WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Microsponge as an Innovative Drug Delivery System

Prabhakar Madvali*, Gangotri Yadav, Ashish Jain, Omkar Tambvekar, Mayuri Mhatre, Nilesh Wakshe

[1]D. D Vispute College of Pharmacy & Research Center. (Pharmaceeutics)
[2]D. D Vispute College of Pharmacy & Research Center. (Assistant Professor)
[3]D. D Vispute College of Pharmacy & Research Center. (Principal M.Pharm, Ph. D Pharmacognosy & Phytochemistry)
Contact details:9405015059, Email id- prabhakarmadvali30@gmail.com

ABSTRACT

For major systemic and cutaneous adverse effects, a novel drug delivery technique that provides extended and regulated drug release, little systemic drug absorption, and minimized side effects is still necessary. A drug delivery system called a microsponge provides the flexibility to load a variety of active compounds to help with the controlled release of active components to reduce systemic exposure and avoid side effects. Microsponge technology has been included in topical medicinal solutions to decrease systemic exposure and reduce local cutaneous reactions to active drugs. The regulated delivery of active medications into the skin is made possible by this technology. Controlled drug release onto the epidermis with assurance that the drug remains primarily localised and does not significantly enter systemic circulation is a challenging field of research.

Microsponges are polymeric sponges with a stiff, porous surface and an interconnected network of gaps. The benefits of microsponge administration technology include increased product stability, increased safety, increased formulation flexibility, increased product efficacy, increased visual appeal, and minimized side effects. This method is used for oral distribution as well as topical treatments. This article provides an overview of microsponge technology, covering its approach, mechanism, programmable release, and characterization of the microsponge delivery system.

Keywords: microsponges, drug release, Quasi-Emulsion Solvent Diffusion, controlled release, solvent diffusion method

Introduction:

The main draw of the microsponge technology is the difficulty of employing standard topical formulations to release active chemicals over an extended period of time. Cosmetics and skin care products are only supposed to have an impact on the epidermis. The typical active ingredient in conventional products is present in a relatively high concentration when applied to the skin, where it may be readily absorbed. The usual result is overmedication, followed by a period of medication until the next application. Rashes and more serious side effects may manifest when the active chemicals quickly penetrate below the skin's surface. Microsponge technology allows for a delayed release of the active substances, potentially lowering adverse effects while preserving therapeutic efficacy. [1]

Drugs whose final destination is the skin cannot be delivered using a transdermal drug delivery system. The formulation's carefully timed release of the drug into the epidermis, which ensures that the majority of the drug remains localized and that only a little amount reaches the systemic circulation, is how adverse effects are managed. Delivery methods are required that will lessen an active ingredient's transdermal penetration into the body and lengthen its time on the skin's surface or inside the epidermis. Additional potential problems with topical drug delivery that may affect patient compliance include the uncontrolled evaporation of the active component, the unpleasant fragrance, and the use of unappealing carriers that may be oily, sticky, or create discolorations.

The carrier technology has the potential to be the answer to these issues. Research on micro- and nanoparticles has expanded in order to enable targeted and sustained drug release. These alter the drug's characteristics of absorption and release and comprise, among other things, nanoparticles, microspheres, and liposomes. It is impossible to regulate how quickly a drug releases from microspheres. Once the exterior wall of the capsule has ruptured, the medication that is inside the microspheres will come out. Preservatives are required due to the limitations of liposomes, including their reduced drug entrapment, formulation challenges, poor chemical stability, and microbiological stability. Overcome the drawbacks of the aforementioned technologies in a distinctive way. To get around issues with the aforementioned technologies, there are special medication delivery methods called microsponges. To get around issues with the aforementioned technologies, there are special medication delivery methods called microsponges. Topical drug products now use Microsponges drug Systems technology to lessen systemic exposure and minimize local cutaneous responses to active drugs. The regulated delivery of active medications into the skin is made possible by this technology. [2]

Microsponges are porous polymeric delivery systems based on microspheres. They are little, spherical particles with sponge-like porous surfaces. They may also enhance stability, reduce side effects, and favourably change drug release. Microsponge technology is a flexible way of medication administration due to its many advantages. Microsponge Systems, which are built on tiny, polymer-based microspheres that may suspend or entrap a wide range of substances, can be used to create a tailored product, such as a gel, cream, liquid, or powder. MDS can successfully increase the effectiveness of medications used topically while also enhancing their safety, product stability, and aesthetic features. [3]

