Int. J. Pharm. Investigation, 2022; 12(2) : 123-128

Review Article

Novel Strategies in the Treatment of Acne: A Review

Sujata Sharma[1], Shweta Vashist[1], Avneet Kaur Lamba[2], Saahil Arora[2], Sucheta[1,*]
[1]School of Medical and Allied Sciences, K. R. Mangalam University, Sohna Road, Gurugram, INDIA.
[2]Department of Pharmaceutical Sciences, Gurugram University, Gurugram, INDIA.

ABSTRACT
Skin break out and eruptions is a typical incendiary issue among people of all age groups, but most common in adolescents. Skin break out development is reliant upon mechanisms, including follicular hyper keratinization, excess sebum secretion, colonization of pathogenic bacteria like *Propionibacterium acnes* and an incendiary course. Treatment strategies predominantly include the use of antibiotics. The use of antibiotics for the treatment of acne is associated with certain side effects like imbalance of skin and gut microbiome and multidrug resistance. This article explains the use of probiotics as a promising tool for the treatment of acne rather than antibiotics. Likewise talk about the favorable conditions and extra advantages offered by probiotics for stability enhancement of topical formulations. This review focuses on the use of bacteriocins in antiacne formulations, use of natural surfactant having additional antiacne properties and bacteriocins having anti-microbial and preservative action. Recent advancements in this field along with the patents are also enlisted.
Keywords: Acne, Skin, Inflammation, Hyperproliferation, Psychological stress.

Correspondence

Dr. Sucheta
School of Medical and Allied Sciences, K. R. Mangalam University, Sohna Road, Gurugram 122103, Haryana, INDIA.

Email id: sucheta@krmangalam.edu.in
DOI: 10.5530/ijpi.2022.2.23

INTRODUCTION

As indicated by contemplates, skin diseases are the most predominant infection among people of all age gatherings. Acne is a skin disease which generally affects the parts like: face, neck, upper chest, upper back, and so forth. Skin aggravation happens because of the excess sebum and oil secreted by the sebaceous gland or which is in any case called as oil organs of the skin. Skin break out preferably known as skin inflammation vulgaris, is a ceaseless provocative disease.[1] The symptoms associated with Acne vulgaris are described by skin with textured red spots (seborrhea), clogged pores due to excess sebum and whiteheads (comedones), scars, pinheads (papules), enormous papules (knobs), pimples.[2] Increase in androgens level like testosterone is primarily responsible for the acne bursts among adolescents.[3] Nodulocystic is a term referred to the huge knobs called as growths and serious fiery skin inflammation over the skin.[4]

Pathogenesis of Acne

Proliferation of pathogenic micro-organisms and aggravation in the pilosebaceous units is the prime cause of skin break outs. Pilosebaceous organ is regulated by hormones, the imbalance in which leads to disorders like acne vulgaris. Follicular epithelial cells form tight intracellular attachments and are therefore shed less. That prompts the emergence of microcomedones, more specifically the hyperkeratotic plugs which extend to shape noninflammatory open or shut comedones.[5] The below enlisted are the causes of acne

Lesion Development

The microcomedo is viewed as the indication for the clinical injuries of acne vulgaris, which include clogged comedones (also known as "whiteheads"), open comedones (may informally be called "clogged pores"), and fiery papules, pustules, and knobs. The four fundamental pathogenic elements which leads to the formation and advancement of microcomedones are as follows:

- Follicular hyper keratinization
- Increased sebum creation by sebaceous glands or the pilosebaceous unit.
- Propionibacterium acnes, anaerobic bacteria responsible for acne bursts.
- Inflammation.[6]

Excess Sebum Production due to Hormones

Sebum formation undertakes a significant role in skin aggravation. The sebum formation is controlled by the hormones specifically androgen and testosterone. Regardless, androgen hormone is considered as an fundamental trigger. Men with more skin inflammation and acne have a high degree of dehydro-epiandrosterone sulfate (DHEAS) and a lesser degree of sex hormone restricting globulin (SHBG). Both these hormones are responsible for hoisting the androgen level.

Role of Propionibacterium acne (P. acne)

Propionibacterium also known as *Cutibacterium*, is a gram-positive, anaerobic bacteria liable for aggravation of the skin. Acne caused by *P. acnes* procedures the triglycerides (separated from sebum) and thus discharges the free unsaturated fat which ultimately stimulates the incendiary reaction leading to skin inflammation. *P. acnes* skin inflammation endorses TLR2. TLR2 are receptors which constitutes part of the natural safe framework for the skin.[7] The initiation of TLR2 by pathogenic microbes on monocytes and neutrophils leads to discharge of different proinflammatory intermediates like cytokines, interleukins 12, 8 and tumor rot factor. Another chemical compound i.e. the CAMP factor more specifically known as the Christie, Atkins, Chomp Peterson factor which is used by microbes like *Staphylococcus* aureus and prompts hemolysis of the skin.[8]

