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MICROSPONGE DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Microsponges are polymeric delivery systems composed of porous microspheres. They are tiny sponge-like spherical particles with a large porous surface. Moreover, they may enhance stability, reduce side effects and modify drug release favorably. Microsponge technology has many favorable characteristics, which make it a versatile drug delivery vehicle. Effective Drug delivery at the targeted or specific site is the significant problem which is being faced by the researchers in the anti-cancer formulation. The development of new colloidal, porous, tiny mesh-like carrier called nanosponges with the size 1µm range wich offers controlled drug delivery at a specific site in cancer treatment. Microsponges play an important role in targeting drug delivery in a controlled manner. A wide variety of drugs, both the lipophilic as well as hydrophilic can be loaded into nanosponge for targeting drug delivery and ultimately improve solubility and bioavailability of the same drug. Nanosponge can circulate around the whole body until they interact with the specific target site and stick on the surface and begin to release the drug in a controlled manner. In this review article, application of nanosponges, its preparation methods, polymers used and characterization have been discussed.

KEYWORDS: Microsponges, Controlled release, Porous microspheres, Solvent evaporation.

INTRODUCTION

Microsponges are polymeric delivery systems composed of porous microspheres. Are small Spherical particles in the form of sponges with large porous surface. In addition, they can be improved stability, reduces side effects and favors drug administration Microsponge technology.

Many favorable features, which makes it a versatile drug delivery vehicle. The systems are based on microscopic microspheres based on polymers that can suspend or capture it a wide variety of substances and can then be incorporated into a gel formulated product, cream, liquid or powder. MDS can provide greater efficiency to local agents. Higher safety, greater product stability and better aesthetic properties effectively mode.[1]

The term "Microsponge" means tiny sponges having porous structures. It offers a solution for several formulation related problems. Microsponges are microparticles with a size of a virus with an average diameter in between 1-100µm. Due to their small size and porous nature they can bind poorly- soluble drugs within the matrix and improve their bioavailability by modifying the pharmacokinetic parameters of drug molecules.[2]

Microsponge is a novel approach which offers controlled drug delivery for cancer treatment. Microsponge is an emerging technology for cancer drug delivery. Microsponge drug delivery system is employed for the improvement of performance of orally, parenteral and topical administered drugs in cancer treatment. Microsponge can circulate into the whole body and release the drug at a specific site in a controlled manner. Microsponges are beneficial for the treatment of many diseases and this technology is more effective at delivering drug for breast cancer than the conventional method. Microsponges are microparticles in which a large number of drug substances can be encapsulated within its core. These microscopic particles are capable carrying both the lipophilic and hydrophilic substances and of improving solubility of drug molecules.[3-5]

Advantages[6,7]

1. Microsponge provides the site-specific drug delivery and predetermined release.
2. A Smaller quantity of the drug contact with the normal tissue hence produces fewer side effects.
3. These formulations are soluble in water and capable of encapsulating hydrophobic drug.
4. Microsponge formulation used to mask unpleasant flavors of drug substance and to convert liquid substances to solids.
5. Particles can be prepared smaller or larger by varying the proportion of cross-linker to polymer
6. Particles can be prepared smaller or larger by varying the proportion of cross-linked to the polymer.
7. Due to their average pore size, 0.25 µm bacteria cannot be penetrate

8. Improved stability, self-sterilizing, increased elegance and enhanced formulation flexibility, improve dissolution.

Disadvantages

1. Microsponge depends upon loading capacities.
2. Formulation of microsponge includes only small molecules.

Characteristics of microsponges[8-11]

1. When these are applied to the skin, the microsponge releases its active ingredient gradually to the skin on a time mode and also in response to stimuli such as rubbing, temperature and pH effect etc. with excellent efficacy and minimal irritation. Characteristics of microsponges are as follows: 10, 12-14 1. Microsponge formulations are stable over range of pH 1 to 11.
2. Microsponge formulations are stable at the temperature up to 1300C.
3. Microsponge formulations are compatible with most vehicles and ingredients.
4. Microsponge formulations are self- sterilizing as their average pore size is about 0.25µm where the bacteria cannot penetrate the pores.
5. Microsponge formulations have high entrapment upto 50 to 60%.
6. Microsponge formulations are free flowing and can be cost effective.
7. Microsponge particles themselves are too large so they are difficult to be absorbed into the skin and this adds a measure of safety to these microsponge materials by avoiding the side effects of the microsponge adjutants.
8. Microsponges formulations can be cost effective even for the cosmetic mass market use where the cost of the materials is important.
9. Microsponges can absorb oil up to 6 times its weight without drying.
10. It provides continuous action up to 12 hours i.e. extended release.
11. They have superior formulation flexibility.

