

A Review on Microsponges Drug Delivery System

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ABSTRACT:

Microsponge technology is a versatile and innovative approach for drug delivery, cosmetics, and personal care products. Microsponges are porous, polymeric microspheres that have emerged as an effective drug delivery system, allowing for the controlled release of active ingredients while minimizing side effects. These tiny, sponge-like particles can entrap a wide range of substances, such as pharmaceuticals, emollients, and sunscreens, making them useful in various cosmetic and pharmaceutical applications. Microsponges are commonly used for topical administration, but they have also been studied for oral use. Their unique structure allows for prolonged drug release, which improves stability and reduces irritation. We examine their role in improving the stability, solubility, and bioavailability of active pharmaceutical ingredients, as well as their potential to reduce irritation and improve product efficacy in topical formulations. This review examines the synthesis, characterization, benefits, and release mechanisms of microsponges, emphasizing their potential to improve the efficacy of topical and oral medications.

Keywords: Microsponge, Controlled release, Topical administration, oral administration, Stability.

I. INTRODUCTION:

Microsponges are polymeric delivery devices made up of porous microspheres. They are little, sponge-like spherical particles with a large porous surface. Furthermore, they may improve stability, reduce side effects, and optimize drug release. Microsponge technology has various advantages that make it an effective medication delivery mechanism. Microsponge Systems are built on microscopic, polymer-based microspheres that can suspend or entrap a wide range of substances.¹ Microsponges are flexible and can hold various active substances due to their porous, cross-linked polymeric structure. With varying release rates, they are mostly used for topical and

oral delivery. Microsponges are polymeric delivery systems composed of permeable microspheres with a molecule size range of 5-300 μm . The microsponge system uses microscopic polymer microspheres to catch and mix various chemicals. The end product may be powder, gel, cream, or liquid. They resemble round sponges with a large porous surface area.²

HISTORY OF MICROSPONGE:

Won devised the microsponge technology in 1987, and Advanced Polymer Systems, Inc. received the original patents. The company developed multiple variations of the technique and applied it to cosmetics, over-the-counter, and prescription medications. Cardinal Health, Inc. has been granted a license to use this promising technology in topical treatments.³

CHARACTERISTICS OF MICROSPONGE:^{4,5}

- Microsponges Drug delivery systems are stable throughout a pH range of 1 to 11.
- Microsponges are stable up to 130°C.
- Microsponges are cost-effective, free-flowing, and may carry a higher payload (50-60%).
- They are affordable, self-sterilizing, and provide free streaming. They are quite adaptive.
- Microsponges are not allergenic, irritant, mutagenic, or poisonous.
- Microsponges may absorb up to six times their weight in oil without drying.

ADVANTAGES OF MICROSPONGES:^{6,7,8}

- The microsponge delivery system allows for the insertion of immiscible elements.
- It shows extended drug release and effect for up to 12 hours.
- Irritation formulas were reduced.
- MDDS works well with most vehicles and substances.
- MDDS have greater formulation flexibility.
- MDDS increases a drug's residence period on the skin's surface or in the epidermis.

- These Microsponges are neither allergic, poisonous, mutagenic, or irritating.
- Microsponges improve the bioavailability of the same drugs.
- It improves condition management.
- It enhances therapeutic efficacy.
- It enhances material processing. For example, liquids can be converted into powders.
- It improves the product's appearance, making it look more magnificent.
- Consumer satisfaction is high due to decreased discomfort and increased tolerance.
- It improves the physical, chemical, and thermal stability, among other things.

LIMITATION:⁹

Organic solvents used as porogens in formulation may provide an environmental risk due to their high flammability. Sometimes traces of Residual monomers can be absorbed, which may be poisonous and harmful to human health.

MECHANISM OF DRUG RELEASE:^{10,11}

Microsponges can release active chemicals based on external triggers over time (fig.1)



Fig.1 Drug Release mechanism

pH-triggered systems:

Modifying the coating on the microsphere can be used to trigger the active's pH-based release. This has a wide range of uses in drug delivery.

Temperature change:

Entrapped active chemicals are typically too viscous to move quickly from microsponges to the skin at normal temperatures. The flow rate increases as the skin's temperature rises. Hence the pace of release.

