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A Review on Drug Delivery System for Microsponges

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ABSTRACT

The delivery system of a microsponge is a highly cross-linked, porous, polymeric microsphere system made up of porous microspheres that have the ability to entrap and release substances into the skin over an extended period of time. Extended release, less discomfort, increased tolerance, and enhanced thermal, physical, and chemical stability are all features of this delivery technology. A variety of techniques are used to create microsponges, including suspension polymerization into a liquid-liquid system and emulsion systems. Microsponges have the ability to ensnare several kinds of drugs and may be used in cream, powder, gel, and lotion formulations. Topical preparations have some drawbacks, such as an offensive smell, greasiness, and skin irritation. These drawbacks are addressed by the delivery system of microsponges, which also helps the preparations reach the systemic circulation. The formulations of microsponge are compatible with the majority of vehicles and ingredients and stable throughout a pH range of 1 to 11. They are also stable at temperatures as high as 130°C. This review provides an overview of microsponge technology, including its synthesis, characterisation, benefits, assessment, and drug delivery system release mechanism. It also includes information on the marketed product and the most recent findings about microsponges.

Keywords:- Sustained release, micro sponges, thermal stable, emulsion system, suspension, polymerization.

INTRODUCTION

The field of medication delivery technologies is becoming more and more competitive and is changing quickly. An increasing number of advancements in delivery methods are being combined to maximize the therapy's effectiveness and financial efficiency. Traditional delivery methods cannot efficiently deliver treatments based on proteins, peptides, or DNA. Biopharmaceuticals, or proteins, peptides, and DNA-based medicines, are new kinds of pharmaceuticals that are driving the quick advancement of drug delivery technology. Usually, these novel medications cannot be administered efficiently by traditional methods. The health care system has been greatly impacted by drug delivery systems (DDS) that are able to precisely manage the release rates or target medications to a specific body location.[1,2]

The current state of medication development is insufficient to meet the needs of drug therapy. However, it also entails creating an appropriate medication delivery mechanism at the action site. The carrier system, which enables a regulated and localized release of the active medication in accordance with the particular needs of the therapy, also plays a role in determining the in-vivo fate of the drug in addition to its inherent qualities. Controlling the pace at which medications are delivered using a variety of contemporary technologies requires a great deal of study and is now the largest problem. Won created the microsponge technique in 1987, and Advanced Polymer Systems, Inc. was given the original patents. This firm created several variants of the techniques, which are used for both prescription and over-the-counter (OTC) medicinal items in addition to cosmetics. As of right now, Cardinal Health, Inc. has a license to utilize this intriguing technology in topical medicines. The microsponge particle's interior structure is shown by scanning electron microscopy as a "bag of marbles." The interstitial gaps between the stones are what cause the porosity. Many different active chemicals, including emollients, perfumes, essential oils, sunscreens, anti-infective agents, and anti-inflammatory agents, can be trapped in the interstitial pores.[3,4]

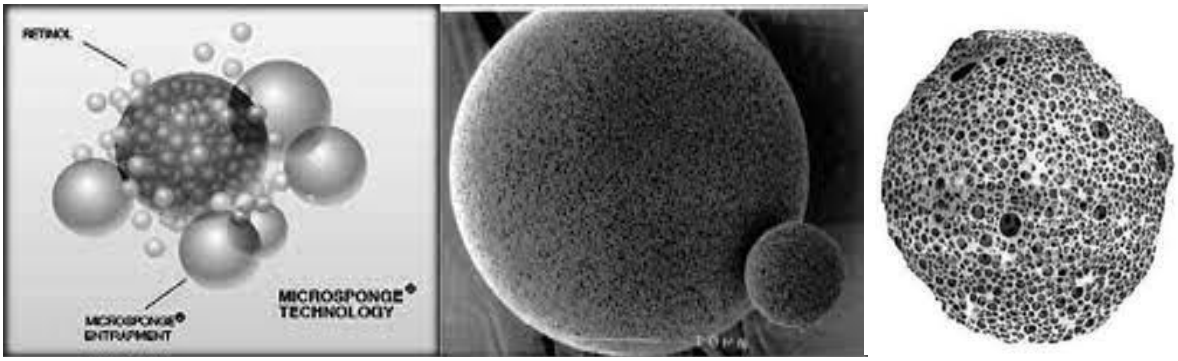

Fig No 1 :- Typical view of Microsponges.