Hyperproliferation of the Follicular Epithelium

Follicular hyper-keratinization also known as ductal hyper cornification. Comedones forms as a result of the hyper keratinization of the skin due to joining of the follicle cells together and their inability to shed appropriately on the skin surface. Unsaturated fats are primarily responsible for the follicular hyper keratinization. Linoleic corrosive is an example of unsaturated fat, when there is an excess of this corrosive then it results in hyper-keratinization.[9]

Abnormal bacterial function

A job of micro-organisms in dermatological disorders has been reinforced since the start of the 20th century. The micro-organisms mainly responsible for diseases like Acne are Staphylococcus epidermidis and Propionibacterium acnes. Among these *P. acnes* affects more.[10] Comedo: A hindered lipid rich lumen with less oxygen pressure is a perfect environment for the growth of *P. acnes*. This abundance of pathogenic microflora like *P. acnes* hydrolyses sebum triglycerides, bringing free unsaturated fats which leads to microcomedo development.

MATERIALS AND METHODS

Databases included Google scholar, PubMed, Elsevier were searched for published articles, reviews and other scientific papers on Probiotics, Skin Acne and inflammation, hypersensitivity and acne vulgaris. More than 75 published papers were examined. The compiled information include the pathogenesis of the *P. acnes*, its lifecycle and inflammatory effects on skin. Existing techniques and antimicrobial/antibacterial serums/products were critically examined and treatment with use of probiotics is discussed. Further novel therapeutic approaches like use of nanoemulsions and other nanoparticles are also discussed and a comparative approach regarding different products available in market for the treatment of acne are illustrated.

APPROACHES TO ACNE TREATMENT

Topical route of administration of antiacne drugs i.e., in the form of creams and gels is the preferred method for the treatment of gentle and moderate skin break out. Though, the oral antibiotics along with NSAIDS are used in combination for extreme skin break out vulgaris.

Fundamental Point of Rewarding Skin breaks out Incorporates

The main targets of antiacne treatment aims at relieving the following symptoms associated with acne:

- Diminishing the aggravation,
- Lessening the hyperproliferation of follicular epithelial cells
- Lower the creation of sebum from the sebaceous organ.
- Forestalling the skin break out scars.
- Maintaining a healthy skin microbiome.

Topical Specialists Engaged with Rewarding Skin Break Out:

Effective Retinoids

Retinoids, also known as comedolytics are primarily obtained from nutrient A. Retinoids are either utilized as monotherapy or are used alongside with other oral antimicrobials for the treatment of acne.

Retinoids are considered to be the first line of treatment for patients having mild moderate skin inflammation.[11]

The principal facts of effective retinoids include

- Increase in the turnover of follicular epithelial cells.
- Dropping or restricting the arrangement of microcomedones.

Topical retinoids utilized to relieve symptoms associated with acne vulgaris can be characterized in the accompanying way

- Tretinoin (Cream, gel or microsphere gel vehicle).
- Adapalene (Cream, gel, salves).
- Tazarotene (Cream, gel or foam)

Tretinoin

Tretinoin has been utilized in the treatment of skin break out since three decades. Tretinoin is a subordinate of nutrient A. It is a comedolytic specialist and hence plays an important role in rewarding skin acne. It has a mitigating property and anticipates the obstruction of the pilosebaceous unit. Tretinoin bonds to different arrangements of a retinoic corrosive receptor-like alpha, beta, and gamma. These receptors are responsible for the adjustment of its movement, adequacy, and decency. Benzoyl peroxide shows an antagonistic action to tretinoin when they are regulated together.[12] Elective planning must be opted prior to administration, to avoid the oxidation and inactivation of tretinoin by benzoyl peroxide.

The reaction of utilizing tretinoin incorporates:

- Dryness in the skin
- Irritation in the skin
- Leads to redness of the skin
- Burning sense
- Contraindicated during pregnancy

In any case, these symptoms can be relieved by use of a rational prescription, the recurrence of use, by keeping away from daylight, utilizing self-protective dress and caps and furthermore by applying appropriate sunscreen.[13]

- Adapalene

Adapalene is utilized as the principal line treatment in the skin break out vulgaris. It is known as a manufactured retinoid compound. It has a mitigating property which follows up on skin break out injuries. The separation in the follicular epithelial cells is standardized.[14] They are less successful when contrasted with different retinoids. Be that as it may, adapalene is having less bothering contrasted with other effective retinoids and likewise, there is no photosensitivity.[15] It is progressively lipophilic in nature, which permits it to enter all the more quickly into the skin. Studies uncovered that a centralization of 0.1% of adapalene and 0.025% of tretinoin are having comparable adequacy. When adapalene is joined with benzoyl peroxide, it is having greater action. Indeed, even a mix of 0.1% adapalene and 1% clindamycin is having a superior movement than utilizing both the medications independently.[16]

