ISSN (O): 2349-5332
CODEN: IRJPHY

MICROSPONGE A PROMISING CARRIER FOR ACNE VULGARIS – A REVIEW

Soumyadip Ghosh[1], Debgopal Ganguly[2*], Subhabrota Majumdar[1], Kiran Kumar[3]

[1]Calcutta Institute of Pharmaceutical Technology & AHS, Banitabla, Uluberia, Howrah, West Bengal
[2]School of Pharmacy, Seacom Skills University, Bolpur, Birbhum
[3]Calcutta Institute of Pharmaceutical Technology & AHS, Banitabla, Uluberia, Howrah, West Bengal

Submitted on: 22.11.2021; **Revised on:** 28.12.2021; **Accepted on:** 29.12.2021

Abstract: In the present era, drug delivery technology is becoming too much competitive, and developing the various strategies to optimize the efficacy with cost-effectiveness is most important. In recent times microsponges drug delivery is gaining much more attention to target various diseases via different routes of administration. It has the potential to control over the release rate to show less toxicity with high effectiveness. Microsponges are the efficient technique for improved bioavailability, high stability, flexibility, and having the high drug loading capacity. Microsponges can make a difference themselves with the other carriers due to their self-sterilization, gaining much more interest to the researchers. Acne vulgaris is the severe disorder nowadays and it is showing the impact on social life. Acne can be characterized by the increase of sebum production, bacterial involvement, alternation of follicular keratinization, and alternation of the follicular barrier. Acne rarely causes serious systemic problems but the quality of life isa very important concern to teenagers and adulthood especially for women which leads to depression, anxiety, and low esteem. Several medications help to reduce the sebum production majorly to reduce the acne formation on the skin. The delivery of drugs using microsponge carriers is gaining access in current drug delivery. The current review is focused on the microsponges as carriers for the drug targeting the acne vulgaris, diagnosis of the disease, and a brief discussion on the present and future aspects of the microsponges to target acne vulgaris.

Keywords: Microsponge, *Acne vulgaris*, drug delivery systems, drug release technology, topical drug delivery.

Corresponding Author: Debgopal Ganguly
E-mail: ghoshs9764@gmail.com

Indian Research Journal of Pharmacy and Science; 30(2021)2601-2615;
Journal Home Page: https://www.irjps.in
DOI: 10.21276/irjps.2021.8.4.6

Introduction: Acne Vulgaris is a chronic inflammatory disease of the skin by Propionibacterium acne affects the pilosebaceous unit due to increasing level of sebum production, alternation of keratinization, bacterial inflammation of hair follicle which is present on skin, neck, chest, back, or any other parts of the body. Acne vulgaris is one of the severe diseases which may impact the social life of teenagers as well as adulthood and affectnearly 85% of the individuals who sufferfrom this disease. Acne is mainly more marked in the age between 12 to 24 during puberty, adolescence and also prevalent in adulthood especially in females because secretion of sebum from sebaceous glands is functioning at peak activity. Acne not only includes pimples but blackheads, nodules and cysts also are involved which is mainly caused by the oil(sebaceous) gland and hair follicle blocked due to hormonal changes. [1]

Several causative factors can be noticed to the acne vulgaris such as genetics, obesity (hyper-androgenism), intake of plenty dietary supplements, environmental factors. Some aggravating factors such as smoking, stress, and facial therapy or facial massage are also involved in acne formation.

Conventional drug delivery systems are not showing proper efficiency and therapeutic effectiveness due to pre-systemic metabolism and lack of concentration at the target site. Due to several adverse effects of the traditional drug delivery systems made to control the active ingredient administered to the human body has been one of the major challenges to the scientists. To overcome this problem multi-particulate drug delivery systems are a suitable carrier for achieving therapeutic effectiveness and low risk of dose dumping and flexibility with controlled or delay the release to the systemic circulation. [2] Various drug carriers are targeting the inflamed tissue and showing activity but the microsponges are the best carrier for local targeting with enhanced stability, formulation flexibility, reduction of adverse effects, and improving elegance.

Microsponges can be defined as porous, crosslinked, microscopic, tiny sponge-like spherical particles with a large surface area that can entrap or sustain a broad range of active ingredients which can be formulated as a lotion,cream,powder, gel, and tablet for delivery drugs. Microsponges have a particle size in the range of 5-300 micrometers in diameter and havea wide range of pores which help to entrap the wide range of drugs for local targeting and show the therapeutic activity. [3] Microsponge delivery system is the new innovative drug delivery systemthat is widely used in skincare products such as anti-fungal, anti-acne, antimicrobial, sunscreen and emollients. Microsponge technology was innovated and developed by "WON" in 1987 and modified and has been licensed to "CARDINAL HEALTH CARE Inc. Originally patent has been named to 'ADVANCED POLYMER SYSTEMS Inc. Microsponge drug delivery has potential to release the active ingredient to the target site by pressure, temperature variation, solubility, and pH trigger system. [4] After applying the formulation to the skin, drug release can be controlled by diffusion mechanism and other various strategies like friction, rubbing, pH, moisture, and skin temperature. Recently microsponges are gaining much more attention in the field of research as oral delivery, bone tissue engineering, cardiovascular engineering, reconstruction of the vascular wall, and topical delivery.

