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A REVIEW ON MICROSPONGES: AN ALTERNATIVE STRATEGY FOR DRUG DELIVERY SYSTEM

Ramisetty Naga Jagadeeswari, Praveen Sivadasu* and Padmalatha K.

Vijaya Institute of Pharmaceutical Science for Women, Enikepadu, Vijayawada-521 108 Krishna District Andhra Pradesh, India.

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***Corresponding Author**
Dr. Praveen Sivadasu
Vijaya Institute of Pharmaceutical Science for Women, Enikepadu, Vijayawada-521 108 Krishna District Andhra Pradesh, India.

ABSTRACT

Microsponge drug delivery system (MDDS) is considered a unique technology to deliver the drug in a controlled manner. These drug delivery systems can also be referred to as polymeric systems with desired drugs loaded in porous microspheres and delivered in the form of gel, cream, liquid, and powder. Further, these are tiny sponge-like spherical particles with a size of 5-300 µm and with a large porous surface. These drug delivery systems possess various advantages like effective delivery of the loaded drug to the target site, stability enhancement, reduced incidence of side effects, and a sustained drug release. In addition, various studies had proved that MDS is non-irritating, non-allergic, and non-toxic. MDS technology facilitates the controlled release of active drugs into the skin to reduce systemic exposure and minimize local cutaneous reactions. These micro-sponges are used mostly for topical use and recent studies suggested that they can also be used for oral administration. The current review focus on history, advantages, limitations, preparation, evaluation, and biomedical applications of micro-sponges.

KEYWORDS: Microsponge; Controlled drug delivery; Topical Drug Delivery; Biomedical application.

INTRODUCTION

Micro-sponges are polymeric delivery systems composed of porous microspheres. They are tiny sponge-like spherical particles with a large porous surface (10-25 µ). Microsponge drug delivery system (MDDS) is a patented, highly cross-linked system and considered a novel technique to deliver the drugs to the targeted site in a controlled manner. In addition, this

drug delivery system possesses enhanced drug stability, reduced adverse effects, and modified drug release. MDDS are microscopic and polymer-based microspheres that can entrap a wide variety of drugs and be incorporated into a gel, cream, liquid, or powder.[1-4] The ever-increasing interest among consumers concerning skincare and skin treatment products have been tampered by the usage of ingredients like α-hydroxy acids and vitamins in cosmetic products which produce severe effects to the skin like aging and damage of skin due to light.[5] To overcome these problems researchers had made several attempts (reducing the concentrations of the excipients and changing the vehicle used) that have led to a product with decreased efficacy. Thus, there is a need for a drug delivery system that can deliver the drugs to a specific site in the body in a controlled manner. Potentially, MDDS can significantly reduce the irritation caused by the drugs without altering the efficacy of the product.[6-9] The micro-sponge 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 over-the-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. The scanning electron microscopy of the micro-sponge particle reveals that its internal structure is the "bag of marbles". As the size of the pore diameter is smaller, the bacteria ranging from 0.007 to 0.2 µm cannot penetrate the tunnel structure of the micro-sponges as shown in Fig 1.[5]

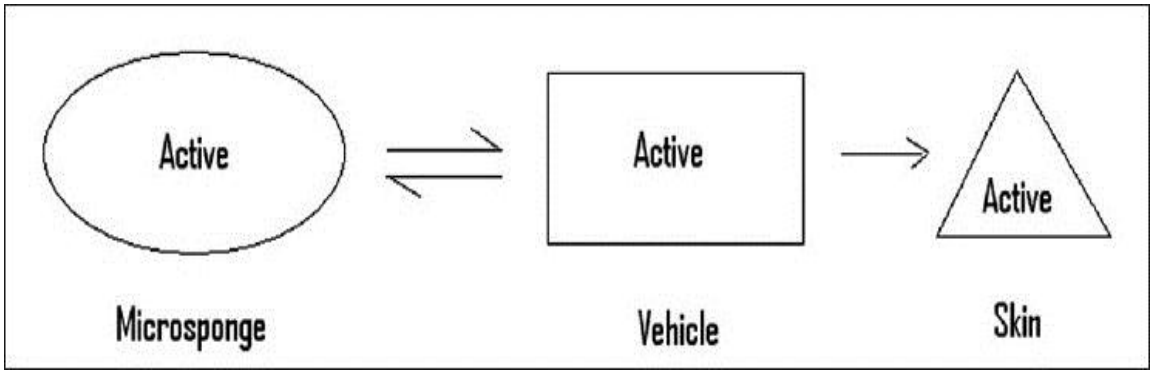

Fig. 1: Schematic representation of the distribution of the loaded material (active) on skin.

