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MICROSPONGE DRUG DELIVERY SYSTEM: A COMPREHENSIVE REVIEW ON FORMULATION, CHARACTERIZATION, APPLICATIONS AND FUTURE PERSPECTIVES

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ABSTRACT

Microsponge drug delivery system is a porous, polymer-based controlled release technology designed to improve therapeutic efficacy and minimize adverse effects of active pharmaceutical ingredients (APIs). These highly cross-linked polymeric microspheres possess a sponge-like architecture capable of entrapping drugs within interconnected void spaces and releasing them in a sustained and controlled manner. Initially developed for topical drug delivery, microsponge systems have expanded to oral, transdermal, and cosmetic applications due to their versatility, stability, and safety profile.

The unique porous structure provides high drug loading capacity, reduced irritation, improved stability of labile drugs, and enhanced patient compliance. Release of drug from microsponges is primarily diffusion-controlled, influenced by factors such as polymer type, cross-linking density, porosity, particle size, and physicochemical properties of the drug.

This review comprehensively discusses the historical development, structure, mechanism of drug release, materials used, methods of preparation, evaluation parameters, pharmaceutical applications, advantages, limitations, and future perspectives of microsponge technology. The article also highlights recent research trends including nanosponges, biodegradable polymers,

and targeted drug delivery strategies. The content is structured to serve as a reference guide for formulation scientists and researchers in pharmaceutical technology.

KEYWORDS: Microsponge, Controlled release, Porous polymeric system, Sustained drug delivery, Entrapment efficiency, Topical drug delivery.

1. INTRODUCTION

The development of novel drug delivery systems (NDDS) has significantly transformed modern pharmaceutics by enhancing therapeutic efficacy and reducing toxicity of conventional drugs. Traditional dosage forms often exhibit limitations such as fluctuating plasma drug concentrations, frequent dosing, poor patient compliance, and systemic side effects.[3] To overcome these drawbacks, controlled and sustained drug delivery systems have been developed to provide predictable and prolonged drug release profiles.[4]

Among various advanced delivery technologies, microsponge drug delivery system has emerged as a promising approach. Microsponges are porous, polymeric microspheres ranging from 5 to 300 µm in diameter. These particles are composed of highly cross-linked polymers forming an interconnected network of pores that act as reservoirs for active pharmaceutical ingredients.[5]

The concept of microsponge technology was first introduced by Won in 1987 for topical application to reduce irritation caused by benzoyl peroxide in acne treatment.[6] Since then, this technology has evolved and found applications in oral, transdermal, and cosmetic formulations. Microsponges provide site-specific and sustained drug release while maintaining drug stability and minimizing adverse reactions.[7]

The increasing interest in microsponge systems is attributed to their ability to incorporate both hydrophilic and lipophilic drugs, compatibility with various dosage forms, and enhanced safety profile compared to conventional systems.[8]

2. HISTORY AND DEVELOPMENT

Microsponge technology was originally patented by Advanced Polymer Systems, USA, to improve topical drug therapy.[6] The first commercial product based on microsponge technology was Retin-A Micro®, which utilized microsponge encapsulation to reduce irritation associated with tretinoin therapy.[9] The early development focused primarily on

dermatological applications. However, researchers later explored the versatility of the porous structure in oral and colon-targeted drug delivery systems.[10]

Advancements in polymer chemistry, cross-linking techniques, and solvent evaporation methods have further expanded the scope of microsponge systems in pharmaceutical sciences.[11]

3. ADVANTAGES OF MICROSPONGE SYSTEM

Microsponges provide sustained drug release, reduced irritation, improved stability, and enhanced patient compliance. They are compatible with creams, gels, tablets, and capsules. Due to small pore size, they prevent bacterial contamination and act as self-sterilizing systems.

They minimize systemic absorption in topical therapy.[12]

4. LIMITATIONS

- Not suitable for very large molecular weight drugs.
- Complex manufacturing process compared to simple emulsions.
- Limited drug loading for highly hydrophilic drugs.[13]

5. STRUCTURE AND MORPHOLOGY OF MICROSPONGES

Microsponges are rigid, spherical particles composed of a highly cross-linked polymeric matrix. The internal structure consists of numerous interconnected pores forming a honeycomb-like architecture.

These pores provide

- Large surface area
- High drug loading capacity
- Controlled diffusion pathways
- Protection of drug from environmental degradation

Scanning Electron Microscopy (SEM) studies reveal that microsponges possess uniform spherical shape with porous surfaces. The pore size typically ranges between 0.1–0.3 µm, preventing bacterial penetration and making the system self-sterilizing. The stability of the microsponge structure depends on polymer type, cross-linking density, and preparation method.[14]

6. MECHANISM OF DRUG RELEASE

Drug release from microsponges occurs primarily by diffusion through the porous network. The interconnected channels allow gradual diffusion of drug into surrounding medium.

