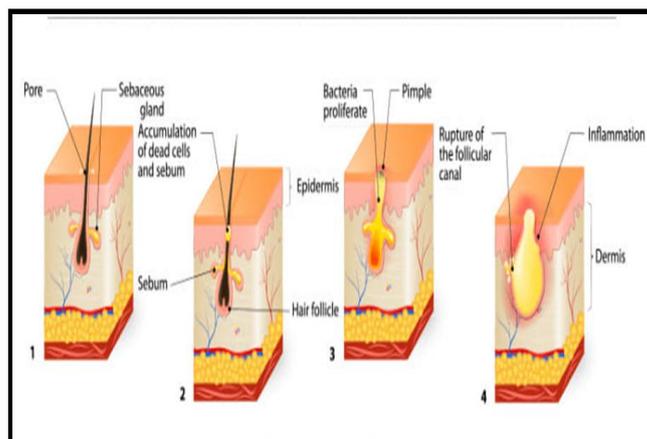


Fig. no. 2: The Flow & formation of acne.^[19]

The medicinal plant used in acne treatment

Medicinal plants are increasingly popular due to their advantages, such as better patient tolerance, history of use, fewer side effects, and relatively few dear. In addition, they have provided good evidence for the treatment of a variety of difficult-to-treat diseases. Healing these plants are used alone or combined with synthetic drugs to treat diseases. More importantly, in addition to consumption as a preventive or curative measure, they can be accompanied by synthetic drugs to reduce their side effects. Without exception, botanical medicines are also used along with other methods or alone to treat acne. Many medicinal plants with anti-inflammatory and antibacterial activities are used in various ways in the treatment of acne and other infectious diseases.^[20]

Matricaria recutita, Calendula officinalis, and Triticum aestivum are commonly used species of these plants. Herbal creams or infusions consisting of astringents and synthetics such as tannins are used topically on the skin after washing or steaming. Hamamelis virginiana has tannins and cuticle extract commonly used to treat acne because it is very safe for a prescription for topical application.

Other plants containing tannin are white oak bark (Quercus alba), walnut leaves (Juglans aqua regia), Agrimonia eupatoria, Syzygium aluminum, Syzygium aluminum plant, natural organic plant, Alchemilla Molli's plant, lavender Angustifolia, Verbascum thapsus, Krameria triandra, Rheum palmatum, Hypericum perforatum, and Rumex Crispus. Other herbs that are

often used topically or as depurative includes *Bellis perennis*, *Viola tricolor*, *Elymus repeat*, and *Taraxacum officinale*. Topical use of ponytail depurative (*Equisetum* species) is recommended due to the high silicic acid content and yellow milky colour of *Aloe Fresh* leaves *ferox* due to anthropoid.^[21]

Vitex agnuscastus is used for acne before menstruation. Whole fruit extract acts on follicle stimulation and Levels of luteinizing hormone in the pituitary gland led to an increase in progesterone and a decrease in estrogen levels through a dopaminergic mechanism, which reduces premenstrual prolactin levels. German Commission E recommends a daily intake of 40 mg of *Vitex agnuscastus* extract for the treatment of acne.^[22]

Pregnant and lactating women should not use this plant. Unwanted side effects such as digestive disorders and skin rashes have been reported. Beyond the traditional usage of herbal medicines as antacids, the antibacterial activities of certain herbs to identify potential for acne herbal treatment have been studied.^[23]

Topical use 50% aloe vera gel with tretinoin cream was well tolerated for eight weeks in a randomized trial double-blind clinical trial with 60 patients with mild to moderate acne and significantly more effective than tretinoin and vehicle. German Commission E has confirmed the topical use of *Solanum dulcamara* and the use of edible *Saccharomyces cerevisiae* as their antibacterial effects as an acne remedy.^[24]

In China, small *Leman* has been used topically to treat acne. A clinical trial documented that the consumption of guggulipid, standardized extraction of oleoresin from an Indian tree called *Commiphora Mukul*, for three months, is effective in the treatment of acne. Interestingly, the patient had oily skin that reacts significantly to guggulipid. It should be noted that the aforementioned studies have some methodological limitations, for example, only 10 individuals in each group (and no placebo), so does not have enough power to determine significant differences between drugs.^[25]

The plant used in treatment

Allium cepa

Onion extract gel has been shown to improve Scar appearance in patients with seborrheic keratosis. This extract gel has been shown to improve the appearance of scars by improving its redness, smoothness, and texture. At the excision site four, 6, and 10 weeks after extract administration.