Potential benefits of microsponges[5, 6]

- Have self-sterilization due to pore size 0.2 5µm which prevents penetration of bacteria; thus, they do not require the addition of a preservative.

- Have high loading capacity ranging from 50 to 60%.
- Free flow properties and can be productive concerning its cost.
- Offer good compatibility with different vehicles and ingredients.
- Have stability at pH extending from 1 to 11.
- They are stable at elevated temperatures up to 130 °C.
- Improves formulation flexibility.
- Extended-release of drug continuous up to 12 hours.
- Microsponge systems are non-irritating, non-mutagenic, non-allergic, and non-toxic.
- Reduce irritation and patient compliance.

Limitations[10,11]

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

Methods of preparation of microsponges

Drug loading in microsposges can be done in two ways i.e. one-step process and two-step process as shown in Fig. 2 which depends on the desired drug that has to be loaded.[12]

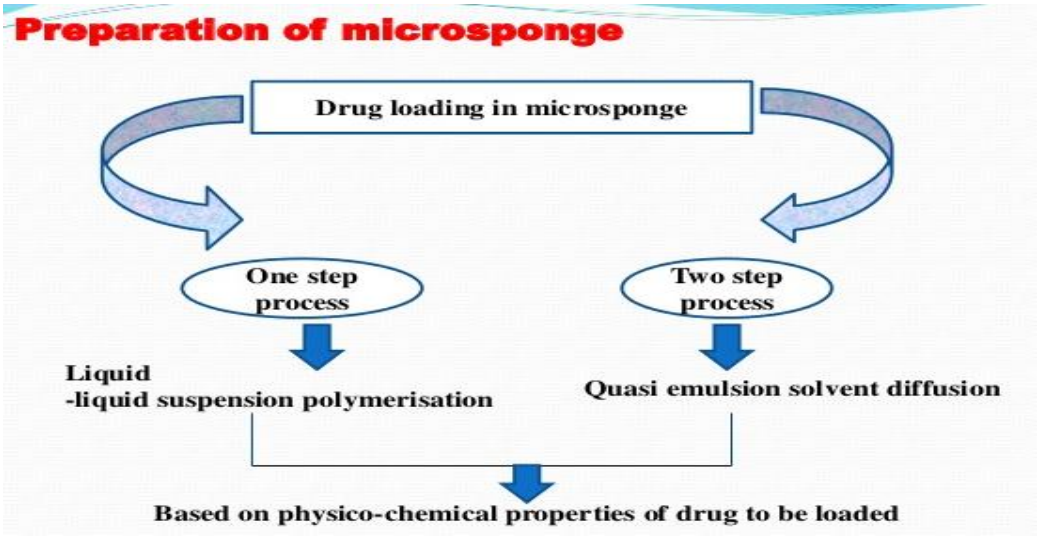

Fig. 2: Drug loading process in microsponges.

Liquid-Liquid suspension polymerization

In this method, MDDS is prepared by suspension polymerization in a liquid-liquid system which is a one-step process as shown in Fig. 3. A typical procedure involves dissolving the monomers with active ingredients in a suitable solvent. Further, the above solution is dispersed in the aqueous phase (consists of surfactants, suspending agents, etc.). The polymerization step is activated by either adding a catalyst or by increasing the temperature and the process is continued until a reservoir of spherical structure is formed. Post completion of polymerization the solvent is removed leading to the forming of microsponges.[13-15]