Several mechanisms contribute to release behavior

1. Diffusion-controlled release
2. Pressure-triggered release (topical application)
3. pH-dependent release
4. Temperature-sensitive release
5. Solubility-controlled release

The release kinetics often follow Higuchi or Korsmeyer–Peppas models, indicating diffusion-controlled mechanism.

Drug release rate depends on

- Polymer concentration
- Particle size
- Porosity
- Drug solubility
- Cross-linking density[15]

7. MATERIALS USED IN MICROSPONGE FORMULATION

Selection of polymer plays a crucial role in determining drug release characteristics. Commonly used polymers include Eudragit RS 100, Eudragit RL 100, ethyl cellulose, polylactic acid, and polymethacrylates. Organic solvents such as dichloromethane, ethanol, acetone, and methanol are used during preparation. Surfactants like polyvinyl alcohol (PVA) are employed to stabilize emulsion systems.

The compatibility between drug and polymer must be evaluated to ensure stability and entrapment efficiency.

8. METHOD OF PREPARATION

Liquid–Liquid Suspension Polymerization

Liquid–liquid suspension polymerization is one of the earliest methods used in microsponge preparation. In this technique, monomers (such as styrene or methacrylates) are dissolved along with the active drug in a suitable organic solvent. The solution is dispersed into an

aqueous phase containing stabilizers under constant stirring to form droplets. Polymerization is initiated by heat, radiation, or chemical catalysts, leading to the formation of cross-linked porous microspheres. The drug is entrapped within the polymer matrix during polymerization. After completion, the formed microsponges are filtered, washed, and dried. This method provides uniform particle size and controlled porosity but requires careful removal of residual monomers and solvents.

Quasi-Emulsion Solvent Diffusion Method

The quasi-emulsion solvent diffusion method is the most widely used technique for microsponge preparation due to its simplicity and reproducibility. In this method, the drug and polymer (e.g., Eudragit RS 100, ethyl cellulose) are dissolved in a volatile organic solvent such as dichloromethane or ethanol to form the internal phase. This internal phase is slowly added into an aqueous external phase containing surfactant (e.g., polyvinyl alcohol) under continuous stirring. As the organic solvent diffuses into the aqueous phase and evaporates, the polymer precipitates, forming rigid porous microsponges. The particles are then filtered, washed, and dried. This method allows better control over particle size, entrapment efficiency, and porosity by adjusting stirring speed, polymer concentration, and solvent ratio.[16]

Solvent Evaporation Method

In the solvent evaporation method, the drug and polymer are dissolved in an organic solvent to form a homogeneous solution. This solution is emulsified into an aqueous phase under mechanical stirring. As the solvent evaporates, the polymer solidifies and forms porous microsponge particles encapsulating the drug. This technique is suitable for heat-sensitive drugs and provides high entrapment efficiency. However, solvent removal must be carefully controlled to avoid residual toxicity.

Oil-in-Oil (O/O) Emulsion Solvent Diffusion Method

This modified technique is particularly useful for incorporating hydrophilic drugs. In this method, the internal phase (drug + polymer in organic solvent) is dispersed into a non-aqueous external phase such as liquid paraffin. The solvent diffuses and evaporates, forming porous microspheres. This approach minimizes drug loss into aqueous phase and enhances entrapment efficiency for water-soluble drugs.

Cross-Linking Polymerization Method

In this approach, cross-linking agents are used to form a three-dimensional polymer network. The drug is incorporated during cross-linking, resulting in a highly porous microsponge matrix. The degree of cross-linking influences porosity, mechanical strength, and drug release rate.40

This method is commonly used in advanced microsponge and nanosponge systems designed for targeted or stimuli-responsive drug delivery.[17,18]

9. CHARACTERIZATION AND EVALUATION PARAMETERS

Characterization of microsponge systems is essential to ensure quality, reproducibility, drug loading capacity, and controlled release behavior. Various physicochemical and performance evaluation parameters are studied to determine the suitability of the formulation for pharmaceutical applications.[19]

Particle Size Analysis

Particle size significantly influences drug release rate, stability, and skin penetration in topical applications. Microsponge particle size generally ranges from 5–300 µm. Smaller particles provide faster drug release due to increased surface area, whereas larger particles offer prolonged release.