- Tazarotene

➢ Tazarotene which is promoted as TAZORAC is a manufactured retinoid with a comedolytic property (causes lysis of comedowns in skin break out). It is utilized in the treatment of mellow to direct skin break out. Financially, it is accessible as a gel (0.05 %, 0.1%) which is applied day by day at night just a single time.[17]

➢ They are having greater movement when contrasted with tretinoin (0.025% and 0.05%). Expanded viability is found by joining tazarotene and clindamycin together. Better viability is seen when utilizing a triple readiness (tazarotene 0.1% gel, clindamycin 1% Benzoyl peroxide 5% gel and erythromycin/ Benzoyl peroxide).[18]

Benzoyl Peroxide (BP)

BP is accessible as cream, gel, and moisturizer and it has against microbial, mitigating and comedolytic property. It is utilized as a stripping specialist in the treatment of skin inflammation. Benzoyl Peroxide is used in rewarding the provocative skin inflammation like papule, pustules, and pimples. The nearness of oil on the skin is diminished just as the size of the sebaceous organ is diminished.[19] It is utilized as a monotherapy in mellow to direct skin break out. So as to diminish the obstruction of the acnes species and to improve the viability, BP is joined with effective

anti-toxins. BP is accessible in different fixations like 2.5%, 5% and 10% including moisturizer, creams, and gels.[20]

Azelaic Corrosive

It is a characteristic dicarboxylic corrosive which prompts restraint of skin inflammation protein combination. Azelaic corrosive restrains the professional provocative cytokines in this manner lessening the aggravation. It likewise causes the enlistment of peroxisome proliferator - actuated receptor - gamma (PPARG). PPARG is likewise called as glitazone receptor which diminishes the fiery reactions.[21]

Effective Anti-infection agents

Topical anti-infection agents fundamentally center around the *Propionibacterium* skin break out. Clindamycin and erythromycin are normally utilized as an effective application for rewarding skin break out. Clindamycin and antibiotic medications are having bacteriostatic movement. Quinolone framework displays its bactericidal movement by communicating with the DNA supercoiling.[22]

Oral antimicrobials and Isotretinoin

Oral anti-microbials:

- The oral anti-microbials are utilized in the treatment of moderate to serious skin inflammation and furthermore the skin inflammation which is impervious to skin treatments. Oral anti-infection agents are for long haul use.
- These mixes express their action by repressing the Propionibacterium acnes and the development of the incendiary middle people.

A list of oral antibiotics used to treat skin breakouts and are available in the market are enlisted in table 1.

Table 1: List of oral anti-microbials used to treat skin break out.

S.No	Antibiotics	D.O.A	Side Effect
1.	Tetracyclines	Duration of 6-8 hours	Including dysphagia, inflammatory lesions .
2.	Doxycycline	Duration of 16 + hours	Including gastro-intestinal upset and photosensitivity.
3.	Minocycline	Duration of 16 + hours	Including vertigo and hyper-pigmentation of the skin.
4.	Erythromycin	Duration of 2 hours	Including gastro-intestinal upset and vaginal candidiasis.
5.	Azithromycin	Duration of 68 hours	Including gastro-intestinal upset

Oral Isotretinoin: It has been utilized in rewarding skin inflammation by displaying its activity against different variables like diminishing sebum discharge, the arrangement of comedeons, colonization of skin with Propionibacterium acnes. They likewise show mitigating action. Initially, the treatment is begun with a low portion and in this manner expanded dependent on the bearableness. At the point when the medication is directed alongside the food, its bioavailability is expanded. In case, in the event that any issue happens during oral isotretinoin treatment, at that point quickly it ought to be accounted for to doctor and research facility checking is required during the treatment.[23]

Hormone based treatment for treatment of skin inflammation

Acne can be adequately rewarded with hormonal medicines. In this treatment, the androgen level has been brought down and their impact on the sebaceous organ has additionally been restricted.

Anti-androgens or androgen receptor blocker, specialists in the ovary or adrenal organ which is answerable for diminishing the creation (endogenous) of androgens, for example, estrogens, a blend of oral contraceptives, gonadotropin-discharging hormone agonists are utilized in hormonal treatments for the treatment of skin inflammation.[24] Oral contraceptives along with medications such as spironolactone can be utilized to treat skin inflammation in women.[25]

Physical treatment

There are a few physical medicines accessible which can be utilized as adjunctive skin break out treatment. From this time forward, these treatments can assume a significant job in the treatment of skin inflammation as the pathogenesis of skin inflammation turns out to be increasingly comprehended and innovation improves.[26]

Comedone Extraction

A few creators have recommended that this method can be utilized simultaneously with isotretinoin treatment to treat macrocomedones (comedones bigger than 1 mm). No remaining scarring ought to be left if this strategy is performing accurately.[27] This mechanical technique for extraction includes the accompanying: the sore ought to be prepared with liquor and the epidermis gently penetrated with a huge bore needle or careful edge. From there on, a comedone extractor is utilized to apply light to medium weight on head of the sore until all the substance are constrained out.[28] Preceding the manual expulsion of the comedone, enzymatic or mechanical shedding can be utilized to diminish hyperkeratosis. After treatment, the skin ought to be treated with a mitigating or antimicrobial specialist.[29]