In another study, the antibacterial and antifungal properties of *A. cepa* and *A. sativum* were revealed against *Malassezia furfur*, *Candida albicans*, and certain other *Candida* species, as well as certain strains of dermatophytes and acne bacteria. The results indicate that *A. cepa* and *A. sativum* may show great promise in the treatment-related bacterial and fungal infections.^[26]

Azadirachta indica

In a study done on an anti-acne formulation prepared from plant extracts, it was revealed that extracts of *Azadirachta indica*, *G. glabra*, *Andrographis paniculata*, *Ocimum sanctum* and green tea possess has the ability to inhibit acne. In this study, in the fight against acne formulation was successfully active against *Propionibacterium* and *Epidermal Staphylococcus*. The aqueous extract of the leaves of *Azadirachta indica* also had chemopreventive activity against skin carcinogenesis in rats. Skin tumours were shown to enhance the expression of proliferative cell antigens compared with the control band. In this study, the skin tumours had a degree of lipid peroxidation.^[27]

Cannabis sativus

The seed oil of *Cannabis sativus* is useful for the treatment of acne rosacea, seborrheic dermatitis, eczema, dermatitis, psoriasis, and lichen planus. The leaves powder of this the plant is very useful as a wound and sore dressing. *Cannabis sativus* extract is externally useful to relieve pain in itchy skin. The seed oil strengthens the skin and makes it more resistant to bacterial, fungal, and viral infections.^[28]

Table 1: Clinical trials with positive effects.

Sr. no.	Medicinal Plants	Family	Used Part(s)	Result	Reference
1	Aloe vera	Xanthorrhoeaceae	extracts	anti-bacterial and anti-inflammatory properties	[29]
2	<i>Azadirachta indica</i>	Meliaceae	extracts	anti-bacterial and anti-inflammatory properties	[30]
3	<i>Curcuma longa</i>	Zingiberaceae	extracts	anti-bacterial and anti-inflammatory properties	[31]
4	<i>Hemidesmus indicus</i>	Apocynaceae	extracts	anti-bacterial and anti-inflammatory properties	[32]
5	<i>Terminalia chebula</i>	Combretaceae	extracts	anti-bacterial and anti-inflammatory properties	[33]
6	<i>Withania somnifera</i>	Solanaceae	extracts	anti-bacterial and anti-inflammatory properties	[34]
7	<i>Butyrospermum</i>	Sapotaceae	Oil	anti-bacterial and anti-	[35]

	paradoxum			inflammatory properties	
8	Camellia sinensis L.	Theaceae	Oil	polyphenol, polyunsaturated fatty acid	[36]
9	Hippophae rhamnoides L.	Elaeagnaceae	fruit extract	vitamins C and E, organic acids, macronutrients, polyunsaturated fatty acid	[37]
10	Melaleuca alternifolia	Myrtaceae	oil	anti-inflammation and Anti-bacterial	[38]

Table 2: Novel drug delivery systems for an antiacne agent.

Novel drug delivery system	Method of preparation	Problem statement	Advantage	Reference
Nanoparticles	Ultrasonication	Low Solubility	Enhanced antimicrobial activity	[39]
	Ion pairing	efficiency due to the hydrophilicity of the drug	Entrapment efficiency and controlled release	[40,41]
Niosomes	Freeze Drying	For Oral Administration only	Topical formulation with enhanced chemical stability	[42,43]
	Thin Film Hydration	Photodegradation	Stratum & stability, Increased drug release & stability, Increase Drug	[44,45]
Liposomes	Sonication	Skin irritation, very low water solubility, difficulty incorporating in topical base, photodegradation	Potential for skin targeting, prolonging drug release, reduction of photo	[46,47]
	Film Formation	Only oral administration	Topical Administration ⁴³ .	[48,49,50]

CONCLUSIONS

In vitro, several plants appear to suppress the development of bacteria, fungus, and viruses. Anti-inflammatory and anti-fatigue effects have also been discovered in the plant. However, there is some evidence of these herbs' usefulness and safety in treating acne and other skin problems. As a result, when it comes to treating acne and skin infections, chemical medications always seem to be the first choice. Synthetic medications, on the other hand, are questioned for their efficacy and safety in treating acne and other skin diseases. The findings of the plant tests in this research are promising. Certain botanicals, especially mountain vine root, tea tree oil, Saccharomyces yeast, and possibly Ocimum basilicum because their efficacy and safety can be compared with alternative medical treatments. composite for mild to moderate acne . Further validated clinical studies with controls are needed to use plants. Clinical efficacy and safety trials on *H. perforatum*, *C. sativum*, *B. serrata*, *U. barbata*, *R. officinalis* and green tea are also essential. in bacterial skin infections.