Two triggers that induce the drug to enter the skin include rubbing and skin temperatures that are higher than ambient. Due to their excellent ability to entrap active ingredients up to three times their weight, microsponge products distinguish themselves from other types of dermatological delivery systems. Payload protection is active. [4] The sustained release of actives to the skin over time is a highly helpful method for extending the effectiveness of strong therapeutic agents like -hydroxy acids, which can cause burning, stinging, or redness in those with sensitive skin. The versatility of microsponge polymers allows them to carry a wide range of actives, improving the efficacy, mildness, tolerability, and prolonged wear of a number of skin therapies. [5]

Drugs explored in MSD: [6-9]

- Tretinoin
- Retinol
- Ibuprofen
- Trolamine
- Benzoyl peroxide
- Ketoprofen
- Fluconazole

Advantages: [10]

1. Without the use of preservatives, shelf life and stability of the product can be improved because bacteria cannot fit within the microsponge due to their size.
2. Due to their highly compartmentalized design, microsponges have a large internal surface area, resulting in a high pay loading capacity.
3. Substances can be made suitable for topical application to the skin by drastically reducing unwanted properties like oiliness and tackiness, or an unpleasant sensation or scent.
4. The capacity to turn liquids into powder that flows easily provides benefits for handling materials.
5. Microsponges help to make the formulation more elegant.
6. MDS allows for the extended release of medications when used topically and boosts their effectiveness.
7. Microsponges are non-collapsible structures comprised of linked gaps with a large porous surface.
8. Stable at temperatures up to 130 °C and a pH range of 1 to 11.
9. Enhanced performance of the product.
10. Extended-release. Better patient compliance is the result of less irritation.
11. The product now boasts improved thermal, physical, and chemical stability along with improved elegance and formulation flexibility.

Characteristics of the drug to be entrapped in microsponges: [11-14]

It needs to be fully miscible or can be made partially miscible by incorporating a third ingredient. Additionally, it must be chemically and physically inert. It has to be solid or water insoluble. The MS structure shouldn't break down due to any physical or chemical changes. It needs to be safe. The solubility of the active components in the vehicle must be kept to a minimum in order to minimise aesthetic problems; not more than 10 to 12% w/w microsponges must be utilized in the vehicle. If not, before applying, the vehicle will run out of microsponges. The polymer structure and payload of the microsponges must be optimised for the required release rate over the allocated time. When in contact with the catalyst for polymerization and under circumstances linked to polymerization, it must be stable.

Need of Microsponges in topical drug delivery system:

The epidermis is the target of topical treatments, which are administered to the skin. There are nevertheless downsides even if some treatments perform better when applied topically, such as lower patient compliance because creams feel greasy and sticky, inflammation, and Allergies, excessive drug evaporation, foul odour, and issues with the drug vehicle are possible side effects for some persons. Furthermore, there are no efficient methods for localised, controlled medication delivery in the stratum corneum and deeper layers. The ineffectiveness of the topical delivery system necessitates the addition of a significant amount of the active ingredient to the vehicle. When a formulation is administered, the medicine swiftly disperses, allowing it to penetrate the skin quickly and produce an excessive buildup of active ingredients.[15]

Instead of penetrating the skin's layers, small, inert, and unbreakable spheres called microsponges become stuck in the skin's crevices and release the therapeutic agent by diffusion in a regulated way that is tailored to the needs of the skin, minimizing skin harm. An unnecessary accumulation of pharmaceuticals in the layers of the skin.[16] Topical agents play a significant role in both cosmetics and the management of dermatological diseases. Conventional dermatological preparations deliver active ingredients in relatively high quantities for a short period of time. This could lead to a cycle of short-term overmedication and long-term under medication. Rashes or other negative side effects may appear when a more active chemical enters the skin. A number of controlled drug-delivery systems, such as microcapsules, microspheres, nano emulsion, liposomes, and niosomes, have been researched to increase the amount of time that active chemicals are present on the epidermis or within skin layers while decreasing their transdermal penetration into the body. The pace at which active drugs are released from microcapsules cannot be adjusted once the capsule wall has been ruptured. Similar to that, making liposomes is expensive and difficult.[17]

Method of Microsponges Preparation:

The liquid-liquid suspension polymerization method and the quasi-emulsion solvent diffusion method are the two most used techniques for entrapping drug material into microsponge particles. As can be seen in Fig. 1, the quasi-emulsion solvent diffusion is a two-step procedure.

A. Quasi-Emulsion Solvent Diffusion Method: [18, 19]

The exterior and interior stages of this approach are separated by a step. Distilled water that contains surfactants makes up the exterior phase. A drug, a polymer, and a solvent make up the interior phase.