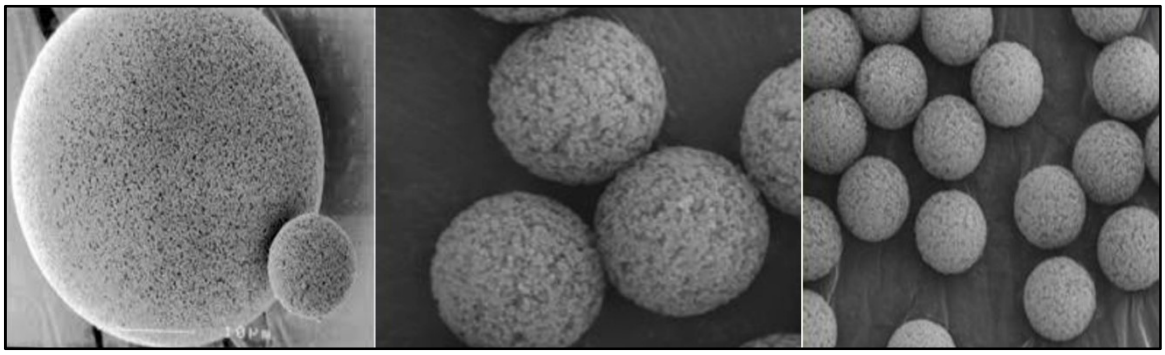

Fig 01 – Various size of microsponge

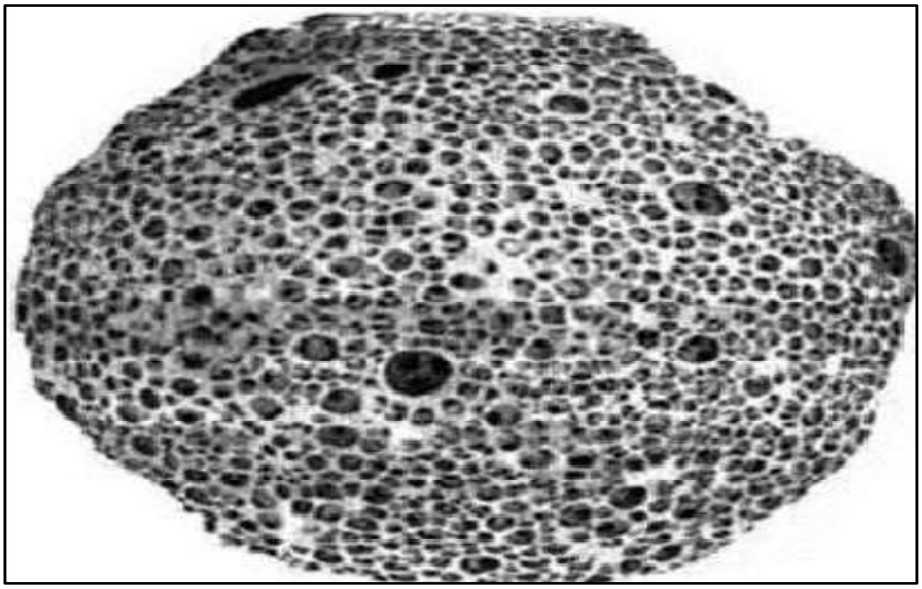

Fig 02 – Highly porous structure of microsponge

Need of microsponge drug delivery for topical delivery systems– [5] [6]

- Microsponge delivery systems have highly cross-linked, porous and polymeric microspheres that can help to entrap the wide range of formulation and can be released at the desired rate.
- Microsponges can prevent excessive accumulation in the dermis and epidermis.
- If the formulation is applied topically, the drug release can be controlled by the diffusion mechanism or other variety of triggers including various factors such rubbing, moisture, pH, friction, and skin temperature.
- It's a suitable carrier because of having high entrapment efficiency.
- Microspongeshave better bioavailability, high stability rate and improved flexibility.

