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A REVIEW ON MICROSPONGES NOVEL DRUG DELIVERY SYSTEM.

Shreya B. Kolhe^{1*}, Darshani D. Taral², Anil A. Danane³, S.P. Kokane⁴, Dr M. S. Kondawar⁵

* 1,2M. Pharm Student, Department of Pharmaceutical Quality Assurance

Appasaheb Birnale College of Pharmacy Sangli 416416.

3Assistant Professor, Department of Quality Assurance

Appasaheb Birnale College of Pharmacy Sangli 416416.

4Assistant Professor, Department of Pharmaceutical Chemistry

5Head and Professor, Department of Pharmaceutical Chemistry, and Pharmaceutical Quality Assurance

Appasaheb Birnale College of Pharmacy Sangli 416416.

Abstract:

Microsponge can be effectively incorporated into topical drug delivery systems for dosage form retention on skin, as well as use for oral drug delivery using bioerodible polymers. Entrapment of ingredients in microsponge drug delivery systems is thought to contribute to reduced side effects, improved stability, reduced systemic exposure and minimise local cutaneous reactions, increased elegance, and enhanced formulation flexibility. The Microsponge Delivery System is a novel technology for the controlled release of topical agents that consists of macroporous beads loaded with active agent that are typically 10-25 microns in diameter. When applied to the skin, the microsponge releases its active ingredient in response to time and other stimuli (rubbing, temperature, pH, etc). Numerous studies have shown that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic. Microsponges delivery technology is currently used in cosmetics, OTC skin care, sunscreens, and prescription products. This review focuses on microsponge preparation, characterization, and application.

Keywords: Control release, Target release, topical formulation, oral administration, Solvent Diffusion Method, Quasi-Emulsion.

1) Introduction ^[3,5]

Microsponges are porous microsphere-based polymeric drug delivery devices. They're round sponge-like particles with a large porous surface. They may also improve stability, lessen side effects, and alter drug release in a positive way. Microsponge technology has a number of advantages that make it a useful medication delivery mechanism. Microsponge Systems are made up of microscopic polymer-based microspheres that can suspend or entrap a wide range of compounds before being mixed into a manufactured product like a gel, cream, liquid, or powder. The microsponge drug delivery technology can give higher efficacy for topically active medicines while also improving safety, product stability, and aesthetic characteristics.

The Microsponge Delivery System (Microsponge drug delivery technology) is a patented porous microsphere-based polymeric system. They are tiny sponge-like spherical particles having a broad porous surface through which active ingredients are delivered in a regulated manner. The microsponges range in size from 5 to 300 m in diameter, with a typical 25 m sphere having up to 250000 holes and an internal pore structure similar to 10 ft in length, resulting in a total pore capacity of roughly 1 ml/g for substantial drug retention.

Won invented the microsponge technique in 1987, and Advanced Polymer Systems, Inc. received the first patents. This company created a huge number of technique modifications, which are used in cosmetics, over-the-counter (OTC), and prescription medicinal items. This fascinating technology has currently been licenced to Cardinal Health, Inc. for use in topical products. The internal structure of the microsponge particle is revealed by scanning electron microscopy as a "bag of marbles." [3] The interstitial spaces between the marbles cause the porosity. Emollients, perfumes, essential oils, sunscreens, anti-infective and anti-inflammatory agents, and other active compounds can be trapped in the interstitial pores.

1.1 Advantages ^[1,12]

- Absorbs up to 6 times its weight in oil without drying
- Product elegance has improved.
- MDS allows for the use of incompatible products.
- Non-irritating, non-mutagenic, non-allergenic, and non-toxic formulations
- Extended-release formulas
- Reduced irritation formulas
- Extended release, sustained action up to 12 hours
- Reduced discomfort, improved tolerance equals broader consumer acceptability
- Enhances product aesthetics, giving it a more exquisite feel
- Increases product stability, including thermal, physical, and chemical stability
- Allows for the introduction of immiscible components
- Improves material processing, such as liquid to powder conversion.
- Increases therapeutic efficacy.
- Confirm cure or control more quickly.
- Improved condition control
- Increased drug bioavailability

1.2 Advantages over conventional formulations ^[8,13]

Topical formulations are often designed for local effects. These products have a high concentration of API and produce a lower result because to their quick absorption into the skin. Microsponges, in comparison to standard formulation, require a substantially smaller amount of API to produce the necessary therapeutic effect because they avoid excessive accumulation of components inside the epidermis and dermis.