Particle size can be determined using

- Optical microscopy
- Laser diffraction method
- Dynamic light scattering (DLS)

Uniform particle size distribution indicates controlled emulsification during preparation.[20]

Surface Morphology

Surface morphology is examined using Scanning Electron Microscopy (SEM). SEM images typically reveal spherical particles with porous, sponge-like surfaces.

The presence of interconnected pores confirms successful formation of microsponges. Surface smoothness and structural integrity also indicate stability of the formulation.[21]

Entrapment Efficiency (EE%)

Entrapment efficiency measures the percentage of drug successfully incorporated into the microsponge matrix. It is calculated using the formula:

$$EE(\%) = \frac{\text{Amount of drug entrapped}}{\text{Total amount of drug added}} \times 100$$

High entrapment efficiency indicates effective drug–polymer compatibility and optimized preparation conditions. Factors affecting EE% include polymer concentration, drug solubility, and stirring speed.

Drug Content Analysis

Drug content analysis ensures uniform distribution of drug within microsponges. The accurately weighed microsponge sample is dissolved in a suitable solvent, filtered, and analyzed spectrophotometrically or by HPLC. Uniform drug content ensures batch-to-batch reproducibility and therapeutic consistency.[22]

Porosity Determination

Porosity is a critical parameter that influences drug loading and release rate. Higher porosity facilitates faster diffusion of drug molecules.

Porosity can be measured using

- Mercury intrusion porosimetry
- Liquid displacement method
- Gas adsorption techniques

Controlled porosity ensures predictable release kinetics.[23]

In Vitro Drug Release Studies

In vitro release studies are performed using USP dissolution apparatus (Type I or II) depending on dosage form. The microsponge formulation is placed in dissolution medium, and samples are withdrawn at predetermined intervals. The amount of drug released is analyzed using UV–Visible spectrophotometry or HPLC. Drug release data are fitted into kinetic models such as

- Zero-order kinetics
- First-order kinetics
- Higuchi model

- Korsmeyer–Peppas model

These models help in understanding the mechanism of drug release (diffusion, erosion, or combined mechanism).[24]

Production Yield

Production yield indicates the efficiency of preparation method. It is calculated as:

$$\textbf{Production Yield (\%)} = \frac{\text{Practical mass of product obtained}}{\text{Total mass of drug + polymer (and other solid excipients)}} \times 100$$

High production yield reflects minimal material loss during formulation.[25]

Compatibility Studies

Drug–polymer compatibility is evaluated using

- Fourier Transform Infrared Spectroscopy (FTIR)
- Differential Scanning Calorimetry (DSC)
- X-ray Diffraction (XRD)

FTIR identifies chemical interactions, DSC detects thermal changes, and XRD determines crystalline or amorphous nature of drug in microsponge matrix.
Absence of significant interaction confirms stability of formulation.[26]

True Density and Bulk Density

Density measurements help in determining flow properties and compressibility for further formulation into tablets or capsules. Bulk density and tapped density are measured, and Carr's Index and Hausner ratio are calculated to evaluate flow characteristics.[27]

Zeta Potential

Zeta potential indicates surface charge of microsponge particles. It helps in predicting stability of suspension systems. High absolute zeta potential values indicate good physical stability due to electrostatic repulsion.[28]

Stability Studies

Stability studies are performed as per ICH guidelines under different temperature and humidity conditions (e.g., 25°C/60% RH and 40°C/75% RH). Formulations are evaluated periodically for changes in drug content, particle size, and release behavior. Stability data ensure shelf-life and safety of product.[29]

10. FACTORS AFFECTING MICROSPONGE FORMULATION

The performance of a microsponge drug delivery system is strongly influenced by formulation and process variables. Proper optimization of these factors is essential to obtain desired particle size, porosity, entrapment efficiency, and controlled drug release behavior.

Polymer Type

The selection of polymer plays a crucial role in determining structural integrity, porosity, and drug release kinetics of microsponges. Polymers such as Eudragit RS 100, Eudragit RL 100, ethyl cellulose, and polymethacrylates are commonly used due to their biocompatibility and controlled permeability characteristics. Hydrophobic polymers generally provide sustained drug release, whereas more permeable polymers allow faster drug diffusion. The molecular weight and permeability of polymer directly influence drug release rate and mechanical stability of microsponges.[30]

Polymer Concentration

Polymer concentration significantly affects particle size, entrapment efficiency, and release profile. Increasing polymer concentration increases viscosity of the internal phase, resulting in larger emulsion droplets and hence larger microsponge particles.