Conflicts of interest

There are no conflicts of interest and disclosures regarding the manuscript.

ACKNOWLEDGMENT

The authors express their sincere gratitude to Kamla Nehru College of Pharmacy University Libraries and all other sources for their cooperation and advice in writing this review.

REFERENCES

- Park S. Cyclic glucans enhance solubility of bioavailable flavonoids. *Molecules*. MDPI AG, 2016; 21.
- Khor TO, Keum YS, Lin W, Kim JH, Hu R, Shen G, et al. Combined inhibitory effects of curcumin and phenethyl isothiocyanate on the growth of human PC-3 prostate xenografts in immunodeficient mice. *Cancer Research*, 2006; 15, 66(2): 613–21.
- Sinha P, Srivastava S, Mishra N, Yadav NP. *New Perspectives on Antiacne Plant Drugs: Contribution to Modern Therapeutics*. BioMed Research International. Hindawi Publishing Corporation, 2014; 2014.
- Nawarathne NW, Wijesekera K, Wijayaratne WMDGB, Napagoda M. Development of Novel Topical Cosmeceutical Formulations from *Nigella sativa* L. with Antimicrobial Activity against Acne-Causing Microorganisms. *Scientific World Journal*, 2019; 2019.
- Charde YM, Sharma PH, Choudhary NG, Avari JG. Development and evaluation of herbal formulation for the treatment of acne. *International Journal of Pharmaceutical Sciences and Research* [Internet], 2014; 5(6): 2250. Available from: <http://dx.doi.org/10.13040/IJPSR.0975-8232.5>
- Kaur N, Puri R, Jain SK. Drug-cyclodextrin-vesicles dual carrier approach for skin targeting of anti-acne agent. *AAPS PharmSciTech*, 2010; 11(2): 528–37.
- Mansu SSY, Coyle M, Wang K, May B, Zhang AL, Xue CCL. Herbal medicine *Eriobotrya japonica* formula for acne vulgaris: A systematic review. Vol.