Furthermore, because of uncontrolled API evaporation, they dramatically reduce side effects caused by API accumulation on the skin surface, improving safety and increasing patient compliance.

1.3 Advantages over microencapsulation and liposomes [8,14]

Microcapsules are utilised to reduce dosage frequency by monitoring the API's release rate. The entire API in it leaked when the walls broke; these are the possible disadvantages of microsponges. Liposomes are spherical vesicles having a phospholipid bilayer that are utilised to transport medicines, peptides, and nucleic acids. Microsponges have an entrapment efficacy of 50% to 60%. Liposomes, on the other hand, have a 30 percent efficiency. Liposomes are therefore difficult to produce, expensive, lack microbiological stability, chemical stability, and have a lesser payload than microsphere.

1.4 Advantages over ointments [8]

Because of their low penetration efficiency, ointments require a high concentration of API for optimal therapeutic activity. Due to the high concentration, it causes adverse effects such as allergic responses and discomfort, and it is often unsightly and sticky, resulting in poor patient compliance. They also have a disagreeable odour and uncontrolled active component evaporation. In comparison to ointments, the microsponges drug delivery system has better permeability with little transdermal penetration into the body, increasing medication retention duration inside the skin's surface layer.

Limitations [3]

Organic solvents are commonly used as porogens, which are hazardous to the environment and may be very combustible, creating a safety risk. Traces of residual monomers have been found in some situations, which could be poisonous and dangerous to one's health.

2. RELEASE MECHANISMS [1]

In reaction to one or more external triggers, microsponges can be programmed to release a specific amount of active chemicals over time.

2.1 Temperature change

At normal temperature, some entrapped actives are too viscous to flow spontaneously from microsponges onto the skin. A rise in skin temperature can lead to an increase in flow rate and, as a result, release. Viscous sunscreens, for example, were shown to release more from microsponges when exposed to greater temperatures; hence, a sunscreen would only be released from a microsphere when exposed to the sun's heat.

2.2 Pressure

The entrapped substance in the microsphere system can be released onto the skin by rubbing or applying pressure to the microsponges. The amount emitted is determined by the sponge's varied features. The microsphere most suited for a certain application can be optimised by adjusting the kind of material and other process variables. Mineral oil containing microsphere had a far greater softening effect than mineral oil containing microcapsules. The microsphere systems also had a substantially longer duration of emolliency.

2.3 PH

PH-activated systems Modifying the coating on the microsphere can be used to trigger the active's pH-based release. This has numerous medication delivery applications.

2.4 Solubility

In the presence of water, microsponges containing water-soluble compounds such as antiperspirants and antiseptics will release the chemical. The release can also be triggered via diffusion, which takes into account the ingredient's partition coefficient between the microsponges and the rest of the system. Microsponges with a long release time can also be created. The following are some of the things to consider when developing such formulations: Entrapped actives' physical and chemical characteristics. Pore diameter, pore volume, resilience, and other physical features of microsphere systems. The characteristics of the vehicle in which the microsponges are disseminated. Microsponges can be constructed to release a

specific amount of actives in response to one or more external triggers, such as particle size, pore features, resilience, and monomer compositions.