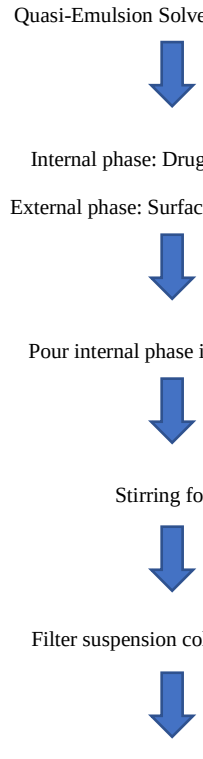

Figure no.1 The Quasi-Emulsion Solvent Diffusion Method

B. Liquid-Liquid Suspension Polymerization Method: [20-24]

Microsponges are primed using the liquid-liquid suspension polymerization technique. The monomer and active component are first separated into the appropriate solvent in this procedure, and then the resulting solution is agitated into the aqueous phase containing the surfactants. During the polymerization process, the solvent is eliminated, producing spherical porous microsponges. As depicted in fig. no.2

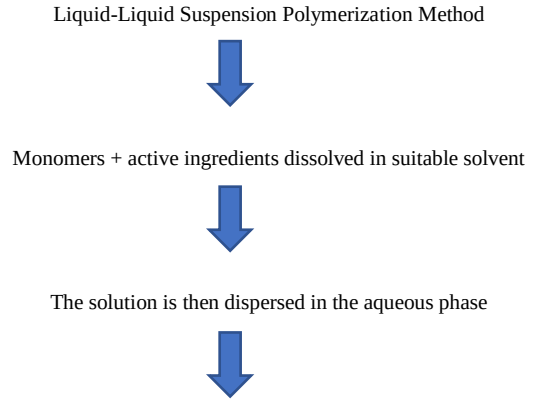

Figure no.2 Liquid-liquid suspension polymerization method

Mechanism: [25]

It's important to formulate carriers for the recommended approach while compounding refined goods to impart the benefits of control consistent release because drugs should not disintegrate too much in the intended vehicle. As an alternative, introducing medications to the solvent in their free form or entrapping microsponges in solvents with less solubilizing power are both workable solutions. A release mechanism that is started by a shift in balance from the microsponge polymer to the carrier vehicle delivers an initial loading dosage of the drug before it is released in microsponge entrapment. The polymer and solvent partition coefficient, surface area, mean pore width moisture, pH, temperature, and pressure all have an impact on the rate of drug release.

Factors Affecting Release Mechanism: [26-28]

Pressure Triggered Systems: Rub the microsponge formulation on the affected area to release the substance it has caught. The features of the sponge created, the type of material trapped, the procedure, and formulation variables all play a role in the pressure trigger mechanism.

Temperature Triggered Systems: In particular, when an excess amount of sticky material is caught, increasing the temperature can improve the rate of flow of the active component entrapped in the microsponge. the potential for a higher release of activity from microsponge with increasing temperature

PH Triggered Systems: The location of the same application affects the formulation's pH. The microsponge's covering can be changed to regulate the active substance's pH-dependent release rate.

Solubility Triggered System: Microsponge loaded with hydrophilic substances that release active components when there is water present. This release rate is dependent on the external medium's ability to suspend the active, the concentration gradient, or the ability to inflate the network of microspores.

Table 1: Applications of microsponges

Active agents Applications	**Active agents Applications**
Sunscreens	Long-lasting product effectiveness, enhanced sunburn and sun-related injury prevention even at high doses, and decreased irritancy and sensitization
• Anti-acne e.g. • Benzoyl peroxide. • Salicyclic acid. • Resorcinol. • Azelaic acid. • Dapsone gel.	Minimized skin sensitivity and irritation while maintaining efficacy.

Anti-inflammatory • e.g. Aspirin (such as Disprin) • Ibuprofen (such as Nurofen) • Naproxen (such as Naprosyn) • Diclofenac (such as Voltaren) • Celecoxib (such as Celebrex)	Long-lasting activity that lessens dermatoses and allergic reactions on the skin.
Antifungals • E.g. • Clotrimazole (Canesten) • Econazole. • Miconazole. • Terbinafine (Lamisil) • Fluconazole (Diflucan) • Ketoconazole (Daktarin) • Nystatin (Nystan) • Amphotericin.	Prolonged active release.
Antidandruff E.g., Salicylic acid and sulfur (Sebex, Sebulex) Salicylic acid (Neutrogena T/Sal) Selenium sulfide (Dandrex, Head & Shoulders Clinical Strength, Selsun) Ketoconazole (Extina, Nizoral A-D, Xolegel)	Extended safety and efficacy, decreased irritation, and decreased offensive odour.
Antipruritic Diphenhydramine (Benadryl) and hydroxyzine.	Improved and prolonged activity.
Skin depigmenting agents e.g.Hydroquinone, arbutin, azelaic acid, kojic acid, ascorbic acid and resveratrol.	Enhanced effectiveness and visual appeal, together with improved stabilisation against oxidation.

