



## Review Article

### ADVANCES IN MICROSPONGE TECHNOLOGY: A COMPREHENSIVE REVIEW

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#### ABSTRACT

Microsponges are polymeric microparticles with an internal porous structure capable of encapsulating various drugs. This abstract provides an overview of microsp sponge formulation, encompassing preparation methods, characterization techniques, and applications. The quasi-emulsion solvent diffusion method is a commonly employed technique for microsp sponge production, involving the formation of an oil-in-water emulsion followed by solvent evaporation. Characterization of microsponges includes particle size analysis, drug loading, encapsulation efficiency, and release kinetics. Microsponges offer advantages such as sustained drug release, improved drug solubility, and enhanced skin penetration. Potential applications span various therapeutic areas, including dermatology, ophthalmology, and oral delivery. Ongoing research focuses on optimizing microsp sponge formulations for specific drug molecules and therapeutic indications to achieve desired drug release profiles and efficacy.

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## INTRODUCTION

The landscape of drug delivery technology is very competitive & rapidly changing. There are many new developments in delivery systems aimed at improving the effectiveness & cost-efficiency of therapies. Conventional methods struggle to deliver peptides, proteins, and DNA-based treatments effectively. Drug delivery systems (DDS) that accurately control the release rates or target drugs to specific areas in the body have significantly influenced healthcare. In recent years, creating new drugs alone isn't enough for effective treatment. It also requires developing suitable drug delivery systems right at the action site.<sup>1</sup>

The fate of a drug inside the body depends not just on its properties. The carrier system also plays a crucial role. It enables controlled & localized release of the active drug based on therapy needs. One key challenge for pharmaceutical scientists is controlling how quickly active ingredients reach specific body sites. The main goal of any drug delivery system? To deliver a therapeutic amount of medication to the appropriate site in the body so that desired drug concentrations are achieved and maintained on time.<sup>2</sup>

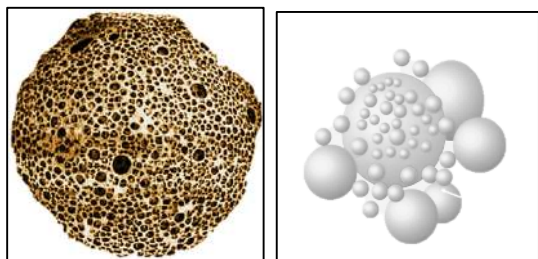
Microsponge technology was first developed by Won in 1987, with original patents assigned to Advanced Polymer Systems, Inc. This company created

numerous variations of these procedures, applied across cosmetics, over-the-counter (OTC) products, and prescription medications. Currently, this innovative technology is licensed to Cardinal Health, Inc., specifically for topical products. Scanning electron microscopy of microsponge particles reveals their internal structure resembles a “bag of marbles.” The porosity occurs because of the spaces between these marbles. These interstitial pores can capture a wide range of active ingredients, including emollients, fragrances, essential oils, sunscreens, anti-infective agents, and anti-inflammatory substances.<sup>3,4</sup>

### Defining Microsponge Delivery System

The Microsponge Delivery System (MDS) is a patented polymeric system consisting of porous microspheres. They are tiny sponge like spherical particles that consist of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface through which active ingredient are released in a controlled manner. The size of the microsponges ranges from 5-300 $\mu$ m in diameter and a typical 25 $\mu$ m sphere can have up to 250000 pores and an internal pore structure equivalent to 10 feet in length, providing a total pore volume of about 1ml/g for extensive drug retention. The surface can be varied from 20 to 500 m<sup>2</sup>/g and pore volume range from 0.1 to 0.3cm<sup>3</sup>/g. This

results in a large reservoir within each microsphere, which can be loaded with up to its own weight of active agent.<sup>5,6</sup>



**Figure 1: Structure of microsphere<sup>59,60</sup>**

#### **Characteristics of microspheres<sup>7-11</sup>**

- Most components & vehicles can be used to create microspheres.
  - These microspheres fully mix with a small amount of nonpolar solvent.
  - Stability is maintained in microsphere formulations across a pH range from 1 to 11.
  - They can withstand high temperatures, reaching up to 130° C.
  - Microspheres show stability when they interact with catalysts and during polymerization processes.
  - Microspheres are self-sterilizing, which keeps bacteria out, because of their 0.25 µm pores,.
  - The compositions of these microsphere formulations can be cost-effective & flow easily.
  - A significant 50–60% of microsphere formulations demonstrate substantial entrapment capacity.
- They offer excellent flexibility in formulation options.
  - Additionally, they allow for a prolonged release of medication, lasting up to 12 hours.

#### **Properties of actives moieties that is entrapped into Microspheres<sup>12-14</sup>**

- Drugs used for microsphere formulation should ideally possess minimal solubility; failing which, the vehicle may degrade the microsphere before application.
- Drug must not react with monomers and must not cause the preparation's viscosity to rise while being formulated.
- It must maintain stability under conditions of polymerization.
- Should be miscible with minimum quantity of solvent.
- Drug must to keep the microsphere's spherical structure intact.
- In order to eliminate cosmetic defects, the vehicle must be restricted to containing only 10 to 12% w/w of microsphere.

#### **Benefits of microsphere drug delivery systems<sup>15,16</sup>**

- Enhanced product performance.
- Extended release.
- Diminish irritation and hence enhanced patient Compliance.
- Improved product elegance.

- Improved oil control as it can absorb oil up to 6 times its weight without drying.
- Allows for novel product forms.
- Improves efficacy in treatment.
- Cure or control confirm more promptly.
- Improve control of condition.
- Improve bioavailability of same drugs
- Flexibility to develop novel product forms.
- Non-irritating, non-mutagenic, non-allergenic and non-toxic
- Improves stability, thermal, physical and chemical stability
- Allows incorporation of immiscible products.
- Improves material processing e.g. liquid can be converted to powders.

#### **Limitations**

- The preparation methods usually use organic solvents as porogens.
- An environmental hazard.
- Highly inflammable.
- Posing a safety hazard.
- In some cases, the traces of residual monomers have been observed, which may be toxic and hazardous to health.