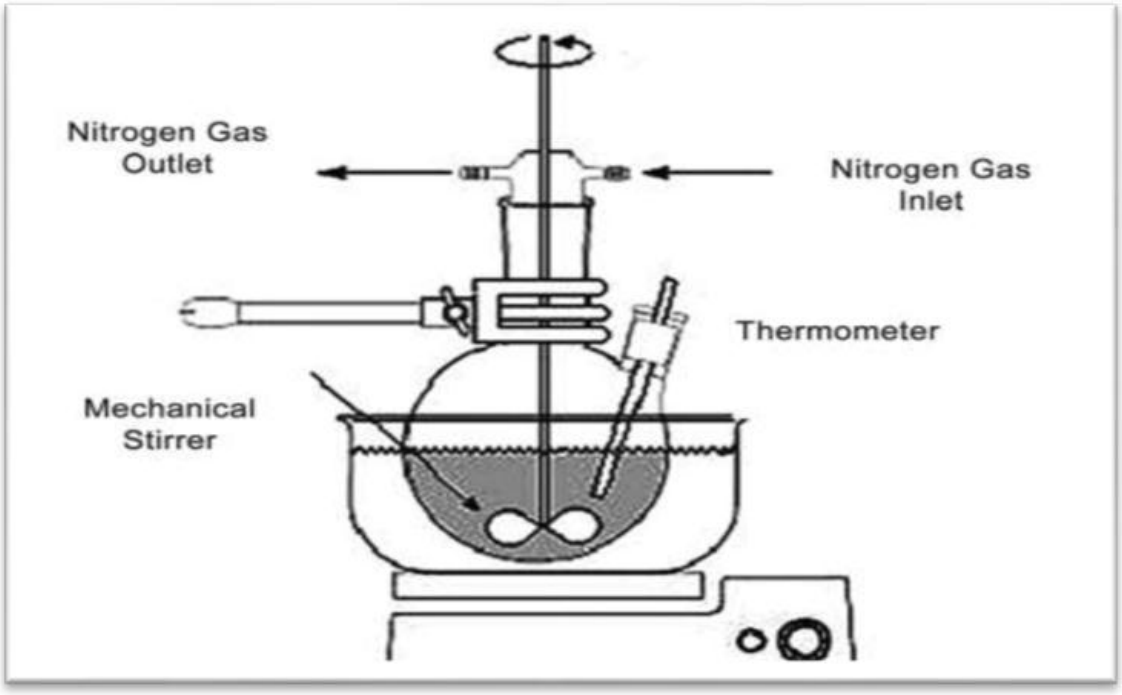

Fig. 3: Microsponge preparation by liquid-liquid suspension polymerization.

Quasi-Emulsion solvent diffusion

MDDS can also be prepared by quasi-emulsion solvent diffusion which is a two-step process as shown in Fig. 4. A typical procedure consists of two phases (internal and external phase). The internal phase consists of a polymer dissolved in a suitable solvent. Then the desired drug is slowly added to the polymer solution and dissolved by using an ultra-sonicator. Further, this internal phase is mixed u with the external phase with a continuous stirring for 2 hours. Post stirring the solution is filtered, washed, and dried to obtain the desired microsponges.[16] A brief description of different methods to prepare microsponges is presented in Table 1.