- 11, Journal of Herbal Medicine. Elsevier GmbH, 2018; 12–23.
8. Sharma M, Dev SK. Preparation and evaluation of anti-acne herbal gel. European Journal of Biomedical AND Pharmaceutical sciences [Internet], 2018; 4(1): 3–6. Available from: <https://www.researchgate.net/publication/32486118>
9. Park S. Cyclic glucans enhance solubility of bioavailable flavonoids. Molecules. MDPI AG, 2016; 21.
10. Fofaria NM, Srivastava SK. STAT3 induces anoikis resistance, promotes cell invasion and metastatic potential in pancreatic cancer cells. Carcinogenesis, 2015; 1, 36(1): 142–50.
11. Park S. Cyclic glucans enhance solubility of bioavailable flavonoids. Molecules. MDPI AG, 2016; 21.
12. Parsaei P, Karimi M, Asadi SY, Rafieian-kopaei M. Bioactive components and preventive effect of green tea (*Camellia sinensis*) extract on post-laparotomy intra-abdominal adhesion in rats. International Journal of Surgery, 2013; 11(9): 811–5.
13. Shahtalebi M, Asghari G, Rahmani F, Shafiee F, Jahanian-Najafabadi A. Formulation of Herbal Gel of *Antirrhinum majus* Extract and Evaluation of its Anti-Propionibacterium acne Effects. Advanced Biomedical Research, 2018; 7(1): 53.
14. Agnihotri S, Wakode S, Agnihotri a. Formulation and evaluation of herbal antiacne gel of myrica esculenta. Asian Journal of Pharmaceutical and Clinical Resarch [Internet], 2016; 9(4): 1–4. Available from: <http://www.patient.info/health/acne-leaflet>
15. Khantal A, Mahajan SC, Sharma S, Sethiya P, Sharma H. Formulation Development and Evaluation of Herbal Gel Containing Smilax China L. Extract for Topical Treatment of Acne. International Journal of Engineering Research & Technology [Internet], 2021; 10(10): 2–4. Available from: www.ijert.or
16. Khadabadi S, Sawarkar HA, Khadabadi SS, Mankar DM, Farooqui IA, Jagtap NS. Development and Biological Evaluation of Herbal Anti-Acne Gel Synthesis View project Multiple adjustable bending machine View project Development and Biological Evaluation of Herbal Anti-Acne Gel [Internet]., Article in International Journal of PharmTech Research, 2010; 29. Available from: <https://www.researchgate.net/publication/26740004>
17. Parsaei P, Karimi M, Asadi SY, Rafieian-kopaei M. Bioactive components and preventive effect of green tea (*Camellia sinensis*) extract on post-laparotomy intra-abdominal adhesion in rats. International Journal of Surgery, 2013; 11(9): 811–5.
18. Parsaei P, Karimi M, Asadi SY, Rafieian-kopaei M. Bioactive components and preventive effect of green tea (*Camellia sinensis*) extract on post-laparotomy intra-abdominal adhesion in rats. International Journal of Surgery, 2013; 11(9): 811–5.
19. Orafiidiya LO, Agbani EO, Oyedele AO, Babalola OO, Onayemi O, Aiyedun FF. The effect of aloe vera gel on the anti-acne properties of the essential oil of *Ocimum gratissimum* Linn leaf - A preliminary clinical investigation. International Journal of Aromatherapy, 2004; 14(1): 15–21.
20. Weckesser S, Engel K, Simon-Haarhaus B, Wittmer A, Pelz K, Schempp CM. Screening of plant extracts for antimicrobial activity against bacteria and yeasts with dermatological relevance. Phytomedicine, 2007; 6, 14(7–8): 508–16.
21. Joshi D, Bahuguna S, Sharma P, Singh B, Semwal N. JOJ Dermatol & Cosmet Novel Approaches In Herbal Medicament For Acne Vulgaris. Dermatol & Cosmet JOJ, 2022; 4(4).
22. Mukherjee S, Dey S, Bhattacharya RK, Roy M. Isothiocyanates sensitize the effect of chemotherapeutic drugs via modulation of protein kinase C and telomerase in cervical cancer cells. Molecular and Cellular Biochemistry, 2009; 330(1–2): 9–22.
23. Weckesser S, Engel K, Simon-Haarhaus B, Wittmer A, Pelz K, Schempp CM. Screening of plant extracts for antimicrobial activity against bacteria and yeasts with dermatological relevance. Phytomedicine, 2007; 6, 14(7–8): 508–16.
24. Chen Y, Mei Liu J, Xin Xiong X, Yao Qiu X, Pan F, Liu D, et al. Piperlongumine selectively kills hepatocellular carcinoma cells and preferentially inhibits their invasion via ROS-ER-MAPKs-CHOP. Mpaact Journals Oncotarget [Internet], 2014; 6(8): 1–16. Available from: www.impactjournals.com/oncotarget
25. Weckesser S, Engel K, Simon-Haarhaus B, Wittmer A, Pelz K, Schempp CM. Screening of plant extracts for antimicrobial activity against bacteria and yeasts with dermatological relevance. Phytomedicine, 2007; 6, 14(7–8): 508–16.
26. Slobodníková L, Košťálová D, Labudová D, Kotulová D, Kettmann V. Antimicrobial activity of Mahonia aquifolium crude extract and its major isolated alkaloids. Phytotherapy Research, 2004; 18(8): 674–6.
27. Parham S, Kharazi AZ, Bakhsheshi-Rad HR, Nur H, Ismail AF, Sharif S, et al. Antioxidant, antimicrobial and antiviral properties of herbal materials. Vol. 9, Antioxidants. MDPI, 2020; 1–36.
28. Sawarkar HA, Khadabadi SS, Mankar DM, Farooqui IA, Jagtap NS. Development and Biological Evaluation of Herbal Anti-Acne Gel. Vol. 2, International Journal of PharmTech Research CODEN (USA): IJPRIF ISSN.
29. Jiao D, Smith TJ, Yang CS, Pittman B, Desai D, Amin S, et al. Chemopreventive activity of thiol conjugates of isothiocyanates for lung tumorigenesis. Carcinogenesis, 1997; 18.
30. Paudel Chhetri H, Shrestha Yogol N, Sherchan J, Mansoor S. Formulation and evaluation of antimicrobial herbal ointment. kathmandu university

