INTERNATIONAL JOURNAL OF
PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

MICROSPONGE: AN INNOVATIVE STRATEGY FOR DRUG DELIVERY SYSTEM, CURRENT STATUS AND FUTURE PROSPECTS

CHAITRA G.[1], SOWMYA B. A.[2]

1. Department of Pharmaceutics, East West College of Pharmacy, Bangalore-91.
2. Department of Pharmacology, East West College of Pharmacy, Bangalore-91.

Accepted Date: 24/11/2019; Published Date: 27/12/2019

Abstract: Microsponge technology has been introduced in topical drug products to facilitate the controlled release of active drug into the skin in order to reduce systemic exposure and minimize local cutaneous reactions to active drugs. Microsponge consists of macroporous beads, typically 10-25µ in diameter, loaded with active agent. When applied to the skin, the microsponge releases its active ingredients on a time mode and also in response to other stimuli. Microsponge drug delivery technology holds a great promise for reaching the goal of controlled and site-specific drug delivery and hence, has attracted wide attention of researchers. This article presents a broad review of Microsponges delivery system discussing the principles and preparation methods. Appropriate analytical techniques for characterization of Microsponges like Particle size and its distribution, surface morphology, porosity, density are covered. These microsponges are used in the sunscreens, creams, ointments, over-the-counter skin care preparations, which are meant for topical application. Microsponge drug delivery can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved aesthetic properties in an efficient and novel manner. They are mostly used for topical use and have recently been used for oral administration.

Keywords: Microsponge, MDS, controlled release, Topical drug delivery, Liquid-Liquid Suspension Polymerization, Quasi emulsion method.

Corresponding Author: CHITRA G.

Access Online On:

www.ijprbs.com

How to Cite This Article:

Chitra G., IJPRBS, 2019; Volume 8(6): 23-36

PAPER-QR CODE

INTRODUCTION

Microsponges are polymeric delivery systems composed of porous microspheres. They are tiny sponge-like spherical particles with a large porous surface. Moreover, they may enhance stability, reduce side effects and modify drug release favorably. Microsponge technology has many favourable characteristics, which make it a versatile drug delivery vehicle.[1] Microsponge Systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances and can then be incorporated into a formulated product such as a gel, cream, liquid or powder. MDS can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved aesthetic properties in an efficient manner. [2]

To control the delivery rate of active agents to a predetermined site in the human body has been one of the biggest challenges faced by Pharmaceutical scientists. Several predictable and reliable systems have been developed for systemic delivery of drugs under the heading of transdermal delivery system (TDS) using the skin as portal of entry.[3] It has improved the efficacy and safety of many drugs that may be better administered through skin. But TDS is not practicable for delivery of materials whose final target is skin itself.[4] Controlled release of drugs onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts is a challenging area of research. [5]

Microsponges consist of non-collapsible structures with porous surface through which active ingredients are released in controlled manner.[6] Depending upon the size, the total pore length may range up to 10 ft. and pore volume up to 1 ml/g. [7] When applied to the skin, the microsponge drug delivery system (MDS) releases its active ingredient on a time mode and also in response to other stimuli such as rubbing, temperature, and p^H[8] Microsponges have the capacity to adsorb or load a high degree of active materials into the particle or onto its surface. Its large capacity for entrapment of actives up to 3 times its weight differentiates microsponges from other types of dermatological delivery systems. [9]

Defining Microsponge: A Microsponges Delivery System (MDS) is “Patented, highly cross-linked, porous, polymeric microspheres, polymeric system consisting of porous microspheres that can entrap wide range of actives and then release them into the skin over a time and in response to trigger”. Micro-sponge polymers possess the versatility to load a wide range of actives providing the benefits of enhanced product efficacy, mildness, tolerability, and extended wear to a wide range of skin therapies. [10]

