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Review On Microsponges- As a New Approach in Innovative Drug Delivery System

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ABSTRACT

Microsponges are porous microsphere-based polymeric delivery devices. They are tiny, spherical particles with a porous surface that resemble sponges. Additionally, they might improve stability, lessen side effects, and favorably alter medication release. The numerous positive aspects of microsponge technology make it a flexible means of drug administration. A designed product, such as a gel, cream, liquid, or powder, can be made using Microsponge Systems, which are based on microscopic, polymer-based microspheres that can suspend or entrap a wide range of compounds. Typically, the outer surface is porous, allowing materials to continuously flow out of the sphere.

Keywords: Microsponge, Controlled drug release, topical formulation, gel.

INTRODUCTION

The health care system is significantly impacted by medication delivery systems that can precisely control the rate of release and direct pharmaceuticals to particular parts of the body [1]. They are polymeric and have a surface that is very porous with small, spherical particles that resemble sponges. Additionally, they improve stability, lessen side effects, and favourably alter medication release.

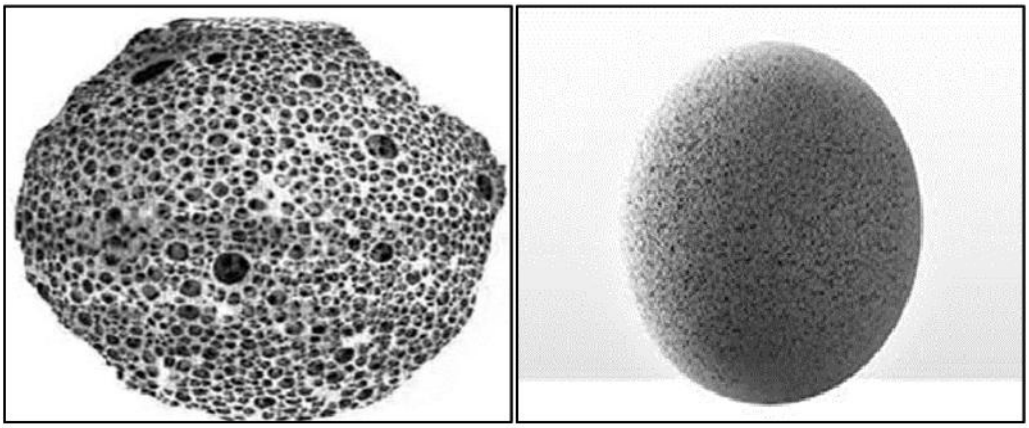
Due to its numerous distribution methods and microsponge technology, it is a flexible medication delivery system. A designed product can be made using Microsponge Systems, which are built on tiny, polymer-based microspheres that can suspend or entrap a range of chemicals [2]. Additionally, microsponges have the ability to transport pharmaceutical active components to a specified region effectively and at a low concentration, which lessens the risk of severe systemic degradation[3,4]. Solid phase porous microspheres are another name for the patented micro particulate system known as the Microsponge Delivery System (MDS)[5]. With a large porous surface to entrap a variety of active agents with varying pharmacological activities administered in different doses that can be released at the desired site for absorption[6], highly crosslinked, polymeric porous microspheres with numerous interconnected voids in the particle, loaded with active agent are highly composed crosslinked [7], polymeric porous microspheres with large porous surfaces[8]. The microsponges can have up to 250000 pores per sphere, and their sizes range from 5 to 300 mm in diameter. Microsponges are made to effectively deliver a pharmaceutical active ingredient at a low dose, minimize side effects, improve stability, and alter the drug release profile. As a result, each microsponge has a sizable reservoir inside of it that can hold up to its own weight in active agent [9–11].

Microsponge drug delivery systems may have the following characteristics [12–15]:
1. Be stable over a pH range of 1 to 11.
2. They maintain their stability at 130 °C.
3. Do not require the addition of a preservative because their pore size of 0.2 mm prevents bacteria from penetrating them.
4. Possess a high loading capacity of between 50% and 60%.
5. Free flow characteristics and is productive compared to its cost.
6. Offer good compatibility with various ingredients and vehicles.