- Having the capability of most of the vehicles and excipients.
- Having self-sterilization capacity as the particle size in the range of 0.25 micrometer thus bacteria can't penetrate
- Microsponges area very well-established carrier because they can be stable in the pH range of 1 to 11 and can be stable till the temperature of 130º.
- Microsponge technology has greater excellent control over the release of the active drug to reduce systemic availability and reduce toxicity.
- Having good bioavailability of active substances.
- Having better physical, chemical, and thermal stability than others novel drug delivery.
- Better formulation flexibility and target specificity.
- Enhancement of formulation performance and product elegancy.
- Microspongeshasa relatively longhalf-life.
- Reduction of irritation, improve patient compliance and extend the release rate up to 12 hrs

Advantages of microsponge for topical delivery –[7][8]

- Microsponges have several benefits over carriers as higher payload capacity, release rate, chemical stability, and self-sterilization.
- Microspongesnon-irritating, non-allergenic, non-mutagenic, and non-systemic toxicity.

Disadvantages of microsponge for topical delivery – [9]

- Using various organic vehicles as porogen which can be highly flammable due it undergoing environmental hazards.
- Some time monomers traces observed which can be toxic.
- Not biocompatible with all solvents and having some safety issues.

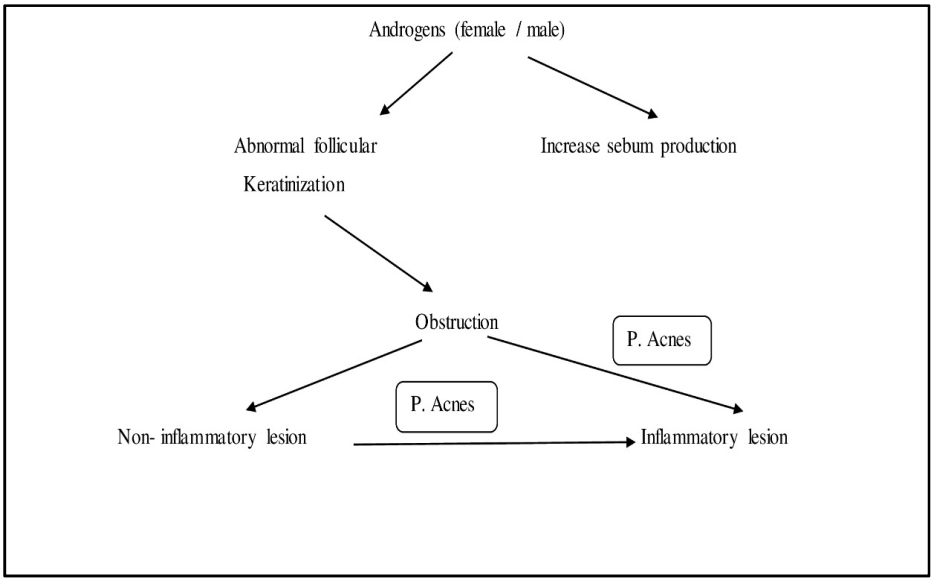

Fig 03 – Flow chart of formation of acne

Pathogenesis : Androgen isa major responsible causative factor for acne by inducing sebum production leading to comedones development. Comedones are nothing but small flesh-colored acne papules. The sebaceous gland consists of the hair follicle and sebaceous gland which is responsible for the secretion of sebum. Sebum and keratinous material clog up a pore on the skin and triggered bacterial colonization which led to the formation of comedones in the acne vulgaris. [11]

Pathogenesis of acne has several factors based on acne formation as non – inflammatory lesions like open and close comedones and inflammatory lesions like papules, pustules and nodules. Some important factors are as follows

- **Increased sebum production** –

  Testosterone is a common hormone for both males and females. When testosterone is secrets to the body it enters to sebaceous gland and conversion of testosterone to di-hydro testosterone by 5-alpha reductase and the formation of sebum. When testosterone level is escalated sebum production goes overdrive because of sensitivity issue of 5-alpha-reductase. A recent study says that sebum is the major impact factor onthe formation of acne. [12]