Characterization of Microsponges: Various methods are used for the characterization of microsponges.

1. **Particle Size and Size Distribution:** The particle size distribution is examined by laser diffraction, microfluidic resistance pulsed detecting, electromagnetic zone, single-particle optical sensing, screening, scattering of dynamic light, permeability to air diameter, and nanoparticle tracker analysis. The assessment and visualisation of information on the size and distribution of a collection of particles that affect the texture of a formulation and predict material representations is done using the particle size analysis technique. Particle size distribution control decreases aggregates or polymerization during dealing with, packaging, research quality assurance, and product development, which improves the powder's ability to flow freely. It is feasible to examine the particle size of both loaded and unloaded microsponges, along with their mean range of sizes and cumulative percentage of drug release, using laser light diffractometry. [35-40]

2. **Morphology and Surface Topography:** The morphology and surface topography of microsponges can be examined using photon correlation spectroscopy (PCS), a combination of scanning electron microscopy (SEM), and transmission electron microscopy, or transmission electron microscopy (TEM). Gold-palladium-encrusted microsponges are investigated for surface morphology at 25°C to 27°C in an argon atmosphere.[41]

3. **Percentage Entrapment:** Microsponges were precisely weighed at 100 mg, powdered, dissolved in 100 ml of methanol, and sonicated. Whatman filter paper was used to filter the solution. The filtrate was then diluted as needed, and the absorbance at 282 nm was measured in a UV-Vis Spectrophotometer using methanol as a reference. Entrapment efficiency was calculated as follows: [42,43]

Entrapment efficiency (%) = $M_{act}/M_{the})*100$

Were,

M_{act} is the actual amount of Terbinafine Hydrochloride in microsponges.

M_{the} is the theoretical amount of Terbinafine Hydrochloride in microsponges.

4. **Percentage yield**: obtained microsponge that was dried and independently weighed. Calculating the beginning weight of the raw materials and the end mass of the microsponges produced allowed for the determination of the microsponges' production yield. The following formula was used to determine the Percentage production yield. [44-46]

5. **Diffusion Test:** A Franz diffusion cell is used to measure the drug release from microsponges. Membranes made of animal skin (rat belly skin, mouse skin, and mucin) and synthetic membranes (cellulose acetate and silastic) are used to analyse the drug release and penetration profiles. For the purpose of conducting diffusion studies, phosphate buffer is employed as a dissolving medium at 37 1 °C in the compartment containing the receptors and a microsponge composition is applied to the membranes in the donor compartment.[47]

Research on Prepared Microsponges:

Author	Drug used	Polymer used	Solvent used	Method of preparation	Result
Sonali et al., (2014)	Prednisolone	Eudragit RS100	Dichloro methane	Quasi- emulsion solvent diffusion	At 8 hours, microsponges had cumulatively discharged 48–87%. [46]
Rajurkar VG et al., (2015)	Naproxen	Eudragit RS100	Dichloro methane	Quasi- emulsion solvent diffusion	A more favourable drug to polymer ratio caused the release of naproxen from microsponges to occur at a controlled rate. [47]
Pande VV et al., (2015)	Sertaconazole nitrate	Eudragit RS100	Dichloro methane	Quasi- emulsion solvent diffusion	Eight hours after Zero-Order kinetics, Batch F5 releases 69.38% of the medicine. [48]
Riyaz Ali M. Osmani et al., (2015)	Domperidone	Eudragit RS100	Dichloro methane	Quasi- emulsion solvent diffusion	A more efficient 1:2 drug-polymer ratio and 76.38% drug release rates after 8 hours. [49]
Charagonda S et al., (2016)	Famotidine	Eudragit RS100	Dichloro methane	Quasi- emulsion solvent diffusion	Entrapment efficiency in the F6 formulation was 88.83%, while cumulative discharge was 86.9%. [50]
Bhandare CR et al., (2016)	Risperidone	Ethylcellulose and Eudragit RS 100	Ethyl alcohol	Quasi- emulsion solvent diffusion	Ethyl cellulose and eudragit offered higher release of drugs and effectiveness in encapsulation comparing to their single-use competitors.[51]
Naji GH et al., (2017)	Piroxicam	Eudragit RS, RL, S -100	Dichloro methane and Ethanol	Quasi- emulsion solvent diffusion	Piroxicam is micro sponge carbopol 934 gel considerably (p0.05) increased the in-vitro release when when compared with pure piroxicam gel. [52]
Selvapriya A et al., (2017)	Nateglinide	Eudragit RS 100	Dichloro methane	Quasi- emulsion solvent diffusion	The regulated releasing via a microsponge that had a drug-polymer ratio of 1:3 proved more effective after 12 hours. [53]
Othman MF et al., (2018)	5Fluorouracil	Eudragit RS 100	acetone	Oil in oil emulsion solvent diffusion	5-FU with MS was more effective than 5-FU alone.[54]