Active molecules that are trapped in microsponges have the following characteristics [16, 17]:
1. Products like creams, gels, powders, lotions, and soaps can contain active ingredients that are trapped in microsponge.
2. In order to achieve the desired product characteristics, a few factors are taken into account when creating the vehicle.
3. It must either be completely miscible in monomer or have the ability to become miscible by adding a small amount of a solvent that is not water miscible.
4. It shouldn't make the mixture more viscous during formulation and should be inert to monomers.
5. It must be water insoluble or almost barely soluble.
6. The spherical structure of the microsponges shouldn't collapse.
7. It must be stable when in contact with the polymerization catalyst and under polymerization conditions.
8. Actives must have a limited ability to dissolve in the vehicle.
9. The microsponges' payload and polymer design must be optimized for the required release rate over the allotted time.

Microsponge drug delivery system benefits: [18, 19]:
1. Improves the performance of the product.
2. Reduces irritation while boosting patient compliance.
3. Enhances the product's elegance. It can be included in various formulations.
4. Has excellent chemical, physical, and thermal stability.
5. Non-allergenic, non-toxic, non-mutagenic, and irritant.
6. Powderizes liquids to facilitate better material handling.
7. enhances medication bioavailability.
8. Boosts the effectiveness of treatment.
9. MDS have a wider range of chemical stability, a higher payload, and are simpler to formulate than other technologies like liposome and microencapsulation.
10. More adaptability in formulation.
11. Flexible enough to create new product forms [20].

Typical View Of Microsponges:



(A) (B)

Fig 1: (A) Highly Porous structure of microsponges (B) Microsponges

Benefits over other formulations: [21]
Microsponges have a number of benefits over other products on the market.

Conventional formulations:
The outer layers of the skin are the target of conventional formulations of topical medications. After use, these products release their active ingredients. They deliver an active ingredient layer that is concentrated and quickly absorbed. The epidermis and dermis subsequently experience an excessive buildup of ingredients. By gradually delivering the active ingredient to the skin, the microsponge system can significantly reduce drug side effects like irritation without reducing its effectiveness.

Microencapsulation and Liposome:
In comparison to other technologies like microencapsulation and liposomes, the MDS may offer some advantages. In microcapsules, the rate of active release is typically unpredictable. Once the wall is broken, the actives that are inside the microcapsules will be released. The capacity, formulation, chemical stability, and microbial stability of liposomes are all limited.

Ointments:
Due to their visually offensive, viscous, and greasy nature, ointments have lower patient compliance. Because ointments are ineffective as drug delivery systems and require high concentrations of active ingredients to be effective, they irritate and sensitize people.

Method Of Preparation:
The preparation process consists of two steps: liquid-liquid suspension polymerization and quasi-emulsion solvent a diffusion technique, both of which are based on the physico-chemical characteristics of the drug to be loaded [22].

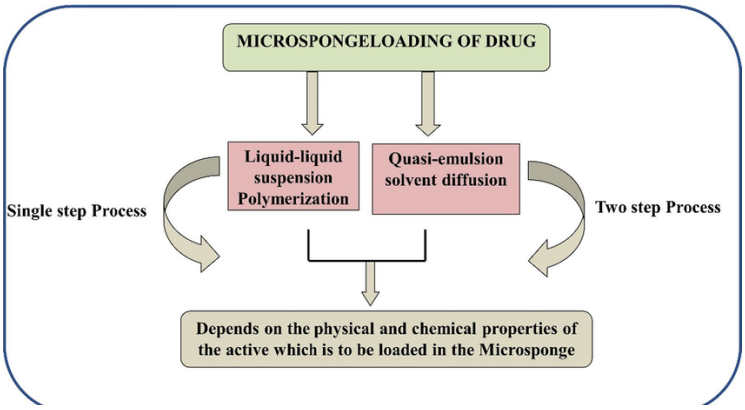


Fig.2: Method Of Preparation

a) Liquid-liquid suspension polymerization
b) Quasi-emulsion solvent diffusion

a) Liquid-liquid suspension polymerization:
In this procedure, the immiscible monomers are first dissolved with the active ingredients in an appropriate solvent before being dispersed in an aqueous phase that contains surfactants or suspending agents to aid in the formation of suspension. Then, either by raising the temperature, applying radiation, or adding a catalyst, the polymerization is triggered. As a result of the polymerization process, a reservoir-type system with a spherical structure is created. The solvent is eliminated following the polymerization process, leaving the microstructure, or microsponges [23-25].