History of Microsponge technique:
Won created the technique in 1987, and Advanced Polymer System, Inc. was granted the initial patents. This corporation created several variants of the procedures and used them for over-the-counter, physician-prescribed, and cosmetic items.[5]

Prospective Features of Microsponge:
Microsponges have demonstrated efficacy as a new, regulated medicinal product. They are capable of capturing a large range of medicines, both liquid and solid. They can absorb more than six times their own weight, demonstrating their great entrapment efficiency. They remain stable in the pH range of 1 to 11 and at high temperatures.When suspended in several types of carriers and dosage forms—liquid or semisolid—they exhibit good compatibility. They create a solution that is elegant and delivers the medicine in a steady, regulated manner that doesn't cause irritation, which increases patient compliance.[6,7,8,9]

CHARACTERISTICS OF MICROSPONGES:[10,11,12,13]
1. Formulations for microsponges remain stable throughout the PH range of 1 to 11.
2. Formulations for microsponges remain stable up to 130 0C in temperature.
3. The majority of vehicles and components are suitable with microsponge compositions.
4. Because the average pore size of microsponge formulations is 0.25µm, which is too small for bacteria to pass through, they are self-sterilizing.
5. Microsponge compositions can be economical and have a larger payload (50–60%) while being free-flowing.

Benefits of using microsponges as a topically active agent carrier system:
The papers in this field show a significant growth in interest in microsponges during the past ten years. When compared to other microparticulate systems, microsponges have the following advantages: easier compositional manufacturing, improved drug loading, and regulated drug release. Several papers propose additional benefits of delivery systems based on microsponge technology (MDS). The leading over-marketed pharmaceutical preparation is Microsponge, which is superior to other formulations.

A) Superior to Conventional Pharmaceutical Formulations:
For topical medication administration, semi-solid or biphasic liquid solutions are often available. On the skin's outermost layer, they release the medication. These traditional formulations demonstrated quick drug releases, which might potentially absorb and deposit in the skin's dermis and epidermis layers. The drug's excessive buildup causes toxicity, inflammation, and adverse effects. The medication delivery method utilizing microsponge technology solves these issues. They deliver the medication to the skin in a regulated, progressive manner.[14,15,16]

B) Over Micro and Nano-formulation:
Pharmaceutical businesses have demonstrated a strong interest in microsponge technology these days, particularly those that create controlled topical dose forms. Because of their high drug loading capacity, simple formulation method, controlled release, physical, chemical, and microbial stability, and compatibility with a wide range of drugs (including ketoprofen, retinol, fluconazole, ibuprofen, tertinoin, trolamine, prednisolone, acyclovir sodium, and ticonazole), microsponges are superior to microspheres, microencapsulation, niosomes, lipid nanoparticles, nanotubes, liposomes, and more.[17,18,19,20,21,22,23.]

METHOD OF PREPARATION OF MICROSPONGE DRUG DELIVERY SYSTEM: A porogen medication is entrapped in a one-step process (liquid-liquid suspension polymerization) and is stable to free radicals. It neither impedes nor activates the polymerization process. The following techniques are appropriate for preparing microsponges:

Liquid-liquid suspension polymerization:[24,25,26]

In liquid-liquid systems, suspension polymerization is used to create porous microspheres. This approach involves dispersing the immiscible monomers in aqueous phases that include a surfactant and suspending agents to help form a suspension after they have been dissolved with the active ingredients in a suitable solvent monomer. Next, a catalyst is added, the temperature is increased, or the polymerization is exposed to radiation. The polymerization process promotes the formation of a reservoir-type system with a spherical shape. After the polymerization process, the solvent is removed and the result is porous microspheres with a spherical structure - also known as microsponges.The following is a summary of the numerous stages that go into making microsponges:

Step 1: Choose the monomer and the monomer mixture.
Step 2: As polymerization begins, chain monomers are formed.
Step 3: Chain monomer cross-linking results in the formation of ladders.
Step 4: The monomer ladder is folded to create spherical particles.
Step 5: Bunches of microspheres are produced when the microspheres agglomerate.
Step 6: Bundles bind together to form microsponges.

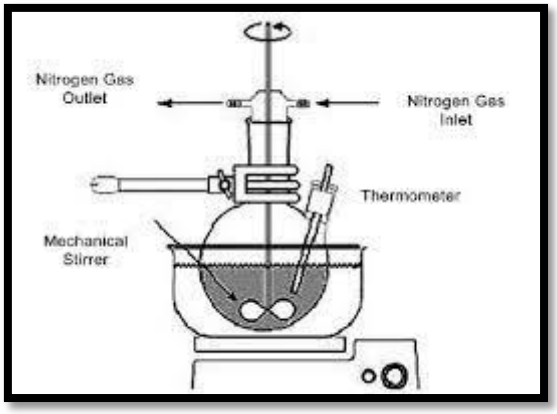

Fig no 2: Liquid-liquid suspension polymerization

Quasi-Emulsion Solvent Diffusion Method:[27,28,29]