Cryotherapy

Cryotherapy includes the controlled and focused on demolition of sick skin tissue by applying a substance with an exceptionally low temperature. Albeit fluid nitrogen is the most widely recognized cryogen utilized, there are a few different cryogens likewise accessible, for example, carbon dioxide and nitrous oxide. Various strategies can be utilized to apply the cryogen, including the cryoprobe, dipstick strategy or the spot freeze method. Cryotherapy is by and large performed without nearby sedation under aseptic conditions and whenever performed effectively it should bring about amazingly great restorative outcomes.[30]

Optical Medicines

Optical medicines for skin inflammation incorporate laser treatment, light sources and photodynamic treatment.[31] Lasers and light-based treatment is normally utilized for the treatment of mellow to direct fiery Skin inflammation vulgaris.[32] The pharmaceutical market is flooded with a range of antiacne formulations. Some of the presently available antiacne formulations are enlisted in Table 2.

ROLE OF PROBIOTICS IN ACNE TREATMENT

The probiotics are live microbial feed supplement which advantageously influences the host creature by improving its intestinal equalization.[33]

Probiotics are live small scale living beings that give a medical advantage to the host. The job of probiotics in the administration of sickness, just as invulnerable change. The most normally utilized microscopic organisms as probiotics are the Lactobacillus and Bifidobacteria, and these are broadly accessible as powders, tablets, drinks, and matured dairy items.[34-35]

Applicability of Probiotics in the Treatment of Acne

Proof of utilization of probiotics in the therapeutic approach towards skin break out is developing through essential science and creature and human clinical preliminaries. Follicular hyperkeratinization, *Propiobacterium acnes* colonization, overabundance sebum creation, and an incendiary cascade are some of the procedures upon which

Table 2: Presently available antiacne formulation in the market.

S.NO	NAME OF THE PRODUCT	MANUFACTURE	FORMULATION
1.	Bio Winter Green Spot Correcting Anti Acne Cream, 15g	Biotique	Antiacne cream
2.	Anti Acne Aloe Vera Massage Cream, 50g	Vaadi Herbals	Antiacne cream
3.	Tea Tree and Cinnamon Anti-Acne Oil Control Face Wash-120g	Lotus Herbals	Antiacne face wash
4.	Retinol serum	The Derma company	Antiacne serum
5.	Foracne PLUS, 15g	Cipla	Antiacne gel combo
6.	Anti Acne serum and Pimple/Acne prone removal serum | Clears scar & Dark Spots |Tea Tree - 15 ml	Amueroz	Antiacne serum
7.	Adapalene gel 15g	Sun pharma	Antiacne gel
8.	VrhAcneonomics Acne Clear Gel, 40 mL	V R Science opcpvt ltd.	Antiacne gel
9.	Chloris Natural Anti Acne Cream, 100 G	Pharmakon	Antiacne cream
10.	Tea Tree And Neem Oil Anti Acne Gel, G	The Good Karma Co.	Antiacne gel

Skin break out arrangement depends[36] Effective skin inflammation are the results affected by normally causing skin obstruction interruption, prompting dryness and bothering. Therefore, considering skin hydration and boundary fix as an essential preventive measure against skin inflammation by quieting the aggravation. Probiotics adjust a few components in the pathophysiology of skin break out turn of events and can conceivably improve consistence also.

The development of antibacterial proteins can play an essential role in repressing the P. acnes and garnering the attention towards Probiotics. A distinct segment of oropharynx of in vitro *Streptococcus salivarius* assembles the A streptococci through the development of bacteriocin-like inhibitory substance (BLIS-like substance), thereby, creating hindrance in the development of *P. acnes*.[37] Comparatively, It has been observed through the emission of bacteriocins, strains of Lactococcus sp. HY 449 show antimicrobial movement and repress the development of *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Streptococcus pyogenes*, and *P. acnes*.[38] Clinically, with an auxiliary increment in antimicrobial properties of the skin the application of probiotics has been increased to alter the boundaries of skin infections. Reports have shown the application of Streptococcus thermophiles (cream) *in vitro* and *in vivo*, appeared to increment ceramide creation when applied for 7 days.[39-40] Probiotics target one factor by diminishing the checks of *P. acnes* adding to skin break out arrangement, outside the skin. By stimulationg the creation of solid ceramides, it restore sound fats, which can benefit skin inflammation straightforwardly and counter regular symptoms appearing because of skin inflammation treatments.

A probiotic can be considered to be novel, feasible, and more secure methodology for treatment of skin inflammation depending on this finding.