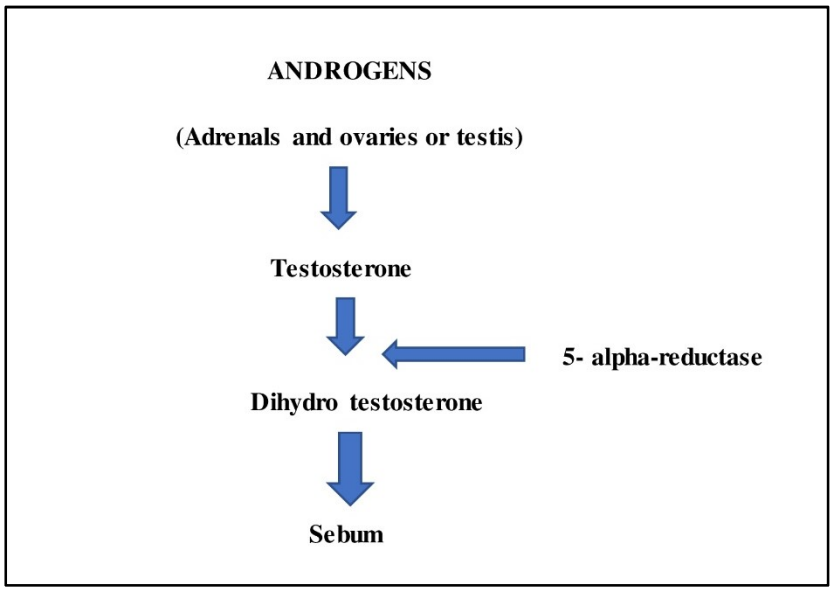

Fig 04 – Diagrammatic representation of sebum formation through sebaceous gland

- **Bacteria involvement** –

  Propionibacterium acne is gram-positive anaerobic bacteria responsible for acne formation and initiation of inflammation by releasing some enzymes like proteinases, lipases and hyaluronidases. These enzymes help to break down the sebum triglycerides into fatty acids and glycerol. A free fatty acid is the waste product thatirritates the lining of the follicle and disease may result in the production of comedones which would expel their contents. [13]

- **Alternation of follicular Keratinization –**

  In a patient with acne, follicular infundibulam can be altered due to the rate of keratinocyte desquamation. The accumulation of cell and sebum leads to the formation of micro- comedones and due to alternation of testosterone production results by the 5- alpha-reductase increase of androgen production and subsequent follicular keratinization. [14]

- **Inflammation of follicular barrier** –

  Bacterial inflammation (P. acne) stimulates CD4 lymphocytes and neutrophils which can penetrate the follicular wall that results in the disruption of the follicular barrier. That's led to the release of some amount of lipids, keratinocytes and spread out over the dermis and thus initiating inflammatory cytokines and neutropeptides. But to reduce the inflammatory reaction the linoleic acid plays an important role to stimulate the control of IL – 8 secretion. Linolenic acid has some drawbacks like enhancement of hyperkeratinization of the epidermis. [15]

Classification of Acne Vulgaris – [16]

Several classifications can be found in acne vulgaris. as

1) Based on characteristics of Acne
2) Based on the morphology of Acne
3) Based on the severity of Acne Vulgaris
4) Based on differential diagnoses of Acne Vulgaris.

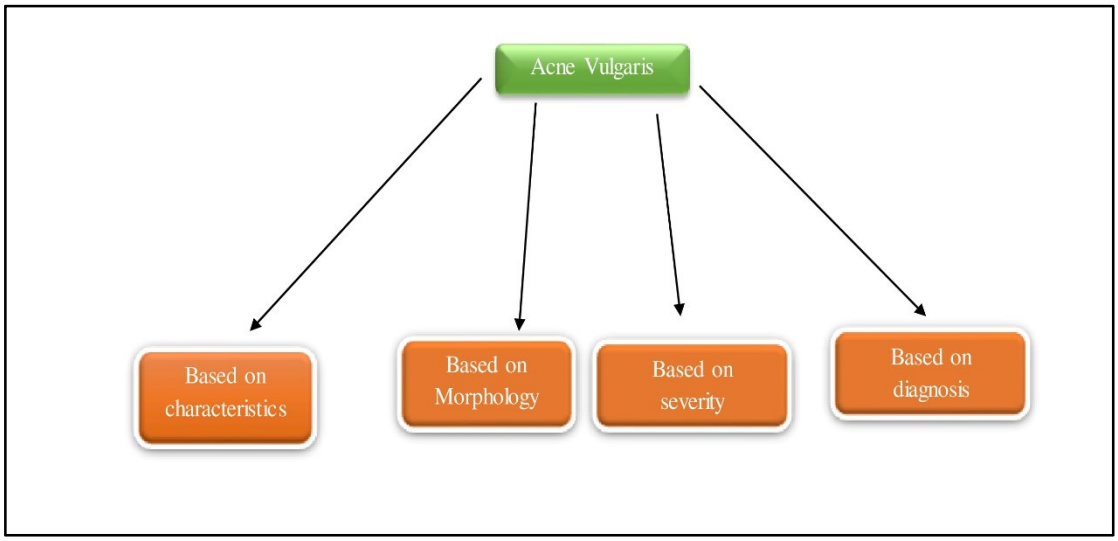

Fig 05 – Classification of Acne Vulgaris

1) Based on the characteristics of Acne –

Several types can be found out as follows –

Table01: Classification of acne based on characteristics [17] [18]