Marketed formulations

Table 1: list of marketed preparation.

Name of product	Content	Uses	Manufacturer
Salicylic peel 20	20% Salicylic acid	Improve fine lines and superior exfoliation.	Biophora
Carac cream	0.5% fluorouracil	In Actinic keratosis	Dermik Laboratories, Inc.
Line Eliminator Dual Retinol Facial Treatment	Vitamin A	Anti-wrinkle cream	Avon
Lactrex TM 12% moisturizing cream	12% lactic acid	As moisturizer	SDR Pharmaceuticals, Inc
NeobenzR Micro	Benzoyl peroxide	As Antibacterial	Intendis Inc.

Future perspective: [55-58]

Micro-sponge is a special drug delivery technique that can be used to distribute drugs in addition to topical distribution, along with controlled orally peptides the delivery process, tissue engineering in cell culture conditions (stem cell culture and cellular restoration), and transdermal delivery system. The development of formulations for extended release without additives, with improved stability, and with less irritation. Microsponge technology is used as a carrier system in cosmetics, toothpaste or mouthwash, long-lasting coloured cosmetics, lipsticks, and concealing powder. Like the parenteral and pulmonary routes, we can develop new drug delivery systems.

Conclusion:

The Microsponge delivery system is a flexible method that is complemented by an original approach to creating dosage forms in pharmaceutical, cosmetic, and biopharmaceutical applications. The controlled dispensing of active substances is carried out by a network of pores in the microsponge. The medicine delivery system termed as the Microsponge increases the durability of substances that are incompatible without the addition of any preservatives. In terms of cosmetics, microsponge is a more sophisticated delivery method than earlier ones because it is porous and can handle oil. As a result of the advantages of a micro-sponge delivery method, MDS is a promising area that requires thorough examination and additional research.

Acknowledgment

We are grateful to Dr. Ashish Jain, the founder and president of Shri D.D. Vispute College of Pharmacy and Research Centre, for his important assistance. We also want to express our gratitude to Mrs. Gangotri Yadav for her help.

Reference:

1. Ingale, D. J.; Aloorkar, N. H.; Kulkarni, A. S.; Patil, R. A. P. Microsponges as Innovative Drug Delivery Systems. *International Journal of Pharmaceutical Sciences and Nanotechnology* **2012**, *5* (1), 1597–1606. https://doi.org/10.37285/ijpsn.2012.5.1.2.
2. .Jadhav, N.; Patel, V.; Siddesh Mungekar; Karpe, M.; Gaurav Bhamare; Vilasrao Kadams. Microsponge Delivery System: An Updated Review, Current Status, And Future Prospects. **2013**.
3. Kapoor, D.; Patel, M.; Vyas, R. B.; Lad, C.; Tyagi, B. L. A Review On Microsponge Drug Delivery System. *Journal of Drug Delivery and Therapeutics* **2014**, *4* (5). https://doi.org/10.22270/jddt.v4i5.978.
4. Pradhan, S. K. Microsponges as a Versatile Tool for Drug Delivery Systems. *IJRPC* **2011**, *1* (2).
5. Delattre, L. Biopharmaceutical Aspects of the Formulation of Dermatological Vehicles. **1995**, *5* (1), S70–S70. https://doi.org/10.1016/0926-9959(95)96020-9.
6. Kawashima, Y.; Niwa, T.; Takeuchi, H.; Hino, T.; Ito, Y. Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity. **1992**, *40* (1), 196–201. https://doi.org/10.1248/cpb.40.196.
7. D Souza , J.; Masvekar , R.; Pattekari , P.; Pudi , S.; More , H. Microspongic Delivery of Fluconazole for Topical Application. *1st Indo-Japanese International Conference on Advances in Pharmaceutical Research and Technology* **2005**, 25–29.
8. Wester, R. C.; 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**, *24* (5), 720–726. https://doi.org/10.1016/0190-9622(91)70109-f.
9. Çomoğlu, T.; Gönül, N.; Baykara, T. Preparation and in Vitro Evaluation of Modified Release Ketoprofen Microsponges. *Il Farmaco* **2003**, *58* (2), 101–106. https://doi.org/10.1016/s0014-827x(02)00007-1.
10. Mahaparale, P. R.; Ikam, S. A. N.; Chavan, M. S. Development and Evaluation of Terbinafine Hydrochloride Polymeric Microsponges for Topical Drug Delivery. *Indian Journal of Pharmaceutical Sciences* **2018**, *80* (6). https://doi.org/10.4172/pharmaceutical-sciences.1000459.
11. Parthiban, K.; Manivannan, R.; Krishnarajan, D.; Chandra, S.; Nidhin, R. Microsponge Role in Novel Drug Delivery System. . *Int J of Pharmaceutical Res and Development* **2011**, *3* (4), 117–125.
12. Panwar, A. S.; Yadav, C. S.; Yadav, P. S.; Darwhekar, G. N.; Jain, D.; Panwar; Agrawal, A. MICROSPONGE a NOVEL CARRIER for COSMETICS. **2011**, *3* (07), 15–24. https://doi.org/10.1234/jgpt.v3i07.406.
13. Kaity, S.; Maiti, S.; Ghosh, A.; Pal, D.; Ghosh, A.; Banerjee, S. Microsponges: A Novel Strategy for Drug Delivery System. *Journal of Advanced Pharmaceutical Technology & Research* **2010**, *1* (3), 283. https://doi.org/10.4103/0110-5558.72416.
14. Yerramchandramouli , S.; Yasmeen , R.; Mahitha , B.; Aruna , U. Microsponges: A Novel Drug Delivery System for Controlled Delivery of Topical Drugs. *International Journal of Pharmaceutical Research &Analysi* **2010**, *2* (2), 79–86.