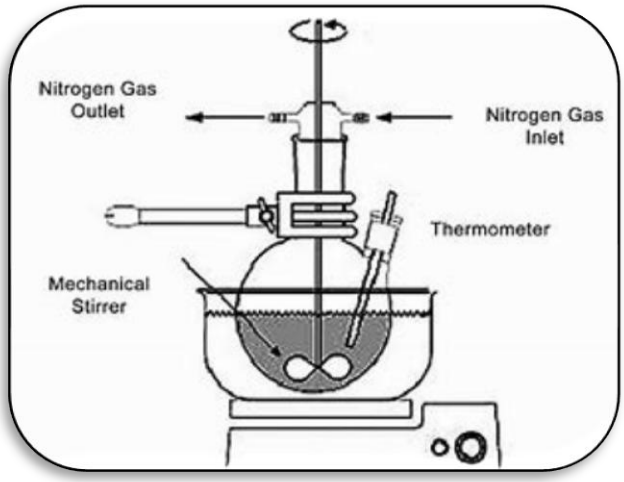


Fig. 3: Liquid-liquid suspension polymerization

b) Quasi-emulsion solvent diffusion:
A quasi-emulsion solvent diffusion method (two-step process) was also used to create microsponges, using an internal phase that contained a polymer, such as Eudragit, dissolved in ethyl alcohol. The drug is then gradually added to the polymer solution and dissolved using ultrasonication at 350 degrees Celsius. To help the plasticity, a plasticizer like triethyl citrate (TEC) was added. The external phase, which contains polyvinyl alcohol and distilled water, is then added to the internal phase while being continuously stirred for two hours.
The solution is then filtered to get rid of the tiny sponges.

The product (micro sponges) was cleaned before being dried for 12 hours in an air-heated oven at 40°C [23-28].

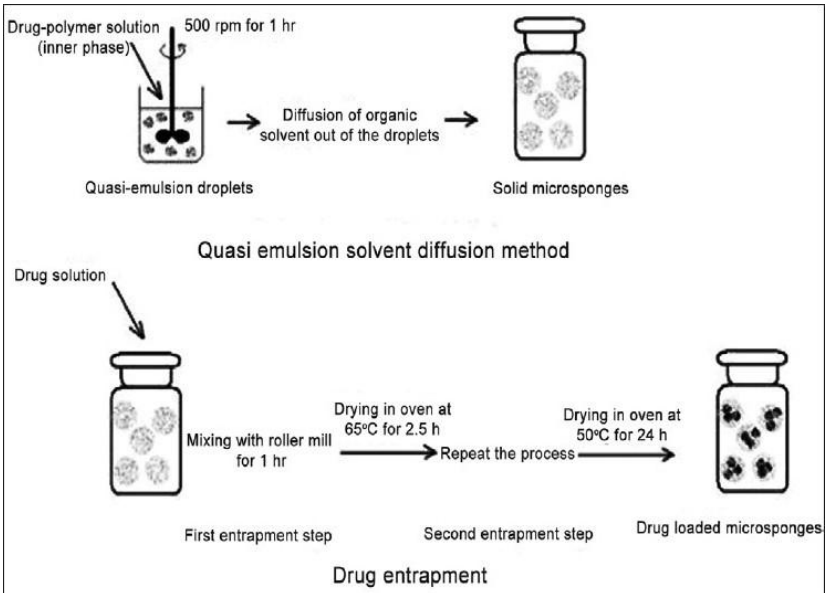


Fig. 4: Quasi-emulsion solvent diffusion

Mechanism of drug release from topical microsponges:
Diffusion was the drug release mechanism, and the microsponge preparation could speed up drug release [29]. It was anticipated that the interaction between microsponges and dermal secretions would be the basis for drug release. Additionally, it might be connected to its porous nature, which allows for the penetration of the release media and accessibility to the drug moiety that is encapsulated [30].