Another approach used to create porous microspheres, or microsponges, was the quasi-emulsion solvent diffusion method, which involves two steps and an interior phase containing a polymer such as Eudragit RS 100 dissolved in ethyl alcohol. Next, a plasticizer like triethylcitrate (TEC) is added to the polymer solution to help with its plasticity, and the medication is gradually added to the mixture and dissolved under ultrasonication at 35 °C. After that, the inner phase is added to the exterior phase, which is made up of distilled water and polyvinyl alcohol, and it is continuously stirred for two hours11. The mixture was then filtered in order to extract the microsponges. The product, microsponges, was cleaned and allowed to dry for 12 hours at 40°C in an air-heated oven.

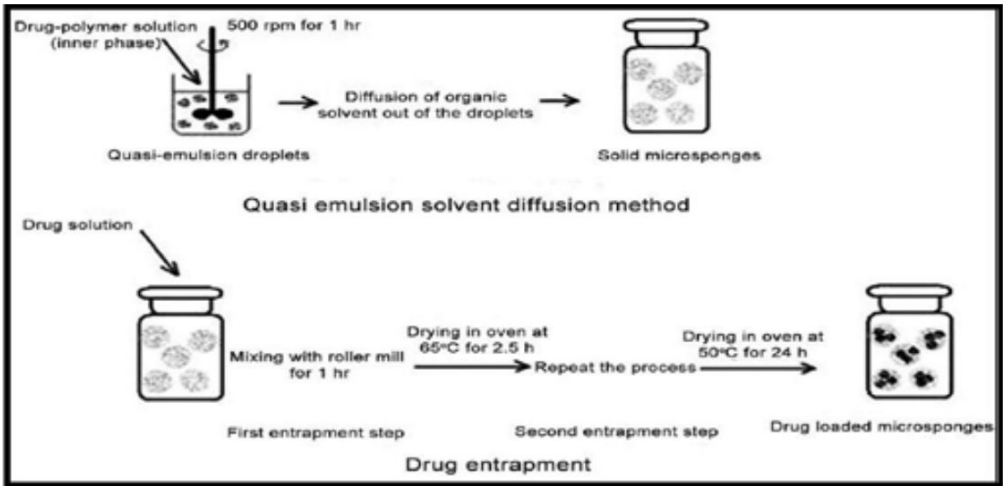

Figure 3: Preparation of microsponges by quasi emulsion solvent diffusion

RELEASE MECHANISMS

The Microsponge delivery system can be designed to release a functional material gradually in response to one or more external stimuli by manipulating the programmable parameters indicated above. This system's primary release method is:

A. Sustained or Time Release

Different physical and chemical characteristics of the entrapped active substance, such as volatility, viscosity, and solubility, will be investigated in the development of a sustained release microsponge. In the case of a polymeric microsponge, pore diameter, volume, and resiliency are assessed to provide the required sustained release effects.[30]

B. Release on Command

In reaction to one or more external triggers, microsponges can be engineered to release the specified quantities of active substances gradually.
accelerated or set off by the subsequent mechanism:

- Systems activated by pressure
- Systems activated by temperature
- pH-triggered mechanisms
- System activated by solubility

Pressure Release: When the microsponge system is compressed or squeezed, fluid or the active ingredient is released, resupplying the skin with the amount of entrapped active component. The sponge's release and the Microsponges' resilience may also have an impact on the amount released.[31]

Temperature Release: Temperature has the power to trigger the release of microsponges' active components.Few encapsulated active compounds may be too viscous to flow from microsponges onto the skin abruptly at room temperature. The flow rate increases along with an increase in skin warmth, which improves release.[32]

pH: It is possible to change the coating on the microsponge in order to initiate the pH-based release of the active. This has a wide range of uses in medication administration.[31]

Solubility: When there is water present, microsponges containing water miscible substances, such as antiperspirants and antiseptics, will release the substance. Diffusion can potentially trigger the release, but this requires accounting for the ingredient's partition coefficient between the microsponges and the external system.[33]

CHARACTERIZATION OF MICROSPONGES

1.Particle size and size distribution

An optical or an electron microscope are used to assess particle size and size distribution. This is a very important phase since the texture and stability of the formulation are significantly impacted by the size of the particles. By adjusting the size of the particles during polymerization, it is possible to produce free-flowing powders with exquisite aesthetic qualities. Particle size analysis of loaded and unloaded microsponges can be carried out using any appropriate technique, such as laser light diffractometry. For any formulation, the values (d50) may be stated as the mean size range. Plotting the cumulative percentage of drug release from microsponges with varying particle sizes versus time will allow researchers to examine how particle size affects drug release.[34]