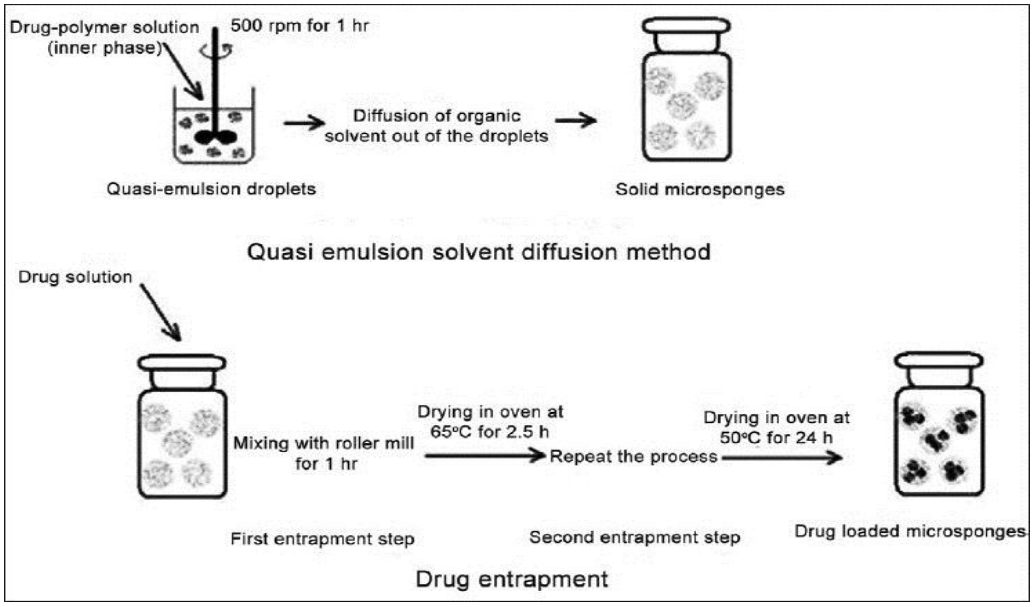

Fig. 4: Preparations of microsponges by Quasi-emulsion solvent diffusion method.

Table 1: Preparation of microsponges by Quasi-emulsion solvent diffusion.

Method	Advantages	Disadvantages
Liquid-liquid suspension polymerization	It can be suitably modified to one-step or two-step methods for drug loading.	Probable entrapment of unreacted monomers and solvent traces. Non-uniform structure. Requires a long time for the reaction of monomers. Requires a two-step method for thermosensitive drugs that have low drug loading efficiency.
Quasi-emulsion Solvent diffusion	No monomer entrapment. Low solvent traces. High drug loading. No exposure of the drug to ambient conditions. The size of microsponges can be easily controlled by controlling the stirring.	Cannot be used for the loading of water-soluble drugs. Requires a long time for the reaction of monomers. The drug should be soluble in a volatile Water-soluble solvent.

Drug release mechanisms of microsponge

The formulated drug-loaded MDDS consists of an open structure where the desired drug can move freely (from particle to the vehicle) as it doesn't have a continuous membrane surrounding the particle. Further, this process continues until the vehicle attains saturation (equilibrium between the particle and the vehicle).[17,18] Post formulation after applying it to the skin the desired drug in the vehicle gets absorbed into the skin and creates a disturbance in the equilibrium between the vehicle and the particle which will lead to a flow of the desired drug from microsponge to the vehicle so that the equilibrium is maintained.

Furthermore, this process is continued until the vehicle is either completely dried off or absorbed. Post absorption the microsponges which are retained on the skin gradually release the desired drug in a controlled manner. This proposed mechanism gives special emphasis on the importance of the vehicles used in the formulation of microsponges. If the desired drug is completely soluble in the selected vehicle the final product will not provide the desirable controlled release.[19,20]

Pressure triggered systems

In this mechanism drug release from the desired MDDS occurs by applying external pressure. Further, the amount of drug released from the microsponge is entirely dependent on the physical properties of the pores (size and number) present on the microsponge, and optimization is done by understanding the type of materials and the process involved in the preparation of the desired MDDS.[21]

Temperature triggered systems

The flow property of the drug-loaded MDDS can be affected by physicochemical properties of the formulation like viscosity (which can be high at room temperature). This limitation can be overcome by increasing the temperature and the flow rate of the drug to the skin can be enhanced.[21]

Solubility triggered systems

Microsponges loaded with water-soluble ingredients like antiperspirants and antiseptics will release the desired drug in the presence of water. The release can be activated by diffusion taking into consideration the partition coefficient of the ingredient between the microsponge and the outside system.[21]