- Defining the reason of symptoms of higher Multireserve obstruction in anti-microbials, probiotics posses mystery normal anti-microbials. For e.g. the issue of Rehashed utilization of anti-infection agents results in multidrug obstruction can be overwhelmed with the utilization of probiotics. They emit normal compound substances called bacteriocins as anti-microbials.
- Oral consumption of anti-infection agents for skin inflammation treatment will lead to increasingly stomach bloating and other related issues as the small-scale unsafe life form present inside the body, in light of the fact probiotics as skin break out treatment is considerably more prevalent than regular techniques.
- Probiotics reduce essential markers of irritation and oxidative worry (from overwhelming smoking, for instance).[41]
- Probiotics minimize white blood cell (WBCs) to intervene skin irritation.[42]
- Probiotics reduce amount of insulin-like development factor 1 (IGF-1) a hormone-like substance drives skin inflammation. Whenever delivered in abundance, builds up irritation just as sebum creation.[43]
- Probiotics provide resistance against both gut-hurting and skin-hurting pathogens.[44]
- Against the interminable pressure i.e. mental worry considered to trigger the skin ailments probiotics diminish constant mental pressure and relieve the harm.
- Probiotics help control glycemic levels, when disturbed can cause skin inflammation.[45]

NOVEL DRUG DELIVERY SYSTEM: ACNE TREATMENT

Microemulsion and nanoemulsion

Microemulsions are bead size 100nm straightforward scatterings of oil and water settled by an interfacial film of surfactant and co-surfactant particles.[46-47] Surfactant and co-surfactant are utilized to reduce the interfacial pressure among oil and water stage.[48] Co-surfactant goes about as an occlusivity enhancer to improve skin infiltration.[49] Dynamic specialists are solubilized in microemulsions and are accessible for rapid infiltration into the skin. Nano emulsions (oil in water or water in oil detailing) are extremely little beads when blended show scattering and are proper bearer for the vehicle of lipophilic mixes. Nano emulsions are also considered as perfect vehicle for skin inflammation. They likewise produce beneficial impacts like expanded skin hydration and viscoelasticity.

Polymers

Polymers comprise of rehashing basic units of monomers associated by covalent bonds. In dermatology, the new acrylic corrosive polymer transforms into gel in nearness of water by catching water into microcells. A steady gel-like appearance with an arrangement of hydrophilic compound and lipophilic compound as suspension is anything but difficult to utilize, and it discharges the dynamic compound after single application. Regardless of the accessibility of various compelling clinical treatments for skin break out vulgaris, issues of security, consistence, and not exactly perfect adequacy help drive the quest for elective medicines for this exceedingly regular clinical issue. Researchers have created a cell divider tied down sialidase of *P. acnes* compelling antibody for *P. acnes*-related provocative skin break out.[50-51] They likewise want to build up a future bacterial treatment for conquering issues seen with the persistent utilization of anti-toxins, for example, a structure up a microscopic organism's obstruction. These researchers of the 21st century are persuaded that skin inflammation isn't because of earth and that

scouring skin can prompt more awful issues. In this way, later on, it is conceivable to investigate the utilization of small scale and nanocarrier-based medication conveyance frameworks in cutting edge structure with increment in viability for treatment of skin inflammation.

PATENTS ON ANTIACNE FORMULATIONS

Patent no: US 9,649,346 B2, Date of Patent: May 16, 2017: This patent features a mixture comprising viable probiotic micro-organisms for topical administration. In one embodiment, this probiotic mixture is packaged as a push-up tube. Also the method of preparing this mixture is also included in this patent. Probiotics from streptococcus, Bifidobacterium and Lactobacillus family are used. The mixture provides for conservation of probiotic micro-organisms in a non-proliferative state. The method also provides for methods of colonizing the skin with viable probiotic micro-organisms. Further, the methods of using the composition to provide skin hydration, decreasing fine lines and wrinkles, preventive and reducing skin inflammation, treating acne and decreasing the occurrence of future acne outbreaks. The pushup stick makes the application of formulation very easier.[52] The design and concept of thymol loaded nano-emulgel for treatment of acne with topical formulations provided by the patents on topical anti-acne formulations (US 7241456B2; US 6897238B2; US 6284234B1). However, a major constraint in the delivery of thymol is deprived aqueous solubility (<1 mg/ml) and low melting point (51°C). Additionally, tea tree oil has been testified with broad-spectrum anti-microbial and anti-inflammatory activity including efficacy against acne causing bacteria like *S. aureus* and *P. acnes*.[53-54]

