INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

From Pores to Performance: The Science and Application of Microsponge Drug Delivery Systems

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ARTICLE INFO

Published: 28 Oct 2025

Keywords:
Microsponges, Porous Drug Delivery, Eudragit, Controlled Release, Quasi-Emulsion Solvent Diffusion.

DOI:
10.5281/zenodo.17464178

ABSTRACT

Advanced micro-particulate drug carriers called Microsponge Drug Delivery Systems (MDDS) are composed of porous polymeric microspheres that reduce side effects and increase therapeutic efficacy. They enable sustained, site-specific, and controlled drug release, guaranteeing a longer duration of therapeutic effect. Both hydrophilic and hydrophobic medications can be entrapped by microsponges, which typically have a diameter of 5 to 300 µm. Their porous surface allows the drug to diffuse gradually in response to stimuli such as moisture, Potential of Hydrogen, pressure, and temperature. The technology, which was created by Won in 1987, has been widely used in targeted, oral, transdermal, and topical drug delivery. In order to preserve drug localization and decrease systemic absorption, microsponges can be made into creams, gels, lotions, and powders. Research indicates improved safety, compatibility, and stability as well as non-toxicity, non-irritability, and non-allergenic properties. Techniques like emulsion solvent Common preparation methods include diffusion, suspension polymerization, and ultrasound-assisted methods. Their morphology and stability are confirmed by characterization methods such as Scanning Electron Microscopy, Differential Scanning Calorimetry, Fourier Transform Infrared Spectroscopy, and X-Ray Powder Diffraction.

INTRODUCTION

Porous, polymeric microspheres called microsponges are made to deliver drugs topically in a controlled and long-lasting manner. They increase therapeutic efficacy, decrease side effects, and improve stability by delivering medications at low dosages. Clinical utility is demonstrated by FDA-approved products such as Retin- A Micro and Carac. Microsponges maximize drug retention on the skin while reducing systemic absorption, in contrast to traditional systems that require high dosages.[(1)] They are mostly made in an oil-in-water (O/W)

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

system using suspension polymerization or emulsion solvent diffusion (ESD).[1] Cardinal Health currently holds a license for the technology, which was created by Won in 1987 and patented by Advanced Polymer Systems. Microsponges have interconnected pores that allow for gradual drug release, giving them the structural appearance of a "bag of marbles." [2,3]

They can tolerate temperatures as high as 130°C and are stable in the pH range of 1 to 11. They are bacteria-proof and self-sterilizing, with a diameter of 0.25 µm. They are economical and efficient due to their high payload capacity (50–60%). Microsponges provide greater stability and better control over drug release than liposomes or microcapsules. Up to 250,000 pores and 1 ml/g of pore volume can be accommodated by each 25 µm microsponge. Creams, gels, lotions, soaps, and powders can all be used with them. By absorbing skin oils, microsponges lessen shine and greasiness. Additionally, they have the ability to trap different substances, such as sunscreens, emollients, and anti-infectives. All things considered, they guarantee minimal adverse effects and localized, controlled drug action. Because of this, microsponge technology is a cutting-edge and promising system for use in cosmetics and pharmaceuticals. [4,5]

Prospective feature of microsponges drug delivery system:

- The microsponge formulation is stable in the pH range from 1 to 11.
- The formulation of the micro-sponge is stable up to 130°C.
- The micro-sponge formulation is compatible with most vehicles and materials.
- The microsponge formulation is self-sterilizing because the average pore size is about 0.25 µm and bacteria cannot pass through the pores.
- The microsponge formulation has high entrapment capacity up to 50 to 60%. [6]

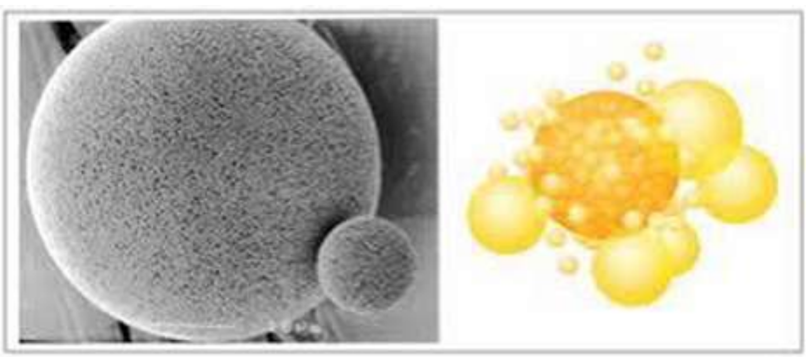

Fig 1: Microsponge Technology [2]