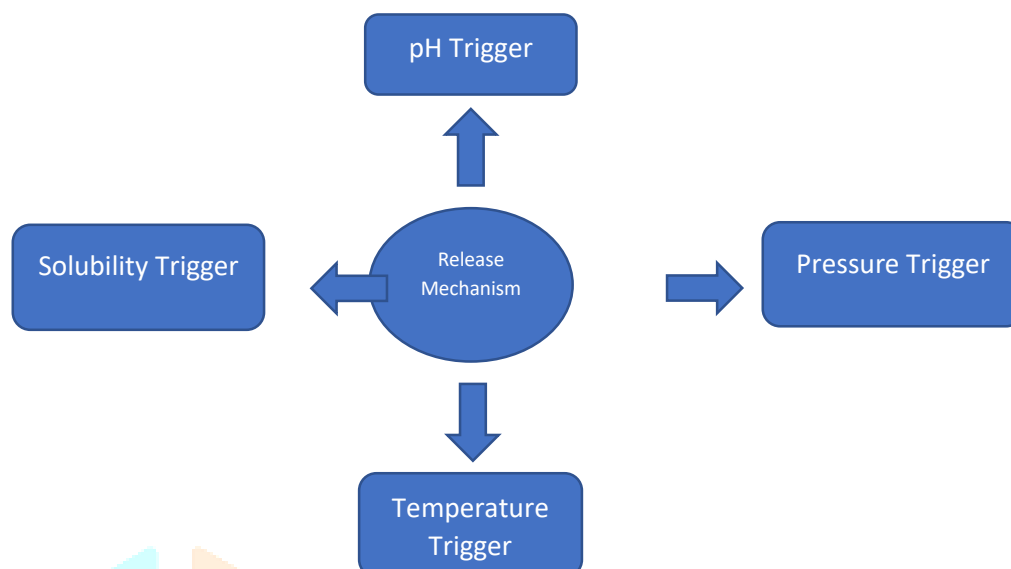


figure 2: schematic representation of release mechanism of microsponges.

3. METHOD OF PREPARATION OF MICROSPONGE DRUG DELIVERY SYSTEM ^[3,15,16,17]

A Porogen medication is entrapped with a one-step procedure and neither hinders nor activates the polymerization process. It is also stable to free radicals (liquid liquid suspension polymerization). The following procedures are suitable for preparing microsponges:

3.1 Liquid-liquid suspension polymerization:

In liquid-liquid systems, suspension polymerization is used to make porous microspheres. In this process, immiscible monomers are first dissolved with active components in a suitable solvent monomer, and then dispersed in aqueous phases containing additives such as surfactants and suspending agents to aid suspension formation. The polymerization is then triggered by raising the temperature, irradiating it, or adding a catalyst. The polymerization process continues to build a reservoir-like system with a spherical shape. The solvent is removed after the polymerization process, leaving spherical structured porous microspheres, or microsponges.

The following are the many steps involved in the preparation of microsponges:

Step 1:

Choose a monomer as well as a monomer combination.

Step 2:

As polymerization begins, chain monomers form.

Step 3:

Ladder formation caused by cross-linking between chain monomers.

Step 4:

The monomer ladder is folded to form spherical particles.

Step 5:

Agglomeration of microspheres results in the formation of microsphere bunches.

Step 6:

Creating microsponges by glueing bunches together.