Higher polymer content enhances entrapment efficiency due to formation of thicker polymer matrix, but excessive polymer may slow down drug release excessively. Therefore, optimization is required to balance sustained release and therapeutic effectiveness.[31]

Drug–Polymer Ratio

The ratio of drug to polymer influences drug loading capacity and release characteristics. Higher drug loading may lead to increased initial burst release due to surface deposition of drug. An optimal drug–polymer ratio ensures uniform distribution of drug within the porous matrix and controlled diffusion through interconnected channels.[32]

Drug Properties

Physicochemical properties of the drug such as solubility, molecular weight, and stability affect microsponge formulation. Highly water-soluble drugs may diffuse out during preparation, resulting in lower entrapment efficiency. Lipophilic drugs are generally better suited for microsponge systems due to stronger affinity with hydrophobic polymers.[11] Drug stability in selected solvent system must also be considered to prevent degradation.

Type of Solvent

The choice of organic solvent affects droplet formation, polymer precipitation, and porosity. Volatile solvents such as dichloromethane and ethanol are commonly used in quasi-emulsion solvent diffusion method. Solvent diffusion rate influences pore formation and internal structure. Rapid solvent removal may create highly porous microsponges, whereas slow evaporation may result in denser particles.

Stirring Speed

Stirring speed during emulsification controls droplet size and hence final particle size. Higher stirring speeds produce smaller droplets, resulting in smaller microsponges with larger surface area and faster drug release. Lower stirring speeds produce larger particles with prolonged release profile. Thus, stirring speed must be optimized to achieve desired particle size distribution.[33]

Surfactant Type and Concentration

Surfactants such as polyvinyl alcohol (PVA) stabilize the emulsion system. Insufficient surfactant concentration may lead to particle aggregation, whereas excessive surfactant can affect porosity and drug loading. Proper surfactant concentration ensures uniform particle formation and stability of dispersion.[34]

Volume of Internal and External Phases

The ratio of internal organic phase to external aqueous phase affects solvent diffusion rate and particle formation. Larger external phase volume enhances solvent diffusion and promotes formation of porous microsponges. Improper phase ratio may cause irregular particle size and reduced production yield.

Temperature

Temperature during preparation influences solvent evaporation rate and polymer solidification. Higher temperature accelerates solvent removal, potentially increasing porosity. However, excessive temperature may degrade heat-sensitive drugs. Therefore, controlled temperature conditions are required during formulation.

Cross-Linking Density

In polymerization-based methods, cross-linking density determines mechanical strength and porosity of microsponges. Higher cross-linking results in rigid structure and slower drug release. Lower cross-linking may increase porosity but reduce structural stability.

Drying Method

Drying conditions (air drying, vacuum drying, oven drying) influence final particle characteristics. Rapid drying may collapse pore structure, whereas controlled drying preserves porous architecture. Proper drying ensures stability and prevents agglomeration.[35]

11. PHARMACEUTICAL APPLICATIONS OF MICROSPONGESX

Topical Drug Delivery

Topical delivery remains the most established application of microsponge technology. Microsponges are widely used in dermatological preparations to reduce irritation and provide sustained drug release. Drugs such as benzoyl peroxide, tretinoin, antifungal agents, and corticosteroids have been successfully formulated into microsponge-based gels and creams. The porous structure reduces direct contact of drug with skin, thereby minimizing irritation and erythema.

Microsponge systems also prevent drug degradation due to environmental exposure, improving stability and shelf life of topical products.[5] Controlled release maintains therapeutic concentration over extended periods, reducing frequency of application and enhancing patient compliance.[36]

Anti-Acne Therapy

Microsponge encapsulation of benzoyl peroxide significantly reduces skin irritation while maintaining antibacterial efficacy against *Propionibacterium acnes*. The gradual release of active ingredient minimizes dryness and peeling associated with conventional formulations.

The commercial success of microsponge-based tretinoin formulations further supports its effectiveness in acne management.

Antifungal and Antibacterial Therapy

Microsponge-based gels loaded with antifungal drugs such as fluconazole and miconazole provide prolonged drug retention at the site of infection. The sustained release enhances therapeutic outcome and reduces dosing frequency. In antibacterial therapy, microsponges

improve local drug concentration while minimizing systemic absorption. This approach is particularly beneficial in superficial infections where localized treatment is required.

Anti-Inflammatory Therapy

Non-steroidal anti-inflammatory drugs (NSAIDs) incorporated into microsponges demonstrate prolonged analgesic effect with reduced gastrointestinal irritation when used in topical preparations. The porous matrix controls diffusion of drug, reducing peak plasma concentration and associated side effects. This application is valuable in arthritis, musculoskeletal disorders, and localized inflammatory conditions.