The drug release measured over the first few hours may be caused by nonencapsulated drug on the surface of the micro carriers, followed by release of the drug entrapped in the pores, leading to sustained drug release [29,31]. This is because the release media first comes in contact with the surface of the microsponge and then gradually into the internal region. So pores' size also has a big impact on how quickly drugs are released. By adjusting the drug and polymer concentrations in the preparation while maintaining a constant content ratio, the porosity of microsponges can be managed [32].

The in vitro release data can be fitted to different drug release kinetic models in order to understand the drug permeation kinetics from microsponge-loaded formulations. These models include zero order (cumulative percentage drug permeated vs time), first order (log cumulative percentage drug remaining to be permeated vs time), Higuchi (cumulative percentage drug permeated vs square root of time), Peppas and Korsmeyer to describe the release mechanism [33].

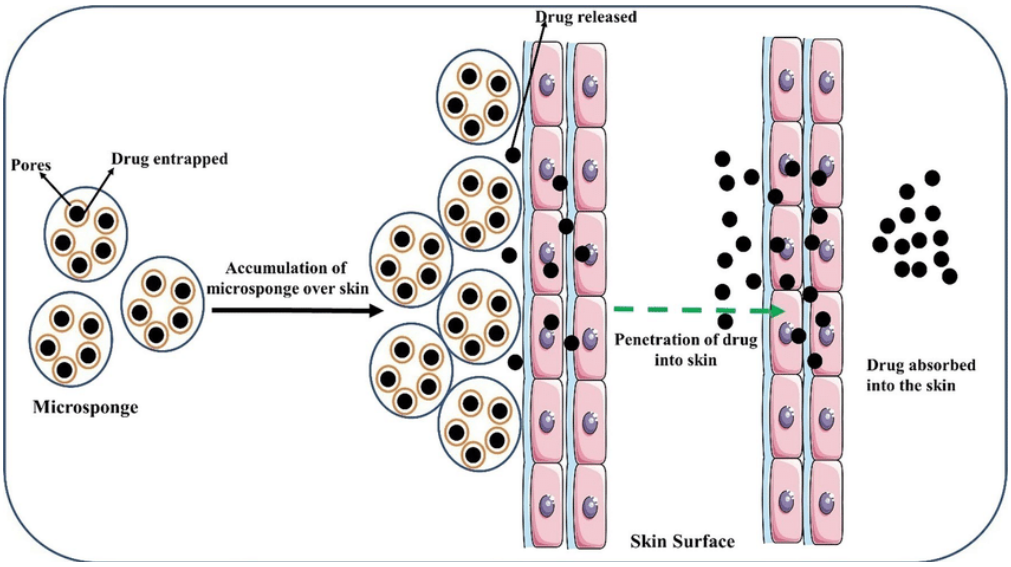


Fig. 5 : Mechanism of drug release from topical microsponges

Characterization of microsponges:

1.Fourier transform infrared (FTIR) spectroscopy:

One of the most important methods for examining the chemical interactions and purity of drugs and excipients is Fourier transform infrared spectroscopy. By comparing the FTIR readings of blank and drug-loaded microsystems, it is possible to assess the stability of the drug in microsponges. Due to molecular interactions between the active moiety and the microsponge, the drug peak shifts or broadens upon drug encapsulation in the FTIR spectrum [34]. After encapsulation, FTIR spectroscopy results showed no new peak appearance or disappearance of existing peaks, demonstrating the drug's compatibility with the chosen polymer and excipients [35].

2. Differential scanning calorimetry:

X-ray diffraction and solid state NMR are more complex and expensive methods of examination than DSC [36].The validation of drug loading in microsponges as well as information on drug purity and interactions with polymers are all provided.