They are tiny sponge like spherical particles that consist of a myriad of interconnecting voids within a noncollapsible structure with a large porous surface through which active ingredient are released in a controlled manner.[11] The size of the microsponges ranges from 5-300µm in

diameter and a typical 25µm sphere can have up to 250000 pores and an internal pore structure equivalent to 10 feet in length, providing a total pore volume of about 1ml/g for extensive drug retention. The surface can be varied from 20 to 500 m/g and 2 pore volume range from 0.1 to 0.3cm/g. This results in a large reservoir within each 3 microsponge, which can be loaded with up to its own weight of active agent. [12]

The microsponge technology was developed by Won in 1987, and the original patents were assigned to Advanced Polymer Systems, Inc. This company developed a large number of variations of the procedures and those are applied to the cosmetic as well as overthe-counter (OTC) and prescription pharmaceutical products. At the current time, this interesting technology has been licensed to Cardinal Health, Inc., for use in topical products.[13] The scanning electron microscopy of the microsponge particle reveals that its internal structure as the "bag of marbles". The porosity is due to the interstitial spaces between the marbles. The interstitial pores can entrap many wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens, anti-infective and anti-inflammatory agents. [14]

These entrapped microsponges may then integrated or formulated into product forms, such as creams, lotions, powders, soaps, capsules and tablets. When these products are applied the entrapped material gets delivered to the skin in a controlled time release pattern or a pre-programmed manner through the use of several different 'triggers', rubbing or pressing the Microsponge after it has been applied to the skin, elevates skin surface temperature introducing solvents for the entrapped materials such as water, alcohol or even perspiration and controlling the rate of evaporation. Active ingredients entrapped in the porous polymeric structure display altered behaviour, with respect to their release, which is restricted and prolonged.[3]

Microsponges are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance stability, reduce side effects and modify drug release profile. [15] The MDS has advantages over other technologies like microencapsulation and liposomes. Microcapsules cannot usually control the release rate of actives. Once the wall is ruptured the actives contained within microcapsules will be released. Liposomesuffer from lower payload, difficult formulation, limited chemical stability and microbial instability. [16]

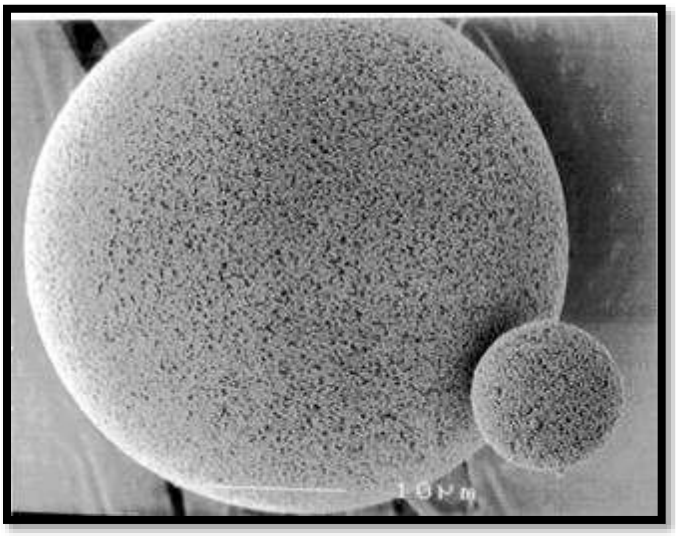

Fig 1: Porous structure of Microsponge

Potential features or characteristic of microsponge drug delivery systems [3,7]

1. Microsponges show acceptable stability over pH ranging from 1 to 11 and at high temperatures (up to130°C).
2. Microsponges exhibit good compatibility with various vehicles and ingredients.
3. Microsponges have high entrapment efficiency up to 50 to 60%.
4. Microsponges are characterized by free flowing properties.
5. The average pore size of microsponges is small (0.25 µm) in a way to prevent the penetration of bacteria, thus they do not need sterilization or addition of preservatives.
6. Microsponges are non-allergenic, non-irritating, nonmutagenic and non-toxic.
7. Microsponges can absorb oil up to 6 times their weight without drying.