Methods of preparation of microsponges

The selection of a particular encapsulation method is primarily determined by the solubility characteristics of the drug and polymer. A popular method for the encapsulation of water-insoluble drugs within water insoluble polymers is the diffusion solvent method. This method can be both readily performed in the laboratory but has scale up potential such that large volumes of water can be handled. When finally developing a microencapsulation procedure then finally selected method should ideally produce.

- High yields of microparticles and free of extensive agglomeration.
- Higher encapsulation of the core material.
- A reproducible release profile from batch to batch.
- An ability to modify in vitro release rates by varying process parameters in order to prepare microparticles with the desired in vivo release characteristics.

Properties of the actives for the entrapment into the microsponge

- 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 and should not increase the viscosity of the mixture during formulation.
- It should be stable when in contact with polymerization catalyst and under conditions of polymerization.
- The spherical structure of the microsponges should not collapse.[12-14]

1. Free Radical Suspension Polymerization: (Bottom up approach)

This is Bottom-up approach starting with monomer. Microsponges were conveniently prepared by free radical suspension polymerization in an emulsified liquid-liquid system. Particles forming polymerization mixtures are usually two phase systems. The monomers are referred to as „monomer phase‟ or „dispersed Phase‟; the immiscible liquid phase containing the dispensed (or dissolved) monomer is defined as "Polymerization medium."

In addition to the monomers and polymerization medium, another liquid (miscible with the monomer and immiscible with the medium) may also be added to the monomer to form a pore network. This liquid is known as „monomer diluent‟ or „porogen‟ and belongs to the category of inert, nonpolar organic solvents when added to the polymerization reaction, polymeric beads with open, porous structures can be obtained and they look just like sponges under SEM, hence the name „microsponges‟. For preparing Microsponge, the requirements are monomer namely Styrene, PHEMA, Cross linking Agents is Divinyl Benzene and Porogen is Toluene.

It is important to maintain the temperature for most efficient operation. Temperature of the reaction mix dictates the rate of decomposition, the initiation into free radicals and hence affecting the rate of polymerization.

Once the suspension is established with discrete droplets of the desired size, polymerization is affected by activating the monomers either by catalysis, increased temperature or irradiation. The result is a series of polymer ladders wrapping around one another into solid Microspheres. As the Polymerization process continues, a spherical structure is produced containing thousands of Microspheres bunched together like grapes, forming interconnecting reservoirs in which the porogen is entrapped. These reservoirs open onto the surface of the spheres through which active ingredient can be released when triggered.

Once polymerization is complete the solid particles that result from the process are recovered from the suspension. The particles are then washed and processed until they are substantially ready for use. Particle formation and incorporation of the functional substance is thus performed as a single step. This may be termed as one step process. When the material is sensitive to the polymerization conditions, polymerization is performed using substitute porogen. The porogen is then removed and replaced by contact absorption assisted by solvents to enhance absorption rate.[15-16]