DSC can be used to acquire the thermograms of the drug, polymer, physical mixture of the drug and excipients, and drug-loaded microsponges. Exothermic and endothermic peaks are produced as a result of sample melting, decomposition, or moisture loss. Broadening of peaks suggests that the medication lost its crystallinity during the creation of the microsponge [37].

3. X-ray diffraction :

A useful analysis technique for examining the physicochemical characteristics of created microsponges is X-ray diffraction.As a result of the scattering of atoms in their lattice planes, the XRD pattern of the microsponge can be calculated. For analyzing variations in drug crystallinity and chemical interactions between the components of microsponges, powder X-ray diffraction has been used [38].

4. Scanning electron microscopy :

Utilizing scanning electron microscopy, the size and shape of the particles are studied. SEM for microsponge formulations showed that they were fine, spherical, and homogeneous. All researchers have consistently used the SEM technique. As a result, characterizing microsponges without SEM could be deemed insufficient [39].

Formulation parameters and process variables on microsponge characteristics :

Particle size, shape, encapsulation effectiveness, manufacturing yield, drug loading, porosity, surface morphology, and drug release are characteristics of microsponges. The sections that follow give an understanding of some of the crucial factors that have a significant bearing on the effectiveness of microsponges [40].

1. Size:

The most crucial thing that must be watched when making microsponges is their size in order to ensure that they work as expected. The chosen preparation process should produce microsponges of the ideal size range with uniform distribution for topical application [41]. These porous microstructures' size is influenced by a number of factors, such as the drug: polymer ratio, internal phase volume, emulsifying agent concentration, and stirring rate. One of these is drug: The prepared microsponges' size is more significantly impacted by the polymer ratio than other factors [42]. It has been noted that the apparent viscosity of the internal phase is directly related to the particle size of microsponges [43].

2. Production yield :

It has been discovered that the drug-polymer ratio, the quantity and kind of emulsifying agent utilized, and stirring speed all have an impact on production yield. A greater ratio of drugs to polymers might boost production yield**.**Increased drug: polymer concentration gives droplet formation more time to occur, improving yield. However, a higher emulsifying agent causes a lower manufacturing yield.

The emulsifier (PVA), which is nonionic, generates some hydrophobic regions as a result of which some of the medicine and polymer dissolve. It is also known that stirring speed affects output yield. A drop in manufacturing yield is shown as stirrer speed is raised, probably because at greater stirring rates, the polymer sticks to the paddle due to the development of turbulence in the exterior phase [35].

3. Entrapment efficiency :

The amount of core material that is successfully entrapped in a formulation is known as entrapment efficiency. It can be determined indirectly by centrifuging a microsponge suspension for ten minutes at 2000 rpm. The resulting supernatant can be appropriately diluted using a suitable solvent, and the amount of free drug contained in the supernatant can be measured using UV-Visible spectroscopy [45].

drug entrapment efficiency (EE %) using the formula below:

$$\frac{\text{Actual drug content in microsponges}}{\text{Theoretical drug content}} \times 100$$

The various parameters described here affect entrapment efficiency. Drug polymer ratio and pore inducer quantity have an impact, according to literature. An increase in the EE could result from a rise in the drug-polymer ratio. The slower rate of drug solution diffusion into the external phase from concentrated polymeric solutions is what is causing the rise in EE. Increased droplet formation time leads to improved microsponge production and entrapment efficiency.
It has been found that production yield and encapsulation efficiency increase with an increase in PVA [44].

4.Characterization of Pore Structure:
Pore volume and diameter play a key role in regulating the extent and time frame of an active ingredient's efficacy, according to a description of the pore structure. The movement of active substances from microsponges into the vehicle in which the material is disseminated is also influenced by pore diameter. To investigate the relationship between pore width and volume and the rate of drug release from microsponges, mercury intrusion porosimetry can be used [46].

Mercury intrusion porosimetry can be used to determine the porosity parameters of microsponges, including intrusion-extrusion isotherms, pore size distribution, total pore surface area, average pore diameters, interstitial void volume percent porosity, percent porosity filled, shape and morphology of the pores, bulk, and apparent density [47].