MICROSPONGES: THE SCIENCE OF POROSITY

1. Definition & Structural Characteristics

Porous, strongly cross-linked polymeric microspheres with a diameter ranging from 5 to 300 µm are known as microsponges. By enclosing active substances in their internal voids and releasing them gradually through linked pores, they behave as drug reservoirs.[7] The interior design consists of a three-dimensional network of pores and channels that are often open to the surface to permit regulated drug diffusion outwards while maintaining the mechanical integrity of the polymer scaffold. [8]

Because of its porous nature, which allows for high surface area, adjustable pore volumes, and flexible pore size distributions, microsponges are helpful for both hydrophilic and hydrophobic drug loading. [9,10]

2. Comparison with Other Carriers (Microcapsules, Liposomes, Nanoparticles)

In contrast to microcapsules, which may rely more heavily on shell degradation or diffusion via a denser matrix, microsponges have internal porosity and void interconnectivity, which allow for more controlled and sustained diffusion. Because of their stiff polymer matrices, microsponges provide greater stability and less leakage than liposomes, which are lipid bilayer vesicles that are prone to instability, leakage, and short-term release. Because of their porous nature, microsponges (microscale) can nevertheless provide significant loading in circumstances where deep penetration or systemic exposure is undesirable. They are also easier to work with and incorporate into topical or semi-solid systems than nanoparticles or nanoscale porous carriers. [11,12]

Table 1 : Polymers and Crosslinkers in Microsponges [13]

Polymer / Crosslinker	Function in Microsponge	Typical Application
Ethyl Cellulose (EC)	Matrix former; mechanical rigidity	Topical, oral, sustained release
Eudragit RS100 / RL100	Matrix & controlled permeability; pH responsive	Oral, dermal formulations
Polyvinyl Alcohol (PVA)	Stabilizer / emulsifier	Quasi-emulsion method
Divinylbenzene / Methacrylic Crosslinkers	Crosslinking agent to stabilize pores	Maintains pore integrity
Hybrid composites (e.g., silica, MOFs)	Enhance functional properties, stimuli-responsiveness	Advanced targeted or hybrid delivery

3. Materials Used (Polymers & Composites)

Ethyl cellulose (EC) is a common polymer used to make microsponges because it is biocompatible and has a stiff structure. [11] Eudragit, especially the RS and RL grades, is used to give the microsponge structure regulated permeability or pH-responsive activity· [14] Crosslinkers, like divinyl benzene and methacrylic cross linkers, are used to make networks that are stable and won't collapse over time and to keep the pores from breaking down. Even though there isn't as much information about these designs, hybrid or composite methods have been looked into to make them work better (for example, by adding inorganic particles or polymers that respond to stimuli). [11,15]

4. Types of Porous Structures &Tunability

The presence of open porosity (channels attached to the surface) or closed or isolated voids (less accessible) in microsponges can affect release rates. They may also have multiscale (hierarchical) porosity, combining macropores (≥50 nm) anmesopores (2–50 nm) to balance loading capacity with controlled diffusion. Gradient porosity, which has larger holes at the shell and smaller ones deeper inside, can enable a slower, longer-lasting release and a higher initial flux. Stimuli-responsive pore gating, including pH-responsive swelling and thermoresponsive expansion/contraction, is a novel method of modulating release on demand that is less frequently studied. To create tunable porosity, one can alter the temperature, crosslink density, stirring rate, solvent selection, polymer/porogen ratio, and porogen removal kinetics. [6,12]

Table 2 : Comparative Features of Microsponges and Microcapsules [13,16]

Feature	Microsponges	Microcapsules
Structure	Highly porous polymeric matrix with interconnected pores	Single core with polymer shell
Size	5–300 µm	1–1000 µm
Drug Loading	High (both hydrophilic & hydrophobic)	Moderate
Release Mechanism	Diffusion through pores; stimuli-responsive possible	Diffusion or shell degradation
Stability	High mechanical & chemical stability	Moderate
Advantages	Tunable porosity, sustained release, low toxicity	Simple fabrication

PREPARATION STRATEGIES

The following section details the preparation methods for microsponges,[17,18,8,19,20]

