**Microsponge : A Novel drug delivery system**

Karishma A. Nikose, Laxmikant N. Barde, Suraj Rajurkar, Shrikant Kamle, Girish Gulhane, Yashkumar Meshram, Rosalin Alexander

*Jagadambha Institute of Pharmacy and Research, Kalamb, Yavatmal (M.S.)*

**Abstract**
Microsponges are small spongy spherical particles with microporous surfaces. They can also increase stability, reduce side effects, and alter drug release. Microsponge systems are based on microscopic polymeric microspheres that can suspend or retain a variety of substances that can be incorporated into products such as gels, creams, liquids, or powders. The outer surface is usually porous, allowing material to flow continuously from the individual. Microsponges are designed to efficiently dispense medicinal ingredients with minimal dosage, increase safety, reduce side effects, and improve drug release. It is considered safe because it does not contain antibiotics in its formula and therefore contains less bacteria. That is why it is used in many sterile preparations such as ophthalmic, parenteral, and others. This review provides an overview of current knowledge on the approach, planning, and process of microsponge technology, and the industrial design, application, and evaluation of microsponges in various forms. Microsponges are mainly used for cosmetic purposes but have also been used orally more recently.

 **Keywords:** Polymer solution, Microsponge.

**MICROSPONGE**

Points to be covered in this topic

* Definition
* Ideal properties
* Preparation of microsponge
* Mechanism of drug release from microsponge
* Microsponge drug delivery system
* Advantages of microsponge based on drug delivery system
* Evaluation of microsponges
* Factor affecting drug release from microsponge
1. **Introduction**

Microsponge particles are small, immobile, non-destructive and do not penetrate the skin. Instead, they fill in small gaps and cracks in the skin and gradually release the drug when the skin needs it. The micro-sponge system prevents excessive accumulation of ingredients in the epidermis and dermis. The micro-sponge technique reduces their irritation without reducing the effects of strong chemicals. In the next wash, the hollow balls are cleaned. In the past few years, the development of new chemical microsponge to modify and control drug release behavior has received a lot of attention. The clinical parameters of the drug and the duration of action can be changed by delivery. Consumer interest in skin care products and treatments is increasing due to the use of ingredients such as alpha-hydroxy acids and vitamins in cosmetics. These ingredients are especially beneficial for aging or damaged skin. Although helpful, many of these ingredients can be irritating. This irritation is characterized by burning, itching or redness and is often seen in people with sensitive skin. Models aware of this problem try to solve it in one of two ways. They reduce the cost of these components but sacrifice quality in the process. Microsponges are polymer delivery systems containing porous microspheres ranging in size from 5 to 300 µm. Microsponge is a porous material that can absorb many substances. They are small porous spheres with a large porous surface. They can also improve safety by changing drug delivery methods while reducing side effects. Microsponges are microporous materials that are often used for cosmetic purposes and more recently for oral care.

**1.1 Definition**

 Microsponges are small globules that can absorb skin secretions, thereby reducing the oil and shine of the skin. Microsponges are polymer delivery systems containing porous microspheres ranging in size from 5 to 300 µm. It is a granular distribution system containing microsponge, porous materials, which can capture various materials. They are small porous like spherical particles with large porous surface. They can also improve safety by changing drug release patterns while reducing side effects. Microsponges are microporous particles used mainly for cosmetic purposes and more recently for oral administration.

**1.2 Ideal properties of Microsponge Delivery System**

1. The structure of the microsponge should not deteriorate, that is, it should preserve its structural integrity.

2. It should be slightly soluble in water.

3. It should be stable when exposed to polymerization catalysts and polymerization conditions.

4. The monomers used in the design should not be forgotten.

5. MDS should not increase the viscosity of the mixture during preparation.

6. The size of the microsponge is about 10 to 25 µm in diameter.

**1.3 Preparation of microsponges**

According to the principles of the human body, there are two ways to package drugs into microsponges: one-step method (liquid-liquid suspension polymerization) or two-step method as discussed in liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques which are based on physicochemical properties of drug to be loaded. If the substance is mostly non-polar, it forms a porous structure called a porogen. Its chemical structure does not inhibit or activate polymerization and is stable against free radicals.



Fig. no. 1 One step and two step preparation of microsponges.