5.In-vitro Dissolution Studies:
The dissolution pattern of the active ingredient of the microsponge can be estimated by USP dissolution apparatus. 900 ml of stimulated solution at 37 ± 0.5 ºC are used to determine to dissolution behavior of the drug [48,49].

6. Stability Studies:
The accelerated stability studies are carried out according to guidelines given by the International Council of Harmonization (ICH guidelines). The formulations are tested for stability at 50 ± 2 ºC, 250 ± 2 ºC/ 60 ±5 RH, 400 ± 2 ºC/ 75 ± 5 RH. Formulations are stored in glass bottles/vials and are evaluated after every 15, 30, 45 days for their physiochemical characteristics [50,51].

7. Drug-Polymer Compatibility Studies:
The sample of drug, excipients, and mixture of drug with excipients (binary (1:1) powder mixtures prepared by triturating drug with the individual excipients) was sealed in vials and kept at room temperature for not less than one month and then samples were analysed by DSC, XRD, and FTIR [52,53]**.**

MICROSPONGE LOADED GEL:

- **Visual examination:**

The colour, texture, and appearance of the microsponges made from the gel formulation were examined visually [34].

- **Measurement of pH:**

A digital pH meter was utilized to ascertain the pH of the gel composition. After dissolving one gram of gel in 100 milliliters of distilled water, it was kept for two hours. It was measured what the formulation's pH was [54].

- **Studies on spreadability:**

Good spreadability is one of the requirements for a gel to satisfy the ideal attributes. This phrase is used to describe the area that gel spreads easily when applied to the skin or other affected area. The spreading value of a formulation also affects how effective it is as a medicine.Glass slides and a wooden block, which was supplied by a pulley at one end, were used to measure spreadability. By using this technique, spreadability was evaluated based on the gels' characteristics of Slip and Drag.
T
he formula below was then utilized to determine spreadability:

$$M \times L/T = S$$

Where S denotes spreadability, M denotes pan weight (fastened to top slide), and L is the length that the glass slide moves. T = is the amount of time it takes to fully isolate each slide from the other [34].

- **Measurement of viscosity:**

Viscosity of the various gel compositions was measured at 25˚C using a Brookfield viscometer at 100 rpm. The viscosity of the optimized formulation was measured using a Brookfield viscometer without any dilution. Rotating spindles of varying sizes are employed and submerged in the test substance. big size spindles (big diameter and surface area) are used for low viscosity liquids, whereas small spindles (small diameter and surface area) are used for high viscosity liquids. Turn the spindle inside the microsponge gel until the viscometer's dial readout remains constant. For repeatable results, this process is carried out three times [54].

- **In vitro diffusion study:**

In vitro studies of the gel were carried out by using Franz diffusion cell apparatus. Selected batches of drug microsponge gel were used for the diffusion study using diffusion cell [34].

- **Drug release kinetics in vitro investigation**

Data on the amount and timing of drug release were used to ascertain the drug release mechanism and analyze the variations in release profiles amongst microsponge gel formulations. Mathematical models such as the Korsmeyer-Peppas, Higuchi matrix, Zero order, First order, and Hixson Crowell models were used to study the drug release kinetics [55].

CONCLUSION

A novel technique for the controlled release of macroporous beads containing an active ingredient that may lessen adverse effects without sacrificing therapeutic efficiency is the microsponge delivery system. Entrapment of components is provided by the microsponge drug delivery method, which is thought to help with less side effects, higher stability, increased elegance, and increased formulation flexibility. Furthermore, a plethora of studies has verified that microsponge systems are non-toxic, non-mutagenic, non-irritating, and non-allergic. At the moment, sunscreens, prescription medications, over-the-counter skin care products, and cosmetics all employ this technology. A greater knowledge of how various diseases are healed might result from the use of this type of medication delivery technology. Therefore, it is anticipated that the drug delivery matrix material based on microsponge technology would be useful for application.

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