RESULTS

In rundown, oral and skin probiotics are emerging as an vitalizing treatment choice or adjuvant treatment for skin inflammation. Skin inflammation is a typical inflammatory skin infection which makes a lot of pain patients continually experiencing it. It has been widely investigated regarding sickness itself just as accessible and potential treatment choices. The objective for skin break out treatment is the four notable pathogenic components answerable for this sickness state. This current survey talked about the various alternatives for rewarding skin inflammation, for example, skin treatments, and physical medicines. Be that as it may, because of the expanding opposition of *P. acnes* towards the accessible anti-toxins. A combination of treatment therapies like use of antibiotics, hormonal therapy, anti-inflammatory drugs, use of essential oils, vitamins, uv-protectants is given. Soaps like Dermadew containing tea tree essential oil are available in the market. But use of semisynthetic antibiotics leads to no. of side effects so, interest of consumers is shifted towards the healthy bugs i.e the probiotics (secreates natural antibiotics i.e bacteriocins). Probiotics along with the therapeutic benefit also leads to stability enhancement. Probiotics maintain a good pH balance on the skin. The emergence of antiacne serum formulations with lime peel essential oil, Patchouli oil, olive oil is also increased tremendously over past few years. Serum containing probiotics proves to be a novel topical drug delivery approach. Serum offers better penetration of the drug to the deeper layers of the skin and probiotics offers additional advantage of stability enhancement and maintain a proper balance of skin microflora. Beyond dermatological benefits probiotics are also increasingly used for stability enhancement of formulation. The concept of pickering emulsion is used to stabilize topical formulations with probiotics, because of their high colloidal stability and their controllable droplet size.

DISCUSSION

Although there is enough support which proves the use of probiotics for acne, several questions remain. First, among them is which will ultimately provides best results: oral ingestion or topical application? Alternatively, will a combination approach of oral and topical prove to be the most effective? Will live probiotic strains or live biotherapeutics offer an additional advantage over using metabolites, probiotic derivatives or supernatants? Will probiotic strains be capable of surviving on the skin, and if yes then how long? What should be the minimum and maximum dose of probiotics?

Each and every person's microbial environment is very complex. So, each and every person should have a different oral and skin care regimen after sampling that patient's unique microbial "fingerprint." A one for all approach is not suitable in this approach. Herbal formulations like use of aloe Vera, Neem, soapwort extract (both antiacne and surfactant properties) with live probiotics offers additional advantages over the synthetic derivatives. Both oral and topical therapy in combination serves the purpose best.

CONCLUSION

Probiotics proves to be a promising tool in the treatment of dermatological disorders like acne. Natural antibiotics (bacteriocins) are better choice than synthetic antibiotics due to lack of multidrug resistance and less adverse effects. Treatment of acne includes a combination approach consisting of use of anti-microbials, a healthy gut microbiome, healthy skin pH, proper hormonal secretion, anti-inflammatory drugs, live biotherapeutics and vitamins.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Ray C, Trivedi P, Sharma V. Acne and its treatment lines. Int J Res Pharm Biosci. 2013;3(1):1-6.
2. Adityan B, Kumari R, Thappa DM. Scoring Systems in Acne vulgaris. Indian J Dermatol venereol Leprol. 2009;75(3):323-6. doi: 10.4103/0378-6323.51258, PMID 19439902.
3. James WD. Clinical practice. Acne. N Engl J Med. 2005;352(14):1463-72. doi: 10.1056/NEJMcp033487, PMID 15814882.
4. Suva MA, Patel AM, Sharma N, Bhattacharya C, Mangi RK. A brief review on acne vulgaris: pathogenesis, diagnosis and treatment. Res Rev J Pharmacol. 2014;4(3):1-2.
5. Brown SK, Shalita AR. Acne vulgaris. Lancet. 1998;351(9119):1871-6. doi: 10.1016/S0140-6736(98)01046-0, PMID 9652685.
6. Imperato-McGinley J, Gautier T, Cai LQ, Yee B, Epstein J, Pochi P. The androgen control of sebum production. Studies of subjects with dihydrotestosterone deficiency and complete androgen insensitivity. J Clin Endocrinol Metab. 1993;76(2):524-8. doi: 10.1210/jcem.76.2.8381804, PMID 8381804.
7. Thiboutot DM. An overview of acne and its treatment. Cutis. 1996;57(1);Suppl:8-12. PMID 8654131.
8. Suva MA, Patel AM, Sharma N, Bhattacharya C, Mangi RK. A brief review on acne vulgaris: Pathogenesis, diagnosis and treatment. Pharmacol Rev. 2014;4(3):1-2.
9. Tuchayi SM, Makrantonaki E, Ganceviciene R, Dessinioti C, Feldman SR, Zouboulis CC. Acne vulgaris. Nat Rev Dis Primers. 2015;1(1):1-20. doi: 10.1038/nrdp.2015.29.
10. Joo SS, Jang SK, Kim SG, Choi JS, Hwang KW, Lee DI. Anti-acne activity of Selaginella involvens extract and its non-antibiotic antimicrobial potential on Propionibacterium acnes. Phytother Res. 2008;22(3):335-9. doi: 10.1002/ptr.2319, PMID 17926337.
11. Benner N, Sammons D. Overview of the treatment of acne vulgaris. Osteopath Fam Phys. 2013;5(5):185-90. doi: 10.1016/j.osfp.2013.03.003.
12. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, *et al.* Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;74(5):945-73.e33. doi: 10.1016/j.jaad.2015.12.037. PMID 26897386.
13. Satine RP, Quan MA. Pearls in the management of acne An Advanced Approach. Dermatology. 2000;27(2):289-08.
14. Sirvi K, Goyal PK, Vyas B. Novel drug delivery system and its uses in the treatment of acne. Int J Pharm Erud. 2016;6(3):12-28.
15. Jain S. Topical tretinoin or adapalene in acne vulgaris: An overview. J Dermatolog Treat. 2004 Jul 1;15(4):200-7. doi: 10.1080/09546630410033006, PMID 15764031.