15. Mandava, S. S.; Thavva, V. Novel Approach: Microsponge Drug Delivery System. *International Journal of Pharmaceutical Science and Research. International Journal of Pharmaceutical Science and Research.* **2012**, *3* (4), 967–980.

16. Tile, M.; Pawar, A. Microsponges: A Novel Strategy for Drug Delivery. *International Journal of Pure and Applied Bioscience* **2015**, *3* (1), 224–235.

17. Borawake, P. D.; Kauslya, A.; Shinde, J. V.; Chavan, R. S. Microsponge as an Emerging Technique in Novel Drug Delivery System. *Journal of Drug Delivery and Therapeutics* **2021**, *11* (1), 171–182. https://doi.org/10.22270/jddt.v11i1.4492.

18. Bhimavarapu , R.; Devi, R.; Nissankararao , S.; Devarapalli , C.; Paparaju , S. Microsponges as a Novel Imperative for Drug Delivery System. *Asian Journal of Research in Chemistry* **2013**, *6* (8).

19. Arora, N.; Agarwal, S.; Murthy, R. S. R. Latest Technology Advances in Cosmaceuticals. *International Journal of Pharmaceutical Sciences and Drug Research* **2012**, *4* (3), 168–182.

20. Kumar, S.; Tyagi, L. K.; Singh, D. MICROSPONGE DELIVERY SYSTEM (MDS): A UNIQUE TECHNOLOGY for DELIVERY of ACTIVE INGREDIENTS. *IJPSR* **2011**, *2* (12), 3069–3080.

21. Patel, E.; Oswal, R. Nanosponge and Microsponges: A Novel Drug Delivery System. *Int J Res Pharm Chem* **2012**, *2*, 237–244.

22. Aldawsari, H. Microsponges as Promising Vehicle for Drug Delivery and Targeting: Preparation, Characterization, and Applications. *African Journal of Pharmacy and Pharmacology* **2013**, *7* (17), 873–881. https://doi.org/10.5897/ajpp12.1329.

23. Pandey, P.; Jain, V.; Mahajan, S. A Review: Microsponge Drug Delivery System. *International Journal of Biopharmaceutics.* **2013**, *4*, 225–230.

24. Patil, R. S.; Kemkar, V. U.; Patil, S. S. Microsponge Drug Delivery System: A Novel Dosage Form. *Am J Pharm Tech Res.* **2012**, *2*, 2249–3387.

25. Bamane, G.; Kakade, T.; Kulkarni, L.; M, V. Microsponges: A Novel Drug Delivery System. *World J Pharm Pharm Sci* **2014**, *3*, 748–762.

26. Osmani, R. A.; Kulkarni, A. S.; Bhosale, R. R.; Harkare, B. R.; Aloorkar, N. H. a New Cornucopia in Topical Drug Delivery: Microsponge Technology. *Asian Journal of Pharmaceutical Science & Technology* **2014**, *4* (1), 48–60.