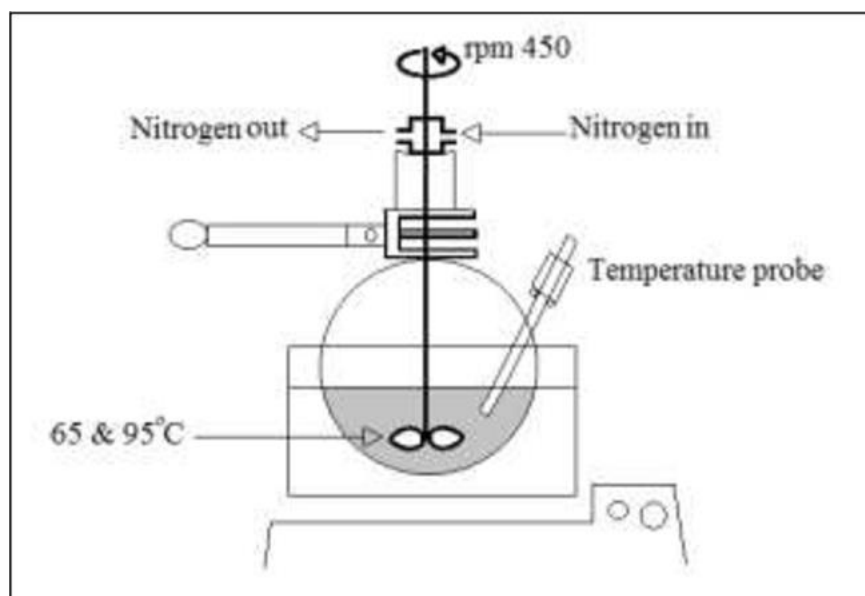


Figure 3: Preparation of microsponges by Liquid-liquid suspension polymerization.

3.2 Quasi-Emulsion Solvent Diffusion Method ^[3,18,19]

Porous microspheres (microsponges) were made utilising a quasi-emulsion solvent diffusion method (two-step procedure) with an internal phase containing polymer like Eudragit RS 100 dissolved in ethyl alcohol. The medication is then gradually added to the polymer solution to improve plasticity. After 2 hours of continuous stirring, the inner phase is placed into the external phase, which contains polyvinyl alcohol and distilled water. The microsponges were then separated by filtering the mixture. The microsponges were washed and dried for 12 hours in an air heated oven at 40 °C.

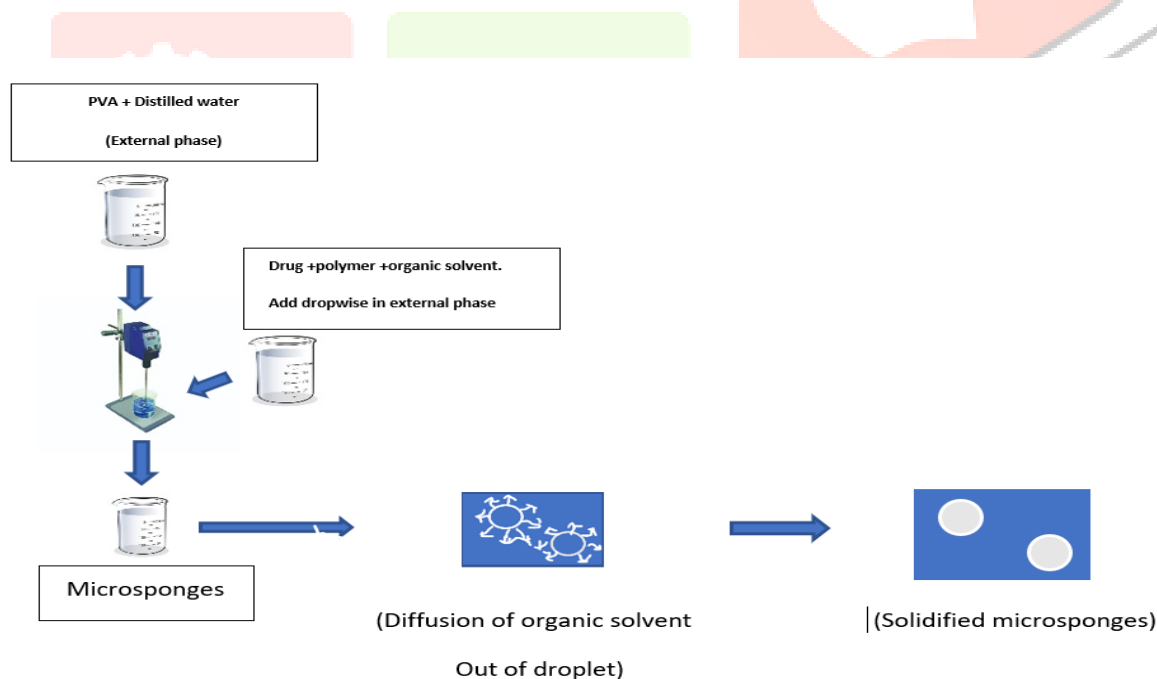


Figure 3.2: Preparation of microsponges by quasi emulsion solvent diffusion method

4 MECHANISM OF ACTION ^[8,10,11]

In an entrapped form, the active ingredient is inserted into the vehicle.