- journal of science, engineering and technology, 2010; 6.
31. Kishan Ghodke S, Bagwan L. Research of formulation and evaluation of anti-acne gel [Internet]. International Journal of Creative Research Thoughts, 2021; 9. Available from: www.ijcrt.org
 32. Dalasanur Nagaprashantha L, Adhikari R, Singhal J, Chikara S, Awasthi S, Horne D, et al. Translational opportunities for broad-spectrum natural phytochemicals and targeted agent combinations in breast cancer., International Journal of Cancer. Wiley-Liss Inc, 2018; 142: 658–70.
 33. Eroğlu İ, Aslan M, Yaman Ü, Gultekinoglu M, Çalamak S, Kart D, et al. Liposome-based combination therapy for acne treatment. Journal of Liposome Research, 2020; 2, 30(3): 263–73.
 34. Isaac VLB, Chiari-Andréo BG, Marto JM, Moraes JDD, Leone BA, Corrêa MA, et al. Rheology as a tool to predict the release of alpha-lipoic acid from emulsions used for the prevention of skin aging. BioMed Research International, 2015; 2015.
 35. Gupta D, Lal Saini S, Sharma T, Professor A, Jammu N, Professor A, et al. Antimicrobial Potential of Polyherbal Formulation Plashbijadi Churna-A Review. International Journal of Research & Review (www.ijrrjournal.com) [Internet], 2017; 4: 11. Available from: www.gkpublication.in
 36. Eroğlu İ, Aslan M, Yaman Ü, Gultekinoglu M, Çalamak S, Kart D, et al. Liposome-based combination therapy for acne treatment. Journal of Liposome Research, 2020; 2, 30(3): 263–73.
 37. Bhupathyaaj M, Mullaicharam AR, Elhadi A. Evaluation of Anti-Acne Property of Poly Herbal Formulation View project Guide-Physical pharmacy View project Evaluation of Anti-Acne Property of Poly Herbal Formulation [Internet]. Journal of Biomedical and Pharmaceutical Research, 2012; 1. Available from: <https://www.researchgate.net/publication/260640743>
 38. Vyas A, Kumar Sonker A, Gidwani B. Carrier-based drug delivery system for treatment of acne. Vol. 2014, The Scientific World Journal. ScientificWorld Ltd, 2014.
 39. Zhou Q, Wang SS, Yang G, Zhao W, Li HL. Development and evaluation of a herbal formulation with anti-pathogenic activities and probiotics stimulatory effects. Journal of Integrative Agriculture, 2016; 1, 15(5): 1103–11.
 40. Vyas A, Kumar Sonker A, Gidwani B. Carrier-based drug delivery system for treatment of acne. Vol. 2014, The Scientific World Journal. ScientificWorld Ltd, 2014.
 41. Gong LH, Chen XX, Wang H, Jiang QW, Pan SS, Qiu JG, et al. Piperlongumine induces apoptosis and synergizes with cisplatin or paclitaxel in human ovarian cancer cells. Oxidative Medicine and Cellular Longevity, 2014; 2014.
 42. Gupta R. Herbal antibiotics: A Review. Bulletin of Environment, Pharmacology and Life Sciences [Internet], 2020; 9(11): 1–8. Available from: <https://www.researchgate.net/publication/349088594>
 43. Gupta P, Wright SE, Srivastava SK. PEITC treatment suppresses myeloid derived tumor suppressor cells to inhibit breast tumor growth. OncoImmunology, 2015; 4(2): 1–8.
 44. Slobodníková L, Košťálová D, Labudová D, Kotulová D, Kettmann V. Antimicrobial activity of Mahonia aquifolium crude extract and its major isolated alkaloids. Phytotherapy Research, 2004; 18(8): 674–6.
 45. Kaur N, Puri R, Jain SK. Drug-cyclodextrin-vesicles dual carrier approach for skin targeting of the anti-acne agent. AAPS PharmSciTech, 2010; 11(2): 528–37.
 46. Bagade VB, Jadhav VM, Kadam VJ. International journal of pharmacy & life sciences Study on Antimicrobial activity of Herbal Formulation. Int J of Pharm & Life Sci (IJPLS), 2013; 4(11): 3099–104.
 47. Isaac VLB, Chiari-Andréo BG, Marto JM, Moraes JDD, Leone BA, Corrêa MA, et al. Rheology as a tool to predict the release of alpha-lipoic acid from emulsions used for the prevention of skin aging. BioMed Research International, 2015; 2015.
 48. Fofaria NM, Srivastava SK. STAT3 induces anoikis resistance, and promotes cell invasion and metastatic potential in pancreatic cancer cells. Carcinogenesis, 2015; 1, 36(1): 142–50.
 49. Nasri H, Bahmani M, Shahinfard N, Nafchi AM, Saberianpour S, Kopaei MR. Medicinal plants for the treatment of acne vulgaris: A review of recent evidence. Jundishapur Journal of Microbiology. Kowsar Medical Publishing Company, 2015; 8.
 50. Slobodníková L, Košťálová D, Labudová D, Kotulová D, Kettmann V. Antimicrobial activity of Mahonia aquifolium crude extract and its major isolated alkaloids. Phytotherapy Research, 2004; 18(8): 674–6.