Characteristics of materials that is entrapped in microsponges [3,16]

1. It should be either fully miscible in monomer as well as capable of being made miscible by addition of small amount of a Water immiscible solvent.
2. It should be water immiscible or nearly only slightly soluble.
3. It should be inert to monomers and should not increase the viscosity of the mixture during formulation.

4. It should not collapse spherical structure of the microsponges.
5. It should be stable in contact with polymerization catalyst and also in conditions of polymerization.(4)
6. The solubility of actives in the vehicle must be limited to avoid cosmetic problems; not more than 10 to 12% w/w microsponges must be incorporated into the vehicle. Otherwise the vehicle will deplete the microsponges before the application.
7. Payload and polymer design of the microsponges for the active must be optimized for required release rate for given period.

Advantages microsponge delivery system (MDS) [3,7]

- Microsponges can absorb oil up to 6 times its weight without drying.
- It provides continuous action up to 12 hours i.e. extended release.
- Improved product elegancy.
- Lesser the irritation and better tolerance leads to improved patient compliance.
- They have better thermal, physical and chemical stability.
- These are non-irritating, non-mutagenic, non-allergenic and non-toxic.
- MDS allows the incorporation of immiscible products.
- They have superior formulation flexibility.
- In contrast to other technologies like microencapsulation and liposomes, MDS has wide range of chemical stability, higher payload and are easy to formulate.
- Liquids can be converted in to powders improving material processing.
- It has flexibility to develop novel product forms.
- MDS can improve bioavailability of same drugs.
- It can also improve efficacy in treatment.

Limitations [9]

The preparation methods usually use organic solvents as porogens, which pose an environmental hazard, as some may be highly inflammable, posing a safety hazard. In some

cases, the traces of residual monomers have been observed, which may be toxic and hazardous to health.

Polymers used in MDDS: [17]

Various polymers can be used for the preparation of microsponge, such as the Polystyrene, Ethyl cellulose, PHEMA, Eudragit RS 100 & acrylic polymers etc.

Table 1: Optimum values for Microsponge formulation [18]

Specification	Optimum values
Drug: polymer ratio	3:1, 4:1 and 5:1
Amount of drug(g)	2
PVA (mg)	30-70
Inner phase solvent	Ethyl alcohol
Amount of inner phage solvent (ml)	10(ml)
Amount of water in outer phage (ml)	200(ml)
Temp in inner phage (°C)	37
Stirrer type	Three blade
Stirring rate (rpm)	500
Stirring time (min)	60

METHODS OF PREPARATION OF MICROSPONGE

Micro sponge's drug delivery system can be prepared in two ways, one-step process or by two-step process that is liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques based that is based on physicochemical properties of drug to be loaded.

Liquid-Liquid Suspension Polymerization

In general, a solution is made comprising the monomers and the functional or the active ingredients which is immiscible with water. Then suspended with agitation in an aqueous phase, usually containing additives such as surfactants, and dispersants to promote suspension.

Once the suspension is established with discrete droplets of the desired size, polymerization is effected by activating the monomers either by catalysis, increased temperature or irradiation. As the polymerization process continues, a spherical structure is produced containing thousands of microsponge bunched together like grapes. When the polymerization is complete the solid particles that results from the suspension. The microsponge product can be made using styrene and methylmethacrylate and ethylene glycol dimethacrylate as starting materials. [4,13]

The various steps involved in the preparation of microsponges are summarized as follows: [2]

Step 1: Selection of monomer as well as combination of monomers.

Step 2: Formation of chain monomers as polymerization starts.

Step 3: Formations of ladders as a result of cross-linking between chain monomers.

Step 4: Folding of monomer ladder to form spherical particles.

Step 5: Agglomeration of microspheres leads to the production of bunches of microspheres.

Step 6: Binding of bunches to produce microsponges.