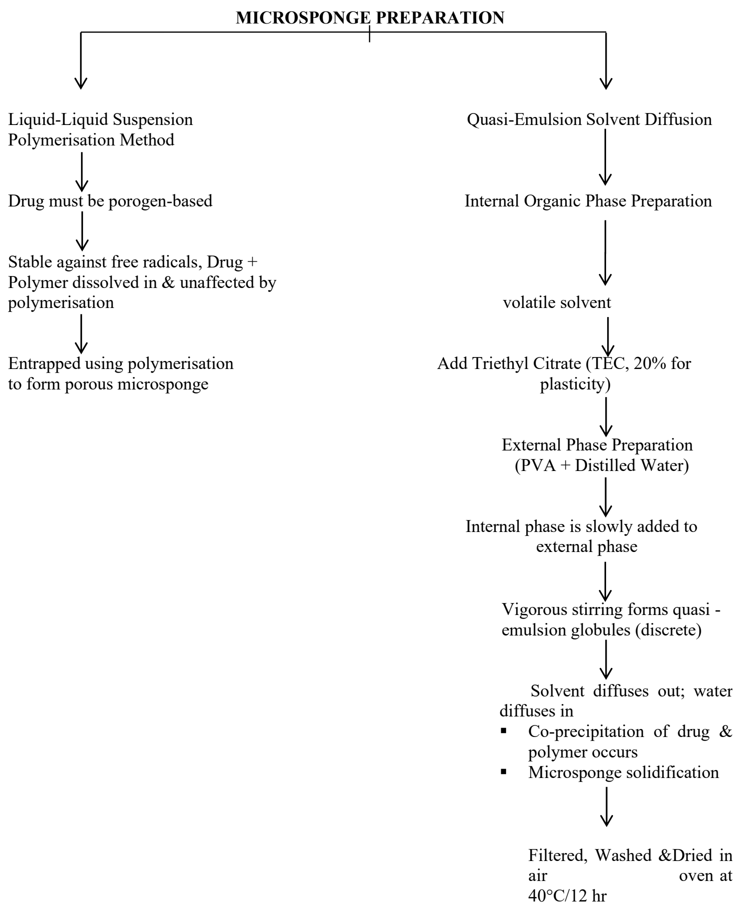

Table 3 : Comparison of Microsponge Preparation Methods [19,20]

Feature	Liquid-Liquid Suspension Polymerisation	Quasi-Emulsion Solvent Diffusion
Step	One step	Two step
Suitable Drug Type	Porogen Stable	Most drugs, including sensitive ones
Environmental Exposure	Possible	Redused
Residual Solvent	Low	Very low due to volatility
Drug Loading Efficiency	Moderate	High
Particle Size Control	Moderate	Easy to modify via stirring
Temperature Sensitivity	Less suitable for thermolabile drugs	Suitable due to post-loading

PHYSICOCHEMICAL CHARACTERIZATION

Characteristic of Micro sponge drug delivery systems

- Micro sponges remain stable at temperatures up to 130 °C and throughout the wide pH range of 1 to 11.
- Micro sponges don't need to be sterilized and work well with a variety of excipients.
- It's possible that between 50 and 60 percent of the drug is trapped in microsponges, which provide good flowing properties.
- These molecules are still free of toxicity, irritation, and allergies.
- It needs to be completely miscible in a monomer or able to be made so by adding a tiny quantity of a solvent that isn't soluble in water.
- It needs to be water insoluble or, at most, barely soluble.
- It must not increase the mixture's viscosity during formulation and be inert to monomers
- It needs to be stable in the polymerization environment and in contact with the catalyst.
- The microsponge's spherical structure must remain intact. [21,22]

Particle size and morphology

a) Particle size determination

Laser light diffractometry or any other appropriate technique can be used to analyze the particle sizes of loaded and unloaded microsponges. For every formulation and size range, the values can be expressed. To examine the impact of particle size on drug release, the cumulative percentage of drug release from microsponges with varying particle sizes will be plotted against time. Particles between 10 and 25 µm are recommended for use in the final topical formulation because particles larger than 30 µm can give off a grainy feeling. [23]

b) Microsponge morphology and surface topography

Scanning electron microscopy (SEM) can be used to examine the surface morphology of prepared microsponges after they have been coated with gold-palladium at room temperature in an argon atmosphere. A fractured microsponge particle's ultra-structure can also be shown using SEM.. [23,24]

c) Electron Scanning Microscopy

A scanning electron microscope (GEOL 5400, USA) running at 20 kV was used to analyze the microsponge morphology. Prior to observation, dried microspheres were coated with a gold-palladium alloy for 45 seconds in an argon atmosphere. An ×500 magnification was used to record the SEM image. [25]

d) Description of the pore structure

Controlling the pore's diameter and volume is essential for regulating the active ingredient's potency and duration. Microsponges' migration of active substances into the vehicle in which they are disseminated is also influenced by pore diameter. To investigate the relationship between pore width and volume and drug release rate from microsponges, mercury intrusion porosimetry can be utilized.