Oral Drug Delivery

Although initially designed for topical application, microsponges have been explored in oral controlled release systems. In oral formulations, microsponges protect drugs from harsh gastric environment and provide sustained release in gastrointestinal tract. They are particularly useful for drugs requiring prolonged therapeutic action and reduced dosing frequency.

Colon-targeted microsponge systems have also been developed for treatment of inflammatory bowel disease and colorectal cancer.[37]

Cosmetic Applications

Microsponge technology is widely used in cosmetic formulations such as sunscreens, moisturizers, anti-aging creams, and deodorants. In sunscreen products, microsponges release UV filters gradually, reducing skin irritation and enhancing long-lasting protection.

In anti-aging products, active ingredients such as retinoids are delivered in controlled manner to minimize irritation while maintaining efficacy. The porous structure also absorbs excess oil from skin, making microsponges useful in oil-control cosmetics.[38]

Controlled Release in Combination Therapy

Microsponge systems allow simultaneous incorporation of multiple drugs with controlled release profiles. Combination therapy using microsponges can enhance synergistic action while minimizing drug interactions and side effects. This approach is particularly promising in dermatological and antifungal treatments.

Targeted Drug Delivery

Recent research focuses on modifying microsponge surfaces for targeted delivery. Functionalization with ligands or antibodies enables site-specific drug delivery, reducing systemic toxicity. Such systems may be applied in cancer therapy, where localized drug release at tumor site is desirable.[39]

12. FUTURE PROSPECTIVES

Development of Nanosponges

Nanosponges represent the nanoscale extension of microsponge technology. These structures provide improved bioavailability and enhanced penetration through biological membranes.

Cyclodextrin-based nanosponges have shown promising results in targeted drug delivery and anticancer therapy.

Biodegradable Polymer Systems

Future research aims to develop biodegradable microsponge systems using polymers such as polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA).

Biodegradable systems eliminate the need for removal after drug release and reduce long-term toxicity concerns.

Stimuli-Responsive Microsponges

Advanced microsponge systems responsive to pH, temperature, enzymes, or external stimuli are under investigation.

Such smart systems release drug only under specific physiological conditions, improving precision of therapy.[40]

Application in Cancer Therapy

Surface-modified microsponge systems may enable localized delivery of chemotherapeutic agents, reducing systemic toxicity.

Targeted delivery using ligand-conjugated microsponges can enhance drug accumulation in tumor tissues.

Gene and Protein Delivery

Emerging research explores microsponge-like porous systems for delivery of proteins, peptides, and nucleic acids.

Such systems may improve stability and controlled release of sensitive biological molecules.

Scale-Up and Commercialization

Although microsponge technology shows promising laboratory results, large-scale manufacturing and regulatory approval remain important challenges.

Standardization of preparation methods and quality control parameters will facilitate commercialization.[41]

13. SUMMARY

This work highlights microsponge technology as an advanced Novel Drug Delivery System (NDDS) designed to overcome limitations of conventional dosage forms such as frequent dosing, fluctuating plasma levels, and systemic side effects. Microsponges are porous, cross-linked polymeric microspheres (5–300 µm) that entrap drugs within interconnected channels, enabling controlled and sustained release. Initially developed for topical acne therapy, their application has expanded to oral, transdermal, cosmetic, and targeted drug delivery systems. Various preparation methods—particularly quasi-emulsion solvent diffusion—allow optimization of particle size, porosity, and entrapment efficiency. Critical formulation variables include polymer type, drug–polymer ratio, solvent system, and stirring speed. Comprehensive characterization using SEM, FTIR, DSC, XRD, drug release studies, and stability testing ensures quality and reproducibility. Overall, microsponge systems provide sustained release, reduced irritation, improved stability, and enhanced patient compliance, making them a versatile and promising platform for modern pharmaceutical applications.

14. CONCLUSION

Microsponge drug delivery systems represent a significant advancement in controlled and sustained release formulations. Their porous, cross-linked polymeric structure enables gradual drug diffusion, minimizing systemic toxicity and improving therapeutic outcomes. These systems are compatible with both hydrophilic and lipophilic drugs and can be incorporated into multiple dosage forms, particularly topical and oral preparations. Optimized formulation parameters such as polymer concentration, cross-linking density, and surfactant

levels are crucial for achieving desired entrapment efficiency and release kinetics. Characterization techniques ensure stability, compatibility, and reproducibility of the final product. Despite challenges in scale-up and regulatory approval, ongoing research into biodegradable polymers, nanosponges, and stimuli-responsive systems is expanding their clinical potential. In conclusion, microsponge technology offers a safe, effective, and adaptable approach for enhancing drug delivery performance and holds strong promise for future pharmaceutical innovations.

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