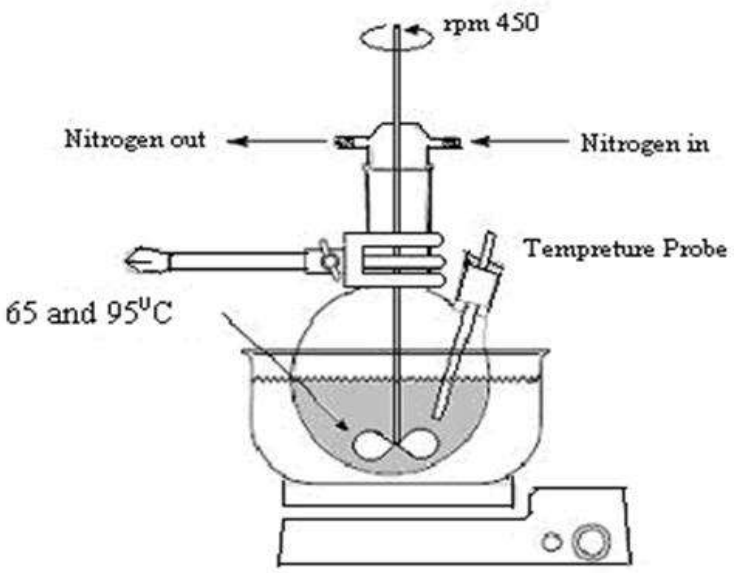

Fig 2: Reaction vessel for Microsponge Preparation by Liquid-liquid suspension polymerization method.

Quasi-Emulsion Solvent Diffusion Method

Microsponges are also prepared by a quasi-emulsion solvent diffusion method (two-step process) using an internal phase containing polymer such as Eudragit RS 100 which is dissolved in ethyl alcohol. Then, the drug is slowly added to the polymer solution and dissolved under ultrasonication at 35º C and plasticizer such as triethylcitrate (TEC) was added in order to aid the plasticity. The inner phase is then poured into external phase containing polyvinyl alcohol and distilled water with continuous stirring for 2 hours. Then, the mixture was filtered to separate the microsponges. The product (microsponges) was washed and dried in an air heated oven at 40°C for 12 hrs. [2]