Evaluation of microsponge

Particle size determination

The particle size of the drug-loaded and plain microsponges can be analyzed by using either a light diffractometer or other suitable methods (light microscopy, scanning electron microscopy Confocal fluorescence microscopy, etc.). Further, results obtained by employing these methods are expressed in the form of mean size either in the nanometer or micrometer. To study the effect of particle size on the dissolution profile of the loaded drug a graph should be plotted between drug release and microsponges of different sizes. Microsponges with a particle size of more than 30 µm give a gritty feeling to the formulation. Therefore,

microsponges with a particle size of 10-25µm are widely used in topical formulations loaded with microsponges.[22]

Morphology and Surface topography of microsponges

The surface morphology of the desired microsponges can be assessed by using scanning electron microscopy (SEM). A typical procedure involves coating the formulated microsponges with gold-palladium at room temperature under an argon atmosphere and the images were recorded to understand the surface morphology of the formulated microsponge.[23]

Determination of true density

Measurement of true density for microsponges was done by using an ultra-pycnometer under the atmosphere of helium gas and calculated by using triplicate data.[24]

Determination of loading Efficiency and Production yield[25]

The loading efficiency (%) and production yield of the microsponges can be calculated according to the following equation given below:

$$\text{Loading efficiency} = \text{Actual drug in microsponge}/\text{Theoretical drug concentration} * 100$$

$$\text{Production Yield} = \text{Practical Mass}/\text{Theoretical Mass} * 100$$

Characterization of pore structure

To study the effect of pore diameter and volume on drug release from microsponges mercury intrusion porosimeter can be used. Further, pore volume and diameter are important in controlling the intensity and duration of release of the desired drug from the microsponge, and pore diameter also influences the migration of microsponges into the vehicle. Furthermore, various porosity parameters like instruction-extrusion isotherms, pore size distribution, total pore surface area, average pore diameter, shape and morphology of the pores, bulk, and apparent density can be calculated by using an intrusion porosimeter.[26]

Compatibility studies

The compatibility of the drug with reaction adjuncts can be studied by thin-layer chromatography (TLC) and Fourier transport infra-red spectroscopy (FT-IR). The effect of polymerization on the crystal unity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC).[27]

Resiliency

Resiliency (viscoelastic properties) of microsponges can be modified 6to produce bead lets that are after or firmer according to the needs of the final formulation. Increased cross-linking tends to slow down the rate of release.[28]

***In-vitro* drug release study**

In-vitro drug release studies can be performed using United States Pharmacopeial (USP) dissolution apparatus equipped with a modified basket consisted of 5 µm stainless steel mesh at 37˚C. The release is selected according to the type of formulation that is topical or oral while considering the solubility of active ingredients to ensure sink conditions.[29]

Biomedical applications of microsponges

For topical administration

A single microsponge particle can be considered as a tiny particle as such of talcum powder with a size less than one-thousand of an inch. Further, these sponges have a myriad of interconnecting voids with a non-collapsible structure that can accept a wide range of drug molecules. A typical microsponge has a porous outer surface which allows the drug molecules to enter and exit the sphere. Microsponges are made up of inert polymers. Even though they are microscopic as the systems are large they cannot cross the stratum corneum of the skin when given as topical products. Benzyl peroxide is commonly used in topical formulations to treat acne with skin irritation as a common adverse effect.[30,31]

For oral administration

The formulated microsponge systems have shown an increasing the solubilization of poorly water-soluble drugs by trapping them in the pores of the sponges when given through the oral route of drug administration. As the size of the pores is in the micro range the size of the trapped molecules will be reduced drastically leading to an increase in surface area by which the solubility of the desired hydrophobic drug can be enhanced. For example, oral delivery of ibuprofen can be improved by formulating in the form of microsponges by using an acrylic polymer Eudragit RS.[32]

For Bone and Tissue engineering[33]

Compounds obtained by mixing polymers like polymethyl methacrylate and liquid methyl acrylate monomers with aqueous dispersions of tricalcium phosphate and calcium-deficient hydroxyapatite powders appeared to be porous and acted as microsponges. Further, the

inclusion of basic fibroblast growth factor (bFGF) in a collagen sponge sustained the release and exhibited local angiogenic activity in a dose-dependent manner. Various marketed formulations of microsponges are depicted in Table 2.