*1. Liquid-liquid suspension polymerization*

Generally, the monomer is first dissolved together with the product in a suitable monomer solution. It is then mixed in the aqueous phase, which often contains additives such as surfactants and dispersants to support the suspension. After a suspension is formed with droplets of the desired size, polymerization is initiated by activating or catalysing the monomers by high temperature or electricity. As polymerization continues, spherical structures are produced, consisting of thousands of microscopic sponges clustered together like fruit, forming a water web (Hainey et al., 1991). After the polymerization is completed, the material is cleaned and stored.

 

Fig. no. 2 Formation of Suspension for Preparation of Liquid-Liquid Suspension Polymerization

*2. Quasi-emulsion solvent diffusion*

When the drug is susceptible to the polymerization process, use the two-step method. Active substances with different chemicals in general: polymer compounds dissolve in organic solvents (internal phase). The solution was then poured into polyvinyl alcohol (external phase) with continuous stirring, allowing the solvent to evaporate, and the mixture was filtered to separate the microsponges. The resulting microsponges were dried and stored in a desiccator to ensure complete removal.

*3. Water-Oil-Water Emulsion Solvent Diffusion*

In this method, an internal aqueous phase containing the emulsifier is dispersed in the organic polymer liquid. The water-in-oil emulsion was redistributed in the aqueous phase containing PVA to form a second emulsion. In this way, both water-soluble and water-insoluble substances will be captured.

*4. Oil-in-Oil Emulsion Solvent Diffusion*

 According to this method, an emulsion with an internal phase containing an organic solvent is prepared. Dichloromethane is used as a volatile solvent in many preparations. The polymer used in it is polylactide glycolic acid with 85 openings as a layer. The internal phase is added dropwise to the dispersion medium and mixed continuously to obtain a microsponge.

 *5. Addition of porogen*

For this, a porogen such as hydrogen peroxide or sodium bicarbonate is present in the inner phase. The porogen is dispersed in the polymer solution to form a homogeneous dispersion and the product is redistributed in the water phase containing PVA. The action of adding hydrogen peroxide results in the formation of interconnected pores 5 to 20 µm in diameter.



Fig. no. 3 Preparation of microsponges by the quasi-emulsion solvent diffusion method

*6. Lyophilization*

In this method, the microspheres are converted into porous microspheres by rapid removal of the solvent, resulting in the formation of porous microspheres. This is done using chitosan hydrochloride. Microspheres were incubated in this solution and then lyophilized. Fragmentation and shrinkage of microparticles may occur due to rapid removal.

 *7. Vibration-hole aerosol generation method*

The vibrating aerosol generation process mainly prepares lipid bilayer silica particles in suspension form. Prepare foundation beads with tetraethyl orthosilicate, ethanol, water and hydrochloric acid heated at reflux to prepare the solution. The solution is diluted with a solvent-containing surfactant and mixed again to obtain a dispersed droplet. The resulting microspheres are encapsulated in liposomes.

 **1.4** **List of drug used in the preparation of microsponges**

Paracetamol

Miconazole

Benzoyl peroxide

Curcumin

Ketoprofen

Tretinoin

Fluconazole

Hydroquinone

Acyclovir sodium

Ibuprofen

Retinol Prednisolone

Erythromycin

Indomethacin

Mupirocin

**1.5 Polymers used for the preparation of microsponges**

Eudragit RS 100 and RL 100

Ethyl cellulose

Polystyrene

Acrylic polymer

PHEMA

Carbopol 934

**1.6 Drug Release Mechanism from Microsponges**

Drug release from microsponges occurs in one or more response times. More external factors such as (temperature, pressure, pH and solubility)

1. Pressure Friction or pressure releases :- Rubbing or pressure applied can release active ingredients from microsponge onto the skin.

2. Temperature :- The production of microsponge components is often affected by changes in temperature. The higher the temperature of the skin, the greater the flow and discharge process.

3. pH value :- By changing the layer of micro sponges, active ingredients can be released according to the pH value.

4. Solubility :- Microsponges contain hydrophilic active ingredients such asantibacterial and antifungal agents that are released when exposed to water. The release can be done by diffusion, but the partition coefficient of the material between the microsponge and the outside must be taken into account.

 **1.7 Properties of microsponges**

In addition, research studies were conducted to determine the following in prepared microsponges:
• Particle size

• Product yield

• Loading Efficiency

**•** Surface topography

**•** In vitro Release studies

***Particle size***

Particle size of microsponge is evaluated by a light microscope or electron microscope. Particle size affects the performance of design. Factors affecting size are chemical Polymer ratio and emulsifier concentration. As that drug: Polymer ratio increases, the particle size decreases, and the increase in emulsifier concentration results in larger particles. The size was determined using a light microscope and a micrometer level spread a small piece of microsponge in a clean glass, put liquid paraffin on it, and cover it with a lid.