2. Quasi-emulsion solvent diffusion method: (Top down approach)

This is top-down approach starting with preformed polymer. This process involved formation of quasi-emulsion of two different phases‟ i.e. internal phase and external phase similar to emulsions. The internal phase of drug--polymer solution made in a volatile solvent like ethanol or acetone or dichloromethane was added to external phase comprising the aqueous polyvinyl alcohol (PVA) solution with vigorous stirring. Triethylcitrate (TEC), which was added at an adequate amount in order to facilitate plasticity. Stirring lead to the formation of discrete emulsion globules called quasi-emulsion globules. Solvent was then extracted out from these globules to form insoluble, rigid microparticles i.e. microsponges. Following sufficient stirring, the mixture was then filtered to separate the microsponges. The microsponges were then dried in an air heated oven. Conceptually, the finely dispersed droplets of the polymeric solution of the drug (dispersed phase) get solidified in aqueous phase via counter diffusion of organic solvent and water out of and into the droplets. The diffused aqueous phase within the droplets decreased the drug and polymer solubility resulting in the co-precipitation of both the components and continued diffusion of the organic phase results in further solidification, producing matrix-type porous microspheres. In comparison with liquid--liquid suspension polymerization method, this method offered the advantage of less exposure of the drug to the ambient conditions, low solvent residues in the

product because the solvent get extracted out due to its solubility in aqueous media or due to its volatile nature.[16-18]

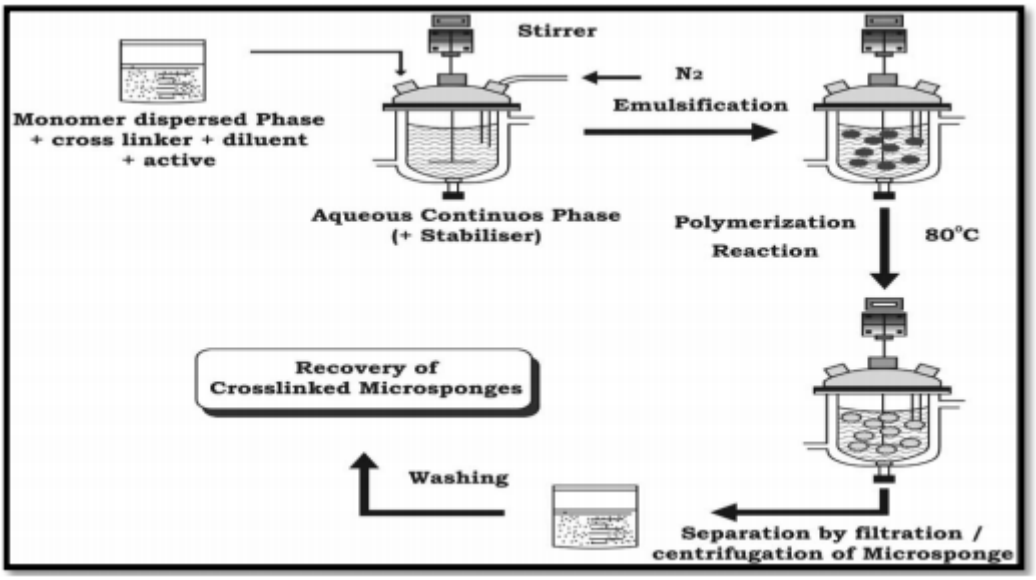

Figure 1: Suspension polymerization- system set up method.