Microsponges' porosity parameters include intrusion-extrusion isotherms. Mercury intrusion porosimetry can be used to measure the bulk and apparent density, distribution of pore sizes, total pore surface area, average pore diameters, and morphology and form of the pores.

The pore diameters, which reflected the pore size distributions, were displayed against the incremental incursion volume scan. [4]

e) Efficacy of drug loading

Calculating the production yield and loading efficiency. The following formula may be used to determine the microsponges' loading efficiency (%):

The real amount of medication in microsponges:-

$$\textit{Loading efficiency} = \frac{\textit{Actual drug content in microsponges}}{\textit{Theoretical drug composition}} X\,100$$

By precisely calculating the initial weight of the raw materials and the final weight of the microsponge produced, the production yield of the microparticles can be ascertained.

Production Yield Y =

$$\textit{Practical mass of microsponges.} = \frac{\textit{Practical mass of microsponges}}{\textit{Theoretical mass}\ (\textit{Drug} + \textit{Polymer})} X\,100$$

f) Release kinetics

The amount of drug released over time was used to ascertain the drug release mechanism and compare the variations in release profiles among microsponges. These mathematical models were used to analyze the release data:

Q=K1tn or log Q=log k1 + n log t………… eq 1

Where,
n = Diffusion exponent that reveals the release mechanism,
K1 = Constant property of the drug–polymer interaction
Q = Amount released at time (h).

Kinetic parameters n and k1 were computed using the slope and intercept of the log Q versus log t plot. Equation (2), a straightforward Higuchi-type equation, was also applied to the data for comparison's sake.

Q = k2t0:5 +C Oh,

if only... The second equation Q is equal to k2t0:5 + C. Equation (2) presents the release profile, where C is a constant and k2 is a root time dissolution rate constant [4]

Information on the amount and duration of drug release was utilized to ascertain the drug release mechanism and analyze the variations in release profiles between microsponge gel formulations.

Using mathematical models such as the Zero order, First order, Higuchi matrix, Hixson Crowell, and Korsmeyer-Peppas model, the drug release kinetics were examined. Numerous kinetic models have been developed term put out to explain a drug's matrix release properties. The release mechanism, or release rate constant (k), correlation coefficient (R), and release exponent (n), was studied using the three parameters in order to identify the best fit model for the optimized formulation.

Using the following mathematical models, the release data was examined:-

1) At zero order kinetics

Drug dissolution from pharmaceutical dosage forms that do not dissolve and release the drug gradually can be represented by the following equation (assuming that area stays unchanged and no equilibrium conditions are reached

Q and K0t are equal.

Where,

Q = Amount of medication released at time t
K0 = Zero-order rate constant expressed in units of concentration/time
t = Time in hours.

This profile is met by pharmaceutical dosage forms that release the same amount of medication in the same amount of time. This model represents the ideal release profile for attaining the extended pharmacological activity.

2) Kinetics of first order

Although it is challenging to theoretically conceptualize this mechanism, this model has also been utilized to explain the absorption and/or elimination of certain medications.

Q1 = Q0 e-K1 t or Log Q1 = Log Q0+K1t 2.303.

Where,
Q0 = Starting drug concentration in the solution
Q1 = Amount of drug released in time t
K1= First order release constant.

The drug is released proportionately to the amount of drug that remains in its interior by the pharmaceutical dosage form that follows this dissolution profile, such as water-soluble medicines in porous matrices.

3) Higuchi matrix model

Water-soluble and low-soluble medications integrated into semisolid and/or solid matrices are studied using this model.

For drug particles distributed in a homogeneous matrix acting as the diffusion media, mathematical expressions were found. Drug release is explained as a diffusion process that is square root time dependent and based on Fick's law.

Q = KH t1/2

Where,
KH= Higuchi dissolution constant
Q = Amount of drug release in time t.