Average Particle Size is calculated by measuring 100 particles per batch.

***Product yield***

The ratio of drug to polymer will also affect the production efficiency, an increase in the drug: polymer ratio will also increase the production efficiency.

production efficiency production capacity = Actual amount / Theoretical Amount x 100

***Loading Efficiency***

The amount of drug loaded into the microsponge is physicochemical depending on its features. There are two ways to transport drugs: active and passive. Passive charging is the most efficient. Increased drug use: polymer ratio to improve drug loading efficiency

Drug loading efficiency is measured as:-

**Drug Loading Efficiency = Drug Loading / Theoretical Drug Loading x 100**.

***Surface* Topography**

Different techniques such as Scanning Electron Microscopy (SEM) and transmission electron are used in topography. microscopy (TEM) etc. SEM is widely used in the preparation of microsponges.

***In******vitro******Release******studies***

In vitro released studies were performed using dissolution apparatus USP XXIII equipped with new baskets containing 5 µm stainless steel mesh. Dissolution rate was measured at 37°C under 150 rpm speed. The dissolution medium is selected according to the solubility of the active ingredient. Remove the sample from the dissolution medium and analyze using the appropriate suitable method.

**1.8 Application area of ​​microsponge**

It offers a structure with many options for pharmaceutical and cosmetic production. Commercial products that use microsponge delivery include a variety of moisturizers, specialty peels, and sunscreens.

*1.* ***Topical drug delivery using microsponge technology***

(A) Benzoyl peroxide (BPO) is often used in topical creams for the treatment of acne and Hong Kong foot. Controlling the release of BPO into the skin through the microsponge delivery system can reduce side effects.

(B) Microsponge-based topical formulation of mupirocin used as an antibiotic for the skin to induce drug release. The absorption of mupirocin in the skin by the microsponge delivery system, compared with conventional mupirocin gel and commercially available mupirocin, indicates that this delivery is a good practice in the treatment of primary and secondary skin diseases.

***2. Microsponges for Oral application***

Microsponge system provides control of the drug from the mouth to the digestive system and after exposure to special enzymes, the drug is released in the intestine. The microsponge system has been shown to improve the decomposition of harmful chemicals by trapping them in their pores. Oral application of ketoprofen by semi-emulsion solvent diffusion method using Eudragit RS100 followed by preparation of micro sponge tablets by direct compression method, the compressibility of the physical mixture of drug and polymer due to plastic deformation of drug and polymer, very good. Sponge-like microsphere structure.

***3. Microsponges for bone and tissue engineering***

Bone-like composites were prepared by mixing pre-prepared polymethyl methacrylate monomer powder with two types of water-dispersed calcium-deficient particles of tricalcium phosphate and hydroxyapatite. The final compound looks porous and grows like a small sponge.

**1.9 Key Features of Microsponge Delivery System**

* Microsponges are stable at pH 1-11. They are thermally stable up to 1300 C.
* The average pore size is 0.25um, it is resistant to bacteria and has antibacterial properties, so there is no need to add preservatives to the milk.
* Microsponges are cost-effective compared to other drug delivery systems.
* They are compatible with most additives and media.
* Micro sponges have a high bearing capacity (50-60% by weight), but remain as an ultra-fine, free-flowing powder.
* Good oil management, oil absorption capacity up to 6 times its weight.
* Easy development of new products. Improved thermal, physical, and chemical stability.

**1.10 Advantages**

***1.10.1 Advantages over Traditional Formula***

Topical topology, because its chemical formula is designed to be applied to the skin. After application, these products release their active ingredients, forming a dense, dense layer. Unlike microsponge, it prevents mixing of components in the epidermis and dermis. Microsponge technology can reduce the irritation of strong drugs while maintaining their effects.

* + 1. ***Advantages over ointments***

Cosmetic products are usually oil, stickiness and so on. are unsatisfactory, and patients rarely follow them. These tools must have active medication to work properly due to their poor use of medication that causes discomfort and is not suitable for many users. Another disadvantage of cosmetics is the uncontrolled evaporation of the active ingredients, the smell and the incompatibility of the drug with the carrier.