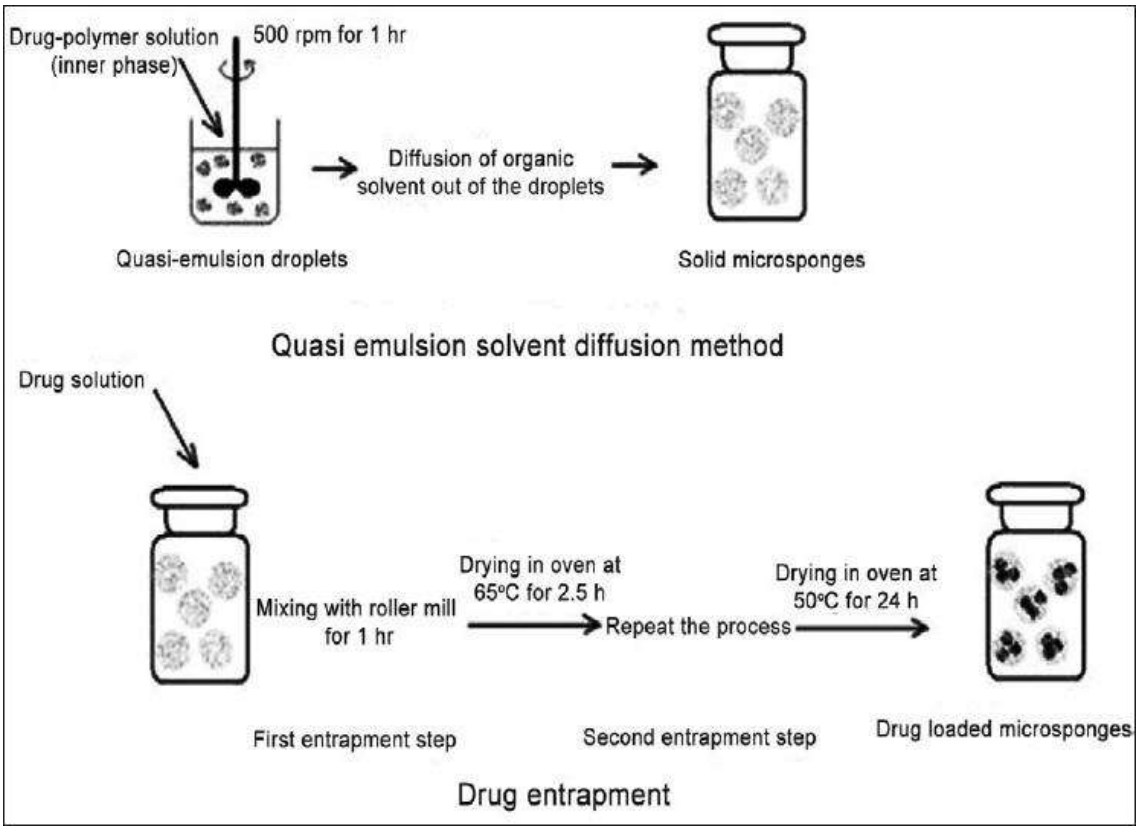

Fig 3: Preparation of Microsponge by Quasi-emulsion solvent diffusion method

Table 2: Applications of microsponge systems [18, 27]

Active agents	Applications
Sunscreens	Long-lasting product efficacy, with improved protection against sunburns

	and sun-related injuries, even at elevated concentration and with reduced irritancy and sensitization
Anti-acne, **e.g., Benzoyl peroxide**	Maintained efficacy with decreased skin irritation and sensitization
Anti-inflammatory **e.g. hydrocortisone**	Long lasting activity with reduction of skin allergic response and dermatoses
Anti-fungals	Sustained release of actives
Anti-dandruffs, **e.g., zinc pyrithione, selenium sulfide**	Reduced unpleasant odor with lowered irritation and extended safety and efficacy
Antipruritics	Extended and improved activity
Skin depigmenting agents, **e.g.,hydroquinone**	Improved stabilization against oxidation with improved efficacy and aesthetic appeal
Rubefacients **e. g. capsaicin**	Prolonged activity with reduced irritancy greasiness and odor

Advance Development

These drug delivery systems were originally developed for topical delivery of drugs. They can also be used for tissue engineering and controlled oral delivery of drugs using biodegradable polymers. It provides a wide range of formulating advantages. Liquids can be transformed into free flowing powders. Formulations can be developed with otherwise incompatible ingredients, with prolonged stability, without the use of preservatives. Therefore, microsponges will be an ideal drug delivery system related to formulations like the transdermal delivery system. As we realize the nanosized particles have immense advantages like a very high surface area to size ratio and a greater potential to modulate the release of actives compared to micro-sized

particles. While inorganic nanosponges have many applications in electronics, the first pharmaceutical nanosponges based on cross linked cyclodextrins have been reported. An interesting application of the microsponge technology could be in oral cosmetics, such as to sustain the release of volatile ingredients, thus increasing the duration of the 'fresh feel'. Microsponges of such volatile ingredients may be easily incorporated in tooth pastes or mouth washes and also colors entrapped in Microsponges may be used in a variety of colored cosmetic products such as rouge or lipsticks to make them long lasting. [28]

Table no. 3: List of Marketed Products using MDS [29, 30]

Product name	Content	Uses	Manufacturer
NeoBenz®Micro,	Benzoyl peroxide, methyl methacrylate/ glycol	Antibacterial properties and is classified as keratolytic.	Intendis Inc. Morristown NJ07962 USA
Retin-A-Micro	0.1% and 0.04% Tretinoin, methyl methacrylate/ glycol dimethacrylate, Aqueous gel base.	Diminishment of fine lines and wrinkles, a noticeable improvement in the skin discolorations due to aging, and enhanced skin smoothness.	Biomedic, Sothys
Retinol cream, Retinol 15 Night cream	Retinol, Vitamin A	For the treatment of actinic keratosis (AK), a common precancerous skin condition caused by over-exposure to the sun.	Dermik Laboratories, Inc. Berwyn , PA 19312 USA
Carac Cream	0.5% Fluorouracil, 0.35%methyl methacrylate / glycol dimethacrylate cross-polymer and dimethicone.	Visibly diminishes appearance of fine lines, wrinkles & skin discolorations associated with aging.	Avon