Pressure:

Rubbing or applying pressure to the Microsphere system can release trapped substances onto the skin. The amount emitted is determined by the sponge's many characteristics. To optimize the microsphere for a specific application, change the material type and process factors. Mineral oil microsphere outperformed mineral oil microcapsules in terms of softening. Microsphere systems have significantly longer emollient durability.

Solubility:

Microsponges containing water-miscible compounds, such as antiseptics and antiperspirants, release their components when exposed to water. Diffusion can also be employed to activate the release; however, the ingredient's partition coefficient between the microsponges and the external environment must be considered.

Characteristics of materials entrapped in Microsponges:^{12,13}

1. The particles have the ability to entrap almost any liquid or soluble substance. The following are the conditions for actives that can be entrapped in microsponges.
2. It must be completely miscible in monomer or can be made miscible by adding a small amount of a water-insoluble solvent.
3. It should be insoluble or slightly soluble in water.
4. The monomer should be inactive.
5. To reduce cosmetic difficulties, the solubility of actives in the vehicle must be controlled; no more than 10 to 12 percent w/w Microsponges should be incorporated into the vehicle. Otherwise, the vehicle's Microsponges will be depleted prior to application. Microsponges' spherical structure should remain intact.
6. The microsponges' polymer design and active payload must be optimized for the desired release rate over a specific time period.
7. It must be stable when in contact with the polymerization catalyst and during polymerization conditions.

METHOD OF MICROSPONGES:¹⁴

PROCESSING

Microsponges are typically generated by two methods: liquid-liquid suspension polymerization and quasi-emulsion solvent diffusion. However, certain new procedures have

lately been invented, and the virtues and downsides of these ways of production have been studied.

1. Liquid-liquid suspension Polymerization: To assist suspension formation, immiscible monomers are first mixed with active components in a competent solvent monomer. They are then disseminated in waterless phases with complements similar to surfactants and suspending agents. A suspension specialist is provided in addition to the other chemicals. To induce polymerization, either a catalyst or a higher temperature might be used. Eventually, the dissolvable is driven out, destroying the porous circular framework. After polymerization, the dissolvable is expelled together with the microsponges. After filtering, the microsponges are dried at 40°C for 12 hours(fig.2). Solvents can be utilized to insert functional chemicals more quickly and effectively. For medications that are susceptible to polymerization, a functional group is used instead of the porogen in the two-step method.¹⁵

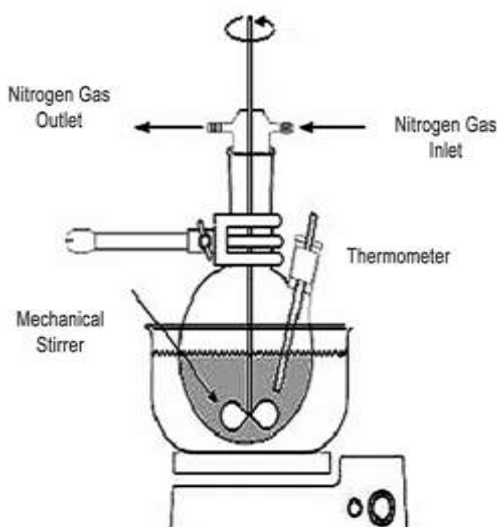


Fig.2 Preparation of liquid-liquid suspension polymerization with a reaction vessel¹⁶

2. Quasi-emulsion solvent diffusion method: The process outlined here is widely used to create topical and oral microsponges. The technique involves the formation of two phases: the inner organic phase, which contains the medicine, and the outer aqueous phase, which is subsequently agitated and filtered before use. The inner phase is then mixed drop by drop into the outer phase using a mechanical stirrer for 60 minutes. Continuous churning produced quasi-emulsion droplets, while additional organic solvent evaporation produced solid microsphere cages. The microsponges were then filtered and dried in an oven for 12

hours(fig.3). The stages involved in producing microsponges using the quasi-emulsion solvent diffusion technique.^{17,18}