Ingredients are free to move in and out of the particles and into the vehicle since they have an open structure and are not surrounded by a continuous membrane, and the vehicle is saturated at equilibrium.



The active will be absorbed into the skin once the product is applied to the skin, depleting the vehicle, which becomes unsaturated, thereby disturbing the equilibrium.



Particles travel from the microsp sponge to the vehicle, then to the skin, until the vehicle is absorbed or dried. The active will then be progressively released into the skin via the microsp sponge particle stored on the stratum corneum surface.

5 Properties of the actives for the entrapment into the microsp sponge ^[9]

- It should be fully miscible in monomer or capable of becoming miscible with the addition of a small amount of a water immiscible solvent.
- It should be water insoluble or only slightly soluble at most.
- It should be monomer inert and not raise the viscosity of the mixture throughout the formulation process.
- When in contact with a polymerization catalyst and under polymerization circumstances, it should be stable.
- The microsponges' spherical structure should not collapse.

6 EVALUATION METHODOLOGY OF MICROSPONGE

6.1 Particle size and size distribution ^[3]

An optical microscope or an electron microscope are used to analyse particle size and size distribution. This is a critical step since particle size has a significant impact on the texture and durability of the formulation. Controlling the size of particles during polymerization allows for free-flowing powders with delicate aesthetic properties. Laser light diffractometry or any other acceptable method can be used to determine the particle size of loaded and unloaded Microsponges. For all formulations, the values (d50) can be represented as a mean size range. To investigate the effect of particle size on drug release, the cumulative percentage drug release from Microsponges of various particle sizes will be plotted versus time.[3]

6.2 Morphology and Surface topography ^[6]

Photon correlation spectroscopy (PCS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), and other techniques have been utilised to study morphology and surface topography. SEM is commonly employed in which prepared. The surface morphology of Microsponges is investigated after they have been coated with gold–palladium in an argon environment at ambient temperature.

6.3 Determination of loading efficiency and production yield ^[8]

The loading efficiency (%) of the Microsponges can be calculated according to the following equation:

$$\% \text{ Loading efficiency} = \frac{\text{actual drug content in microsp sponge}}{\text{theoretical drug content}} \times 100 \quad \dots (A.1)$$

The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the SPM obtained.³⁰

$$\% \text{Production yield} = \frac{\text{Production yield}}{\text{theoretical mass (polymer + drug)}} \times 100 \quad \dots (A2)$$

6.4 Determination of true density ^[2]

Microsponges' real density can be determined using an ultra-pycnometer under helium gas and calculated from a mean of multiple measurements.

6.5 Characterization of pore structure ^[1]

Pore volume and diameter are critical in determining the active ingredient's strength and duration of action. The migration of active substances from Microsponges into the medium in which the material is disseminated is also influenced by pore diameter. Mercury intrusion porosimetry can be used to investigate the relationship between pore width and volume and drug release rate from Microsponges.

Intrusion–extrusion isotherms are one of Microsponges' porosity metrics. Mercury intrusion porosimetry can be used to evaluate pore size distribution, total pore surface area, average pore diameters, pore shape and morphology, bulk and apparent density.

Pore diameters that reflected pore size distributions were shown against incremental incursion volume scans. The Washburn equation can be used to compute the pore diameter of Microsponges:

$$D = \frac{-4 \gamma \cos \theta}{P} \quad \dots (B.1)$$

Where D is the pore diameter (μm); γ the surface tension of mercury (485 dyn cm^{-1}); θ the contact angle (130°); and P is the pressure (psia).