2.Morphology and Surface topography of SPM

Numerous methods, including photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), and others, have been employed to study morphology and surface topography. SEM is frequently used to examine the surface morphology of prepared microsponges that have been coated with gold–palladium at room temperature in an argon environment.[35]

3.Determination of loading efficiency and production yield

The loading efficiency (%) of the Microsponges can be calculated according to the following equation:

$$\%\text{loading efficiency} = \frac{\text{actual drug content in microsponges}}{\text{Theoretical drug content}} \times 100$$

The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and last weight of the SPM obtained.

$$\%\text{Production yield} = \frac{\text{Production yield}}{\text{Theoretical mass (polymer + drug)}} \times 100$$

4.Determination of true density[36]

An ultra-pycnometer operating in helium gas may be used to estimate the real density of microsponges, which is determined by taking the mean of several measurements.

5. Characterization of pore structure

The width and volume of the pores play a crucial role in regulating the duration and potency of the active component. The migration of Microsponges' active components into the dispersion vehicle is influenced by pore diameter as well. To investigate the relationship between pore width and volume and the rate of drug release from microsponges, mercury intrusion porosimetry can be utilized. Microsponges' porosity characteristics include isotherms for incursion and extrusion. Mercury intrusion porosimetry may be used to measure the pore size distribution, total pore surface area, average pore diameters, shape and morphology of the pores, bulk, and apparent density. The plotting of incremental incursion volume scan against pore diameters, which indicated pore size distributions, was done. The following Washburn equation can be used to determine the pore diameter of microsponges:

$$D = \frac{-4\gamma\cos\Theta}{P}$$

Where D is the pore diameter (μm); γ the surface tension of mercury (485 dyn cm−1); θ he contact angle (130o); and P is the pressure (psia).

EVALUATION OF MICROSPONGE

1) Particle size determination:[37]

Particle size analysis of loaded and unloaded microsponges is done using laser light diffractometry or any other appropriate technique. Every formulation and size range has an expression for the values. To investigate the impact of particle size on drug release, the cumulative percentage of drug released from microsponges with varying particle sizes will be plotted versus time. Particles bigger than 30 μm have the potential to produce a gritty feeling; thus, for usage in the final topical formulation, particles between 10 and 25 μm are preferable.

2) Scanning electron microscope study:[38]

Prepared microsponges can be coated with gold palladium for surface topography and morphology at room temperature in an argon environment. Scanning electron microscopy (SME) can then be used to examine the microsponges' surface morphology. The ultra structure of a shattered microsponge particle may be obtained via SEM.

3) Determination of loading efficiency and production yield:

The loading efficiency (%) of the microsponges can be calculated according to the following equation: Loading efficiency = Actual Drug Content in Microsponge ×100
Theortical Drug Content

4) Production yield:

Accurately calculating the beginning weight of the raw materials and the final weight of the microsponge generated will provide the production yield of the microparticles.

$$\text{Production Yield (PY)} = \frac{\text{Practical Mass of Microsponges}}{\text{Theortical Mass Theoretical mass (Polymer+drug)}} \times 100$$

5) Determination of true density:[39]

Using an ultra-pycnometer and helium gas, one may determine the real density of Microsponges by averaging several measurements.

6) Compatibility studies:[40]

Fourier transform infrared spectroscopy (FT-IR) and thin layer chromatography (TLC) can be used to examine a drug's compatibility with reaction adjuncts. Differential scanning calorimetry and powder X-ray diffraction (XRD) can be used to examine how polymerization affects the drug's crystallinity (DSC).

7) Polymer/monomer composition:[41]

The drug release from microspheres is controlled by variables such polymer composition, drug loading, and microsphere size. The polymer composition of the MDS can have a direct impact on the rate of release of the entrapped medication by affecting the partition coefficient of the drug between the microsponge system and the vehicle. A useful method for studying drug release from microsponge systems with varying polymer compositions is to plot the cumulative percentage of drug release versus time.

MECHANISM OF RELEASING

In reaction to one or more external triggers, a microsponge can be engineered to release a certain quantity of active chemicals gradually.

a) Temperature change: Some entrapped active substances may be too viscous to leak from microsponges onto the skin abruptly at room temperature. The flow rate increases along with an increase in skin warmth, which improves release.

b) Pressure: The active component in microsponges can be released onto skin by rubbing or applying pressure.

c) Solubility: When water is present, microsponges containing water-miscible substances, such as antiperspirants and antiseptics, release the substance. Diffusion can potentially trigger the release, but this requires accounting for the ingredient's partition coefficient between the microsponges and the external system.

d) PH-triggered systems: By altering the microsponge's coating, the pH-based release of the active can be started.

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