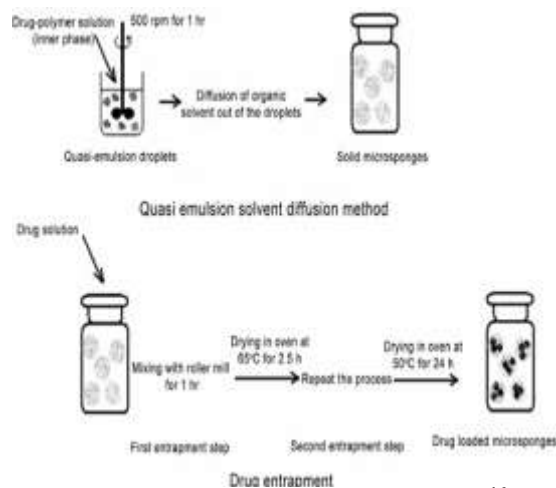


Fig.3 Quasi-emulsion solvent diffusion¹⁶

3. Ultrasonic-Assisted Production: To make nanosponges, the process was modified to use diphenyl carbonate as a cross-linker and alpha-cyclodextrin (beta-CD) as the monomer. To control the size of the microparticles, the mixture is heated and sonicated. After cooling the reaction mixture, it was crushed into big particles and washed with ethanol and distilled water. Beta-CD microparticles can be cross-linked with porosity microparticles to form drug carriers. The approach retains cross-linking residues, which may pose a risk.¹⁹

4. Expansion of Porogen: Porogen expansion involves replacing emulsions with porogens, such as hydrogen peroxide or sodium bicarbonate. To do this, a single-phase framework was formed by dissolving the porogen in a polymeric arrangement. The framework was spread in a water stage containing polyvinyl liquor. To produce distinct emulsions, an initiator was introduced. Microsponge was created by assessing the natural dissolvability and eliminating any remaining particles.¹⁶

5. Lyophilisation: Lyophilisation creates porous microspheres by rapidly removing the solvent from them. This is accomplished using a solution of chitosan hydrochloride. The microspheres are grown in this solution and subsequently lyophilized. Quickly removing the solvent may cause microparticles to shrink or break.²⁰

6. Water in oil in water emulsion solvent diffusion: In this process, an emulsifying agent-containing internal aqueous phase was dispersed in an organic polymeric solution. To create a double emulsion, the water in the oil emulsion was

dispersed in an external aqueous phase containing PVA. This technique captures both water-soluble and water-insoluble drugs.²¹

7. Oil in oil emulsion solvent dissuision: This process was used to create the emulsion, which contains volatile organic substances in its interior. Dichloromethane is the most common volatile solvent used in preparations. The polymer used is polyactide glycolic acid with a span of 85 for the external phase. To create the microsp sponge, the internal phase was added to the dispersion medium dropwise with constant stirring.²²

Characterization of Microsp sponge^{23,24,25}

1. Physical/chemical properties

a) Particle size distribution: An optical microscope or electron microscope can be used to determine particle size and distribution. The particle size impacts the texture and stability of formulations. Diffractometry or other appropriate methods can be used to analyze particle size in loaded or unloaded microsp sponge. To determine the impact of particle size on drug release, graph particle size vs time.

b) Determining pH: A sophisticated pH meter can be used to determine the pH of microsp sponge gel or other topical formulations.

c) True density: It is measured using an ultrapyanometer under helium gas.

2. Surface Topography of Microsp sponges: Techniques including photon correlation spectroscopy (PCS), SEM, and TEM can be utilized to analyze microsp sponges surface topography.

3. Calculating Loading Efficiency and Production Yield: The % loading efficiency of microsp sponges is estimated using the following formula.

$$\frac{\text{It's the actual drug content of microsp sponges X}}{100}$$

Theoretical Drug Content

4. Production yield: Microsp sponges' production yield can be determined using the following equation.

$$\frac{\text{Practical Mass of Microsp sponges}}{\text{Theoretical Mass}} \times 100$$

5. Pore Structure Characterization: Pore volume and diameter significantly affect drug release. It also transports drugs from the microsp sponge to the vehicle. Intrusion porosimetry can be used to determine the pore surface area, average pore

diameter, shape, morphology, mass, and density. To determine the pore diameter of a microsp sponge, use the Washburn equation:

$$\text{Production Yield } D = \frac{-4 \gamma \cos \theta}{P}$$

Where D is the pore diameter (μm), γ is the surface tension of mercury (485 dyn cm⁻¹), θ is the contact angle (130°), and P is the pressure (psi). To compute the total pore area (A_{tot}), use the following equation. Mercury intrusion-extrusion profiles in microsp sponges can provide insight into pore shape.