Types of Acne	Cause	Comedones severity	Lesions Area
Acne Conglobata	Increasing the level of sebum production.	Multiparous comedones	Face,hand, back
Occupational Acne	Exposure to industrial chemicals.	Predominantly comedones	Forearms
Cosmetic Acne	Using cosmetics especiallyoil-based.	Always comedones	Chin
Drug-induced acne	Using drugs like steroids, androgens, anti- TB drugs, iodides and anti-convulsant.	Predominantly comedones	Back and Face
Infantile Acne	Presence of maternal hormone in the child.	Predominantly comedones may last for 3 years	Face
Late-onset Acne	Increase secretion of androgen, i.e. polycystic ovarian syndrome	Predominantly comedones	The lower half of the face
Acne Excoriee	Conscious, repetitive and uncontrollable desire to pick, scratch or rub acne lesions.	Predominantly comedones	Face
Post Facial massage Acne	Acneiform eruption during facial massage	Few or No comedones	Cheeks, Mandible
Acne fulminans	After the massage and hypersensitive reaction due to allergic cosmetics, Fever, myalgia and arthralgia	Predominantly comedones	Face, back, hand

2)Based on the morphology of Acne–[19]

Based on the morphology they can be classified into 3 types

1) Comedonal acne – Major 2 classed undergoes as open (blackheads) and closed comedones (whiteheads)
2) Inflammatory acne – Papules and pustules
3) Nodulocystic acne – nodules and cysts.

3)Based on the severity of Acne Vulgaris–

Table 02: Classification based on severity of Acne Vulgaris [20]

AcneSeverity	Clinical Type	Comedones	Papulesand/or Pustules	Nodules	Nodule, cysts & sinus tracts
Mild	Comedonalacne and Papulopustular acne	Comedones are the main lesions (< 20)	Small and Fewinnumber(<10)	None	None
Moderate	Papulopustular acne and Nodular acne	10 – 40	10 –40	0 – 10	None
Severe	Nodulocystic acne & Conglobate acne	40 – 100& Fused	>40	>10	many

4)Based on the differential diagnosis of acne vulgaris – [21]

Table03: Classification of Acne Based on Diagnosis

Disease	Clinical findings
Acne Rosacea	Commonly observed in middle age or later in life
Folliculitis and boils	Present with pustular lesion
Milia	Small non-follicular keratin papules

Treatment of Acne vulgaris – [22] [23]

- To prevent bacterial inflammation by reduction of bacterial colonies.
- To reduce sebum production activity by decreasing the sebaceous gland activity.
- To prevent the follicles from becoming plugged
- To minimize the scar.
- To maintain remission and prevent relapse
- To prevent several physicals, physiological and social complications.
- To eliminate that factors that predispose the person to acne
- To give proper medication and giving support for social health.
- Reduction of hyperkeratinization.
- Rebalance the hormones.

Table04: Current treatment of Acne vulgaris [24] [25]

Route of Administration	Drug or Dosage form	Treatment features
Oral	Tetracycline, Doxycycline, Minocycline,Isotretinoin(13- cis-retinoicacid)	Drugs should be taken daily, Highpatientcompliance, Adverse effects limit the use of the drugs
Topical	Benzoylperoxide, Clindamycin, Erythromycin, Tetracycline, Tretinoin, Tazarotene, Green tea extracts	Local administration of drugs, Ease of termination of drug action, Adverse effects limit the use of the drugs
Particle-based DDS	Liposomes,Solid lipid nanoparticles, Nanostructured lipidcarriers, Microemulsions	Sustained release of drugs,More effective than topical gel,the higher fluxofdrugacrosstheskin, Effective for follicular targeting
Light-basedtherapy	Endogenousporphyrins (coproporphyrin III), 5- amino-levulinicacid	Fewer adverse effects than systemic/topical administration and Drug delivery system, Light therapy alone or along with liposomal drugs reported, Not a first-line therapy foracnevulgaris

Table05: Consideration of Management of Acne Vulgaris [26] [27]

Type of Treatment	Mild Acne	Moderate Acne	Severe Acne
First-line medication	Topical retinoid or Benzoyl peroxide or Topical combination therapy	Topical combination therapy;or Oral antibiotics, topical retinoid and benzoyl peroxide; orOral antibiotic, topical retinoid, benzoyl peroxide and topical antibiotic.	Oral antibiotics and topical combination therapy;or Oral isotretinoin.
Alternative medication	Add topical retinoid or benzoyl peroxide (in case one is not used already); or Consider alternative retinoid; or Consider topical dapsone.	Consider alternativecombinationtherapy; or Consider a change in oral antibiotic; or Add combinedoral Contraceptiveororal spironolactone(female patients); or Consideroral isotretinoin.	Consider a change in oral antibiotic; or Add combinedoral contraceptive or oral spironolactone (female patients); or Consider oral isotretinoin.

