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Review Article

# A REVIEW: MICROSPONGE-AN EFFECTIVE DRUG DELIVERY SYSTEM

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***ABSTRACT***

*Microsponge Delivery System (MDS) is a unique technology for controlled delivery of drug. MDS technology has been introduced in topical drug products to facilitate the controlled release of active drug into the skin in order to reduce the systemic exposure and minimize local cutaneous reactions to active. Microsponge technology has been clinically tested with many active ingredients in full formations, providing strong product claims. Microsponge literally means a collection of very small, sponge like particles, having a large porous surface, used for drug delivery. Microsponge particles are also referred to as microsphere beads or microspheres. The chemical manufacture of Microsponge involves careful polymerization using specific inert monomers, which may be selected based on their compatibility with individual active ingredients. The method of Microsponge manufacture is dependent on the chemical characteristics and "fragility" of the active ingredient.*

*KEYWORDS: Microsponge, controlled delivery of drug, topical drug products, compatibility,*

## INTRODUCTION

Microsponges are porous, polymeric microspheres that are mostly used for prolonged topical administration. Microsponge are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance stability, reduce side effects, and modify drug release profiles. Microsponge drug delivery system (MDDS) is a patented, highly cross-linked, porous, polymeric microspheres polymeric system (10-25 µ) consisting of porous microspheres particles consisting of a myriad of inter connecting voids within non-collapsible structures with a large porous surface that can entrap wide range of actives (cosmetics, over-the-counter (OTC) skin care, sunscreens and prescription products) and then release them onto the skin over a time and in response to trigger. A typical 25µm sphere can have up to 250000 pores and an internal pore structure equivalent to 10ft in length providing a total pore volume of about 1ml/g. Microsponge do not pass through the skin (capable of holding four times their weight in skin secretions

Microsponge technology has many favorable characteristics, which make it a versatile drug delivery vehicle. Microsponge Systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as a gel, cream, liquid or powder.

## HYPOTHETICAL MECHANISM OF MICRO SPONGE

The active ingredient is added to the vehicle in an entrapped form. As the Microsponge particles have an open structure (i.e., they do

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not have a continuous membrane surrounding them), the active is free to move in and out from the particles and into the vehicle until equilibrium is reached, when the vehicle becomes saturated. Once the finished product is applied to the skin, the active that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore, disturbing the equilibrium. This will start a flow of the active from the Microsponge particle into the vehicle, and from it to the skin, until the vehicle is either dried or absorbed. Even after that the Microsponge particles retained on the surface of the stratum corneas will continue to gradually release the active to the skin, providing prolonged release over time. This proposed mechanism of action highlights the importance of formulating vehicles for use with Microsponge entrapments. If the active is too soluble in the desired vehicle during compounding of the finished products, the products will not provide the desired benefits of gradual release. Instead they will behave as if the active was added to the vehicle in a free form. Therefore, while formulating microsponge entrapments, it is important to design a vehicle that has minimal solubilizing power for the actives. This principle is contrary to the conventional formulation principles usually applied to topical products. For these conventional systems it is normally recommended to maximize the solubility of the active in the vehicle. When using microsponge entrapments, some solubility of the active in the vehicle is acceptable, because the vehicle can provide the initial loading dose of the active until release from the Microsponge is activated by the shift in equilibrium from the polymer into the carrier. Another way to avoid undesirable premature leaching of the active from the Microsponge polymer is to formulate the product with some free and some entrapped active, so the vehicle is pre-saturated. In this case there will not be any leaching of the active from the polymer during compounding. The rate of active release will ultimately depend not only on the partition coefficient of the active ingredient between the polymer and the vehicle (or the skin), but also on some of the parameters that characterize the beads. Examples of these include surface area and primarily, mean pore diameter. Release can also be controlled through diffusion or other triggers such as moisture, pH, friction or temperature .