16. Dréno B. What is new in the pathophysiology of acne, an overview. J Eur Acad Dermatol Venereol. 2017 Sep;31;Suppl 5:8-12. doi: 10.1111/jdv.14374, PMID 28805938.
17. Usatine RP, Quan MA. Pearls in the management of acne: An advanced approach. Prim Care. 2000;27(2):289-308. doi: 10.1016/s0095-4543(05)70196-2, PMID 10815044.
18. Kosmadaki M, Katsambas A. Topical treatments for acne. Clin Dermatol. 2017;35(2):173-78. doi: 10.1016/j.clindermatol.2016.10.010, PMID 28274355.
19. Webster G. Combination azelaic acid therapy for acne vulgaris. J Am Acad Dermatol. 2000;43(2 Pt 3):S47-50. doi: 10.1067/mjd.2000.108318, PMID 10898830.
20. Hubbard WH. Clinical dermatology: a color guide to diagnosis and therapy. Arch. Fam. Med. 1994;3(1):23.
21. Aytekin M, Gursoy RN, Ide S, Soylu EH, Hekimoglu S. Formulation and characterization of liquid crystal systems containing azelaic acid for topical delivery. Drug Dev Ind Pharm. 2013;39(2):228-39. doi: 10.3109/03639045.2012.671829, PMID 22480294.
22. Ghosh S, Sinha M, Bhattacharyya A, Sadhasivam S, Megha J, Reddy S, *et al*. A reasonably designed multifunctional antibiotic for the cure of drug-resistant acne. J.Inves. Dermatology. 2018;138(6):1400-08.
23. Moore A, Ling M, Bucko A, Manna V, Rueda MJ. Efficacy and Safety of Subantimicrobial Dose, Modified-Release Doxycycline 40 mg Versus Doxycycline 100 mg Versus Placebo for the treatment of Inflammatory Lesions in Moderate and Severe Acne: A Randomized, Double-Blinded, Controlled Study. J Drugs Dermatol. 2015;14(6):581-6. PMID 26091383.
24. Katsambas AD, Dessinioti C. Hormonal therapy for acne: Why not as first line therapy? facts and controversies. Clin Dermatol. 2010;28(1):17-23. doi: 10.1016/j.clindermatol.2009.03.006.
25. Bershad SV. The contemporary age of acne remedy: A examination of present treatment options. Mt Sinai. J Med. 2001;68:279-85.
26. Kim RH, Armstrong AW. Present state of acne conduct: Highlighting lasers, chemical peels and photodynamic therapy. Dermatol Online J. 2011;17.
27. Wise EM, Graber EM. Clinical pearl: Comedone extraction for persistent macrocomedones while on isotretinoin therapy. J Clin Aesthet Dermatol. 2011;4(11):20-1. PMID 22132254.
28. Kaminsky A. Less common methods to treat acne. Dermatology. 2003;206(1):68-73. doi: 10.1159/000067824, PMID 12566807.
29. Steventon K. Expert opinion and review article: The timing of comedone extraction in the treatment of premenstrual acne–a proposed therapeutic approach. Int J Cosmet Sci. 2011;33(2):99-104. doi: 10.1111/j.1468-2494.2010.00610.x, PMID 20807258.
30. Sharma VK, Khandpur S. Guidelines for cryotherapy. Indian J Dermatol Venereol Leprol. 2009;75:S90-S100.
31. Simonart T. Newer approaches to the treatment of acne vulgaris. Am J Clin Dermatol. 2012;13(6):357-64. doi: 10.2165/11632500-000000000-00000, PMID 22920095.
32. Elman M, Lebzelter J. Light therapy in the treatment of acne vulgaris. Dermatol Surg. 2004;30(2 Pt 1):139-46. doi: 10.1111/j.1524-4725.2004.30053.x, PMID 14756640.
33. Fuller R. Probiotics in man and animals. J Appl Bacteriol. 1989;66(5):365-78. doi: 10.1111/j.1365-2672.1989.tb05105.x, PMID 2666378.
34. Kumar S, Mahajan BB, Kamra N. Future viewpoint of probiotics in dermatology: An aged wine in fresh bottle. Dermatol Online J. 2014;20:11.
35. cosmeceutical_corner/probiotics-play-a-key-role-in-maintaining-skin-health.
36. Benefits of probiotics in Skincare. Available from: https://www.nourishedlife.com.au/article/1055030/benefits-of-probiotics-inskincare.html [cited 6/4/2022].
37. Baquerizo Nole KL, Yim E, Keri JE. Probiotics and prebiotics in dermatology. J Am Acad Dermatol. 2014;71(4):814-21. doi: 10.1016/j.jaad.2014.04.050, PMID 24906613.