Microsponge drug delivery for Acne vulgaris –

Microsponge is the perfect carrier for acne vulgaris as they have high entrapment efficiency, high stability rate with high bioavailability with accurate flexibility and can prevent excessive accumulation in the dermis and epidermis. It is novel delivery technology that can be delivered the optimized product including facial shine and oily shine. Microsponge drug delivery has clinical over efficacy and tolerability in the treatment of acne by reducing the facial sebum accumulation relative to control. [28]

M. Jelvehgari, M.R siahi-Shadbad et al, purpose of the study preparation, characterization and release study of the benzoyl peroxide microsponge delivery system to the treatment of Acne Vulgaris. Microsponge was prepared by an emulsion solvent diffusion method. Benzyl peroxide microsponge using ethyl cellulose with a different drug: polymers ratio and done the proper comparison of release rate and flux of benzoyl peroxide incorporated topical formulation with that same formulation prepared with pure benzoyl peroxide. [29]

Jakhar, Seema et al reported Preparation, characterization andantimicrobial activity of dapsone loaded microsponge gel for Acne Management. The drug-loadedethyl cellulose microsponge preparation was done by quasi emulsion solvent diffusion technique. The development of micro formulation showed effectivity against the chosen acne bacteria and

improved stability and also showedan effective strategy for acne management. [30]

Sheefali Mahant, Sunil Kumar et al review the microsponge for dermatological application and having some perspective and challenges can face during topic delivery especially for acne. Done successfully review on the important factors affecting the performance and mechanism of drug release from topically applied microsponges along with the characterization techniques. [31]

James E. Fulton, JR., et al didstudy the mechanism of action of topical benzoyl peroxide and vitamin A acid in acne vulgaris.This resulted that the benzoyl peroxide with a combination of vitamin A showing the perfect activity to control the sebum production and keratinization and control over the acne formation.[32]

Sonali sayal, Vinay Pandit et al, studied to develop the microsponge containing havan ash composed gel formulation for the treatment of Acne. The preliminary investigation was carried out of the formulation of Havan Ash-loaded microsponges by the quasi emulsion solvent diffusion method (MSF1-MSF6). Different gel-based formulation (G1-G3) using Carbopol- 934 (1,1.5,2.0%) prepared by emulsification method. Successfully optimize (f3) showing the better result to targeting the sebum production and successfully reduce the activity of acne formation. [33]

Current Trends and Future Aspect of Microsponge For Topical Delivery –

Recently several advances of microsponge were successfully targeted to the local delivery and improvedbioavailability, high drug loading capacity to show the therapeutic efficacy. Now-a-days several microsponge formulations have been modified as nanosponge, nanoferrosponge and porous microbeads.

Studies say that nanosponge can deliver gases that can have the potential to target the cancerous cell and reduction of the cytotoxic effects. Nanoferrosponge is the emerging delivery thathas the potency of penetration to the targeted area due to having the external magnetic trigger which enforces to penetrate deeper tissue. [34] [35]

Beta cyclodextrin nanosponge is a wonder carrier for hydrophobic as well as hydrophilic drugs which compatible with nano or microsponge delivery. Nanosponges were developed by reacting the beta-cyclodextrin with diphenyl carbonate. Several drugs are formulated through this method as oral administration of dexamethasone, flurbiprofen, doxorubicin hydrochloride, itraconazole and sebum albumin etc. [36] [37]

Microsponge drug delivery systems havebecome more spirited, rapidly on the rise and holding the opportunity for the upcoming generation as it has extended-release, elegancy, improved drug release profiles, physical, physiological and chemical stability, improved bioavailability and specific targeting and attends local concentration to show the therapeutic efficacy. Real challenging of the future in the development and delivery of protein, peptide and gene to the site-specificity.For neoplastic delivery of the drugs microsponge is sometimes not suitable due to the toxic effect and stability issue. [38] [39] [40]

The porous delivery has been studied for the pulmonary route and it was established to show the efficacy and it should be formulated the alternative route of administration as a parenteral route. To give importance of protein and peptide microsponge delivery used as the stem cell culture

media and cellular regeneration in the body and show the effectiveness. [41] [42]

Microsponge drug delivery has elegance and penetration capacity due to the small size range is used in the cosmetics and cosmeceutical industries. These all these upcoming developments gaining much more interest to the researcher to target the special tissue or cells to get proper therapeutics attributes. [43] [44] [45]

Conclusion: Microsponge drug delivery is the innovative drug delivery systems various therapeutics application in upcoming trends and gaining too much attention to the researcher because of their several exciting advantages. Microsponge is the suitable delivery for acne vulgaris as perfect loading capacity, encapsulation efficiency, target specificity, prevent the excessive accumulation in the dermis as well as the epidermis. This is the specific technology for controlling the release rate of the active ingredients and can be also available for oral as well as biopharmaceutical drug delivery. For topical drug delivery, maximum carriers are failed to control the efficacy and release of the drugs but the microsponge technology significantly controls the release rate as well as reduces the systemic toxicity without affecting the active activity of the drug. Microsponge drug delivery holds fantastic promises tolocation-specific drug targeting and reduced the nearby cutaneous reaction to control over it and also suitable for the cosmetics products that attracted huge attention of the researchers. Microsponges getting a significant part in their small size and excellent characteristics.