Total pore area (A_{tot}) was calculated by using equation,

$$A_{\text{tot}} = \frac{1}{\gamma \cos \theta} \int_0^{V_{\text{tot}}} P \cdot dV \quad \dots (B.2)$$

Where P is the pressure (psia); V volume (mL g^{-1}); V_{tot} is the total specific intrusion volume (mL g^{-1}). The average pore diameter (D_m) was calculated by using equation,

$$D_m = \frac{4V_{\text{tot}}}{A_{\text{tot}}} \quad \dots (B.3)$$

Envelope (bulk) density (ρ_{se}) of the Microsponges was calculated by using equation,

$$\rho_{\text{se}} = \frac{W_s}{V_p - V_{\text{Hg}}} \quad \dots (B.4)$$

Where W_s is the weight of the SPM sample (g); V_p the empty penetrometer (mL); V_{Hg} is the volume of mercury (mL).

Absolute (skeletal) density (ρ_{sa}) of Microsponges was calculated by using equation,

$$\rho_{\text{se}} = \frac{W_s}{V_{\text{se}} - V_{\text{tot}}} \quad \dots (B.5)$$

Where V_{se} is the volume of the penetrometer minus the volume of the mercury (mL). Finally, the % porosity of the sample was found from equation,

$$\text{Porosity \%} = \left(1 - \frac{\rho_{\text{se}}}{\rho_{\text{sa}}}\right) \times 100 \quad \dots (B.6)$$

Pore morphology can be characterized from the intrusion– extrusion profiles of mercury in the Microsponges.

6.6 Compatibility studies ^[1]

Thin layer chromatography (TLC) and Fourier Transform Infrared spectroscopy can be used to investigate drug compatibility with reaction adjuncts (FT-IR). Powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC) can be used to investigate the effect of polymerization on medication crystallinity 26, 27, 28. For DSC, roughly 5mg samples can be accurately weighed into aluminium pans, sealed, and run at a heating rate of 150 c/min in a nitrogen atmosphere over a temperature range of 25–4300C.

6.7 Polymer/ Monomer composition ^[2]

The drug release from microspheres is governed by factors such as microsphere size, drug loading, and polymer composition. The polymer composition of the MDS can affect the entrapped drug's partition coefficient between the vehicle and the microsphere system, and hence have a direct impact on the entrapped drug's release rate. Plotting cumulative percent drug release against time can be used to investigate drug release from microsphere systems with various polymer compositions. The rate of drug release and total amount of drug released from the methyl methacrylate/ethylene glycol dimethacrylate system is slower than that of the styrene/ divinyl benzene system. The qualities of the active substance to be entrapped and the vehicle into which it will be disseminated both influence monomer selection. To give flexibility in the release of active substances, polymers with variable electrical charges or degrees of hydrophobicity or lipophilicity can be created. The drug release profiles of various monomer combinations will be studied to determine their compatibility with the medicines.

6.8 Resiliency (viscoelastic properties) ^[2]

Microspheres' resiliency (viscoelastic characteristics) can be tweaked to produce softer or stiffer beadlets, depending on the final formulation's requirements. The rate of release is slowed by increased cross-linking. As a result, the resiliency of microspheres will be investigated and optimised in accordance with the requirements, taking into account release as a function of cross-linking with time.

6.9 Dissolution tests ^[3]

The dissolution release rate of microspheres can be investigated using the USP XXIII dissolving apparatus and a modified basket made of 5m stainless steel mesh. To ensure sink conditions, the dissolution medium is chosen while considering the solubility of the actives. The samples from the dissolution medium were analysed using appropriate analytical procedures at various intervals. [3]

6.10 In-vitro diffusion studies ^[1]

In vitro diffusion investigations of the produced microsphere gel were conducted in a Keshary–Chien diffusion cell with a cellophane membrane. The receptor compartment was made out of 100 ml of phosphate buffer, and then 500 mg of gel containing 10 mg of medication was evenly disseminated across the membrane. The temperature was fixed at 37.50 and the donor compartment was kept in contact with a receptor compartment. Externally driven Teflon coated magnetic bars were used to agitate the solution on the receptor side at specified time intervals, pipette out 5 ml of solution from the receptor compartment, and immediately replace it with fresh 5 ml phosphate buffer. The drug concentration in the receptor fluid was measured using spectrophotometry in comparison to a suitable blank. The experiment was repeated three times.