Line Eliminator **Dual Retinol Facial Treatment**	Vitamin A	Improve fine lines, pigmentation, and acne concerns.	Biophora
Salicylic Peel 20	Salicylic acid 20%,	Improve fine lines, pigmentation and acne concerns.	Biophora
Salicylic peel 30	Salicylic acid 30%,	Freeing the skin of all dead cells while doing no damage to the skin.	Biomedic
Dermalogica Oil **Control Lotion**	Niacinamide, Zinc Gluconate, Yeast Extract, Caffeine, Biotin,SalicylicAcid, Enantia Chlorantha Bark Extract.	To reduce oily shine on skin's surface.	John and Ginger Dermalogica Skin Care Products
Ultra Guard	Dimethicone	To protect a baby's skin from diaper rash, hypoallergenic and skin protectants.	Scott Paper Company

CONCLUSION

The Microsponge delivery system is a unique technology for the controlled release of macroporous beads, loaded with active agent, offering a potential reduction in side effects, while maintaining their therapeutic efficacy. The Microsponge drug delivery system offers entrapment of its ingredients and is believed to contribute toward reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. In addition, numerous studies have confirmed that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and nontoxic. This technology is being used currently in cosmetics, over-the-counter skin care, sunscreens, and prescription products. This kind of drug delivery technology may lead to a better understanding of the healing of several diseases.

Hence, the Microsponge-based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future.

BIBLIOGRAPHY

1. Kapoor D, Vyas RB, Lad C, Patel M, Tyagi BL, A review on microsponge drug delivery system. Journal of Drug Delivery and Therapeutics. 29-35;4(5):2014.

2. Garish Joshi, Rajandeep Kaur, Harpreet Kaur, Microsponges: A Novel Drug Delivery System. IRJPBS. 01-11; 3(1): 2016.

3. Raju. Manda, Dr. R. Suthakaran, Choppadandi. Mounika, Abhkishek chawan, R. K. Prasanna, Naresh. G, A Review: Microsponge a Novel New Drug Delivery System. Journal of Scientific Research in Pharmacy.,1-5; 4(1): 2015.

4. Saroj Kumar Pradhan, Microsponges as the versatile tool for drug delivery system. IJRPC., 243-258;1(2):2011.

5. Nikhil B Sinkar, Sheetal B Gondkar, Ravindranath B Saudagar, A review: Microsponge a innovative strategy for drug delivery system Current status and future prospects. International Journal of Institutional Pharmacy and Life Science., 226-243;5(3):2015.

6. N.H Aloorkar, Kulkarni AS, Ingale DJ, Patil RA, Microsponges as Innovative Drug Delivery Systems. Int J Pharm Scl Nanotech., 1597-1606; 5(1):2012.

7. Kajal P. Badhe, Dr. R.B. Saudagar, A Review on Microsponge a Novel Drug Delivery System. Asian J. Pharm. Tech., 51-57;6(1):2016.

8. Manisha K, Tile,A.Y. Pawar, Microsponges: A Novel Strategy for Drug Delivery. Int. J. Pure App. Biosci., 224-235; 3 (1): 2015.

9. Shital S. Patil, Vaishali Dandekar, Asawari Kale, Dr. S. D. Barhate, Microsponge drug delivery system: An overview. European Journal of Pharmaceutical and Medical Research.,212-221;3(8):2016.

10. Ankaj Kaundal, Rohit Bhatia, Amit Sharma, Pankaj Sukrial, A review on microsponges drug delivery system. International Journal of Advanced Pharmaceutics. Vol 4(3); 177-181:2014.

11. M. S. Charde, P. B. Ghanawat, A. S. Welankiwar, J. Kumar and R. D. Chakole, Microsponge A Novel New Drug Delivery System: A Review. International Journal of Advances in Pharmaceutics. 63-70; 2 (6):2013.