6. Compatibility studies: TLC and FT-IR can be used to determine the compatibility of active ingredients, such as drugs. The effects of polymerization on crystallinity are investigated using powder X-ray diffraction (XRD) and DSC.

7. Polymer/monomer composition:²⁶ A polymer composition analysis is required to determine the release rate of microsp sponges. Polymer composition may affect the partition coefficient between the entrapped drug vehicle and the microsp sponge system, hence influencing the release rate. It can be investigated by charting the cumulative percentage of medication release over time.

8. Viscoelastic characteristics: Viscoelastic properties can be changed depending on the requirements of the final product. As cross-linking rises, the rate of release lowers.

9. Dissolution tests:²⁷ The drug release study involves dissolving microsp sponge in a customized basket with 5 μm stainless steel mesh. The rotational speed is fixed at 150 rpm. In the dissolution investigation for microsp sponge-formed tablets using USP apparatus II, the rotation speed was 50 rpm at 37 °C.

10. Kinetics of Release:²⁸ To understand drug release mechanisms, many mathematical models were utilized to assess release data.

Applications of microsp sponges as drug delivery system²⁹

Microsp sponges are commonly used for topical and oral medication delivery, including biopharmaceuticals. The following uses have been proven or are under research.

I. Burn wound therapy: Silver sulfadiazine-loaded microsp sponges were produced for burn wound therapy using the water-in-oil-in-water quasi-emulsion solvent diffusion approach. Adding loaded microsp sponges to

- the gel base improved medication efficacy by lowering cytotoxicity to keratinocytes and fibroblasts while maintaining antibacterial characteristics. Microsponges enhance the transport of silver sulfadiazine to burn sites while limiting cytotoxicity to host cells.³⁰
- II. **Anti-fungal**-Eberconazole nitrate-loaded microsponges were created utilizing the quasi-emulsion solvent diffusion method. After dispersing the microsponges in a gel, an in-vivo skin deposition investigation revealed that the loaded microsponges had four times higher retention in the stratum corneum layer than the commercial cream.³¹
 - III. **Anti-acne** - Retinoic acid-loaded microsponges were evaluated for drug release and anti-acne effectiveness. Entrapping tretinoin in the microsphere resulted in statistically significant decreases in both inflammatory and non-inflammatory lesions.
 - IV. **Colon-specific drug targeting for treating rheumatoid arthritis**-A commercial Microsphere 5640 system was used for regulated distribution of flurbiprofen to treat rheumatoid arthritis at the colon level. In-vitro investigations show that compression-coated colon-specific tablet formulations release medication for 8 hours, which corresponds to the proximal colon arrival time. The addition of the enzyme results in a changed release pattern. Drug release from colon-specific formulations generated by pore-plugging microsponges increased for 8 hours after the enzyme was added.³²
 - V. **Anti-glaucoma** - The Quasi-emulsion solvent diffusion technique was used to create stable acetazolamide microsponges for anti-glaucoma treatment. Ex-vivo studies showed that the in-situ gel formulation was effective for treating glaucoma while avoiding systemic side effects compared to oral acetazolamide.³³
 - VI. **Anti-cancer** -A topical gel formulation of 5-fluorouracil (5-FU) based on microsponges can effectively treat skin cancer while minimizing skin irritation. Brunauer-Emmett-Teller analysis revealed increased surface area and pore volume in the developed microsponges formulation. The improved formulation outperformed the commercial cream formulation in terms of thixotropy and texture. The modified formulation resulted in a 5.5-fold increase in skin deposition, as proven by an in-vivo local bioavailability study. Additionally, it reduced skin irritation significantly compared to the commercial version. The microsponges-based formulation provides better topical administration of 5-FU compared to commercial formulations.³⁴
 - VII. **MDS for Oral Drug Delivery:** MDS is appropriate for oral medication administration because it has the ability to improve the release rate of pharmaceuticals that are poorly soluble in water by trapping these compounds in the microsphere's pore system. The microsphere regulates the pH of oral drug administration. When removed from the mouth, the medicine is protected by gastric juice (pH 1-3) due to its enteric coating. The coating dissolves in the gut due to the action of colonic enzymes (glycosidases), and the drug starts to disperse after 6 hours. MDS mainly transports medications through the descending colon of the large intestine. Microsphere delivery technology can safely transport medicines to the lower portion of the gastrointestinal tract. The microsphere method is ideal for administering drugs to the colon since actives smaller than 200 µm are easily absorbed by macrophages, resulting in targeted drug activity.^{35,36}
 - VIII. **MDS for Topical Delivery:** Traditional topical medication compositions are assumed to work only on the skin's surface layers. When these traditional materials are applied to the skin, they release pharmaceutically active medicine, creating a highly concentrated film that is quickly absorbed. To prevent excessive build-up of active components in the skin's epidermis and dermis layers, medicines can be packaged in a microsphere delivery system. This microsphere technology significantly reduces drug irritation while preserving efficacy. Drug-containing porous microspheres can be used in several dosage forms, including creams, gels, powders, and lotions.^{37,38}