#### **ADVANTAGES OF MICROSPONGE OVER VARIOUS DELIVERY SYSTEMS**

##### **Advantages over conventional formulations:**

Traditional topical treatments are made to target the layers of the skin. When you

apply products, they gradually let out active ingredients. This creates a concentrated layer that absorbs quickly. Because of this, both the dermis and epidermis can build up too much medicine. In contrast, microsponges can help solve this issue by slowly releasing the active ingredients into the skin over time. Therefore, the microsp sponge system might greatly reduce side effects like irritation while still being effective. A good example is MDS with benzoyl peroxide, which shows minimal irritation along with strong results.<sup>17</sup>

##### **Advantages over ointments:**

Patients often don't like ointments because they feel greasy. Since ointments require high amounts of active ingredients, they don't work well as drug delivery systems. This can lead to irritation or sensitivity issues. On top of that, there are unpleasant smells, issues with how quickly active ingredients evaporate, & possible incompatibilities between drugs & vehicles. However, the microsp sponge system can keep working beneath the skin without causing irritation or other problems that typical ointments have.<sup>18</sup>

##### **Advantages over liposomes and microencapsulation:**

MDS has its advantages when looked at beside methods like liposomes and microencapsulation. Microcapsules often struggle to control how fast active substances leak out. Once the wall breaks,

everything inside is released too quickly. Liposomes also face issues—like having less drug capacity, lower heat stability, tricky formulation steps, & being more vulnerable to bacterial instability. On the other hand, the microsp sponge system is tough! It can handle temperatures of up to 130 °C and stays stable in a range from pH 1 to 11. This sets it apart from other systems. Furthermore, it has an average pore size of 0.25 µm which allows it to self-sterilize by blocking harmful germs while still being compatible with various substances and vehicles. Plus, it keeps flowing smoothly & has the ability to load more drugs—between 50% & 60% capacity.<sup>19</sup>

## **METHODS OF PREPARATION OF MICROSPONGES**

Some of the methods used to develop microsp sponge-based drug delivery systems include liquid-liquid suspension polymerization, quasi-emulsion solvent diffusion, water-in-oil-in-water (w/o/w) emulsion solvent diffusion, oil-in-oil emulsion solvent diffusion, the addition of porogen method, vibrating orifice aerosol generator method, electro-hydrodynamic atomization method, and ultrasound-assisted production method.

### **Liquid-liquid suspension**

#### **polymerization:<sup>20-22</sup>**

The porous microspheres are made using the suspension polymerization method

within liquid systems. First, the monomers, which don't well with each other, dissolved together with active in a suitable solvent. Next, this mixture is dispersed into aqueous phases containing additives, like surfactants and suspending agents. These help to create a stable suspension. Once everything is set up, the polymerization begins. This can be triggered by raising the temperature, using irradiation, or adding a catalyst. As polymerization continues, it forms a spherical structure that acts like a reservoir. Afterward, the solvent gets removed, leaving behind the spherical porous microspheres. Porous microspheres are created using the suspension polymerization method in liquid-liquid systems. In this approach, immiscible monomers are first combined with active ingredients in a suitable solvent. Then, they are dispersed in aqueous phases that contain additives like surfactants and suspending agents. These additives help to form the more effectively. To initiate polymerization, we can increase the temperature, use irradiation, or add a catalyst. As polymerization continues, it results in a reservoir-like spherical structure. Once this process is complete, the solvent is removed, leaving behind the spherical porous microspheres—often referred to as microsponges.

Here's a quick summary of the steps involved in making microsponges:

*Step 1:* Choose the monomer(s) and their combinations carefully.

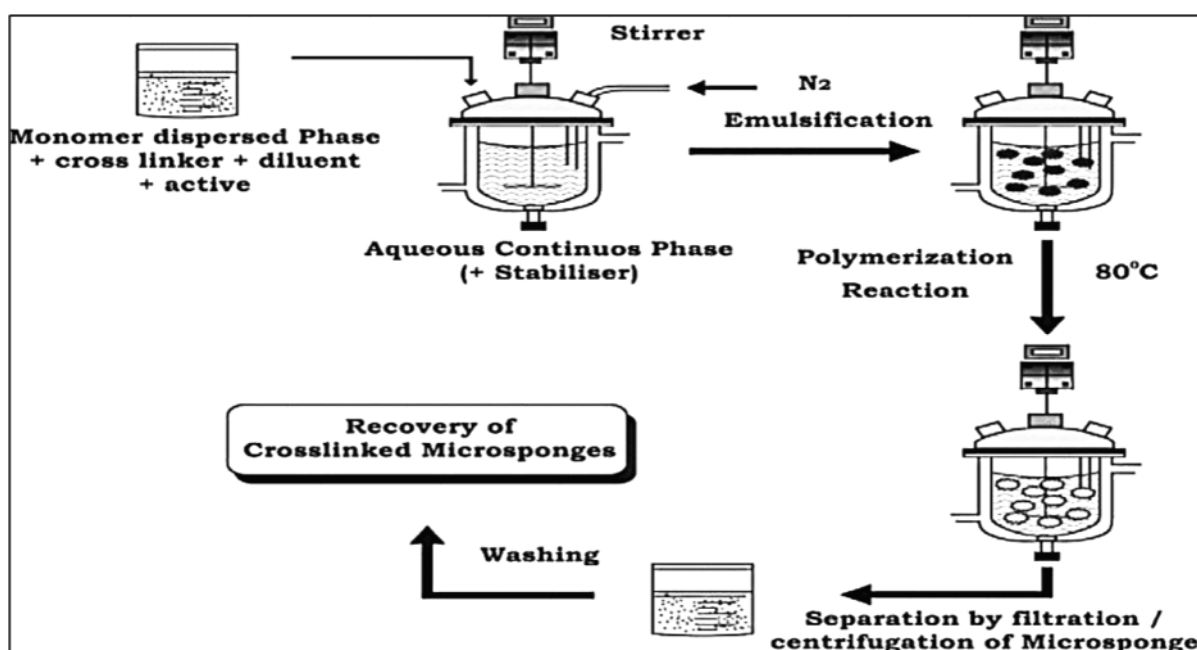
*Step 2:* As polymerization begins, chain monomers start to form.

*Step 3:* Cross-linking occurs between these chain monomers, creating ladder-like structures.