12. Shubhrajit Mantry, Arnab Bagchi, Sujit Das, Sudip Das, Microsponge as a novel stratergy of drug delivery System, UJPSR., 32-38; 1 (1):2015.

13. Goutam Pal, An overview on Microsponge delivery system. International Journal of Drug Discovery and Medical Research., 1-3;1(2):2012.

14. Namrata Jadhav, Vruti Patel, Siddesh Mungekar, Gaurav Bhamare, Manisha Karpe, Vilasrao Kadam,. Microsponge Delivery System: An updated review current status and future prospects. Journal of Scientific and Innovative Research. 1097-1110;2 (6):2013.

15. S. Kavya Lalitha, M. Shankar, D. Likhitha, J. Dastagiri, M. Niranjan Babu, A current view on microsponge drug delivery system. European Journal of Molecular Biology and Biochemistry.,88-95;3(2):2016.

16. Poornima Pandey, Vikas Jain and SC Mahajan, A review: Microsponge drug delivery system. International Journal of Biopharmaceutics. 225-230;4(3):2013.

17. Upadhye shashikant S, kothali B.K, Apte A.K, Patil A.A, Danole A.B. A review on Microsponge drug delivery system. IJPRBS., 152-166; 5(1): 2016.

18. Mohite P.B, Khanage s.g, Harishchandre v.s, Shirsath yogita, Recent advances in microsponges drug delivery system. J Crit Rev., 9-16;3(1): 2016.

19. Sandhyarani R. Sagavkar, Dr. Shrinivas K Mohite, Innovative and novel strategy: microsponges drug delivery system. International Journal of Universal., Pharmacy and Bio Sciences.,79-92; 3(4):2014.

20. Shelke PK, Gadhave M V, Gaikwad D, Rajpure P.B, International Journal of Universal Pharmacy and Life Sciences., 1-17;3(4):2013.

21. M.Sarat Chandra Prasad, M. Ajay, B. Nagendra Babu, P. Prathyusha, N. Audinarayana, Dr. K. Bhaskar Reddy, Microsponge Drug Delivery System: A Review. Journal of Pharmacy Research. 1381-1384; 4(5):2011.

22. Hamid Hussain, Divya Juyal, Archana Dhyani, Microsponges: An Overview. International Journal of Drug Delivery Technology. 58-66;4(4):2014.

23. Ravi R, S K Senthilkumar, S Parthiban, Microsponges drug delivery system: A review. International Journal of Pharmacy Review & Research., 6-11; 3:2013.

24. Rahul Shivaji Patil, Vishnu Uddhav Kemkar, S. S. Patil, Microsponge Drug Delivery System: A Novel Dosage Form. Am. j. Phar Tech., 227-251; 2(4):2012.

25. Hussain hamid, Juyal divya, Dhyani archana, Microsponges: An Overview. Indian Journal of Novel Drug delivery., 198-207; 6(3):2014.

26. Ramadevi Bhimavarapu, Ramesetti RamaDevi, Srinath Nissankararao, Microsponges as a Novel Imperative for Drug Delivery System. Research J. Pharm. and Tech., 842-848; 6(8):2013.

27. Santanu Kaity, Sabyasachi Maiti, Ashoke Kumar Ghosh, Dilipkumar Pal, Animesh Ghosh, Microsponges: A novel strategy for drug delivery system. Journal of Advanced Pharmaceutical Technology & Research., 283-290; 1(3): 2010.

28. Navneet Kumar Verma, Prabhudutta Panda, J. N. Mishra, D. K. Vishwakarma, Gulzar Alam, A.P. Singh, Microsponges: An Approach to Novel Drug Delivery System-A Review. IJCPS., 1719–1725;3(5): 2015.

29. Arijit Gandhi, Sougata Jana, Kalyan Kumar Sen, Tailoring effect of Microsponge for targeted drug delivery. Journal of Scientific and Innovative Research. 1073-1082;2 (6): 2013.

30. Jagtap S.C, Karale A.A, Ambekar A.W, Microsponge: A novel topical drug delivery system. Journal of drug delivery research. 1-9; 3(4):2014.