S.n.	Active agent	Application
1.	Sunscreens	Sunscreens provide long-lasting protection against sunburns and related ailments. Increased concentration with reduced irritation and sensitivity.
2.	Anti-acne treatments, such as benzoylperoxide.	Efficacy was maintained while skin irritation and sensitivity decreased.
3.	Anti-inflammatory For example, hydrocortisone	Long-term activity with lowering of skin allergic reactions and dermatoses
4.	Anti-fungals	Sustained release of actives
5.	Anti-dandruffs include zinc pyrithione and selenium sulfide	Reduced unpleasant odor, reduced irritation, and increased safety and efficacy.
6.	Antipruritics	Extended and improved activity.
7.	Skin depigmenting chemicals, such as hydroquinone	Improved oxidation resistance, effectiveness, and aesthetic appeal.
8.	Rubefacients	Longer activity with less irritability, greasiness, and odor.

Table 1: List of commercialized products with microsp sponge drug delivery systems:³⁹

Future Prospects:

Microsponges are a unique medication delivery method designed for topical use. They can also be employed for tissue engineering and regulated oral medication administration using biodegradable polymers. It offers a variety of formulation benefits. Liquids can become free-flowing powders. Formulations with incompatible constituents can achieve long-term stability without using preservatives. Microsponges are a suitable medication delivery method for transdermal formulations. Higher concentrations of vehicles are needed to dissolve the API for successful therapy, however, this can produce irritation and hypersensitivity reactions in users. Topical formulations have drawbacks such as uncontrolled component evaporation, bad odor, and drug compatibility issues with automobiles. Topical medication compositions often target the skin's outer layers. These formulations release active chemicals upon application, resulting in a concentrated coating that is quickly absorbed. A mechanism is needed to maximise the duration an active substance remains on the skin's surface or within the epidermis. Some microsp sponge-based products are already approved, while others are being developed and clinically evaluated.

II. CONCLUSION:

The microsp sponge delivery system is a unique technology that allows for the controlled release of macroporous particles containing active substances. Microsponges can reduce adverse

effects while still providing therapeutic benefits. Microsponges offer improved stability, elegance, and formulation flexibility. Previous investigations have proven that microsponges are non-irritating, non-allergenic, non-mutagenic, and non-toxic. This technique is being employed in cosmetics, sunscreens, and prescription medications. Microsp sponge-based drug delivery technology is a promising option for therapeutic uses in the future. Microsp sponge delivery technologies may be more effective for future cosmetics and pharmaceuticals. Microsponges are an innovative technique for the topical active chemicals are released in a regulated manner, similar to consuming medications, providing an advantage over typical topical dose forms for treating local disorders. Microsponges can reduce pain and mutagenicity associated with medicines. Future uses for these microsponges include topical preparations with prolonged release. Microsp sponge drug delivery allows for the regulated administration of active substances to specific regions. Microsponges have greater physical, chemical, and thermal stability, allowing for more flexible dosage forms during manufacture.

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