*Step 4:* The monomer ladders then fold to shape spherical particles.

*Step 5:* These microspheres agglomerate into groups of microspheres.

*Step 6:* Finally, these bunches bind together to create microsponges.



**Figure 2: Preparation of microsponges by Liquid-liquid suspension polymerization.<sup>6</sup>**

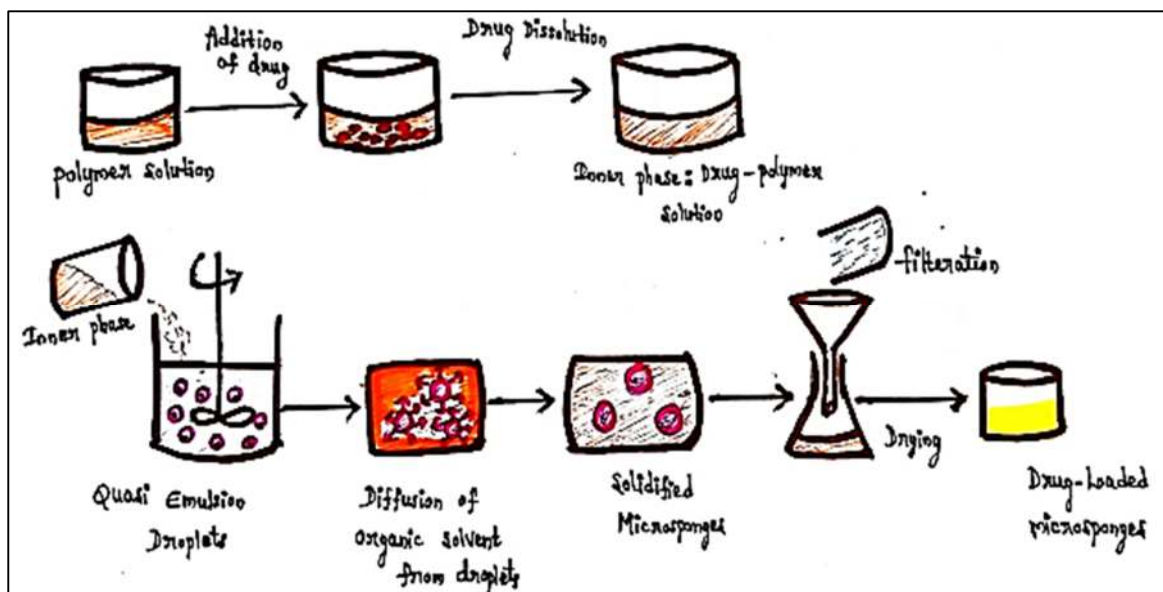
**Quasi-Emulsion Solvent Diffusion Method:<sup>23-25</sup>**

Microsponges are created using a quasi-emulsion solvent diffusion method. First, you dissolve the polymer in an appropriate solvent, most commonly ethanol. This creates what we call the inner phase. After that, add the drug into this inner phase. Let the mixture sit and dissolve for about 15 at 35 ° under ultrasonication.

Next comes the outer phase. This is made by mixing polyvinyl alcohol (PVA) with

distilled water at normal room temperature. Once prepared, combine the inner phase with the outer phase at room temperature. Stir this mixture continuously for two hours at 500 rpm. This process leads to the formation of microsponges.

Afterward, we filter the preparation to separate the microsponges. Finally, clean and dry the resulting product in an oven set to 40 °C.



**Figure 3: Preparation of microsponges by quasi emulsion solvent diffusion.**

### **Water-in-oil in Water (w/o/w) Emulsion Solvent Diffusion Method:**

This technique for producing biodegradable porous microspheres is simple. This approach separated an emulsifying agent such as span, polyethyleneimine, or spaced repetition from an organic polymeric solution utilizing an internal aqueous phase. The w/o emulsion was then dispersed in an external PVA-containing aqueous process to create a double emulsion. Entrapment is a benefit of this method. Several investigations have identified xanthan gum as an emulsifier that stabilizes the internal water-in oil emulsion. While this technique has the benefit of entrapping both water-soluble and water-insoluble compounds, the use of water-insoluble surfactants, which might retain residues inside the microsponges, is a major drawback.<sup>26-28</sup>

### **Oil-in-oil Emulsion Solvent Diffusion Method:**

The oil-in-oil (o/o) emulsion was made by using a volatile organic liquid as the internal stage, instead of the w/o/w method, which involved letting the water slowly evaporate while stirring. Dichloro-methane was the internal phase, polylactic glycolic acid was the polymer, and span-85, which is a mixture of fixed oil (Corn or Mineral) and dichloro-methane, was the external phase. To make the microsponges, the internal step was slowly added to the dispersion medium while stirring constantly. Hydroxyzine HCl-loaded Eudragit RS-100 microsponges were made using this method, with acetone as the dissolver and liquid paraffin as the continuous medium. The physicochemical properties of the drug and the polymer used

to make the microsponges affect the choice of an organic solvent and an outer phase. No surfactant residues were found in the microsponges, which is a big plus for this method. The main problems with this method are that you must eliminate all traces of alcohol and use organic solvents.<sup>7,29–31</sup>

#### **Addition of Porogen Method:**

In this method, the internal aqueous stage of the water-in-oil-in-water (w/o/w) emulsion was replaced with a porogen, such as hydrogen peroxide or sodium bicarbonate. The porogen was distributed throughout the polymeric solution to provide a consistent dispersion framework. This framework was then redispersed in a PVA-containing aqueous phase. The organic solvent was removed from the w/o/w emulsion after the addition of an initiator, leaving the microparticles behind. Hydrogen peroxide inclusion resulted in equally spaced and overlapping holes ranging in size from 5 to 20 μm. While it may be damaged, this porous architecture featured regularly distributed and linked pores.<sup>32</sup>

#### **Lyophilisation:**

This method was utilized to transform the microspheres into porous microspheres. At this step, the microspheres were grown in a chitosan hydrochloride solution before being lyophilized. The rapid removal of the solvent resulted in the formation of pores in the microspheres. Microsponges may be

made fast, simply, and frequently with this process. This process is simple and efficient, but it produces microparticles that are fractured or shrunken because the solvent is withdrawn too quickly.<sup>33</sup>

#### **Vibrating Orifice Aerosol Generator Method:**

The initial use of a vibrating orifice aerosol generator was producing lipid-bi-layered mesoporous silica particles (VOAG). Surfactant microdroplet evaporation-driven thermal deposition generated porous particles using the VOAG technique. Initially, a stock solution for the core particle was made by refluxing a hydro-ethanolic mixture of tetra-ethyl-orthosilicate in diluted HCl. This stock solution was diluted with a surfactant-containing solvent and stirred to generate monodisperse droplets, encased in microsponges.<sup>34</sup>

#### **Ultrasound-assisted Microsponge Production Method**

This technique was developed to produce the nano-sponge by modifying liquid-liquid suspension polymerization to employ -cyclodextrin as a monomer and di-phenyl carbonate as a cross-linking agent. To control the range of the microparticles, the reaction mixture was heated and sonicated. The reaction mixture was allowed to cool before being pulverized to generate particles that were first rinsed with distilled water and then ethanol. Cross-linked-CD



permeable microparticles molar medications effectively load medications. The results are easily reproducible, and no solvent residues were found. Nevertheless,

this approach has the disadvantage of trapping potentially hazardous cross-linking agent residues.<sup>6,8</sup>

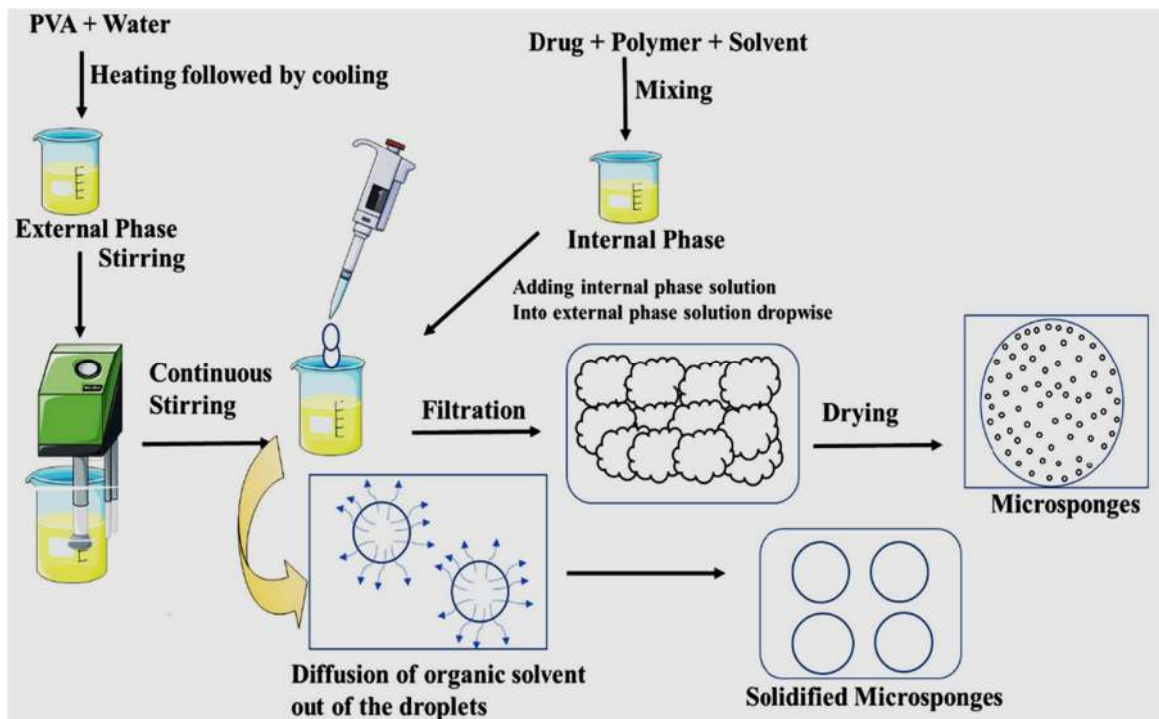


Figure 4: Ultrasound-assisted microsphere method.<sup>62</sup>

### FACTORS AFFECTING OF DRUG RELEASE FROM THE MICROSPONGE

**Solubility:** The discharge rate of agents from microsponges can be by aqueous media, like sweat. Important factors include how soluble the drug is in that external medium, the concentration gradient, & microsphere networks to expand.<sup>36</sup>

**Pressure release:** When you compress or squeeze the microsphere system, fluids or active ingredients get released. This process replenishes the skin with the entrapped components. Additionally, both the resilience of the sponge & its ability to

release may affect how much is released.<sup>37,39</sup>

**Temperature change:** Temperature plays a key role in initiating drug release from microsponges. At room temperature, many encapsulated active ingredients might show high viscosity, which can make it hard for them to flow directly from microsponges onto skin. However, raising the skin's temperature can enhance this flow rate, leading to increased release.<sup>38</sup>

**pH-triggered systems:** By modifying the coating or coverings of microsponges, they can effectively release drugs based on pH levels.<sup>39</sup>

## CHARACTERIZATION OF MICROSPONGES

Various methods are used for the characterization of microsponges.

### 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.<sup>40</sup>

### Drug content:

Equivalent microsponges are precisely weighed and mixed in 100 millilitres of phosphate buffer solution (PBS) (pH 6.8). The mixture should be filtered through a 0.45- $\mu$ m membrane filter and the samples are to be analysed at a suitable wavelength

using ultraviolet-visible (UV) spectrophotometer. The drug content can be calculated using the following formula.<sup>41</sup>

### 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.<sup>6,42,43</sup>

### Percentage Entrapment & Drug content:

Theoretically 50mg equivalent weight of microsponges that were weighed and placed to a 50 ml volumetric flask containing methanol in 10 ml were kept in a water bath shaker for 6 hr. at 35° C. Volume was make up to the mark by using suitable solvent and go for filtration, following proper dilution and spectrophotometric test at working wave length. Utilizing the following formula, the medication content and encapsulation effectiveness were determined:<sup>12,44</sup>

$$\text{Drug content} = \frac{\text{Con.} \times \text{Dil. factor} \times \text{volume}}{1000}$$

$$\text{Loading efficiency} = \frac{\text{Calculated drug contents}}{\text{Theoretical drug content}} \times 100$$

### **Percentage yield:**

Obtained microsp sponge 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.<sup>45</sup>

### **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 microsp sponge composition is applied to the membranes in the donor compartment.<sup>21,46</sup>

### **In vitro drug release:**

Accurately and the in vitro drug release studies can be done using USP dissolution testing apparatus type II (USP II). An aliquot of microsp sponge suspension is administered onto a dialysis membrane (pore size 14,000 Da, diameter 17.5 mm, HI-media) to determine the drug release. The dialysis bags must be fastened using paddles and positioned within dissolution vessels filled with buffer solution.

Subsequently, the vessels are subjected to stirring at 50 rpm once the temperature is stabilized to 37 ± 1 °C. Evaluation of drug release into the surrounding solution, attributed to membrane diffusion, is conducted by periodically collecting samples from the solution at specified time intervals. UV visible spectrophotometer can be used to quantify the amount of drug released from microsp sponge formulation.<sup>41,47</sup>

## **PHARMACEUTICAL UTILIZATION OF MICROSPONGES**

Microsp sponge delivery systems are valuable tools for improving the safety, effectiveness, & aesthetic appeal of various products—like topical prescriptions over-the-counter items, & personal care products. These microsponges have many uses. Mostly, they're applied topically; however, recently they've started being used for oral administration as well. Numerous patents indicate that these systems can work as excipients due to their ability to load a lot of substance & release it steadily.

### **Long lasting Coloured Cosmetics:<sup>48,49</sup>**

Colors that are trapped in microsponges can be integrated into a range of colored cosmetics, including rouges or lipsticks—making them last longer. As mentioned earlier, microsponges aid in spreading evenly and boost the covering power. Consequently, colored cosmetics that

incorporate microsponges tend to have a sophisticated touch.

**For topical administration:**<sup>50,51</sup>

A single microsphere is merely as small as a grain of talcum powder. It's less than one-thousandth of an inch wide! Each microsphere resembles a sponge: it's made up of countless tiny voids inside a solid structure that can hold many different substances. Typically, the outer surface is porous—this allows substances to flow in & out smoothly. During production, specific characteristics of the microsphere system can be set to get spheres just right for particular applications & compatibility with other products. Generally speaking, microsphere systems consist of biologically inert polymers. Comprehensive safety studies confirm that these polymers are non-irritating, non-mutagenic, non-allergenic, non-toxic, & will not biodegrade. This means human bodies cannot break them down into other substances. Even if they are tiny, these systems can't pass through the stratum corneum when used in topical items. Benzoyl peroxide is often included in topical patches for acne treatment but may cause skin irritation.

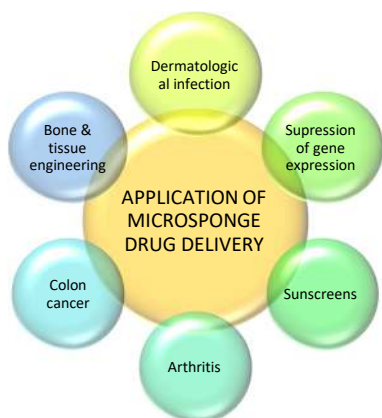
**For oral administration:**<sup>52</sup>

When used orally, the microsphere system has proved to elevate the solubilisation speed of drugs that don't dissolve well in water by trapping them within its tiny

pores. Since these pores are very small, the drug tends to become microscopic particles; hence there is a significant increase in surface area which greatly boosts solubilization rates. Controlled oral delivery of ibuprofen microspheres is implemented by using acrylic polymer Eudragit RS. Adjustments to their intraparticle density allow for sustained release formulations of chlorpheniramine maleate through powder-coated microspheres created by dry impact blending methods.

**For Bone and Tissue Engineering:**<sup>53,54</sup>

Compounds were gathered by blending pre-polymerized powders of polymethyl methacrylate with liquid methyl methacrylate and two types of aqueous dispersions: tricalcium phosphate grains & calcium-deficient hydroxyapatite powders. The resulting composites appeared porous and acted like microspheres. Basic fibroblast growth factor (bFGF) was integrated into a collagen sponge sheet and released steadily within mouse subcutis—according to how fast the sponge matrix biodegraded—which showed local angiogenic activity based on dosage



**Figure 5: Summarized uses of microsponges in various formulations.<sup>60</sup>**

### RECENT ADVANCEMENTS OF MICROSPONGES AS DRUG DELIVERY SYSTEMS

$\beta$ -CD microsponges have been developed for use with both hydrophobic & hydrophilic drugs. This is different from traditional polymeric micro or microsponges. Researchers studied these advanced systems, focusing on the oral administration of dexamethasone, flurbiprofen, doxorubicin hydrochloride, itraconazole, & serum albumin as example drugs. The creation of these microsponges involved cross-linking the  $\beta$ -CD molecule by re-acting it with diphenyl carbonate.

Interestingly, some researchers have noted that these microsponges serve as effective

carriers for gas delivery. Furthermore, they found that adding a cytotoxic agent into a microsponge carrier could enhance the drug's potency. This finding suggests potential applications for targeting cancer cells.<sup>55</sup>

Another innovative concept is the nanoferrosponge. It's made up of self-performing carriers which are designed to penetrate targeted sites more efficiently thanks to an external magnetic trigger. This mechanism forces the carriers to reach deeper tissues and enables the subsequent removal of magnetic material, resulting in a porous system.<sup>56</sup>

To improve the characteristics of porous microspheres, a process was crafted to produce these porous microbeads. This method involves a High Internal Phase Emulsion (HIPE) that integrates a continuous oil phase with monomers, cross-linking agents, & an aqueous internal phase. Researchers also noted enhanced RNA stability and an effective encapsulation process for siRNA. Such an approach might open up new therapeutic avenues for delivering siRNA.<sup>57</sup>

**Table: 1 Examples of microsp sponge drug delivery system with their formulations.**<sup>23,42-58</sup>

Sl. No.	Drug Delivery System	Active Moiety	Method of Preparation	Composition for Microsponge	Composition for DDS
1	Delayed release Capsule	Lansoprazole	Quasi emulsion solvent diffusion technique	Lansoprazole Eudragit L100 Eudragit LS 100 Polyvinyl alcohol (PVA) Methanol Ethyl acetate	Lansoprazole Microsponge Lactose SD Polyox N750 HPMC K15 Colloidal Silicon Dioxide
2	Tablet	Olsalazine	Quasi emulsion solvent diffusion technique	Olsalazine Eudragit s 100 Pectin Dibutyl phthalate PVA	Olsalazine Microsponge Inulin Locust bean gum MCC PVP K 30 Mg. Stearate Talc
3	Colon specific Tablet	Naproxen	Quasi emulsion solvent diffusion technique	Naproxen Eudragit RS100 PVA	Naproxen microsponge Starch MCC Lactose Mg. Stearate Croscarmellose
4	CR Colon specific Tablet	Aceclofenac	Quasi emulsion solvent diffusion technique	Aceclofenac EUDRGIT RS 100 DCM PVA	Aceclofenac microsponge Starch MCC Directly compressible Lactose Mg. Stearate Talc
5	Once daily Tablet	Fexofenadine Hydrochloride	Quasi emulsion solvent diffusion technique	Fexofenadine Hydrochloride Eudragit EPO DCM Ethanol Glycerine PVA	
6	Capsule		Quasi emulsion solvent diffusion technique	Domperidone Eudragit RS 100 DCM Ethanol PVA	

**Table 2: List of Marketed Products based on Microsponges**<sup>18,42,46</sup>

Product Name	Pharmaceutical Uses	Manufacturer
Glycolic Acid Moisturizer w/SPF 15	Anti-Wrinkles, soothing	AMCOL Health & Beauty Solution
Retin A Micro	Acne vulgaris	Ortho-McNeil Pharmaceutical, 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
Dermalogica Oil Control Lotion	Skin protectant	John and Ginger Dermalogica Skin Care Products
Ultra Guard	Protects baby's skin	Scott Paper Company
Oil free matte block SPF 20	Sunscreen	Dermalogica

### FUTURE PROSPECTS

A microspunge is made up of several interconnected voids housed in a non-collapsible A microspunge consists of many interconnected voids, all contained within a strong framework. This design enables it to hold a wide variety of materials. Nowadays, scientists are really concentrating on how to deliver things like sunscreen, anti-acne products, and anti-dandruff agents. It's also useful for delivering sensitive substances such as

vaccines, proteins, peptides, & DNA-based therapies.

In addition, these sponges play a role in tissue engineering and in controlled drug release systems for medicines that need to be given over longer periods. Typically, the outside of the microspunge is porous, which helps substances move in and out easily. During research, optimization techniques are employed to achieve the best outcomes from different formulations. They use efficient & safe ways to deliver active ingredients. Plus, there has been research

on using these porous devices for parenteral and pulmonary drug administration.

As it turns out, microsp sponge particles are also helpful as a medium for cell culture, which opens doors for stem cell growth and cellular regeneration in living organisms. The potential applications of microsp sponge carrier systems are quite vast—especially in cosmetics. Moreover, the adaptability of these formulations brings benefits across various sectors and sets the stage for new medication delivery systems.<sup>48</sup>

## **CONCLUSION**

Microsp sponge delivery technology represents a controlled release system. Here, active pharmaceutical ingredients get loaded into macro porous beads. This setup aims to reduce side effects while boosting therapeutic effectiveness. The use of microsp sponge can be quite effective in topical drug delivery systems. It helps retain the dosage form on the skin. Additionally, it can also aid in oral drug delivery, particularly using bio-erodible polymers. This is especially important for colon-specific and controlled release systems. Such methods can improve patient compliance by enabling site-specific drug delivery & prolonging dosing intervals.

With a growing demand for innovative and efficient pharmaceutical & cosmetic products, the market offers considerable potential for microsp sponge technology. The versatility it provides is significant.

Formulators are exploring new & creative ways to deliver actives, which means they can tap into the full capabilities of these unique materials. This includes enhanced safety, improved stability, fewer side effects from actives, and better compatibility with ingredients. Using novel development approaches alongside creative formulation techniques could make the microsp sponge delivery system a winning strategy for the next generation of the pharmaceutical & cosmetic industries. Manufacturing is straightforward, ingredients are simple, and a wide range of actives can be encapsulated. Plus, the programmable release feature makes microsponges especially appealing.

Originally, microsponges were developed for delivering topical drugs such as anti-acne treatments, anti-inflammatory agents, antifungals, anti-dandruff solutions, antipruritics, and rubefacients. The future looks promising for the Microsp sponge Delivery System in various pharmaceutical applications due to its unique properties like enhanced performance & elegance, extended-release profiles, reduced irritation levels, and improved thermal, physical, and chemical stability.

Microsponges hold distinct advantages over conventional topical dosage forms when treating tropical diseases. They offer a unique method for controlling the release of topical agents and can also be used for



oral as well as biopharmaceutical drug delivery. Compared to other products, they are non-mutagenic, nontoxic & non-irritant. Therefore, the microsp sponge drug delivery system holds a lot of potential. It's an emerging field that clearly needs further exploration through research studies in the future.

#### DECLARATION

There is no conflict of interest in publishing this review article.

#### REFERENCES

1. Shaha V., Jain H., Jethva K., Patel P. Microsp sponge drug delivery: A Review. *Int. J. Res. Pharm. Sci.* 2010; Vol-1, Issue-2: 212-218.
2. Kydonieus A.F., Berner B. *Transdermal Delivery of Drugs*. CRC Press, Raton: 1987.
3. Namrata Jadhav, Vruti Patel, Siddhesh Mungekar, Manisha Karpe, Vilasrao Kadam, Microsp sponge delivery system: an updated review, current status and future prospects, *World Journal of Pharmacy and Pharmaceutical Sciences*, Volume 2, Issue 6, 6463-6485.
4. Won R: Method for delivering an active ingredient by controlled time release utilizing a novel delivery vehicle which can be prepared by a process utilizing the active ingredients as a Porogen. 1987; US Patent No. 4690825.
5. Embil K., Nacht S. The Microsp sponge Delivery System (MDS): A topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. *J. Microencapsul.* 1996; 3(5), 575-588
6. Nacht S, Kantz M. The microsp sponge: A novel topical programmable delivery system. *Top Drug Deliv Syst.* 1992; 42:299- 325.
7. Won R: Method for delivering an active ingredient by controlled time release utilizing a novel delivery vehicle which can be prepared by a process utilizing the active ingredients as a Porogen. 1987; US Patent No. 4690825.
8. Chadawar V., Shaji J. Microsp sponge Delivery System. *Current Drug Delivery.* 2007; 4: 123-129.
9. Aritomi H., Yamasaki Y., Yamada K., Honda H, Koshi M. Development of sustained release formulation of chlorpheniramine maleate using powder coated microsp sponges prepared by dry impact blending method. *Journal of Pharmaceutical Sciences and Technology.* 1996; 56(1): 49-56.
10. D'souza J.I., Masvekar R.R., Pattekari P.P., Pudi S.R., More H.N. Microsp ongi c delivery of fluconazole for topical application. *Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech.* 2004;76.

11. Parthiban K.G., Manivannan R., Krishnarajan D., Chandra S., Nidhin R. Microsponge role in novel drug delivery system. *Intl. J. Pharm. Res. Devel.*, 2011; 3(4): 117-125.
12. Patidar K, Soni M, Saxena C, Soni P, Sharma DK. Microspongea versatile vesicular approach for transdermal drug delivery system. *J Global Pharm Tec*, 2(3), 2010, 154- 164.
13. N.H. Aloorkar, A.S. Kulkarni, D.J. Ingale and R.A. Patil, Microsponges as Innovative Drug Delivery Systems, *International Journal of pharmaceutical Sciences and Nonotechnology*, 5(1), 2012.
14. D'souza J.I., More H.N. Topical Anti-Inflammatory Gels of Fluocinolone Acetonide Entrapped in Eudragit Based Microsponge Delivery System. *Res J Pharm Tech* 1(4), 2008,502-506.
15. Abdel-Mottaleb MM, Mortada ND, El-Shamy AA, Awad GA. Physically cross-linked polyvinyl alcohol for the topical delivery of fluconazole. *Drug Dev Ind Pharm* 2009; 35:311-20.
16. Yehia SA, El-Gazayerly ON, Basalious EB. Fluconazole mucoadhesive buccal films: In-vitro/In- vivo performance. *Curr Drug Deliv* 2009; 6:17-27.
17. Ahmed A, Makram M, Sayed M, Louis D (2018) An overview of microsponge as a novel tool in drug delivery. *MADD* 2(3):1–7. <https://doi.org/10.31031/madd.2018.02.000537>
18. Jyothi KN, Kumar PD, Arshad P, Karthik M, Panneerselvam T (2019) Microsponges: a promising novel drug delivery system. *J Drug Deliv Therap* 9(5-s):188–194. <https://doi.org/10.22270/jddt.v9i5-s.3649>
19. Pradhan SK (2011) Microsponges as the versatile tool for drug delivery system. *Int J Res Pharm Chem* 1(2):243–258
20. 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.
21. 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.
22. Brunton LL, Lazo JS, Parker KL. Goodman and Gilman's, *The Pharmacological Basis of Therapeutics*°. 11th Edition. 2006, 1021.
23. 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.
24. Comoglu T, Gonul N, Baykara T, Preparation and in vitro evaluation of modified release ketoprofen microsponges, II, *Farmaco*, 58, 2003, 101-106.
25. Neelam Jain, Pramod Kumar Sharma, Arunabha Banik, Recent advances on microsphere delivery system, *International Journal of Pharmaceutical Sciences Review and Research*, Volume 8, Issue 2, May – June 2011.
26. Arya P, Pathak K. Assessing the viability of microsponges as gastro retentive drug delivery system of curcumin: optimization and pharmacokinetics. *Int J Pharm*. 2014;460(1-2):1-12. doi: 10.1016/j.ijpharm.2013.10.045, PMID 24184218.
27. Rawat A, Majumder QH, Ahsan F. Inhalable large porous microspheres of low molecular weight heparin: in vitro and in vivo evaluation. *J Control Release*. 2008;128(3):224-32. doi: 10.1016/j.jconrel.2008.03.013, PMID 18471921.
28. Maiti S, Kaity S, Ray S, Sa B. Development and evaluation of xanthan gum-facilitated ethyl cellulose microsponges for controlled percutaneous delivery of diclofenac sodium. *Acta Pharm*. 2011; 61(3): 257-70. doi: 10.2478/v10007-011-0022-6, PMID 21945905.
29. Giri TK, Choudhary C, Ajazuddin AA, Alexander A, Badwaik H, Tripathi DK. Prospects of pharmaceuticals and biopharmaceuticals loaded microparticles prepared by double emulsion technique for controlled delivery. *Saudi Pharm J*. 2013;21(2):125-41. doi: 10.1016/j.jsps.2012.05.009, PMID 23960828.
30. Mandal TK, Bostanian LA, Graves RA, Chapman SR, Idodo TU. Porous biodegradable microparticles for delivery of pentamidine. *Eur J Pharm Biopharm*. 2001;52(1):91-6. doi: 10.1016/S0939-6411(01)00150-3, PMID 11438428.
31. Zaki Rizkalla CM, latif Aziz R, Soliman II. In vitro and in vivo evaluation of hydroxyzine hydrochloride microsponges for topical delivery. *AAPS PharmSciTech*. 2011;12(3):989-1001. doi: 10.1208/s12249-011-9663-5, PMID 21800216.
32. Ramaiya A. Detecting torsional motion of kinesin motor proteins using birefringent microspheres and high-resolution optical tweezers. *Universität Tübingen*; 2018.
33. Trotta F, Cavalli R, Tumiatti W, et al. Ultrasound-assisted synthesis of

- cyclodextrin-based nanosponges. WO2006002814A1, 2008.
34. Gan Y, Zhang Y, Cheng D, Shetty A, Rathi P, Katarki N, et al. editors. An open-source benchmark suite for microservices and their hardware-software implications for cloud and edge systems. In: Proceedings of the Twenty-Fourth International Conference on Architectural Support for Programming Languages and Operating Systems; 2019:3-18. doi: 10.1145/3297858.3304013.
35. Mahant S, Kumar S, Nanda S, Rao R. Microsponges for dermatological applications: perspectives and challenges. Asian J Pharm Sci. 2020;15(3):273-91. doi: 10.1016/j.ajps.2019.05.004, PMID 32636947.
36. Mansi H (2019) A review on micro sponge delivery system. J Drug Deliv Therap | EBSCOhost. openurl.ebsco.com. <https://doi.org/10.22270/jddt.v9i3-s.2938>
37. Jadhav N, Patel V, Mungekar S, Bhamare G, Karpe M, Kadams V (2013) Microsponge delivery system: an updated review, current status and future prospects. J Sci Innov Res 2(6):1097–1110
38. Thakur R, Kumar S, Gaba P (2020) A review: novel method for microsponge drug delivery system. J Pharm Biol Sci 15(4):35–44. <https://doi.org/10.9790/3008-1504023544>
39. Lalitha SK, Shankar M, Likhitha D, Dastagiri J, Babu MN (2016) A current view on microsponge drug delivery system. Eur J Mol Biol Biochem 3(2):88–95
40. Farsana T, Geetha VS, Jumana KK, Mubashira NP (2023) Formulation development and evaluation of antimicrobial drug loaded microsponges for topical drug delivery. World J Pharm Res. <https://doi.org/10.20959/wjpr202311-28698>
41. Mohan D (2019) Microsponge based drug delivery system of voriconazole for fungal infection: formulation development and In-vitro evaluation. [jddtonline.info](http://jddtonline.info). <https://doi.org/10.22270/jddt.v9i3.2840>
42. Dineshmohan S, Gupta VRM (2016) Transdermal delivery of fuconazole microsponges: preparation and in vitro characterization. J Drug Deliv Therap 6(6):1334. <https://doi.org/10.22270/jddt.v6i6.1334>
43. Eshwarlall MR, Kishan CV, Krishnarao PV, Motiram CH. Formulation and evaluation of sertaconazole nitrate microsponge gel
44. Emerging implementation of drug loaded with microsponges technology and their antifungal activity. J Pharm Negat Results 13(S01) (2022).

- <https://doi.org/10.47750/pnr.2022.13.s01.103>
45. Halder S, Poddar S, Khanam J (2021) Optimization and scale-up methodology in preparing microsphere loaded with 5-fluorouracil (5-FU). *Drug Deliv Transl Res.* <https://doi.org/10.21203/rs.3.rs-989826/v1>
46. Rajurkar VG, Tambe AB, Deshmukh VK (2015) Topical anti-inflammatory gels of naproxen entrapped in eudragit based microsphere delivery system. *J Adv Chem Eng* 5(2):0122. <https://doi.org/10.4172/2090-4568.1000122>
47. Syed SM (2020) Formulation and evaluation of gel containing fuconazole microspheres. [www.ajprd.com](http://www.ajprd.com). <https://doi.org/10.22270/ajprd.v8i4.75>
48. Peppas N.A., Analysis of Fickian and non-Fickian drug release from polymers. *Pharm. Acta Helv.* 1985; 60: 110– 111.
49. Rekha U, Manjula BP. Formulation and evaluation of microspheres for topical drug delivery of mometasone furoate. *Int J Pharm Pharm Sci*, 3(4), 2010, 133-137.
50. D'souza JI, The Microsphere Drug Delivery System: For Delivering an Active Ingredient by Controlled Time Release. *Pharma. info.net*, 2008, 6 (3): 62.
51. Sarat C. P. M., Ajay M., Nagendra B.B., Prathyusha P., Audinarayana N., Bhaskar R.K. Microsphere Drug Delivery System . A Review. *J. Pharm. Res.* 2011; 4(5): 1381-1384.
52. D'souza JI. In-vitro Antibacterial and Skin Irritation Studies of Microspheres of Benzoyl Peroxide. *Indian Drugs.* 2001, 38(7): 23.
53. Wester R., Patel R., Natch S., Leyden J., Melendres J., Maibach H., Controlled release of benzoyl peroxide from porous microsphere polymeric system can reduce topical irritancy, *J. Am. Acad. Derm.*, 1991, 24, 720-726.
54. John I. D'souza, Jagdish K. Saboji, Suresh G. Killedar, Harinath N. More "Design and Evaluation of Benzoyl Peroxide Microspheres to Enhance Therapeutic Efficacy in Acne Treatment", Accepted for presentation in 20th FAPA Congress, Bangkok , Thailand , Nov Dec 3, 200428.
55. Trotta F, Cavalli R, Tumiatti W. Cyclodextrin-based microspheres for drug delivery. *J Incl Phenom Macrocyclic Chem.* 2006;56:209-13.
56. Hu S.H., Liu T.Y., Liu D.M., Nanospheres for controlled drug release. *J Control Release.* 2007; 121(3):181-9.
57. Li NH., Benson JR., Kitagawa N . Polymeric microbeads and method of

- preparation. International publication number. WO1995033553; 2003. <https://doi.org/10.1186/s43094-022-00421-9>
58. Lee JB, Hong J, Bonner DK., Self-assembled RNA interference microsponges for efficient siRNA delivery. *Nat Mater.* 2012; 11(4): 316-22
59. Pawar Vitthal, Salunkhe Anuradha, A Review on Microsponges Drug Delivery System, *International Journal of Research and Analytical Reviews (IJRAR)*, 2020: 7 (1), 2349-538 [www.ijrar.org](http://www.ijrar.org)
60. Srinatha, Sowjanya Battu and Vishwanath B. A, Microsponges: a promising frontier for prolonged release-current perspectives and patents, *Beni-Suef University Journal of Basic and Applied Sciences*, 2024, N et al. *Beni-Suef Univ J Basic Appl Sci* (2024) 13:60 <https://doi.org/10.1186/s43088-024-00519-4>
61. Shereen Sultana, Dr. Shahid Mohammed, Review on Microsponge Drug Delivery System, *International Journal for Research Trends and Innovation*, 2020: 5(6), 2456-3315
62. Abhishek Tiwari<sup>1</sup>, Varsha Tiwari<sup>1</sup>, Binita Palaria<sup>2</sup>, Manish Kumar, Deepak Kaushik, Microsponges: a breakthrough tool in pharmaceutical research, *Future Journal of Pharmaceutical Sciences* (2022) 8:31