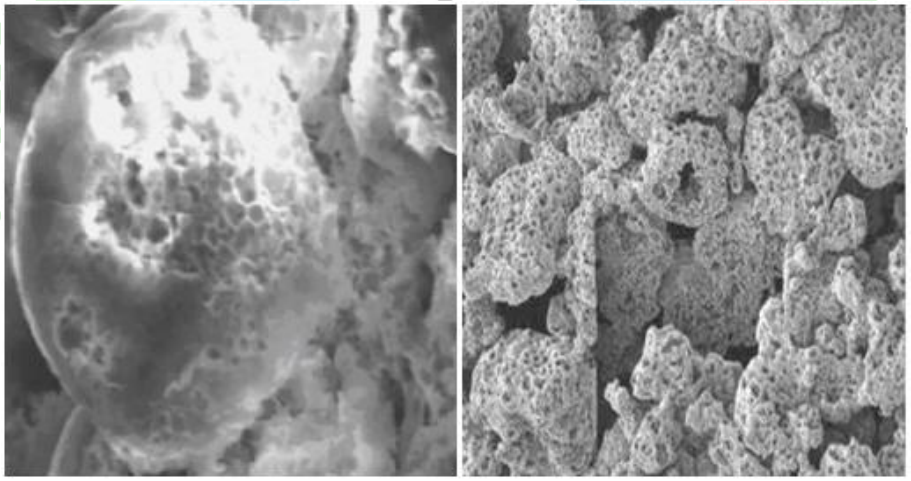

**Fig. 1. Structure of Microsponge**

**Characteristics of microsponges**

- Microsponge formulations are stable over range of PH 1 to 11
- Microsponge formulations are stable at the temperature up to 1300C;
- Microsponge formulations are compatible with most vehicles and ingredients;
- Microsponge formulations are self sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate;
- Microsponge formulations have higher payload (50 to 60%), still free flowing and can be cost effective

**Advantages**

- Advanced oil control, absorb up to 6 times its weight without drying
- Improved product elegancy.
- MDS allows the incorporation of immiscible products.
- Extended release
- Reduced irritation formulas
- Allows novel product form
- These are non-irritating, non-mutagenic, non-allergenic and non-toxic.
- Improved product aesthetics
- Extended release, continuous action up to 12 hours
- Reduced irritation, better tolerance means broader consumer acceptance
- Improved product aesthetics, gives product an elegant feel
- Improves stability, thermal, physical and chemical stability
- Allows incorporation of immiscible products.
- Improves material processing e.g. liquid can be converted to powders
- Improves efficacy in treatment.
- Cure or control confirm more promptly.
- Improve control of condition

**METHODS OF PREPARATION OF MICRO SPONGES**

Initially, drug loading in micro sponges is mainly take place in two ways depending upon the physicochemical properties of drug to be loaded. If the drug is typically an inert non-polar material which will generate the porous structure then, it is known as porogen. A Porogen drug neither hinders the polymerization process nor become activated by it and also it is stable to free radicals is entrapped with one-step process (liquid-liquid suspension polymerization).

Microsponge are suitably prepared by the following methods

***Liquid-liquid suspension polymerization***

Microsponge is prepared by suspension polymerization process in liquid-liquid systems (one-step process). Firstly, the monomers are dissolved along with active ingredients (non-polar drug) in an appropriate solvent solution of monomer, which are then dispersed in the aqueous phase with agitation. Aqueous phase typically consist of additives such as surfactants and dispersants (suspending agents) etc in order to facilitate the formation of suspension. Once the suspension is established with distinct droplets of the preferred size then, polymerization is initiated by the addition of catalyst or by increasing temperature as well as irradiation. The polymerization method leads to the development of a reservoir type of system that opens at the surface through pores. During the polymerization, an inert liquid immiscible with water however completely miscible with monomer is used to form the pore network in some cases. Once the polymerization process is complete, the liquid is removed leaving the micro sponges which is permeate within preformed micro sponges then, incorporates the variety of active substances like anti fungal, rubefacients, anti acne, anti inflammatory etc and act as a topical carriers. In some cases, solvent can be used for efficient and faster inclusion of the functional substances. If the drug is susceptible to the condition of polymerization then, two-step process is used and the polymerization is performed by means of alternate porogen and it is replaced by the functional substance under mild conditions.

The various steps involved in the preparation of microsponges are summarized as follows:

**Step 1**: Selection of monomer as well as combination of monomers.

**Step 2**: Formation of chain monomers as polymerization starts.

**Step 3**: Formations of ladders as a result of cross-linking between chain monomers.

**Step 4**: Folding of monomer ladder to form spherical particles.

**Step 5**: Agglomeration of microspheres leads to the production of bunches of microspheres.

**Step 6:** Binding of bunches to produce microsponge

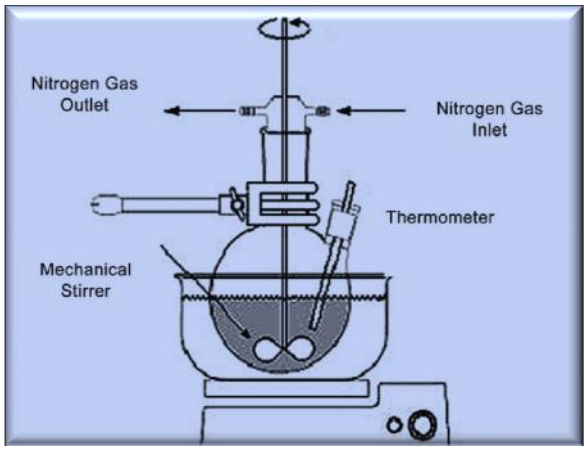


**Fig. 2. Reaction vessel for Microsponge**

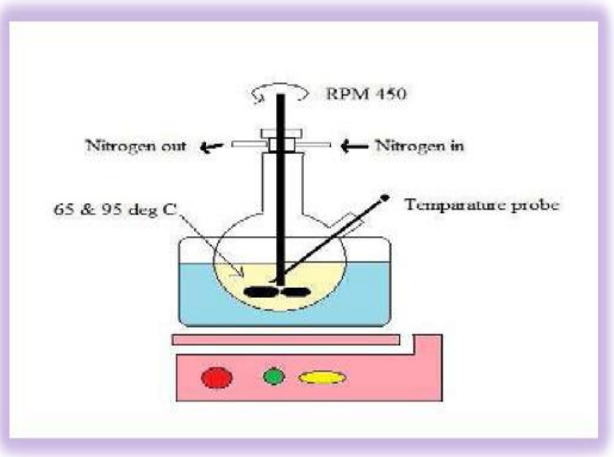


**Fig.3. Liquid-liquid polymerization preparation**

***Quasi-Emulsion Solvent Diffusion Method***

Porous microspheres (microsponges) were also prepared by a quasi-emulsion solvent diffusion method (two-step process) using an internal phase containing polymer such as Eudragit RS 100 which is dissolved in ethyl alcohol. Then, the drug is slowly added to the polymer solution and dissolved under ultrasonication at 35oC and plasticizer such as triethylcitrate (TEC) was added in order to aid the plasticity. The inner phase is then poured into external phase containing polyvinyl alcohol and distilled water with continuous stirring for 2 hours11. Then, the mixture was filtered to separate the microsponges. The product (microsponges) was washed and dried in an air heated oven at 40°C for 12 hrs Ingredients can be entrapped in microsponge polymers either at the time of synthesis, or if too labile to withstand polymerization conditions, they can be postloaded after the microsphere structure has been preformed. In general, the latter process is the preferred mode, as many cosmetic ingredients, and most pharmaceutical ones, would decompose at the temperatures employed for polymerization

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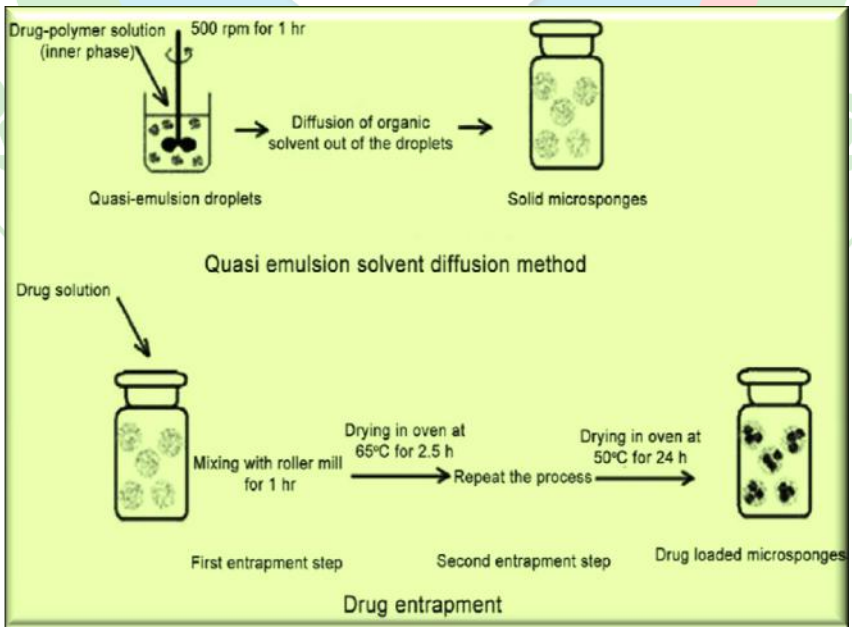


**Fig.4. Method of quasi-emulsion solvent diffusion**

**MECHANISM OF DRUG RELEASE**

The active ingredient is added to the vehicle in an entrapped form. As the Microsponge particles have an open structure (i.e., they do not have a continuous membrane surrounding them), the active is free to move in and out from the particles and into the vehicle until

equilibrium is reached, when the vehicle becomes saturated. Once the finished product is applied to the skin, the active that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore, disturbing the equilibrium. This will start a flow of the active from the Microsponge particle into the vehicle, and from it to the skin, until the vehicle is either dried or absorbed. Even after that the Microsponge particles retained on the surface of the stratum corneum will continue to gradually release the active to the skin, providing prolonged release over time.

***Pressure triggered systems***

Microsponge system releases the entrapped material when pressurized/rubbed; the amount released depends upon various characteristics of the sponge. By varying the type of material and different process variables, the microsponge best suited for a given application may be optimized. When compared with mineral oil containing microcapsules, mineral oil containing microsponge showed much more softening effect. The duration of emolliency was also much more for the microsponge systems.

***Temperature triggered systems***

Some entrapped active ingredients can be too viscous at room temperature to flow spontaneously from microsponges onto the skin. Increased in skin temperature can result in an increased flow rate and hence release. So it is possible to modulate the release of substances from the microsponge by modulation of temperature. For example, viscous sunscreens were found to show a higher release from microsponges when exposed to higher temperatures; thus a sunscreen would be released from a microsponge only upon exposure to the heat from the sun.

***pH triggered systems***

Triggering the pH-based release of the active can be achieved by modifying the coating on the microsponge. This has many applications in drug delivery.

**Solubility triggered system**

Microsponges loaded with water-soluble ingredients like anti-prespirants and antiseptics will release the ingredient in the presence of water. Presence of an aqueous medium such as perspiration can trigger the release rate of active ingredients. Thus release may be achieved based on the ability of the external medium to dissolve the active, the concentration gradient or the ability to swell the microspore network.

**FACTOR AFFECTING MECHANISM OF DRUG RELEASE**

- Physical and chemical properties of entrapped actives.
- Physical properties of Microsponge system like pore diameter, pore volume, resiliency etc. Properties of vehicle in which the microsponges are finally dispersed.
- Particle size, pore characteristics, resiliency and monomer compositions can be considered as programmable parameters and microsponges can be designed to release given amount of actives in response to one or more external triggers like; pressure, temperature and solubility of actives.
- Pressure Rubbing/ pressure applied can release active ingredient from microsponges onto skin.
- Temperature change some entrapped actives can be too viscous at room temperature to flow spontaneously from microsponges onto the skin. Increased in skin temperature can result in an increased flow rate and hence release.
- Solubility Microsponges loaded with water-soluble ingredients like antiperspirants and antiseptics will release the ingredient in the presence of water. The release can also be activated by diffusion taking into consideration the partition coefficient of the ingredient between the microsponges and the outside system.

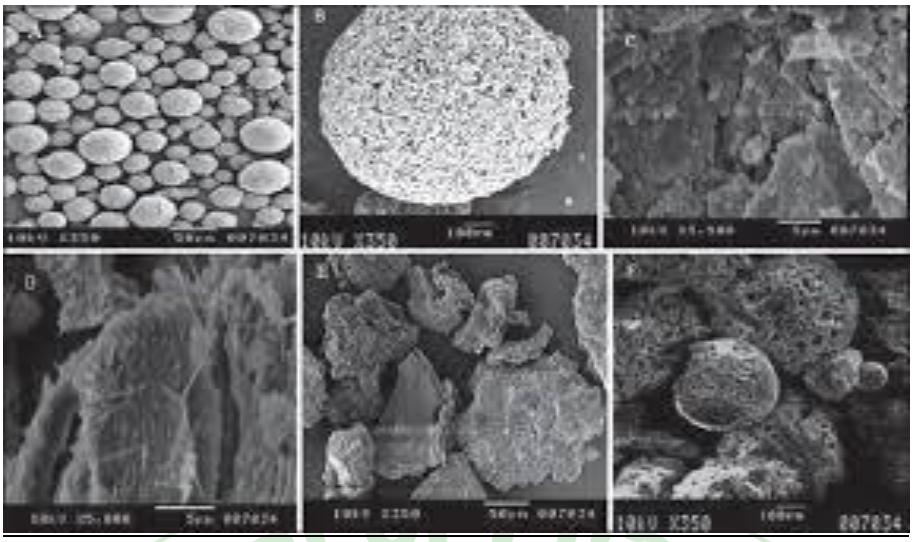

**Fig.5. Scanning electron microscopy of microsponges**

## EVALUATION PARAMETERS OF MICRO SPONGES

- Particle size (Microscopy)
- Morphology and Surface topography
- Loading efficiency and production yield
- Resiliency
- Compatibility studies
- Drug release study

## Applications of micro sponges:

### Micro sponge for topical delivery

The Micro sponge systems are based on microscopic, polymer-based microspheres that can bind, suspend or entrap a wide variety of substances and then be incorporated into a formulated product, such as a gel, cream, liquid or powder. A single Micro sponge is as tiny as a particle of talcum powder, measuring less than one-thousandth of an inch in diameter.

### Micro sponge for oral delivery

In oral applications, the micro sponge system has been shown to increase the rate of solubilisation of poorly watersoluble drugs by entrapping such drugs in the micro sponge system's pores. As these pores are very small, the drug is in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increases the rate of solubilisation.

### Micro sponge for Bone and Tissue Engineering Bone-substitute

Compounds were obtained by mixing pre polymerized powders of polymethyl methacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium deficient hydroxyapatite powders. The final composites appeared to be porous and acted as micro sponges.

### Recent advances in micro sponge drug delivery system:

Various advances were made by modifying the methods to form Nan sponges, nanoferrosponges and porous micro beads. β - CD nanosponges were also developed that can be used for hydrophobic as well as hydrophilic drugs, in contrast to polymeric micro or nanosponges. These advanced systems were studied for oral administration of dexamethasone, Flurbiprofen, doxorubicin hydrochloride, itraconazole and serum albumin as model drug

### Micro sponges for biopharmaceuticals delivery

The micro sponge delivery system (MDS) is employed for both in the delivery of biopharmaceuticals as well as in tissue engineering.

## SOME OTHER APPLICATION OF MICRO SPONGE

| Active agents | Applications |
|---|---|
| Sunscreens | Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization. |
| Anti-acne e.g. Benzoyl peroxide | Maintained efficacy with decreased skin irritation and sensitization. |
| Anti-inflammatory e.g. hydrocortisone | Long lasting activity with reduction of skin allergic response and dermatoses. |
| Antifungals | Sustained release of actives. |
| Antidandruffs e.g. zinc pyrithione, selenium sulfide | Reduced unpleasant odor with lowered irritation with extended safety and efficacy. |
| Antipruritics | Extended and improved activity. |
| Skin depigmenting agents e.g. hydroquinone | Improved stabilization against oxidation with improved efficacy and aesthetic appeal. |

### Marketed formulations of Microsponge

| Product name | Manufacturer | Marketed Product |
|---|---|---|
| Retin-A-Micro | Ortho-Mcneil pharmaceutical, inc |  |
| Anew | Avon |  |
| Retinol 15 night cream | Sothys |  |
| carac cream 0.5% | Dermik Labratories |  |
| EpiQuin micro<br>Skin Medica inc | EpiQuin micro<br>Skin Medica inc |  |
| Salicylic peel 30 | Biomedic |  |
| Oil free matte block spf-20 | Dermalogica |  |
| LactrexTM 12% moisturizing cream | SDR pharmaceuticals, inc. |  |

## CONCLUSION

The Microsponge delivery system is a unique technology for the controlled release of macro porous beads, loaded with active agent, offering a potential reduction in side effects, while maintaining their therapeutic efficacy. The Microsponge drug delivery system offers entrapment of its ingredients and is believed to contribute toward reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. In addition, numerous studies have confirmed that Microsponge systems are nonirritating, no mutagenic, no allergenic, and nontoxic. This technology is being used currently in cosmetics, over the counter skin care, sunscreens, and prescription products. This kind of drug delivery technology may lead to a better understanding of the healing of several diseases. Hence, the Microsponge based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future.

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