Table 2: Marketed formulation of MDS.[34]

Product name	Treatment	Manufacturer	Active ingredient
Retin-A-Micro	Acne vulgaris	Ortho-McNeil Pharmaceutical, Inc.	0.1%-0.4% tretinoin in an aq. gel
carac cream 0.5%	Actinic keratosis	Dermik Laboratories	0.5% fluorouracil
Lactrex™ 12% moisturizing cream	Long-lasting moisturization	SDR Pharmaceuticals, Inc.	12% lactic acid as the ammonium lactate.
Micro peel plus/ Acne peel	Remove all dead cells without damaging the skin	Bio medic.	Salicylic acid in the forms of microcrystals
Oil control lotion	Acne-prone, oily skin condition	Fountain cosmetics	Natural antibiotics
Ultra-guard	Protect baby's skin from diaper rash	Scott paper company	Dimethicone

CONCLUSION

Microsponge drug delivery systems have various advantages like enhanced product performance, elegancy, extended-release, improved thermal, reduced irritation physical and chemical stability which can be incorporated in the development of various novel pharmaceutical products. Additionally, various research studies suggested that the formulated microsponges are non-irritating, no mutagenic, no allergenic, and non-toxic. Further, these drug delivery systems were developed with a new technology where the product stability was enhanced without incorporating preservatives into the final product. This novel drug delivery system is currently used in the formulation of cosmetics (skincare, sunscreen, etc.) and there is still scope to explore this drug delivery system to treat various diseases. Therefore, from the above findings, it can be concluded that this novel microsponge drug delivery system can be used as an alternative approach to transport the drug to the desired location and releases the drug in a controlled manner.

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CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

REFERENCES

1. M.S. Charde, P.B. Ghanawat, A.S. Welankiwar. A Novel New Drug Delivery System: A Review. Int. J. Adv. Pharm, 2013; 2(6): 63-70.
2. Shivani Nanda, Mandeep Kaur, Nikhil Sood, Sahil Nagpal. Microsponge drug delivery system: an overview. World J Pharm Pharm Sci, 2013; 2(3): 1032-43.
3. Kaity S, Maiti S, Ghosh AK, Pal D, Ghosh A, Banerjee S. Microsponges: A novel strategy for drug delivery system. J Adv Pharm Techno Res, 2010. 1(3): 90-283.
4. Chadawar, V. and J. Shaji. Microsponge delivery system. Curr Drug Deliv, 2007; 4(2): 9-123.
5. Tile MK, Pawar AY. Microsponges: a novel strategy for drug delivery. *Int J* Pure Appl Biosci, 2015; 3(1): 224-35.
6. Kapoor D, Vyas RD, Lad C, Patel M, Tyagi BL. A Review on Microsponge Drug Delivery System. J. Drug Deliv. Ther, 2014; 4(5): 29-35.
7. Kirti Deshmukh, Sushil Kumar S Poddar. Solid porous microsphere: emerging trend in pharmaceutical technology. Int J pharm Bio Sci, 2011; 2(1): 364-77.
8. Patel SB, Patel HJ and Seth AK. Microsponge drug delivery system: an overview. J Global Pharm Tech, 2010; 2(8): 1-9.
9. Viral Shaha, Hitesh Jain, Jethva Krishna, Pramit Patel. Microsponge drug delivery: A Review. Int. J. Res. Pharm. Sci, 2010; 1(2): 212-8.
10. Kale S, Shalini R. Microsponge: Comprehensive Review of Application. Int J Pharm Chem, 2013; 3(1): 214-26.
11. Hussain H, Juyal D. Microsponges: An Overview. Ind J Novel Drug Delivery, 2014; 6(3): 198-207.
12. Sagavkar SR and Mohit SK. Innovative and Novel Strategy: Microsponges drug delivery System. IJUPBS, 2014; 3(4): 79-92.
13. Jyothi KN, Kumar PD, Arshad P, Karthik M, Panneerselvam T. Microsponges: A Promising Novel Drug Delivery System. J. Drug Deliv. Ther, 2019; 9(5-s): 188-94.
14. Çomoğlu T, Gönül N, Baykara T. Preparation and in vitro evaluation of modified release ketoprofen microsponges. Il farmaco, 2003; 58(2): 101-6.