4) Korsmeyer-Peppas model

Korsmeyer developed a simple empirical model in which the drug release was exponentially related to the elapsed time (t): ft= a. tn. The drug release mechanism is indicated by equation (7), where n is the release exponent, an is a constant that takes into account the geometric and structural characteristics of the drug dosage form, and t is Mt/M∞ (fractional release of drug)

5) Model Hixson-Crowell

Hixson and Crowell (1931) acknowledged that the cube root of a particle's volume is proportional to its regular area. They arrived at the following equation:

κ t = W0 1/3-Wt 1/3

Where,
W0 = The starting amount of drug in the pharmaceutical dose form
Wt = Remaining amount at time t
κ (kappa) = Constant that incorporates the surface volume relation.

The release from systems where the diameter and surface area of the particles or tablets fluctuate is described by the equation. Data from in vitro drug release tests were shown as the cube root of the drug % remaining in matrix vs time in order to examine the release kinetics. [26]

MECHANISM OF DRUG RELEASE FROM MICROSPONGES

Microsponges are novel drug delivery systems that use external triggers such as changes in pH, temperature, pressure, and solubility to release active ingredients in a controlled manner. Certain encapsulated medications may be too viscous to flow at room temperature, but viscosity reduces and release is improved as skin temperature rises. The drug can also be released onto the skin through mechanical rupture brought on by pressure or friction, such as rubbing. [27]

According to the partition coefficient between the microsponge and the skin surface, solubility-based release happens when microsponges that contain water-miscible ingredients (such as deodorants or antiseptics) come into contact with moisture and start to diffuse. Modifying the coating in pH-triggered systems enables drug release in response to particular pH levels, which is helpful for targeted delivery. [28,26]

Because of these programmable characteristics, microsponges are extremely versatile for regulated and long-term topical treatment.

- They minimize systemic absorption and adverse effects by keeping medications localized within the epidermis.
- Through creams and gels, microsponges are effectively used to treat dandruff, eczema, psoriasis, acne, and skin cancer.
- Their structure improves therapeutic efficacy by facilitating effective drug entrapment and gradual release.
- Their biocompatibility and non-irritating nature are confirmed by safety evaluations, which include toxicity tests, allergenicity, eye irritation, and mutagenicity tests.
- All things considered, microsponge technology provides a flexible, secure, and effective method for contemporary pharmaceutical and dermatological applications. [29,30,31]

THERAPEUTIC APPLICATIONS

Topical applications:

Only the technological aspects of micro sponges, which are employed for topical distribution in dermatological and cosmetic applications, differ. The market demand, industrial scalability, regulatory restrictions, and brief product launch period for dermatologicals could all be contributing factors. The market currently offers a variety of micro sponge-loaded deodorants, sunscreens, and antiperspirants due to the high absorbent nature of porous micro sponges. Acne, psoriasis, skin cancer, wounds, wrinkles, hyperhidrosis, sunburn, alopecia, and other topical conditions can all benefit from MDDS's localised and site-specific action, which also avoids needless medication retention in the percutaneous blood circulation. Micro sponges loaded in Carbopol gel exhibit 77.5% curcumin penetration in 24 hours, according to ex vivo drug deposition tests. Nevertheless, these substances are linked to adverse effects like bacterial resistance or dryness, irritation, and peeling of the skin. These problems hinder patient compliance and jeopardise treatment. Novel drug delivery mechanisms must be proposed in order to overcome these problems and reduce the dosage of anti-acne medications. Potentially innovative vesicular and particulate drug delivery technologies include with benefits like continuous supply of curcumin to reduce administration recurrence and increase its bioavailability, curcumin-loaded micro sponges may therefore be a viable substitute for topical delivery systems. [32]

a) Microsponges for medications that prevent acne:

The pilosebaceous unit (PSU) is linked to chronic inflammatory illnesses like acne, which are characterised by varying immunological host responses, sebum production, bacterial growth, follicular epithelial desquamation, and inflammation. The face, chest, and back are where acne most commonly appears. The pathophysiology of acne is regulated by the overproduction of sebum in malformed follicles, which causes follicular hyperproliferation and microcomedones, which in turn causes inflammation and manifests as pustules, papules, cysts, and nodules. First-line keratolytic drugs (retinoids and their derivatives, benzoyl peroxide, azelaic acid, and salicylic acid) and antibiotics (erythromycin and its zinc complexes, clindamycin) are the main ingredients in localised topical acne treatment. Usually, these are applied as topical agents. For better topical treatment of acne, research has been conducted on solid lipid nanoparticles, liposomes, microemulsions, microspheres, and nano-lipid carriers. [32,33]

b) Micro sponges for medications that treat psoriasis:

Another chronic inflammatory skin condition that affects about 2% of people is psoriasis. The innate and adaptive immune systems' cells and molecules step in to help. Chronic plaque psoriasis, pustular psoriasis, nail psoriasis, guttate psoriasis, and erythrodermic psoriasis are all types of psoriasis. Due to its vasoconstrictive, anti-inflammatory, and antiproliferative properties, clobetasol propionate (CP) is a highly effective Di halogenated topical corticosteroid used to treat psoriasis. Steroid acne, skin shrinkage, allergic contact dermatitis, hypopigmentation, and systemic penetration are among its eleven common adverse effects. The adverse effects associated with CP are addressed by the introduction of innovative topical carriers and delivery systems, which provide a prolonged duration of action through regulated drug release. Additionally, carbopol gel base was used to manufacture CP-loaded micro sponges. Additionally taken into account were the ratio of polymer to medication, the amount of the aqueous and organic phases, the velocity of stirring, and surfactants. The entrapment efficiency of micro sponges is improved when the drug to polymer ratio is increased. With the fewest harmful effects, micro sponges as a delivery mechanism resulted in better therapeutic efficacy and prolonged release of CP. [32]

c) Skin cancer micro sponges:

The most common type of cancer is skin cancer, which affects almost one million Americans annually, particularly in Caucasian (white-skinned) populations Any malignant lesion of the skin is referred to as skin cancer. Melanoma and non-melanoma skin cancer (Nmicrosponges C) are the two basic categories into which skin cancers can be divided based on their nature. One option for first-line treatment is 5-FU topical cream (5%). Its low skin penetration and local tolerance, however, result in irritation, itching, and inflammation. Hydrophilic petrolatum or a basic propylene gel base for topical use was present in FU. Both human and pig skin have been used to test the in-vitro medication release. [32,34]

Cosmeceuticals:

One of the areas of the skin care industry that is expanding quickly is cosmetics. Examples of cosmeceutical chemicals include vitamin K, alpha-hydroxy acids (AHAs), retinol, and others. Although these substances have many advantages, they also have some drawbacks, including as erythema, dryness, and peeling. Therefore, microsponge polymers containing cosmeceutical compounds may be a superior option. Retinol, a very pure form of vitamin A, is very effective at preventing wrinkles and maintaining the appearance of young skin. A visually appealing moisturising base contained retinol. These products can retain 90% of their original concentration and have a two to three year shelf life. Retinol was encapsulated within a visually appealing moisturizing base. These products possess a shelf life of 2-3 years and can maintain 90% of their original concentration. Formulations containing entrapped retinol, combined with other cosmeceutical agents such as vitamin K (phytonadione), which is also included in the encapsulated structure, help to reduce the appearance of dark circles under the eyes. These encapsulated active ingredients render the formulations gentler and, consequently, suitable for regular use. [32]

Microsponge for Sustained Release Drug Delivery

The effects of tablets and capsules start to work in about 30 minutes and can last for up to 47 hours. Five to seven hours after oral administration, the drug is typically eliminated by the body in healthy individuals. Nifedipine's short half-life (t1/2, 2 hours) necessitates frequent administration, despite the fact that it may be useful in treating cardiovascular issues. Nifedipine-containing tablet formulations of sustained-release microsponges have been created to enhance patient compliance and clinical use. 91 Doperidone provides an extra option for sustained-release formulations because it is intended for long-term treatment and requires high dosages. Capsules based on extended-release domperidonemicrosponge technology enhance release kinetics and efficacy while lowering side effects for conditions like gastroparesis, emesis, and other disorders. [18]

Anti-allergic and anti- inflammatory drug delivery via microsponge

Notwithstanding their adverse effects on the gastrointestinal tract, non-steroidal anti-inflammatory medications (NSAIDs) are useful in reducing fever, inflammation, and discomfort. In allergic locations, a number of trustworthy and cutting-edge medicine delivery methods are now being assessed. To overcome some of the physicochemical difficulties and restrictions connected to conventional pharmaceutical formulations, topical anti-inflammatory gels with naproxen enclosed in a Eudragit-based microsponge delivery system have recently been created (e.g., inadequate solubility and penetration, penetration through the skin, shelf life). Eudragit RS-100, carbopol, and PVA were used to create a quasi-emulsion to create naproxen microsponges. 106 By delivering drugs continuously, the microsponge delivery technique successfully treats a variety of allergy-related problems (Table 8). When compared to traditional formulations, a microsponge formulation of diclofenacdiethylamine showed a delayed release of the medication when tested for its effectiveness against musculoskeletal disorders and arthritis.