**2. Microsponge Drug Delivery System**

Microsponge Delivery System (MDS) is a combination of porous polymer containing porous microspheres that can store various components such as perfume, sunscreen, emollient, antifungal, anti-bacterial and anti-inflammatory. , VESAIR. They are used only to prolong the life of cosmetics. Microsponges are small spherical spongy particles that have a lot of interaction on the uneven surface, and microsponges can vary in size, often in diameter. 5 to 300 μm, depending on the level of nap. In addition, they can increase stability, reduce side effects, change drug release and control the amount of drug release, thus making them suitable for cosmetic use. Therefore, optimized microsponges can be prepared by optimizing formulation parameters such as drug:polymer ratio and mixing/mixing speed. Microsponges have many advantages that make them versatile in drug delivery. Microsponges can remove or trap many chemicals, which can be formulated into gels, creams, liquids or powders for topical use. When the formula is applied to the skin, MSD rapidly releases ingredients in response to other stimuli (friction, temperature, pH). Recent studies have shown that microsponges can be used in oral diseases. Microsponge systems have been shown to improve the separation of water-insoluble chemicals by using chemicals in the pores of the microsponge system.

***Advantages of microsponge based delivery system***

1. The microsponge cannot be penetrated by bacteria due to its size.
2. There is no need to use preservatives to extend shelf life and product stability similar conditions of microsponges make the internal space very high and therefore they have a high charging capacity
3. Undesirable properties such as oiliness and stickiness or ingredients with an undesirable feel or odor can be greatly reduced, making them suitable for topical application to the skin
4. A useful product can be obtained by converting the liquid into powder without water
5. Formulation MDSs increase efficacy and increase the release of cosmetic substances.
6. Microsponges have interconnected cavities in a non-collapsing structure with a large porous surface.
7. It is stable in the pH range of 1-11 and at temperatures up to 130°C.
8. Microsponges in Pharmaceutical Applications: Cosmetic, over-the-counter, and personal care products use microsponge delivery systems to improve their efficacy, safety, and aesthetic appeal. Microsponges have many uses, especially in cosmetics, but recently they have also taken orally. It is stated in many certificates that it is used as a reinforcement due to its high loading capacity and long-term release capacity.
9. Long-lasting cosmetics: Microsponges can capture the colors in various cosmetic products such as blush and lipstick, helping them to last longer. As mentioned earlier, microsponge helps to spread evenly and increases protection. Cosmetics made with microsponges will be very soft.

**3. Evaluation method of microsponge**

**3.1. Particle Size Evaluation**

Other particle size distribution using an optical machine or an electron machine. Determination of the size of microsponges can be done by laser diffraction or other suitable methods. The value (d50) of all formulations will be displayed as average dimensions. Particle sizes greater than 30 µm give a sandy appearance, so use sizes between 10 and 25 µm in the final formulation.

**3.2. Morphology and Surface Topography**

Various techniques such as photon correlation spectroscopy (PCS), transmission electron spectroscopy (TEM), and scanning electron microscopy (SEM) are used to examine the morphology of microsponge morphology.

**3.3. Determination of loading efficiency:** The loading efficiency (%) of the microsponges can be calculated as follows:-

$Loading efficiency=\frac{Actual Drug content in microsponges }{Theoretical drug content }$ **× 100**

**3.4. Determination of production yield:** The production yield of the microsponges can be determined by:

$Production yield =\frac{Practical mass of microsponges }{Therotical mass (polymer+ drug) }$ **× 100**

**3.5. Determination of true density**- The actual density of microsponges can be measured using a pycnometer in the presence of helium and is several orders of magnitude better. can be calculated from the average.

**3.6. Compatibility study**- The search can be done using Thin Layer Chromatography (TLC) and Fourier Transform Infrared Spectroscopy (FT-IR). The effect of polymerization on crystallinity can be studied by powder X-ray diffraction (XRD) and differential scanning calorimetry.

 **3.7. Release evaluation:** The release of microsponges can be controlled by contamination or other factors (such as humidity, pH, friction, temperature). This version is used to improve the quality of the product.

**3.8. Resiliency:** The viscoelastic properties of softer or harder microsponges for bullet production can be adjusted according to the needs of the final formulation. Increasing the number of connections will decrease the output.