27. Joshi, G.; Rajandeep, H. Microsponges: A Novel Drug Delivery System. *IRJPBS* **2016**, *3*, 1–11.

28. Lalitha, S. K.; Shankar, M.; Likhitha, D.; Dastagiri, J.; Babu, M. N. A Current View on Microsponge Drug Delivery System. *European Journal of Molecular Biology and Biochemistry* **2016**, *3* (1), 33–38.

29. Pawar, A. P.; Gholap, A. P.; Kuchekar, A. B.; Bothiraja, C.; Mali, A. J. Formulation and Evaluation of Optimized Oxybenzone Microsponge Gel for Topical Delivery. *Journal of Drug Delivery* **2015**, *2015*, 1–9. https://doi.org/10.1155/2015/261068.

30. Jelvehgari, M.; Siahi-Shadbad, M. R.; Azarmi, S.; Martin, G. P.; Nokhodchi, A. The Microsponge Delivery System of Benzoyl Peroxide: Preparation, Characterization and Release Studies. *International Journal of Pharmaceutics* **2006**, *308* (1-2), 124–132. https://doi.org/10.1016/j.ijpharm.2005.11.001.

31. Grime, P. A Microsponge Formulation of Hydroquinone 4% and Retinol 0.15% in the Treatment of Melasma and Postinflammatory Hyperpigmentation. *Cutis* **2004**, *4* (6), 362–368.

32. Deshmukh, K.; Poddar, S. S. Tyrosinase Inhibitor-Loaded Microsponge Drug Delivery System: New Approach for Hyperpigmentation Disorders. *Journal of Microencapsulation* **2012**, *29* (6), 559–568. https://doi.org/10.3109/02652048.2012.668955.

33. Bothiraja, C.; Gholap, A. D.; Shaikh, K. S.; Pawar, A. P. Investigation of Ethyl Cellulose Microsponge Gel for Topical Delivery of Eberconazole Nitrate for Fungal Therapy. *Therapeutic Delivery* **2014**, *5* (7), 781–794. https://doi.org/10.4155/tde.14.43.

34. Li, S.-S.; Li, G.-F.; Liu, L.; Jiang, X.; Zhang, B.; Liu, Z.-G.; Li, X.-L.; Weng, L.-D.; Zuo, T.; Liu, Q. Evaluation of Paeonol Skin-Target Delivery from Its Microsponge Formulation: In Vitro Skin Permeation and in Vivo Microdialysis. *PLoS ONE* **2013**, *8* (11), e79881. https://doi.org/10.1371/journal.pone.0079881.

35. Kesharwani, R.; Ansari, M. S.; Patel, D. K. NOVEL TECHNOLOGY USED in the PREFORMULATION STUDY: A REVIEW. *Journal of Drug Delivery and Therapeutics* **2017**, *7* (4). https://doi.org/10.22270/jddt.v7i4.1487.

36. Orlu, M.; Cevher, E.; Araman, A. Design and Evaluation of Colon Specific Drug Delivery System Containing Flurbiprofen Microsponges. *International Journal of Pharmaceutics* **2006**, *318* (1-2), 103–117. https://doi.org/10.1016/j.ijpharm.2006.03.025.

37. Vyas, L.; Tapar, K.; Laddha, B.; Lahoti, A.; Nema, R. Formulation and Development of Anti-Blemish Preparations Using Microsponge Technology. *J Chem Pharm Res* **2010**, *2*, 562–571.

38. Panday, P. Design and Characterization of Microsponge Loaded Controlled Release Epicutaneous Gel of Lornoxicam. *Applied Medical Research* **2015**, 1–6. https://doi.org/10.47363/amr/2015(1)105.

39. 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). https://doi.org/10.4314/tjpr.v9i1.52039.

40. Sharma, N.; Banik, P. Recent Advances in Microsponge Delivery System. *Int J Pharm Sci.* **2011**, *2* (1), 13–23.

41. Sareen, R.; Nath, K.; Jain, N.; Dhar, K. L. Curcumin Loaded Microsponges for Colon Targeting in Inflammatory Bowel Disease: Fabrication, Optimization, and *Vitro*and Pharmacodynamic Evaluation. *BioMed Research International* **2014**, *2014*, 1–7. https://doi.org/10.1155/2014/340701.

42. Hussain, H.; Archana Dhyani; Divya Juyal; Abhishek Bahuguna. Formulation and Evaluation of Gel-Loaded Microsponges of Diclofenac Sodium for Topical Delivery. **2014**, *3* (10), 58–63.