6.11 Other In-vitro studies ^[1]

6.11.1 Fourier transforms infrared (FTIR) analysis:

To determine compatibility, FTIR spectra of the medicine, a physical mixture of the drug and Eudragit RS-100, and formulations FPRS1nFPRS4 were recorded in a potassium bromide disc using a Shimadzu Model 8400 FTIR spectrometer.

6.11.2 Differential scanning calorimetric (DSC) analysis:

The drug, a physical mixture of the drug, and Eudragit RS-100 were thermally analysed by DSC; properly weighted samples were put into aluminium pans and sealed. Over a temperature range of 40-430°C, all samples were heated at a rate of 20°C/min.

6.11.3 Statistical analysis:

Using Graph Pad stat software, the data from each experiment was statistically analysed using the student t-test and one-way analysis of variance (ANOVA). A significance level of P 0.05 was judged significant.

6.11.4 Stability studies:

In the pharmaceutical industry, stability is defined as a formulation's ability to remain within its physical, chemical, microbiological, therapeutic, and toxicological specifications in a certain container or closure system. A product's durability can be defined as a formulation's capacity to maintain physical, chemical, microbiological, therapeutic, and toxicological specifications in a specified container. The storage stability of Microsponge gel formulations is a major source of resistance in the development of commercialised preparations. The stability of the obtained formulation was tested by storing it at $4 \pm 1^\circ\text{C}$, $25 \pm 2^\circ\text{C}$, and $37 \pm 5^\circ\text{C}$ with a RH (Relative Humidity) of 75 percent. They were assessed for the following parameters after one month and three months: appearance, pH, drug content analysis, drug release profiles, rheological properties, and so on.

7. Marketed products of microsponges ^[9]

Table 7.1: Marketed products of microsponges.

Product Name	Pharmaceutical Uses	Manufacturer
Glycolic Acid Moisturizer w/SPF 15	Anti-Wrinkles, soothing	AMCOL Health & Beauty Solution
Solution Retin A Micro	Acne vulgaris	Ortho-McNeil Pharmaceutical, Inc.
Carac Cream	0.5% Actinic keratoses	Dermik Laboratories, Inc.
Line Eliminator Dual Retinol Facial Treatment	Anti-wrinkle	Avon
Retinol 15	Night cream Anti-wrinkles	Sothys
Retinol cream	Helps maintain healthy skin	Biomedic
EpiQuin Micro	Hyper pigmentation	SkinMedica Inc
Sports cream RS and XS	Anti-inflammatory	Embil Pharmaceutical Co. Ltd
Salicylic Peel 20	Excellent exfoliation	Biophora
Oil free matte block SPF 20	Sunscreen Dermalogica	Dermalogica

Ultra Guard	Protects baby's skin	Scott Paper Company
Dermologica Oil Control Lotion	Skin protectant	John and Ginger Dermologica Skin Care Products
Lactrex™ 12% Moisturizing	Cream Moisturizer	SDR Pharmaceuticals, Inc

8. Application of microsp sponge ^[4]

Table 8.1: application of microsp sponge.

Active agents	Applications
Sunscreen	Increase efficacy and protection against sunburns and other sun-related injuries.
Anti-acne e.g., Benzoyl peroxide	Reduced skin irritation and sensitivity while maintaining efficacy
Anti-inflammatory e.g., Hydrocortisone	Long-lasting activity that reduces allergic skin reactions
Anti-fungal	Sustained release of actives
Anti-dandruffs e.g. Zinc pyrithione, selenium sulfide	Reduced odour and irritation, as well as increased safety and efficacy
Rubefacients	Prolonged activity with less irritability
Skin depigmenting agent e.g. Hydroquinone	Improved oxidation resistance with increased efficacy

CONCLUSION:

The microsp sponge delivery system is a novel technology that allows for the controlled release of macroporous particles containing active ingredients. Microsponges have the potential to reduce side effects while maintaining therapeutic effect. Furthermore, microsponges improve stability, elegance, and formulation flexibility. Previous research has shown that microsponges are non-irritant, non-allergenic, non-mutagenic, and non-toxic. This technology is currently used in cosmetics, sunscreens, and prescription medications. As a result, microsponges-based drug delivery technology is likely to become a valuable drug delivery matrix substance in the future for a variety of therapeutic applications.