38. Bowe WP, Filip JC, DiRienzo JM, Volgina A, Margolis DJ. Inhibition of propionibacterium acnes by bacteriocin-like inhibitory substances (BLIS) produced by *Streptococcus salivarius*. J Drugs Dermatol. 2006;5(9):868-70. PMID 17039652.
39. Oh S, Kim SH, Ko Y, Sim JH, Kim KS, Lee SH, *et al*. Effect of bacteriocin produced by Lactococcus sp. HY 449 on skin-inflammatory bacteria. Food Chem Toxicol. 2006;44(8):1184-90. doi: 10.1016/j.fct.2005.08.008.
40. Di Marzio L, Centi C, Cinque B, Masci S, Giuliani M, Arcieri A, *et al*. Effect of the lactic acid bacterium *Streptococcus thermophilus* on stratum corneum ceramide levels and signs and symptoms of atopic dermatitis patients. Exp Dermatol. 2003;12(5):615-20. doi: 10.1034/j.1600-0625.2003.00051.x, PMID 14705802.
41. Pavicic T, Wollenweber U, Farwick M, Korting HC. Anti-microbial and -inflammatory activity and efficacy of phytosphingosine: An *in vitro* and *in vivo* study addressing acne vulgaris. Int J Cosmet Sci. 2007;29(3):181-90. doi: 10.1111/j.1467-2494.2007.00378.x, PMID 18489348.
42. Naruszewicz M, Johansson ML, Zapolska-downar D, Bukowska H. Effect of Lactobacillus plantarum 299v on cardiovascular disease risk factors in smokers. Am J Clin Nutr. *2002*;76(6):1249-55. doi: 10.1093/ajcn/76.6.1249, PMID 12450890.
43. Hacini-rachinel F, Gheit H, Le Luduec JB, Dif F, Nancey S, Kaiserlian D. Oral probiotic control skin inflammation by acting on both effector and regulatory T cells. PLOS ONE. *2009*;4(3):e4903. doi: 10.1371/journal.pone.0004903, PMID 19300508.
44. Kang SH, Kim JU, Imm JY, Oh S, Kim SH. The effects of dairy processes and storage on insulin-like growth factor-I (IGF-I) content in milk and in model IGF-I-fortified dairy products. J Dairy Sci. *2006*;89(2):402-9. doi: 10.3168/jds.S0022-0302(06)72104-X, PMID 16428610.
45. [cited Aug 24, 2021]Available from: http://probiotics101.probacto.com/effects-of-probiotics-on-nutrient-synthesis/.
46. Ait-belgnaoui A, Braniste V, Colom A. Probiotic gut effect prevent the chronic psychosomatic stress-induced brain action anomaly in mice. J Neurogastroenterol Motil. *2014*;26(4):510-20.
47. Zareie M, Johnson-Henry K, Jury J, Yang PC, Ngan BY, McKay DM, *et al*. Probiotics prevent bacterial translocation and improve intestinal barrier function in rats following chronic psychological stress. Gut. *2006*;55(11):1553-60. doi: 10.1136/gut.2005.080739, PMID 16638791.
48. Bagwe RP, Kanicky JR, Palla BJ, Patanjali PK, Shah DO. Improved drug delivery using microemulsions: Rationale, recent progress, and new horizons. Crit Rev Ther Drug Carrier Syst. 2001;18(1):77-140. PMID 11326744.
49. Mann MW, Ellis SS, Mallory SBInfantile acne as the initial sign of an adrenocortical tumor. J Am Acad Dermatol. 2007;56(2):S15-8. doi: 10.1016/j.jaad.2006.04.028.
50. Shalita AR, Thiboutot DM, Bersonet DS. Effects of tazarotene 0.1% cream in the management of facial acne vulgaris: Pooled outcome from two multicenter, randomized, double-blind, parallel-group trials, vehicle-controlled. Clin Ther. 2004;26(11):1865-73.
51. Patel MR. Micro emulsions: As NDD vehicle. Pharmainfo.net. 2007.
52. Nakatsuji T, Rasochova L, Huang CM. Vaccine therapy for *P. acnes*-associated diseases. Infect Disord Drug Targets. 2008;8(3):160-5. doi: 10.2174/187152651080803016O, PMID 18782033.
53. Vyas A, Kumar Sonker A, Gidwani B. Carrier-based drug delivery system for treatment of acne. Scientific World Journal. 2014;2014:276260. doi: 10.1155/2014/276260, PMID 24688376.

Article History: Submission Date : 04-02-2022; Revised Date : 17-03-2022; Acceptance Date : 03-04-2022.
Cite this article: Sharma S, Vashist S, Lamba AK, Arora S, Sucheta. Novel Strategies in the Treatment of Acne: A Review. Int. J. Pharm. Investigation. 2021;12(2):123-8.