**3.9. Stability study:** Gel formulations are tested for safety according to ICH specifications. Collect the gel in clean, painted, collapsible aluminum tubes and store in several replicates in a vacuum chamber at 40 ± 2 °C and 75 ± 5% relative humidity. Changes in gel shape, pH, and in vitro release profile were evaluated at 30, 60, and 90-day intervals.

**Table 1:** List of marketed products based on microsponges

|  |  |  |
| --- | --- | --- |
| 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 | SkinMedicaInc |
| Sports cream RS and XS | Anti-inflammatory | Embil Pharmaceutical Co. Ltd. |
| Salicylic Peel 20 | Excellent exfoliation | Biophora |
| Oil free matte block SPF 20 | Sunscreen | Dermalogica |
| Lactrex™12% | Moisturizing Cream | SDR Pharmaceuticals, Inc |
| Ultra Guard | Protects baby’s skin | Scott Paper Company |

1. **Drug release mechanism from microsponges**

It causes a slow release of one or more external stimuli or components contained in microsponges.

**4.1.** **Temperature-triggered** **release**

In this process, active substances are released into the body when the temperature changes. At room temperature some substances flow very viscous without interfering with porous systems. However, when applied to the skin, the temperature of the skin causes an increase in pressure, which causes the drug to be released.

**4.2. Pressure-triggered release**

In this device, the micro sponge releases the trapped drug when the dosage form is brushed on the skin. The amount of drug released is determined by many properties of the microsponge, including process, strength and material type.

* 1. **Solubility Triggered Release**

Porous systems containing water-soluble excipients release drugs upon contact with water. Diffusion mechanisms include the distribution coefficient of the drug and sometimes external processes that lead to its release.

**4.4. pH triggered release**

In this method, a change in pH causes the drug to be released by changing the layer of the microsponge to achieve the pH function.

**4.5. Hypothetical drug release mechanism**

The drug is encapsulated and added to the carrier. Due to its open structure, the drug can enter and exit the microsponge system with the carrier until it is stabilized. This causes chemical saturation of the carrier. When the formulation is applied to the skin, it causes the carrier to become unsaturated and unstable. To create this balance, the drug will flow from the carrier to the skin until the carrier dries or is absorbed. Then, over time, active substances are gradually released from the micro-sponge located on the surface of the stratum corneum. Carriers play an important role in the creation of microsponges as they allow slow absorption and support of the active ingredients. Accordingly, the carrier must be chosen in such a way as to reduce the solubility of the components. The dosage form will have both free and embedded drug moieties to prevent premature leaching of the drug from the polymer.

**5. Factors affecting drug release by microsponges**

1. Physicochemical properties of embedded API.

2. Physical parameters of microsponges such as pore size, volume, particle size, and flexibility.

3. Properties of micro sponge dispersion carrier.

4. Pore properties, monomer composition, etc.

Microsponges are a new technology developed for drug delivery systems and more recently for oral control. It has many advantages. Microsponges are well-designed medical devices that can deliver drugs to the area with a small amount of drug, increase safety, reduce side effects, and control drug release. The main future challenge is to develop delivery systems for oral peptide delivery with different types of polymers. Microsponges would be an excellent drug delivery system. The search for microsponge drug delivery systems that can control release rates for specific parts of the body will be further refined with significant health implications in the coming years, and many microsponge products have been approved; Many are currently under development and evaluation.

1. **Future prospects**

Microsponges are new devices designed for drug delivery systems and more recently for oral drug delivery. It has many advantages. Microsponges are well-designed medical devices that can deliver drugs to the area with a small amount of drug, increase safety, reduce side effects, and control drug release. The main future challenge is developing a delivery system for oral peptide delivery with different polymers. Microsponges would be an excellent drug delivery system. The search for microsponge drug delivery systems that can control the rate of release to specific parts of the body will be further refined in the coming years, with important therapeutic implications, and many microsponge products have been approved; Many products are currently under development and evaluation.

**7. Conclusion**

Microsponge delivery system is a new technology that controls the release of microporous beads with active ingredients that can reduce side effects and control treatments. Microsponge drug delivery systems are believed to reduce side effects, increase safety, increase elegance, ease of construction, and also allow entry of their products. The microsponge system is non-mutagenic, non-irritating, non-toxic and non-allergenic. The technology is currently used in pharmaceuticals, cosmetics, (OTC) over-the-counter skin care, and sunscreens. Today, drug delivery technology can lead to a better understanding of the treatment of many diseases and conditions.

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