References –

1) Oulès B, Philippeos C, Segal J, Tihy M, Rudan MV, Cujba AM, Grange PA, Quist S, Natsuga K, Deschamps L, Dupin N. Contribution of GATA6 to homeostasis of the human upper pilosebaceous unit and acne pathogenesis. Nature communications. 2020 Oct 20;11(1):1-7.
2) Yoon HY, Yang HM, Kim CH, Goo YT, Kang MJ, Lee S, Choi YW. Current status of the development of intravesical drug delivery systems for the treatment of bladder cancer. Expert Opinion on Drug Delivery. 2020 Nov 1;17(11):1555-72.
3) Junqueira MV, Bruschi ML. A review about the drug delivery from microsponges. AAPS PharmSciTech. 2018 May;19(4):1501-11.
4) Rajeswari S, Swapna V. Microsponges as a Neoteric Cornucopia for Drug Delivery Systems. International Journal of Current Pharmaceutical Research. 2019;11(3):4-12.
5) Mantry S, Bagchi A, Das S, Das S. Microsponge as A Novel Strategy of Drug Delivery System. Universal Journal of Pharmaceutical Sciences and Research. 2015 May 15;1(1):32-8.
6) Kappor D, Patel M, Vyas RB, Lad C, Tyagi BL. A review on microsponge drug delivery system. Journal of Drug Delivery and Therapeutics. 2014 Sep 14;4(5):29-35.
7) Tiwari A, Mishra MK, Shukla A, Yadav SK. Microsponge: An augmented drug delivery system. American Journal of PharmTech Research. 2016;6(6):79-95.

8) Jyothi KN, Kumar PD, Arshad P, Karthik M, Panneerselvam T. Microsponges: A Promising Novel Drug Delivery System. Journal of Drug Delivery and Therapeutics. 2019 Oct 15;9(5-s):188-94.
9) Mantry S, Bagchi A, Das S, Das S. Microsponge as A Novel Strategy of Drug Delivery System. Universal Journal of Pharmaceutical Sciences and Research. 2015 May 15;1(1):32-8.
10) Brown SK, Shalita AR. Acne vulgaris. The Lancet. 1998 Jun 20;351(9119):1871-6.
11) Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J. Acne vulgaris: a disease of Western civilization. Archives of dermatology. 2002 Dec 1;138(12):1584-90.
12) Burke BM, Cunliffe WJ. The assessment of acne vulgaris—the Leeds technique. British Journal of Dermatology. 1984 Jul;111(1):83-92.
13) Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. Journal of the American Academy of Dermatology. 2003 Sep 1;49(3): S200-10.
14) Pawin H, Beylot C, Chivot M, Faure M, Florence PO, Revuz J, Dréno B. Physiopathology of acne vulgaris: recent data, a new understanding of the treatments. European Journal of Dermatology. 2004 Jan 1;14(1):4-12.
15) Tuchayi SM, Makrantonaki E, Ganceviciene R, Dessinioti C, Feldman SR, Zouboulis CC. Acne vulgaris. Nature reviews Disease primers. 2015 Sep 17;1(1):1-20.
16) White GM. Recent findings in the epidemiologic evidence, classification, and subtypes of acne vulgaris. Journal of the American Academy of Dermatology. 1998 Aug 1;39(2): S34-7.
17) Plewig G, Kligman AM. Classification of acne vulgaris. InAcne 1975 (pp. 162-167). Springer, Berlin, Heidelberg.
18) Barinova AN. Etiology, pathogenesis, classification and clinical picture of acne vulgaris. Modern view of the problem. Russian Family Doctor. 2018 Nov 15;22(3):14-22.
19) Ogé LK, Broussard A, Marshall MD. Acne vulgaris: diagnosis and treatment. American family physician. 2019 Oct 15;100(8):475-84.
20) Boen M, Jacob C. A review and update of treatment options using the acne scar classification system. Dermatologic Surgery. 2019 Mar 1;45(3):411-22.
21) Rathi SK. Acne vulgaris treatment: the current scenario. Indian journal of dermatology. 2011 Jan;56(1):7.
22) Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita AR, Siegfried EC, Thiboutot DM, Van Voorhees AS, Beutner KA, Sieck CK, Bhushan R. Guidelines of care for acne vulgaris management. Journal of the American Academy of Dermatology. 2007 Apr 1;56(4):651-63.
23) Rathi SK. Acne vulgaris treatment: the current scenario. Indian journal of dermatology. 2011 Jan;56(1):7.
24) Simonart T. Newer approaches to the treatment of acne vulgaris. American journal of clinical dermatology. 2012 Dec;13(6):357-64.