When applied to the skin, 12 flurbiprofen microsponges show enhanced reactivity to pH, temperature, and agitation while releasing biologically active compounds in a regulated way. 107 There are several benefits of entrapping drugs in microsponge devices beyond controlling drug release. [18]

Starch microsponges-based topical sunscreen product

Topical sunscreens protect against damaging solar rays by acting as ultraviolet (UV) shields that absorb both UVA and UVB wavelengths. However, because they are absorbed from the skin into the systemic circulation, many sunscreens cause allergic responses and raise safety concerns. Although the USFDA has authorized oxybenzone/benzophenone-3 (BNZ) as a sunscreen, topical retention is significantly hampered by its high penetrability. Excellent spreading properties, a rich texture, a non-sticky feel, and great patient compliance are all displayed by the starch microsponges-based sunscreen product [82]. Compared to commercial creams, starch microsponges offer a greater SPF, better photoprotection, and less skin penetration, according to in vitro and ex vivo investigations. Clinical experiments verified the safety and biocompatibility of the developed starch micro-sponge enriched sunscreen lotion after preclinical research. (32,35)

COMPARATIVE ADVANTAGE OVER OTHER SYSTEMS

a) Microsponge

- Loading Capacity for Drugs: The porous structure makes it high.
- Offers a regulated and prolonged release of the medication.
- Provides controlled release and shields the medication from external influences, improving stability.
- Excellent absorption of oil; helps to make the skin less oily.
- Both hydrophilic and lipophilic medications might be included.
- Because it is non-irritating and has a lasting effect, patient compliance is improved. (36,37)

b) Microcapsule

- Moderate Drug Loading Capacity; restricted by core size.
- Less controlled release happens when the capsule wall bursts.
- Increases stability by encasing the drug; nevertheless, the substance breaks down more quickly if it is ruptured.
- Limited ability to absorb oil.
- Most appropriate for hydrophobic or lipophilic medications.
- Depending on the integrity of the capsule, moderate. (38,37)

LIMITATIONS & CHALLENGES

1. Utilization of Organic Residuals and Solvents

A variety of microsponge manufacturing techniques, such as suspension polymerization and quasi-emulsion solvent diffusion, rely on organic solvents or porogens like acetone, dichloromethane, and chloroform. Any leftover solvent must be totally removed because even trace levels can result in toxicity or regulatory noncompliance. (21)

2. Batch Uniformity, Scale-up, and Reproducibility

When microsponge production is moved from laboratory to industrial scale, issues include variable mixing, changes in heat/mass transfer, inconsistencies in pore size, and irregularities in drug administration and release between batches. (39)

3. Pore integrity and mechanical fragility

The microporous network may collapse or deform under mechanical stress (compression, shear, blending into formulations like creams or gels), changing the kinetics of release or resulting in premature leakage. Damage to a few pores close to the surface could result in burst release. (6)

4. Variability in Release Profiles and Burst Release

It may not be advantageous for drug molecules adsorbed close to or in surface-accessible pores to cause an initial burst release. Significant variation in release profiles is also caused by slight variations in pore wall thickness or interconnectivity between batches. [29]

5. Stability & Durability of Porous Materials

Environmental elements like humidity, temperature fluctuations, and mechanical vibration can cause pore collapse, structural creep, or polymer chain rearrangement over prolonged storage, changing the porosity's original design and, consequently, the way drugs release. [4]

6. Safety and Regulatory Issues

Regulators may need to carefully describe the internal pore architecture, residue solvents, degradation actions, and reproducibility due to the complexity of the process. For long-term use, particularly in internal applications, the polymeric matrix must also be demonstrated to be biocompatible, non-toxic, non-immunogenic, and safe. [14]

7. Restrictions on Deep and Internal Tissue Delivery

In contrast to nanoparticles, microsponges may not be able to pass through certain biological barriers or penetrate deeply into tissues due to their relatively large size (micron-scale). This could limit their ability to deliver medications in a systemic or deeply targeted manner. [29]

