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# MICROSPONGES DRUG DELIVERY SYSTEM: A REVIEW

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**ABSTRACT**

The drug delivery technology landscape has become highly competitive and rapidly evolving. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. Peptides, proteins and DNA-based therapeutics cannot be effectively delivered by conventional means. To control the delivery rate of active agents to a predetermined site in human body has been one of the biggest challenges faced by drug industry. Controlled release of drugs onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts is an area of research that is successively done by the microsponge delivery system. The present review introduces Microsponge technology along with its synthesis, characterization, programmable parameters and release mechanism of MDS.

**Key words**: Microsponge, Controlled release, Topical drug delivery, Oral drug delivery.

## INTRODUCTION

The area of drug delivery technology is evolving rapidly and becoming highly competitive day by day. The developments in the delivery systems are being utilized to optimize the efficacy and the cost effectiveness of the therapy. The challenges faced by drug development industry are:

• Sustained release technology for reducing irritation of a wide range of APIs and other skin care actives thereby increasing patient/client compliance and results.

• Enhanced formulation stability ensuring long term product efficacy and extended shelf life.

• Superior skin feel and exceptional product esthetics [1].

Several predictable and reliable systems were developed for systemic drugs under the heading of transdermal delivery system (TDS) using the skin as portal of entry. It has improved the efficacy and safety of many drugs. But TDS is not practical for delivery of materials whose final target is skin itself. Thus the need exists for system to maximize amount of time that an active ingredient is present either on skin surface or within the epidermis, while minimizing its transdermal penetration in the body [2].

The microsponge delivery system fulfills these requirements. Microsponge deli-very systems are uniform, spherical polymer particles. Their high degree of cross-linking results in particles that are insoluble, inert and of sufficient strength to stand up to the high shear commonly used in manufacturing of creams, lotions, and powders. Their characteristic feature is the capacity to adsorb or "load" a high degree of active materials into the particle and on to its surface. Its large capacity for entrapment of actives, up to three times its weight, differentiates micro-sponge products from other types of dermatological delivery systems. While the active payload is protected in the formulation by the microsponge particle, it is delivered to skin via controlled diffusion. This sustained release of actives to skin over time is an extremely valuable tool to extend the efficacy and lessen the irritation commonly associated with powerful therapeutic agents such as Retinoid or Benzoyl Peroxide. Micro-sponge polymers possess the versatility to load a wide range of actives providing the benefits of enhanced product efficacy, mildness, tolerability, and extended wear to a wide range of skin therapies [3].

### Advantages

- Advanced oil control, absorb up to 6 times its weight without drying
- Extended release
- Reduced irritation formulas
- Allows novel product form
- Improved product aesthetics

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- 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 eg. liquid can be converted to powders
- Allows for novel product forms.
- Improves efficacy in treatment.
- Cure or control confirm more promptly.
- Improve control of condition.
- Improve bioavailability of same drugs [4].

**CHARACTERISTICS OF MATERIALS THAT IS ENTRAPPED IN MICROSPONGES**

Most liquid or soluble ingredients can be entrapped in the particles. Actives that can be entrapped in microsponges must meet following requirements,

- It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers.
- The solubility of actives in the vehicle must be limited to avoid cosmetic problems; not more than 10 to 12% w/w microsponges must be incorporated into the vehicle. Otherwise the vehicle will deplete the microsponges before the application.
- The spherical structure of microsponges should not collapse.
- Polymer design and payload of the microsponges for the active must be optimized for required release rate for given time period.
- It should be stable in contact with polymerization catalyst and conditions of polymerization

**METHODS OF PREPARATION OF MICRO SPONGES [6-10]**

Initially, drug loading in microsponges 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). Microsponges are suitably prepared by the following methods:

**a) Liquid-liquid suspension polymerization**

Microsponges are 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 microsponges which is permeate within preformed microsponges 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 microsponges.

**a) 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.

**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 [11].

**EVALUATION PARAMETERS OF MICRO SPONGES**

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

**Particle size and shape**

The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). Both can be used to determine the shape and outer structure of microparticles. LM provides a control over coating parameters in case of double walled microparticles. The microparticles structures can be visualized before and after coating and the change can be measured microscopically. SEM provides higher resolution in contrast to the LM. SEM allows investigations of the microparticles surfaces and after particles are cross-sectioned, it can also be used for the investigation of double walled systems.

Conflocal fluorescence microscopy is used for the structure characterization of multiple walled microparticles. Laser light scattering and multi size coulter counter other than instrumental methods, which can be used for the characterization of size, shape and morphology of the microparticles (microsponges) [12].

**Morphology and surface topography of microsponges**

For morphology and surface topography, prepared microsponges can be coated with gold-palladium under an argon atmosphere at room temperature and then the surface morphology of the microsponges can be studied by scanning electron microscopy (SEM). SEM of a fractured microsponge particle can also be taken to illustrate its ultra structure [13].

**Determination of Loading Efficiency and Production Yield**

The loading efficiency (%) of the microsponges can be calculated according to the following equation [14]:

$$\text{Loading Efficiency} = \frac{\text{Actual Drug Content in microsponges}}{\text{Theoretical Drug Content}} \times 100$$

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

**Compatibility studies**

Compatibility of drug with reaction adjuncts can be studied by thin layer chromatography (TLC) and Fourier Transform Infra-red spectroscopy (FT-IR).

Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC). For DSC approximately 5 mg samples can be accurately weighed into aluminum pans and sealed and can be run at a heating rate of 15 C/min over a temperature range 25–430 C in atmosphere of nitrogen [15].

**Resiliency (viscoelastic properties)**

Resiliency (viscoelastic properties) of microsponges can be modified to produce beadlets that is softer or firmer according to the needs of the final formulation.

Increased cross-linking tends to slow down the rate of release [16].

**Drug release kinetics**

The dissolution profile of each formulation have been subjected to various models such as Zero order kinetics (percentage drug release against time), First order kinetics (log percentage drug unreleased against time), Higuchi (percentage drug released against square root of time) and Korsemeyer-Peppas (log percent drug released against log of time) were applied to assess the kinetics of drug release from prepared microsponges [17].

**Future Perspective**

**Nanosponges**

Today, as we realize the immense advantages offered by the nano-size, the micro sized products are likely to be outdated. The nanosized particles have a very high surface area to size ratio and a greater potential to modulate the release of actives compared to micro-sized particles. While inorganic nanosponges have many applications in electronics, the first pharmaceutical nanosponges based on cross linked cyclodextrins have been reported. These are Nano sized, highly porous materials composed of beta-cyclodextrins cross linked with carbonate bonds. Econazole nitrate nanosponges loaded carbopal hydrogel were recently developed. These are prepared using ethyl cellulose and poly vinyl alcohol by emulsion solvent evaporation method [19].

**Going the natural way using a Functional Active**

Although natural actives are important consumer attractants, now the focus has shifted on using multifunctional natural ingredients. For example, Marinosomes®, liposomes made from natural anti-inflammatory lipid extracts, have set a new paradigm in using such functional 'active excipients'. The possibility of using such substances for constructing a microsponge structure appears to be cost effective and innovative.

**Microsponges in Oral Care Cosmetics**

An interesting application of the microsponge technology could be in oral cosmetics, such as to sustain the release of volatile ingredients, thus increasing the duration of the 'fresh feel'. Microsponges of such volatile ingredients may be easily incorporated in tooth pastes or mouth washes.

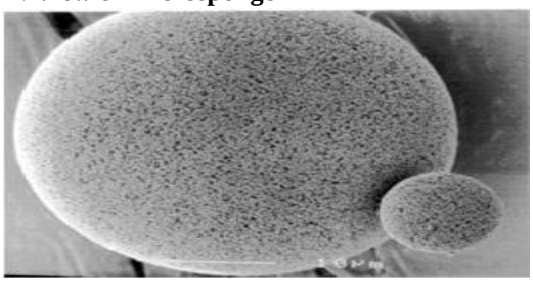
**Long lasting Coloured Cosmetics; a new application for Microsponges**

Colours entrapped in microsponges may be used in a variety of coloured cosmetic products such as rouge or lipsticks to make them long lasting. As stated above, microsponges help in uniform spreading and improving covering power. Thus, colored cosmetics formulated with microsponges would be highly elegant [20,21].

**Table 1. Therapeutic application of microsponges [18]**

| Product Name | Advantages | Manufacturer |
|---|---|---|
| Retin-A-Micro$^{tm}$ | and 0.04% tertinoin entrapped in MDS, for topical treatment of acne vulgaris. | Ortho-Mcneil pharmaceutical, inc |
| Carac cream, 0.5% | Carac cream contains 0.5% flurouracil,with0.35 being incorporated into a patented porous microsponge composed of methyl methacrylate cross polymer and dimethicone | Dermik Labratories, inc. |
| Line eliminator dual retinal Facial treatment | Lightweight cream with a retinal in MDS,Delivers both immediate and time releasedWrinkle-fighting action. | Avon |
| Retinol cream | The retinol molecule is kept in microsponge System to protect the potency of vitamin A. This helps to maximize the retinol dosage. While reducing the possibility of irritation | Biomedic |
| Retinol 15 night cream | A night time treatment with microsponge Technology using a stabilize formula of pure Retinol and vitamin A | Sothys |
| EpiQuin micro | The microsponge system uses microscopic. Reserviours that entrap hydroquionone and Retinol | Skin Medica inc |
| Spots cream RS and XS | Topical analgic-antiinflammatory and Counter Irritant activities in microsponge delivery System for management of musculoskeletal Condition. | Embil pharmaceutical co. Ltd |
| Salicylic peel 20 | Deep BHA peeling agent for salicylic acid 20% microsponge technology. Excellent Exfoliations and stimulation of skin for more Resistant skin types or for faster results. | Biophora |
| Salicylic peel 30 | Deep BHA peeling agent for salicylic acid 30% microsponge technology. Excellent Exfloliation and stimulation of skin for more Resistant skin types or for faster results. | Biomedic |
| Oil free matte block spf-20 | The invisible sun screen provides a shield for the skin from damaging uv rays and controls oil production. Microsponge technology absorps the oil. Maintain an all day matte finish and preventing shinewithout any powdery residue. | Dermalogica |
| Lactrex$^{TM}$ 12% moisturizing cream | Lactrex$^{TM}$ 12% moisturizing Cream contains 12% lactic acid as the neutral Ammonium salt and lactate microsponge Technology has been included for comfortable Application and long lasting moisturization. | SDR pharmaceuticals, inc. |

**Figure 1. View of Microsponge**



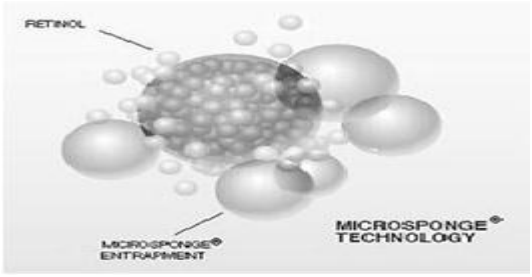


**Figure 2. Reaction vessel for microsponge preparation by liquid-liquid suspension polymerization**

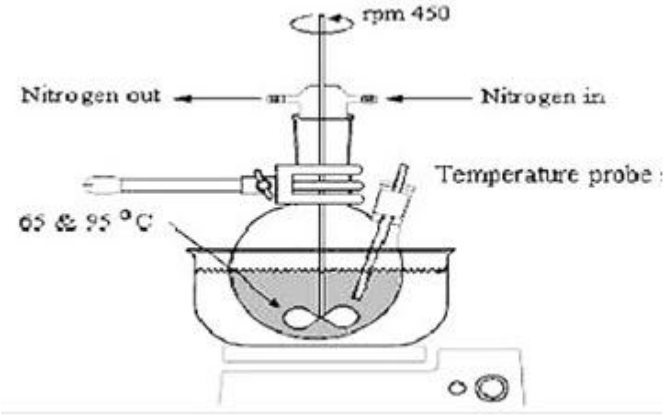
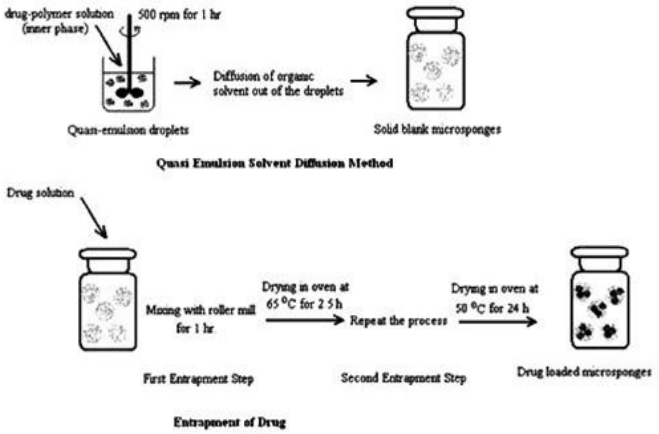



**Figure 3. Method of quasi-emulsion solvent diffusion**




## CONCLUSION

Ease manufacturing, simple ingredients and wide range actives can be entrapped along with a programmable release make microsponges extremely attractive. MDS is originally developed for topical delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, antipruritics, rubefacients etc. Microsponge Delivery System holds a promising future in various pharmaceutical applications in the coming years as they have unique properties like enhanced product performance and elegancy, extended release, reduced irritation, improved thermal, physical, and chemical stability so flexible to develop novel product forms. Researchers are continuously trying to develop a drug delivery system which is cost effective and having better therapeutic efficacy. MDS technology showed such promises to meet researchers expectations. It's a very unique technology to control drug release of topical agents as well as oral drug delivery. The MDS system offers entrapment of its ingredients with reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. On the other hand, numerous studies reveal that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic. The versatile and unique properties of MS made it ideal carrier of drugs with shorter half-lives and drugs which are suffering from first pass metabolism.

A Microsponge Delivery System can entrap wide range of actives and then release them onto the skin over a time and in response to trigger. It is a unique technology for the controlled release of topical agents and consists of microporous beads loaded with active agent and also use for oral as well as biopharmaceutical drug delivery. A Microsponge Delivery System can release its active ingredient on a time mode and also in response to other stimuli. Thus microsponge has got a lot of potential and is a very emerging field which is needed to be explored.

## REFERENCES

1. Kirti Deshmukh, Sushilkumar S Poddar. Solid porous microsphere: emerging trend in pharmaceutical technology. *Int J Pharm Bio Sci*, 2(1), 2011, 364-377.
2. Patel SB, Patel HJ and Seth AK. Microsponge drug delivery system: an overview. *J Global Pharm Tech*, 2(8), 2010, 1-9.
3. Viral Shaha, Hitesh Jain, Jethva Krishna1, Pramit Patel. Microsponge drug delivery: A Review. *Int. J. Res. Pharm. Sci*, 1(2), 2010, 212-218.
4. Patidar K, Soni M, Saxena C, Soni P, Sharma DK. Microspongea versatile vesicular approach for transdermal drug delivery system. *J Global Pharm Tec*, 2(3), 2010, 154-164.
5. Saroj Kumar Pradhan. Microsponges as the versatile tool for drug delivery system. *IJRPC*, 1(2), 2011, 243-258.
6. Mahajan Aniruddha G, Jag tap Leena S, Chaudhari atul L, Swami sima P, Mali Prabha R. Formulation and evaluation of microsponge drug delivery system using Indomethacin. *IRJP*, 2(10), 2011, 64-69.
7. Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Gary P Martin, Ali Nokhodchi. The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies. *Int J Pharm*, 308, 2006, 124–132
8. Tansel C¸, Omog˘Lu, Nursin Gonu, Tamer Baykara. Preparation and *invitro* evaluation of modified release ketoprofenMicrosponges. *Il Farmaco*, 58, 2003, 101-106.
9. Saboji J. K, Manvi FV, Gadad AP. & Patel BD. Formulation and evaluation of ketoconazole microsponge gel by quassi emulsion solvent diffusion. *Journal of Cell and Tissue Research*, 11(1), 2011, 2691-2696.
10. Neelam Jain, Pramod Kumar Sharma, Arunabha Banik. Recent advances on microsponge delivery system. *Int J Pharm Sci Review and Res*, 8 (2), 2011, 13-23.
11. Panwar AS, Yadav CS, Yadav P, Darwhekar GN, Jain DK, Panwar MS, Agrawal A. Microsponge a novel carrier for cosmetics. *JGPT*, 3(7), 2011, 15-24.
12. Vikrant K, Nikam, RT Dolas, Somwanshi SB, Gaware VM, Kotade KB, Dhamak KB, Khadse AN and Kashid VA. Microparticles: a novel approach to enhance the drug delivery - a review. *IJPRD*, 3(8), 2011, 170- 183.
13. Madhu Sharma, Baibhav Joshi. Microsponges: A comprehensive Review. *The Global J Pharm Res*, 1(3), 2012, 359-377.

14. Saurabh Kumar, Tyagi LK, and Dashrath Singh. Microsponge delivery system (MDS): A unique technology for delivery of active ingredients. *IJPSR*, 2(12), 2011, 3069-3080.
15. Patel EK and Oswal RJ. Nanosponge and micro sponges: A novel drug delivery system. *Int J Res in Pharm and Chem*, 2(2), 2012, 237-244.
16. Saroj Kumar Pradhan. Microsponges as the versatile tool for drug delivery system. *IJRPC*, 1(2), 2011, 243-258.
17. Swetha, Gopal Rao, Venkata Ramana K, Niyaz Basha B and Koti Reddy V. Formulation and *in-vitro* evaluation of etodolac entrapped in microsponge based drug delivery system. *Int J Pharma*, 1(2), 2011, 73-80.
18. Santanu Kaity, Sabyasachi Maiti, Ashoke Kumar Ghosh,Subham Banerjee. Microsponge: A novel strategy for drug delivery system. *J. Adv. Pharma. Tech. Res*, 1(3), 2010, 283-290.
19. Shyam Sunder Mandava and Vedavathi Thavva. Novel approach: microsponge drug delivery system. *IJPSR*, 3(4), 2012, 967-980.
20. Bhumika Sharma, Arvind Sharma. Future prospect of nanotechnology in development of anti-ageing formulations. *Int J Pharm Pharm Sci*, 4(3), 2012, 57-66.
21. Rekha U, Manjula BP. Formulation and evaluation of microsponges for topical drug delivery of mometasone furoate. *Int J Pharm Pharm Sci*, 3(4), 2010, 133-137.
22. Mallik Santanu, Kshirsagar MD, Saini Vipin, Patial Rajan, Khokhar Atin, Ghosh TK. Revealing drug release pattern with revolutionary porous microsponges-a review. *NSIJPS*, 1, 2012, 11-24.