15. Potts RO, Guzek DB, Harris RR, McKie JE. A noninvasive, In Vivo technique to quantitatively measure water concentration of the stratum corneum using attenuated total-reflectance infrared spectroscopy. Arch. Dermatol. Res, 1985; 277(6): 489-95.
16. D'Emanuele A, Dinarvand R. Preparation, characterisation, and drug release from thermoresponsive microspheres. Int. J. Pharm, 1995; 118(2): 237-42.
17. Khopade AJ, Jain S, Jain NK. The microsponge. Eastern pharmacist, 1996; 39(459): 49-53.
18. Aloorkar NH, Kulkarni AS, Ingale DJ, Patil RA. Microsponges as innovative drug delivery systems. Int J Pharm Sci Nanotechnol, 2012; 5(1): 1597-606.
19. Jain N, Sharma PK, Banik A. Recent advances on microsponge delivery system. Int J Pharm Sci Rev Res, 2011; 8(2): 13-23.
20. Sharma M, Dev SK, Kumar M, Shukla AK. Microspheres as suitable drug carrier in sustained release drug delivery: an overview. Asian J Pharm Pharmacol, 2018; 4(2): 102-8.
21. Shah CN and Shah DP. Microsponges: A revolutionary path breaking modified drug delivery of topical drugs. Int. J. Pharm. Res, 2014; 6(2): 2-11.
22. Vikrant K, Nikam, RT Dolas, Somwanshi SB, Gaware VM, Kotade KB, Dhamak KB, Khadse AN and Kashid VA. Microparticles: a novel approach to enhance the drug delivery -a review. IJPRD, 2011; 3(8): 170- 83.
23. Madhu Sharma, Baibhav Joshi. Microsponges: A comprehensive Review. The Global J Pharm Res, 2012; 1(3): 359-77.
24. Kawashima YNT, Takeuchi HH, Tomoaki IY. Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity. Chem. Pharm. Bull, 1992; 40(1): 196-201.
25. Saurabh Kumar, Tyagi LK, and Dashrath Singh. Microsponge delivery system (MDS): A unique technology for delivery of active ingredients. IJPSR, 2011; 2(12): 3069-80.
26. Patel EK and Oswal RJ. Nanosponge and Microsponges, a Navel Drug Delivery System. Int. J. Res. Pharm. Sci, 2012; 2(2): 2281-781.
27. Patel EK, Oswal RJ, Nano sponge And Microsponges: A Novel Drug Delivery System. Int J Res, Pharm Chem, 2012; 2(2): 237-43.
28. Saroj Kumar Pradhan. Microsponges as the versatile tool for drug delivery system. IJRPC, 2011; 1(2): 243-58.

29. Swetha, Gopal Rao, Venkata Ramana K, Niyaz Basha B and Koti Reddy V. Formulation and in-vitro evaluation of etodolac entrapped in microsponge based drug delivery system. Int J Pharma. 2011; 1(2): 73-80.
30. Sarat C. P. M., Ajay M., Nagendra B.B., Prathyusha P., Audinarayana N., Bhaskar R.K. Microsponge Drug Delivery System: A Review. J. Pharm. Res, 2011; 4(5): 1381-4.
31. Disouza JI, Saboji JK, Jyothi MH, Patil CS. In-vitro antibacterial and skin irritation studies of microsponges of benzoyl peroxide. Indian Drugs, 2001; 38(7): 361-2.
32. Wester R., Patel R., Natch S., Leyden J., Melendres J., Maibach H., Controlled release of benzoyl peroxide from aporous microsphere polymeric system can reduce topical irritancy, J. Am. Acad. Derm, 1991; 24: 720-6.
33. Sinkar NB, Gondkar SB, Saudagar RB, Microsponge A Innovative Strategy for Drug Delivery System, Current Status and Future Prospects-A Review, Int J Inst Pharm Life Sci, 2015; 5(3): 226-42.