8. Economic viability, awareness, and market adoption

Persuading pharmaceutical companies, physicians, and regulatory agencies of the benefits of microsponge-based therapies is necessary for their adoption. Unless the advantages are obvious and observable, economic reluctance may result from the higher cost and complexity compared to traditional dose forms. [40]

FUTURE PERSPECTIVES

1. Microsponges in Cancer Therapy and Targeted Oncology:

One promising approach is the development of microsponge devices that release anticancer drugs preferentially in the tumor microenvironment. To selectively activate release in tumor tissue, for example, pH-sensitive gating, which opens pores under an acidic tumor pH, or enzyme-responsive linkers can be used. Hybrid systems that combine magnetic or photothermal agents with external stimuli like heat, light, or a magnetic field can cause localized release. [14]

2. Delivery of Vaccines and Immunotherapy:

Microsponges may serve as antigen/adjuvant depots, enabling the pulsatile or gradual release of immunogens to mimic prime-boost regimens. Surface targeting to antigen-presenting cells (APCs) and co-loading adjuvants and antigens in different pore domains are promising but understudied areas. [29]

3. Probiotics, Biologics, and Microbiome Modulation

Another creative strategy is to use microsponges to encapsulate live probiotics, enzymes, or proteins, shield them in a porous environment, and then release them gradually in the mucosal or gut areas. Trigger-responsive release (e.g., pH in GI, enzymatic breakdown) enabled the delivery of biologics to specific locations. [41]

4. Perceptive and Flexible Microsponges

Making multi-stimuli sensitive microsponges that respond to several external stimuli, including pH, temperature, redox conditions, enzymes, light or magnetic fields, and others, is one innovative strategy. Particularly interesting is the use of molecular "gates" or switching moieties to open and close pore entrances in response to certain stimuli. [14]

5. Mucoadhesive, gastroretentive, and floating microsponges

It might be feasible to increase the duration of microsponges' residence in the GI tract or on mucosal surfaces by producing them with buoyant or floating properties or mucoadhesive polymers (like chitosan or carbopol). This would result in a prolonged local release under these circumstances. [14]

6. Hybrid and Multistage Delivery Systems

It is possible to develop hybrid systems in which microsponges have nanoparticles or other carriers in their pores to allow for a two-stage release (first from the sponge, then from the nanoparticle). Similarly, porosity, functionalization, and mechanical stability could be integrated into the microsponge by incorporating mesoporous silica, MOFs, or inorganic nanostructures. [29]

7. Clinical Translation, Standardization, and Regulatory Strategy

For true impact, future research should focus on using quality-by-design (QbD) techniques, standardizing characterization (mechanical testing, repeatability, and porosity measurements), and engaging with regulatory bodies early on. Clinical and in vivo trials must proceed, especially for topical or local applications. Examining biodegradable or bioresorbable sponge matrices that decompose after release would also allay worries about residual carriers. [41,16]

CONCLUSION

Microsponges represent a novel and versatile platform in controlled drug delivery, bridging the gap between traditional and modern therapeutic systems. They are perfect for both topical and systemic applications due to their distinct porous structure, high loading capacity, and adjustable release profiles. The transition from microcapsules and microspheres to microsponges has yielded notable benefits in terms of stability, patient adherence, and the effectiveness of targeted delivery.

Their broad commercial adoption is still hampered by issues like reproducibility, large-scale manufacturing, and formulation scientists' lack of awareness, despite encouraging laboratory results. But these obstacles are gradually being overcome thanks to developments in polymer engineering, nanotechnology, and green synthesis techniques.

Looking ahead, microsponges hold immense potential in next-generation therapeutics such as cancer-targeted delivery, peptide stabilization, vaccine carriers, and probiotic encapsulation. Their adaptable design allows integration with stimuli-responsive systems, offering personalized and intelligent drug delivery opportunities. Thus, microsponges stand as a “bridge technology” connecting the reliability of conventional dosage forms with the innovation of smart delivery systems paving the way for a future where drug delivery is not only controlled but also condition responsive and patient oriented.

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HOW TO CITE: Sonal Bangar, Shriram Dhandrut, Manshi Tiwari, Dipali Ghatal, Swapnil Solase, Shrutika Patil, From Pores to Performance: The Science and Application of Microsponge Drug Delivery Systems, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 10, 2989-3004. https://doi.org/10.5281/zenodo.17464178