Reference:

- 1) Patil RS, Kemkar VU, Patil SS. Microsponge drug delivery system: a novel dosage form. *Am J PharmTech Res.* 2012 Jul;2(4):227-51.
- 2) Shaha V, Jain H, Krishna J, Patel P. Microsponge drug delivery: A Review.
- 3) 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.
- 4) Vitthal P, Anuradha S. A Review on Microsponges Drug Delivery System. *IJRAR-International Journal of Research and Analytical Reviews (IJRAR), E-ISSN.* 2020:2348-1269.
- 5) Patel UB, Patel HM, Shah CN, Barse R. Review-Recent research on microsponge a novel new drug delivery system. *Int J Adv Pharm.* 2018;7(03):10-6.
- 6) Roy A. Microsponges-A Novel Drug Delivery System-A Review. *European Journal of Molecular & Clinical Medicine.* 2020 Dec 1;7(1):2429-37.
- 7) Gad S, Elosaily G, Mahrous R, Moustafa Y, Khafagy E. Drug Delivery from Microsponges: A Review Article. *Records of Pharmaceutical and Biomedical Sciences.* 2021 Jan 1;5(Pharmacology-Pharmaceutics):21-7.
- 8) Thakur R, Kumar S, Gaba P. A review: novel method for microsponge drug delivery system. *Journal of Pharmacy and Biological Sciences.* 2020;15(4):35-44.
- 9) 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.
- 10) Jain N, Sharma PK, Banik A. Recent advances on microsponge delivery system. *International Journal of Pharmaceutical Sciences Review and Research.* 2011 May;8(2):13-23.
- 11) Deore Mayuri B, Salunkhe KS, Pawbake G, Chaudhari SR, Gaikwad PR. Microsponges as a modified drug delivery system. *World Journal of Pharmaceutical Research.* 2015 Jan 3;4(3):657-67.
- 12) Delattre L, Delneuve I: Biopharmaceutical aspects of the formulation of dermatological vehicles. *J Eur Acad Dermatol Venereol* 1995; 5:70-71.
- 13) Kaity, S, Maiti, S, Ghosh A.K, Pal, D, Ghosh, A., & Banerjee, S: Microsponges: A novel strategy for drug delivery system. *Journal of Advanced Pharmaceutical Technology & Research* (2010);1(3):283-290.
- 14) Osmani, R.A., Aloorkar, N.H., Kulkarni, P.K., MHani, U., Thirumaleshwar, S., & Bhosale, R.R. Novel cream containing microsponges of anti-acne agent: Formulation development and evaluation. *Journal of Current Drug Delivery* (2015) ;12(5):504-516.
- 15) Panwar AS, Yadav CS, Yadav P, Darwhekar GN, Jain DK, Panwar MS, Agrawal A. Microsponge a novel carrier for cosmetics. *JGPT*, 3(7), 2011, 15-24.
- 16) 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*, 3(8), 2011, 170- 183.
- 17) Brunton LL, Lazo JS, Parker KL. Goodman and Gilman's „The Pharmacological Basis of Therapeutics“. 11th Edition. 2006, 1021.
- 18) John I D' Souza and Harinath N. Topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. *Research J Pharm and Tech*, 1(4), 2008, 502.
- 19) Comoglu T, Gonul N, Baykara T, Preparation and in vitro evaluation of modified release ketoprofen microsponges, *II, Farmaco*, 58, 2003, 101-106.