43. Osmani, R. M.; Moin, A.; Deb, T.; Bhosale, R.; Hani, U. Fabrication, Characterization, and Evaluation of Microsponge Delivery System for Facilitated Fungal Therapy. *Journal of Basic and Clinical Pharmacy* **2016**, *7* (2), 39. https://doi.org/10.4103/0976-0105.177705

44. Li, S.-S.; Li, G.-F.; Liu, L.; Jiang, X.; Zhang, B.; Liu, Z.-G.; Li, X.-L.; Weng, L.-D.; Zuo, T.; Liu, Q. Evaluation of Paeonol Skin-Target Delivery from Its Microsponge Formulation: In Vitro Skin Permeation and in Vivo Microdialysis. *PLoS ONE* **2013**, *8* (11), e79881. https://doi.org/10.1371/journal.pone.0079881.

45. Pokharana, M.; Vaishnav, R.; Goyal, A.; Shrivastava, A. STABILITY TESTING GUIDELINES of PHARMACEUTICAL PRODUCTS. *Journal of Drug Delivery and Therapeutics* **2018**, *8* (2). https://doi.org/10.22270/jddt.v8i2.1564.

46. Prajapati , S.; Sonali , S. Formulation and Evaluation of Prednisolone Loaded Microsponges for Colon Drug Delivery: An In-Vitro and Pharmacokinetic Study. *Int J Pharm Sci Res* **2014**, *5*, 1994–2005.

47. VG, R. Topical Anti-Inflammatory Gels of Naproxen Entrapped in Eudragit Based Microsponge Delivery System. *Journal of Advanced Chemical Engineering* **2015**, *5* (2). https://doi.org/10.4172/2090-4568.1000122.

48. Kadnor, N.; Pande, V.; Kadam, R.; Upadhye, S. Fabrication and Characterization of Sertaconazole Nitrate Microsponge as a Topical Drug Delivery System. *Indian Journal of Pharmaceutical Sciences* **2015**, *77* (6), 675. https://doi.org/10.4103/0250-474x.174986.

49. Osmani, R. M.; Moin, A.; Deb, T.; Bhosale, R.; Hani, U. Fabrication, Characterization, and Evaluation of Microsponge Delivery System for Facilitated Fungal Therapy. *Journal of Basic and Clinical Pharmacy* **2016**, *7* (2), 39. https://doi.org/10.4103/0976-0105.177705.

50. Charagonda, S.; Puligilla, R. D.; Ananthula, M. B.; Bakshi, V. FORMULATION and EVALUATION of FAMOTIDINE FLOATING MICROSPONGES. *International Research Journal of Pharmacy* **2016**, *7* (4), 62–67. https://doi.org/10.7897/2230-8407.07440.

51. Katti, S.; Bhandare, C. Formulation of Microsponges of Risperidone HCl. *Int J Res Pharm Chem* **2016**, *6*, 18–27.

52. Hameed, S.; Naji, G. Study the Effect of Variables on Piroxicam Microsponge Formulated as a Topical Gel for Transdermal Drug Delivery. *Int J Pharm Sci Rev Res.* **2017**, *42*, 1241–1249.

53. Selvapriya, A.; Keerthana, K.; Kumari, S.; Elango, K. Formulation and Evaluation of Nateglinide Microsponges or the Treatment of Type II Diabetes Mellitus. *World Journal of Pharmacy and Pharmaceutical Sciences* **2017**, *6*, 1685–1694.

54. Othman, M. H.; Zayed, G. M.; El Sokkary, G. H.; F Ali, U.; Abdellatif, A. A. Preparation and Evaluation of 5-Fluorouracil Loaded Microsponges for Treatment of Colon Cancer. *Journal of Cancer Science & Therapy* **2017**, *09* (01). https://doi.org/10.4172/1948-5956.1000433.

55. Junqueira, M. V.; Bruschi, M. L. A Review about the Drug Delivery from Microsponges. *AAPS PharmSciTech* **2018**, *19* (4), 1501–1511. https://doi.org/10.1208/s12249-018-0976-5.

56. Gupta, V.; Verma, P.; Madhav, N. A Review Article on Pharmaceutical Validation and Process Controls. *The Pharma Innovation* **2012**, *1*, 51.

57. Chadawar, V.; Shaji, J. Microsponge Delivery System. *Current Drug Delivery* **2007**, *4* (2), 123–129. https://doi.org/10.2174/156720107780362320.

58. Rosen, Y.; Gurman, P.; Elman, N. *Drug Delivery*; CRC Press, 2017.