25) Jain V, Singh R. Dicyclomine-loaded Eudragit®-based microsponge with potential for colonic delivery: preparation and characterization. Tropical Journal of Pharmaceutical Research. 2010;9(1).
26) Gollnick HP, Krautheim A. Topical treatment in acne: current status and future aspects. Dermatology. 2003;206(1):29-36.
27) Embil K, Nacht S. The microsponge® delivery system (MDS): a topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. Journal of microencapsulation. 1996 Jan 1;13(5):575-88.
28) Iwai S, Sawa Y, Ichikawa H, Taketani S, Uchimura E, Chen G, Hara M, Miyake J, Matsuda H. Biodegradable polymer with collagen microsponge serves as a new bioengineered cardiovascular prosthesis. The Journal of Thoracic and Cardiovascular Surgery. 2004 Sep 1;128(3):472-9.
29) Mandava SS, Thavva V. Novel approach: microsponge drug delivery system. International Journal of Pharmaceutical Sciences and Research. 2012 Apr 1;3(4):967.
30) Jakhar S, Kadian V, Rao R. Dapsone-Loaded Microsponge Gel for Acne Management: Preparation, Characterization and Anti-Microbial Activity. Micro and Nanosystems. 2021 Jun 1;13(2):211-22.
31) Mahant S, Kumar S, Nanda S, Rao R. Microsponges for dermatological applications: Perspectives and challenges. Asian journal of pharmaceutical sciences. 2020 May 1;15(3):273-91.
32) Wester RC, Patel R, Nacht S, Leyden J, Melendres J, Maibach H. Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy. Journal of the American Academy of Dermatology. 1991 May 1;24(5):720-6.
33) Syal S, Pandit V, Ankalgi AD, Verma CP, Ashawat MS. Formulation and Evaluation of Microsponges Gel of Havan Ash for the Treatment of Acne. Journal of Drug Delivery and Therapeutics. 2020 Nov 15;10(6):74-85.
34) Jadhav N, Patel V, Mungekar S, Bhamare G, Karpe M, Kadams V. Microsponge delivery system: an updated review, current status and future prospects. Journal of Scientific and Innovative Research. 2013 Sep 21;2(6):1097-110.
35) Kumari A, Jain A, Hurkat P, Verma A, Jain SK. Microsponges: a pioneering tool for biomedical applications. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2016;33(1).
36) Gangadharappa HV, Vishal Gupta N, Chandra Prasad M S, Shivakumar HG. Current trends in microsponge drug delivery system. Current drug delivery. 2013 Aug 1;10(4):453-65.
37) Jadhav N, Patel V, Mungekar S, Bhamare G, Karpe M, Kadams V. Microsponge delivery system: an updated review, current status and future prospects. Journal of Scientific and Innovative Research. 2013 Sep 21;2(6):1097-110.
38) Borawake PD, Kauslya A, Shinde JV, Chavan RS. Microsponge as an Emerging Technique in Novel Drug Delivery

System. Journal of Drug Delivery and Therapeutics. 2021 Jan 15;11(1):171-82.

39) Bharathi M, Mullaikodi O, Rajalingam D, Gnanasekar N, Kesavan M. A Review on Microsponge Drug Delivery System. International Journal of Review in Life Sciences. 2020 Sep 19;10(2):53-9.

40) Kshatriya PJ, Shinde JV, Chavan RS. As Review on Microsponge Gel as Topical Drug Delivery System. Journal of Drug Delivery and Therapeutics. 2020 Dec 15;10(6-s):125-33.

41) Nivedita M. Formulation and Evaluation of Diacerein Loaded Microsponges in Capsule (Doctoral dissertation, College of Pharmacy Madras Medical College, Chennai).

42) Pawar AP, Gholap AP, Kuchekar AB, Bothiraja C, Mali AJ. Formulation and evaluation of optimized oxybenzone microsponge gel for topical delivery. Journal of drug delivery. 2015;2015.

43) Wadhwa G, Kumar S, Mittal V, Rao R. Encapsulation of babchi essential oil into microsponges: Physicochemical properties, cytotoxic evaluation, and anti-microbial activity. Journal of food and drug analysis. 2019 Jan 1;27(1):60-70.

44) Caso MF, Carotenuto F, Di Nardo P, Migliore A, Aguilera A, Lopez CM, Venanzi M, Cavalieri F, Rinaldi A. Nanoporous microsponge particles (NMP) of polysaccharides as universal carriers for biomolecules delivery. Nanomaterials. 2020 Jun;10(6):1075.

45) Nagula RL, Wairkar S. Cellulose microsponges based gel of naringenin for atopic dermatitis: Design, optimization, in vitro and in vivo investigation. International journal of biological macromolecules. 2020 Dec 1; 164:717-25.

CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED