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Review Article

Beyond Conventional Drug Delivery: The Expanding Role Of Microsponge Technology In Controlled Therapeutics

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ABSTRACT

Microsponges are highly porous polymeric microspheres that are intended for regulated and targeted distribution of active medicinal substances. They have a sponge-like structure that can entrap and release medicines in a prolonged manner. The microsphere delivery system has gained popularity in pharmaceutical and cosmetic formulations because it improves therapeutic efficacy, reduces adverse effects, improves stability, and allows for longer drug release. Microsponges are ideal for topical, oral, and dermatological uses. Their production involves a variety of preparation processes, including quasi-emulsion solvent diffusion and liquid-liquid suspension polymerisation. Particle size, production yield, drug entrapment efficiency, surface morphology, and in vitro drug release studies are all considered evaluation factors. This review summarizes the concept of microsponges, their need, materials used, preparation methods, evaluation techniques, advantages, disadvantages, and applications. In addition, a brief review of previously reported microsphere formulations is presented to highlight recent advances and future prospects of this promising drug delivery system

INTRODUCTION

Novel drug delivery methods have emerged as a major area of pharmaceutical research in order to overcome the constraints of traditional dosage forms, such as frequent dosing, fast drug release, changing drug concentrations, and increased adverse effects [1]. These limitations have prompted the development of controlled drug

delivery systems that can improve treatment efficacy, increase patient compliance, and provide prolonged drug release [2]. Among these, the microsphere drug delivery method has shown promise and versatility [3].

Highly porous polymeric microspheres with a sponge-like structure, microsponges are able to

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contain active medicinal substances and release them gradually over time[4]. They are typically spherical particles with a diameter of 5–300 μm and many interconnecting pores that serve as drug molecule repositories. In order to maintain therapeutic drug levels while reducing local irritation and systemic side effects, the medication is gradually released through diffusion or in reaction to external stimuli like pressure, temperature, pH, or moisture [5].

Won created microsphere technology in the late 1980s for topical medication administration, and it has subsequently acquired popularity in pharmaceutical and cosmetic applications [6]. Microspheres' porous nature allows them to successfully encapsulate both hydrophilic and lipophilic medicines, protecting them from environmental degradation and improving their stability. Polymers such as Eudragit®, ethyl cellulose, and polymethyl methacrylate are often employed in their production, with procedures such as quasi-emulsion solvent diffusion and liquid-liquid suspension polymerization [7].

Microsphere-based formulations have been extensively studied for the treatment of acne, fungal infections, inflammatory skin disorders, wound healing, oral controlled-release systems, and cosmetic items [8]. Their capacity to offer continuous drug release, reduce dose frequency, improve drug stability, and increase patient compliance makes them a desirable drug delivery platform. As a result, microsphere technology has emerged as a key research area for developing safer and more effective pharmaceutical formulations [9].

This review provides a comprehensive overview of microsphere drug delivery systems, including their purpose, materials used, formulation

methods, evaluation techniques, benefits, drawbacks, applications, and recent research developments, emphasising their potential as an effective controlled drug delivery strategy.

1.1 Need for Microspheres

The limits of traditional dosage forms and the need for focused and regulated medication delivery lead to the necessity of microsphere drug delivery devices. The following are the main justifications for creating formulations based on microspheres.

- To provide prolonged therapeutic action and minimise variations in drug concentration by offering controlled and sustained medication release.
- To improve patient compliance and treatment adherence by lowering the frequency of drug administration [10]
- To reduce systemic adverse effects and local discomfort by releasing the medication gradually at the place of action.
- To improve the stability of medications by shielding them from oxidation, light, heat, and moisture [11].
- To increase the bioavailability of medications that are poorly soluble by using controlled release and improved drug dispersion.
- To accomplish targeted or site-specific medication delivery, especially in topical and dermatological applications.
- To boost drug loading capacity since a wide range of active medicinal substances can be effectively trapped by the porous nature of microspheres [12].
- To enhance formulations' physicochemical and aesthetic qualities, such as decreasing greasiness, improving spreadability, and giving topical treatments a pleasing skin feel.



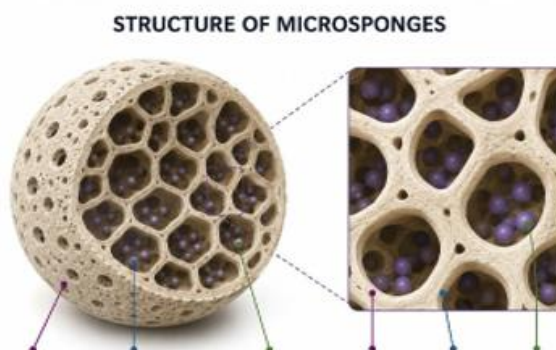


Figure 1 Structure of microsponges

1.2 Structure of Microsponges

Microsponges are highly porous, spherical polymeric microspheres with a three-dimensional network of interconnected pores. These porous structures consist of numerous tiny cavities that can encapsulate active pharmaceutical ingredients and gradually release them over an extended period.[14] Typically ranging from **5 to 300 μm** in diameter, microsponges possess a rigid outer surface and an internal porous matrix, allowing

them to entrap drugs efficiently while protecting them from environmental degradation [15]. Their unique architecture enables controlled and sustained drug release, improves drug stability, and minimizes local irritation, making them particularly suitable for topical drug delivery applications [16].

2. MATERIALS AND METHODS:

2.1 MATERIALS

Table 1 Materials used in microsponges

Category	Examples	Function
Polymers	Eudragit® RS100, Eudragit® RL100, Ethyl Cellulose, PMMA, PCL	Form the porous microsphere matrix and control drug release.
Organic Solvents	Dichloromethane, Ethanol, Acetone, Ethyl Acetate	Dissolve drug and polymer; evaporate to create porous microsponges.
Stabilizers/Emulsifiers[17]	PVA, Tween 80, Span 80, SLS	Stabilize emulsion droplets and ensure uniform particle formation.
Plasticizers	Triethyl Citrate, PEG 400, Dibutyl Phthalate	Improve flexibility and mechanical strength of the polymer matrix.
Porogens[18]	Sodium Chloride, Sodium Bicarbonate, Ammonium Bicarbonate	Generate pores and enhance controlled drug release.
Active Pharmaceutical Ingredients (APIs)	Benzoyl Peroxide, Clindamycin, Ketoconazole, Diclofenac Sodium, Berberine, Adapalene	Provide therapeutic activity through sustained drug delivery.

Aqueous Phase	Purified Water, Distilled Water	Act as the external phase during emulsion preparation.
Preservatives[19]	Methyl Paraben, Propyl Paraben, Phenoxyethanol	Prevent microbial growth and improve formulation stability.
pH Adjusters	Triethanolamine, Sodium Hydroxide, Citric Acid	Maintain optimum pH for stability and skin compatibility.

2.2 METHODS

2.2.1 Preformulation Studies

The preliminary research done prior to the creation of microsphere formulations is known as preformulation studies. These investigations aid in determining the appropriate formulation components, guaranteeing compatibility, and comprehending the physicochemical characteristics of the medicine and excipients. For stable microspheres with optimal drug loading, entrapment efficiency, and controlled drug release, proper preformulation studies are crucial. Among the notable preformulation investigations are:

- **Organoleptic Evaluation:** To verify the drug's identification and purity, its colour, odour, look, and physical condition are assessed.
- **Solubility Studies:** The drug's solubility is tested in several solvents, including water, ethanol, methanol, acetone, dichloromethane, and phosphate buffer. These studies help to determine optimal solvents for microsphere preparation. [20]
- **Melting Point Determination:** The capillary method or device is used to measure the purity and thermal properties of a medication.
- A UV-visible spectrophotometer is used to determine the drug's maximum absorption wavelength (λ_{max}). This wavelength is

utilised for quantitative estimate in drug content and release research.

- **Calibration Curve Preparation:** The absorbance of standard drug solutions at λ_{max} is measured to create a calibration curve. In formulation research, it is employed to ascertain drug concentration [21].
- **Drug-Polymer Compatibility Studies:** Analytical methods like Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) are used to assess the drug's compatibility with particular polymers. These investigations aid in locating any chemical interactions that might have an impact on the stability of the formulation.
- **Partition Coefficient:** To assess a drug's lipophilic or hydrophilic nature, which affects drug entrapment and release behaviour, the partition coefficient is calculated [22].
- **Thermal Analysis:** To evaluate thermal stability and potential interactions, the drug's and formulation's thermal behaviour is examined using DSC or Thermogravimetric Analysis (TGA).
- **Drug Stability:** Prior to formulation, the drug's stability is assessed under various environmental circumstances, including temperature, humidity, and light [23].

2.2.2 Formulation Techniques:

Various techniques have been employed for the preparation of microsphere drug delivery systems. The selection of the method depends on the nature



of the drug, polymer, and the desired characteristics of the final formulation.

• Quasi-emulsion Solvent Diffusion Method

Principle: The idea behind this technique is that a volatile organic solvent diffuses and evaporates from the internal phase into the external aqueous phase. The polymer precipitates around the medication when the solvent diffuses and evaporates, creating porous microsponges[24]

Steps:

- ✓ The chosen polymer should be dissolved in a volatile organic solvent such as acetone, ethanol, or dichloromethane.

- ✓ To prepare the internal phase, add the medication to the polymer solution.
- ✓ Dissolve Polyvinyl Alcohol (PVA) or similar stabiliser in distilled water to prepare the exterior aqueous phase.
- ✓ With constant stirring, gradually incorporate the internal phase into the external phase.
- ✓ To enable the organic solvent to diffuse and evaporate, keep swirling.
- ✓ The polymer solidifies as the solvent evaporates, creating porous microsphere particles.
- ✓ Gather the generated microsponges using centrifugation or filtration.
- ✓ To eliminate any remaining stabiliser, wash the microsponges with purified water.

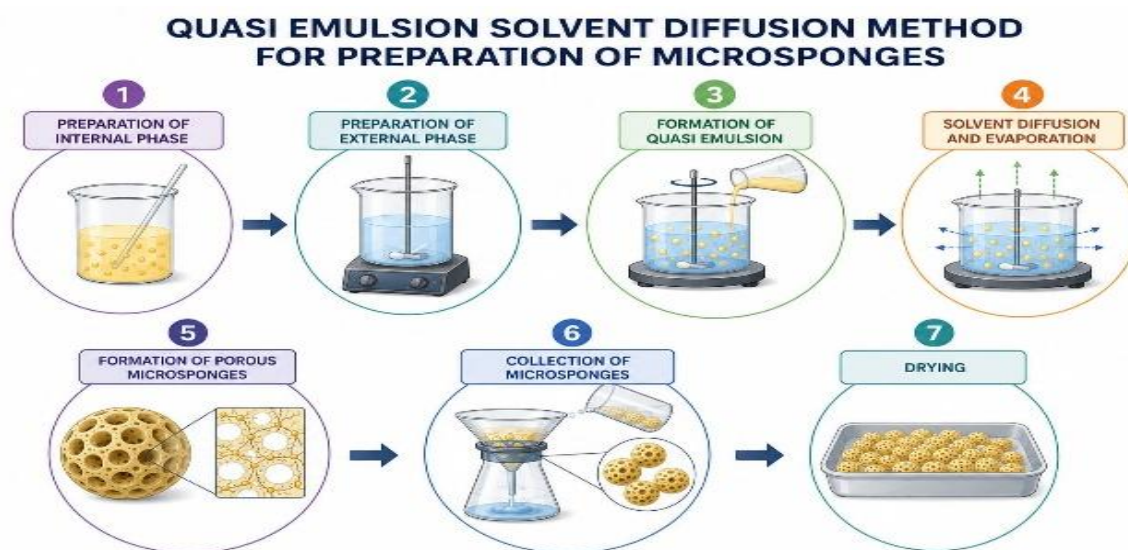


Figure 2Quasi-emulsion Solvent Diffusion Method

Liquid–Liquid Suspension Polymerization

Steps:

- ✓ Dissolve the drug in the monomer solution.
- ✓ Add initiators and cross-linking agents.
- ✓ Disperse the mixture into an external liquid phase under stirring.

- ✓ Initiate polymerization using heat, radiation, or chemical catalysts.
- ✓ Continue stirring until porous microsponges are formed.
- ✓ Filter, wash, and dry the obtained microsponges [25]

Liquid-Liquid Suspension Polymerization Method of Preparation of Microsponges

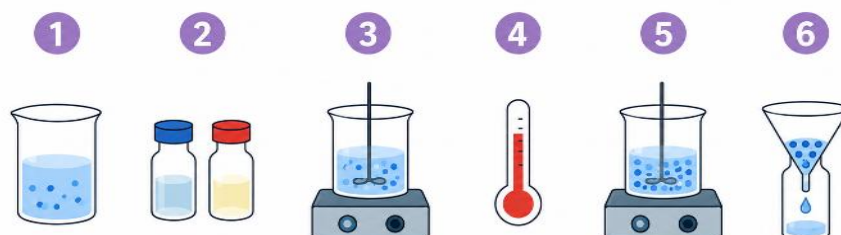


Figure 3 Liquid-Liquid Suspension Polymerization method.

• Double Emulsion Solvent Evaporation

Method

Principle: This method is mainly used for hydrophilic drugs by forming a water-in-oil-in-water (W/O/W) emulsion [26].

Steps:

- ✓ Prepare a primary water-in-oil (W/O) emulsion.
- ✓ Add the primary emulsion into an external aqueous phase to form a W/O/W emulsion.
- ✓ Stir continuously to evaporate the organic solvent.
- ✓ Allow the polymer to solidify and form microsponges.
- ✓ Collect, wash, and dry the particles.

Double Emulsion Solvent Evaporation Method

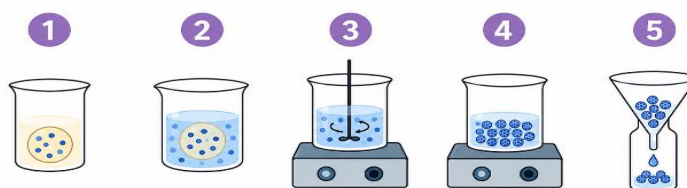


Figure 4 Double emulsion Solvent Evaporation method

• Solvent Evaporation Method

Principle: Microsponges are formed by evaporation of a volatile solvent from an emulsion system [27].

Steps:

- ✓ In a volatile organic solvent, dissolve the medication and polymer.
- ✓ Emulsify the mixture into a stabilizer-containing aqueous phase.
- ✓ Continue stirring until the solvent evaporates.
- ✓ Permit the development of microsponges and polymer precipitation.

- ✓ The microsponges should be filtered, cleaned, and dried.

SOLVENT EVAPORATION METHOD FOR PREPARATION OF MICROSPONGES



Figure 5 Solvent Evaporation Method

- **Oil-in-Oil Emulsion Solvent Diffusion Method** Principle: This method is suitable for moisture-sensitive drugs and employs two immiscible organic phases [28].

Oil-in-Oil Emulsion Solvent Diffusion Method for Preparation of Microsponges

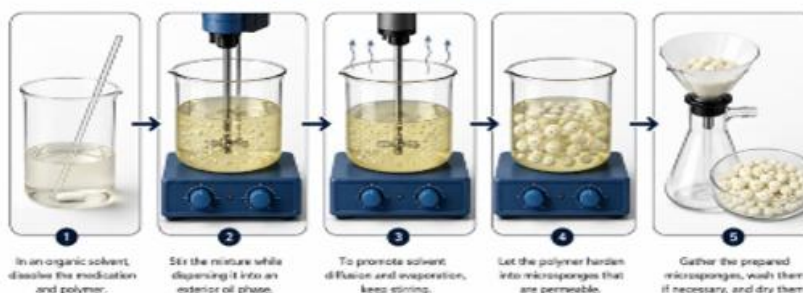


Figure 6 Oil-in-Oil Emulsion Solvent Diffusion Method

Steps:

- ✓ In an organic solvent, dissolve the medication and polymer.
- ✓ Stir the mixture while dispersing it into an exterior oil phase.
- ✓ To promote solvent diffusion and evaporation, keep stirring.
- ✓ Let the polymer harden into microsponges that are permeable.
- ✓ Gather the prepared microsponges, wash them if necessary, and dry them.

• Lyophilization (Freeze-Drying) Method



Principle: Porous microsponges are produced by freezing the formulation followed by sublimation of the solvent [29].

Steps:

- ✓ Get the drug-polymer dispersion ready.
- ✓ The dispersion should be frozen at a low temperature.
- ✓ Freeze-dry the frozen sample.
- ✓ Sublimate the frozen solvent to remove it.
- ✓ Gather the permeable microsponges that have dried.

3. EVALUATION TECHNIQUES

The following criteria are used to assess the prepared microsponges' physicochemical properties, morphology, release behaviour, and drug loading efficiency

- **Particle Size Analysis:** Using optical microscopy, laser diffraction, or a particle size analyser, the average particle size and size distribution of microsponges are ascertained. Particle size influences drug loading, release rate, and stability.
- **Surface Morphology:** The surface morphology and porous structure of microsponges are examined using Scanning Electron Microscopy (SEM). SEM provides information on particle shape, surface characteristics, and pore distribution [30].
- **Production Yield:** Production yield indicates the efficiency of the preparation process and is calculated using the following equation:

$$\text{Production Yield (\%)} = (\text{Practical Yield} / \text{Theoretical Yield}) \times 100$$

- **Drug Content:** Drug content is determined by dissolving a known quantity of microsponges

in a suitable solvent and analyzing the solution using a UV–Visible spectrophotometer or High-Performance Liquid Chromatography (HPLC)[31].

- **Entrapment Efficiency:** Entrapment efficiency determines the percentage of drug successfully encapsulated within the microsponges.

$$\text{Entrapment Efficiency (\%)} = (\text{Actual Drug Content} / \text{Theoretical Drug Content}) \times 100$$

- **In-vitro Drug Release Study:** The drug release profile is evaluated using a USP dissolution apparatus in a suitable dissolution medium under controlled conditions. Samples are withdrawn at predetermined intervals and analyzed using UV spectrophotometry or HPLC.
- **Drug Release Kinetics:** The release data are fitted into various kinetic models such as:
 - ✓ Zero-order kinetics
 - ✓ First-order kinetics
 - ✓ Higuchi model
 - ✓ Korsmeyer–Peppas model

These models help determine the mechanism of drug release from the microsphere system[32].

- **Differential Scanning Calorimetry (DSC):** DSC is used to study the thermal behavior of the drug, polymer, and microsphere formulation, confirming drug encapsulation and compatibility.
- **Stability Studies:** Stability studies are conducted according to ICH guidelines by storing the formulation under accelerated and long-term storage conditions. The formulation is periodically evaluated for changes in



appearance, drug content, entrapment efficiency, and drug release profile[33].

4. ADVANTAGES OF MICROSPONGES

The microsphere drug delivery system is a promising method for targeted and controlled drug delivery because it has a number of advantages over traditional dosage forms. Provides controlled and sustained drug release.

- Reduces the frequency of drug administration, improving patient compliance.
- Minimizes local irritation and systemic side effects[34].
- Enhances the stability of drugs by protecting them from light, heat, moisture, and oxidation.
- Increases drug entrapment efficiency due to its porous structure. • Can encapsulate both hydrophilic and lipophilic drugs.
- Improves bioavailability and therapeutic efficacy.
- Offers site-specific delivery, particularly for topical applications[35].
- Enhances the aesthetic properties of topical formulations by reducing greasiness and improving spreadability.

- Compatible with various dosage forms, including gels, creams, lotions, capsules, and tablets.

3. DISADVANTAGES OF MICROSPONGES

Microsphere medication delivery devices have several drawbacks despite their many benefits.

- The preparation techniques need careful optimisation and are somewhat complicated.
- Residual solvent problems could arise from the usage of organic solvents.
- More expensive to produce than traditional formulas [36].
- It can be difficult to scale up for industrial output.
- Unsuitable for medications that need a high loading capacity.
- Environmental factors and polymer type may have an impact on drug release.
- Characterisation and evaluation frequently call for specialised equipment [37].
- Because there are several processing steps, preparation takes a long time.
- The biodegradability of certain polymers may be restricted.

6. REVIEW OF PREVIOUS FORMULATIONS

Table 2 Review of Previous Formulations

S. No.	Author (Year)	Drug	Polymer	Method	Major Findings
1	Khattab&Nattouf (2021) [38]	Clindamycin	Eudragit RS100	Emulsion Solvent Diffusion	High entrapment efficiency with sustained drug release (90.38% over 12 h) and porous spherical microsponges.
2	Bhagat <i>et al.</i> (2024) [39]	Ketoconazole	Eudragit RS100	Quasi-emulsion Solvent Diffusion	High drug loading, controlled release, and reduced skin irritation.



3	Budarapuet <i>al.</i> (2025) [40]	Ketoconazole	Ethyl Cellulose	Quasi-emulsion Solvent Diffusion	High entrapment efficiency (94.78%) with sustained release over 12 h and good compatibility.
4	El-Housinyet <i>al.</i> (2020) [41]	Berberine + Cinnamaldehyde	Carbopol Hydrogel	Microemulsion– Hydrogel System	Improved topical delivery and antimicrobial activity against acne-causing bacteria.
5	Atabayet <i>al.</i> (2022) [42]	Benzoyl Peroxide	Eudragit RS100	Quasi-emulsion Solvent Diffusion	Sustained drug release with reduced skin irritation and enhanced antibacterial activity.
6	Ghorpade&Atram (2023) [43]	Adapalene	Eudragit S100, Eudragit RS100	Quasi-emulsion Solvent Diffusion	Controlled drug release with improved topical efficacy against acne vulgaris.
7	Amrutiyaet <i>al.</i> (2009) [44]	Mupirocin	Eudragit RS100	Emulsion Solvent Diffusion	Developed sustained- release microsponges with enhanced skin deposition and prolonged antibacterial activity.

7. FUTURE PERSPECTIVES

Microsponge drug delivery systems have emerged as a promising platform for controlled and targeted drug administration, with important implications for future pharmaceutical and biological applications. Advances in polymer science, nanotechnology, and material engineering are predicted to improve the design of microsponges with higher drug-loading capacity, controlled release properties, and biocompatibility. The development of biodegradable and stimuli-responsive polymers may broaden their utility by allowing for site-specific medication release in response to changes in pH, temperature, enzymes, or other physiological parameters.

Future research will also focus on combining microsponge technology with novel therapeutic techniques such as nanocarriers, hydrogels, microneedles, and three-dimensional (3D) printing

to create enhanced drug delivery platforms. In addition to topical formulations, microsponges have great potential for oral, ophthalmic, transdermal, and targeted drug delivery applications. Furthermore, the inclusion of natural bioactive chemicals and herbal medications into microsponge systems is gaining popularity due to its ability to boost therapeutic efficacy while minimising side effects. Despite these advancements, further studies are required to optimize large-scale manufacturing processes, evaluate long-term safety, and conduct extensive clinical trials to establish the efficacy and commercial feasibility of microsponge-based formulations. Continued research and technological innovations are expected to broaden the scope of microsponge drug delivery systems and facilitate their translation from laboratory research to clinical practice.

9. CONCLUSION



The microsphere drug delivery system represents an innovative and versatile approach for achieving controlled, sustained, and site-specific drug delivery. Its highly porous polymeric structure enables efficient drug encapsulation, improved stability, prolonged drug release, and reduced local as well as systemic side effects. These unique characteristics have made microspheres a valuable carrier system for a wide range of pharmaceutical and cosmetic applications, particularly in topical drug delivery. Various preparation techniques, especially the quasi-emulsion solvent diffusion method, have demonstrated the ability to produce stable microspheres with high drug entrapment efficiency and desirable release profiles. Numerous studies have reported improved therapeutic efficacy, enhanced patient compliance, and better formulation stability compared with conventional dosage forms. With continuous advancements in polymer technology and drug delivery research, microsphere systems are expected to play an increasingly important role in the development of next-generation pharmaceutical formulations. Future innovations focusing on biodegradable polymers, targeted delivery, and combination with emerging technologies are likely to further expand the clinical and commercial applications of microsphere-based drug delivery system.

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