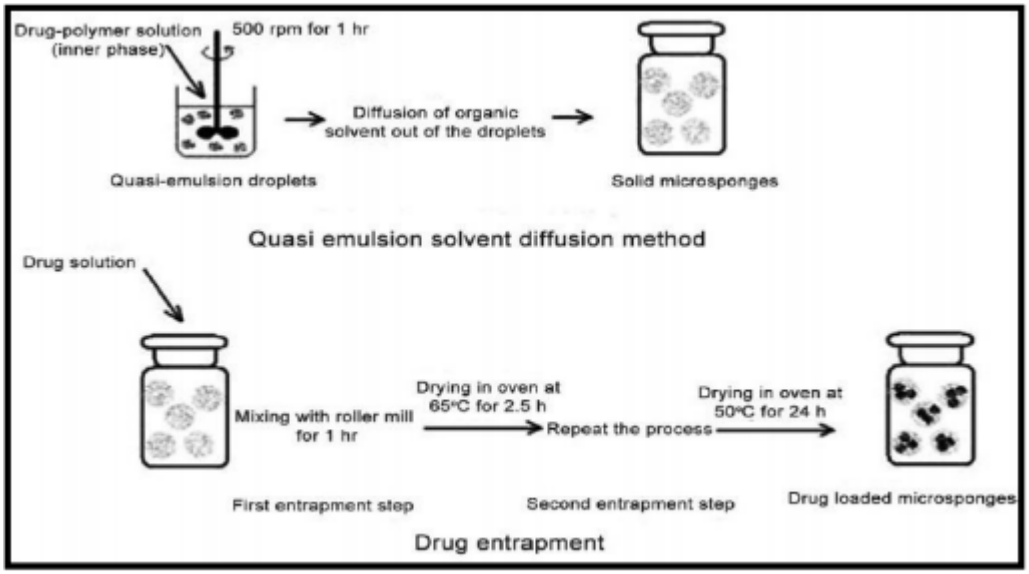

Figure 2: Preparation of microsponges by quasi emulsion solvent diffusion.

Characterization of microsponges

1. Particle size and size distribution

Particle size and size distribution are evaluated using either an optical microscope or an electron microscope. This is an extremely crucial step, as the size of the particles greatly affects the texture of the formulation and its stability. Free flowing powders with fine aesthetic attributes are possible to obtain by controlling the size of particles during

polymerization. Particle size analysis of loaded and unloaded Microsponges can be performed by laser light diffractometry or any other suitable method. The values (d50) can be expressed for all formulations as mean size range. Cumulative percentage drug release from Microsponges of different particle size will be plotted against time to study effect of particle size on drug release.[19]

2. Morphology and Surface topography of SPM

For morphology and surface topography, various techniques have been used like photon correlation spectroscopy (PCS), Scanning electron microscopy (SEM), transmission electron microscopy (TEM) etc. SEM is used widely for which prepared Microsponges are coated with gold–palladium under an argon atmosphere at room temperature and then the surface morphology of the Microsponges is studied.[20]

3. Compatibility studies

The drug-excipients compatibility studies are carried out in order to ensure that there is no inadvertent reaction between the two when formulated into a dosage form. These studies are commonly carried out by recording the differential scanning Calorimetry (DSC) of the chemicals viz., API and excipients individually and also together and checking for any addition or deletion of any peaks or troughs. For DSC approximately 5 mg samples can be accurately weighed into aluminium pans and sealed and can be run at a heating rate of 15oC/min over a temperature range 25–430oC in atmosphere of nitrogen.

Infrared (IR) spectroscopy can also reveal the incompatibilities between the chemical moieties. Compatibility of drug with reaction adjuncts can also be studied by thin layer chromatography (TLC) and FT-IR. Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC).[21-23]

4. Drug Release

Dissolution profile of Microsponges can be studied by use of dissolution apparatus USP XXIII with a modified basket consisted of 5µm stainless steel mesh. The speed of the rotation is 150 rpm. The dissolution medium is selected while considering solubility of actives to ensure sink conditions. Samples from the dissolution medium can be analyzed by suitable analytical method at various intervals.[24]

Applications of microsponges with respect to their advantages

Sl. No.	Applications	Advantages
1	Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization
2	Anti-acne e.g. Benzoyl peroxide	Maintained efficacy with decreased skin irritation and sensitization.
3	Anti-inflammatory e.g. hydrocortisone	Long lasting activity with reduction of skin allergic response and dermatoses.
4	Anti-dandruffs e.g. zinc pyrithione, selenium sulfide	Reduced unpleasant odour with lowered irritation with extended safety and efficacy.
5	Skin depigmenting agents e.g. hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.

CONCLUSION

With demand for innovative and highly efficient Pharmaceutical as well as Cosmetic products, the market holds considerable potential for Microsponge technology and the versatility they offer. As formulators consider new and creative ways to deliver actives, they can realize the full capabilities of these unique materials providing enhanced safety, improved stability, reduced side effects from actives, enhanced multifuntionality and improved ingredient compatibility. Complemented by novel development approaches and creative formulation techniques, Microsponge delivery system can be a winning strategy for a new generation of Pharmaceutical and Cosmetic industry. Microsponges have a distinct advantage over the existing conventional topical dosage forms for the treatment of tropical diseases; it is a unique technology for the controlled release of topical agents also use for oral as well as biopharmaceutical drug delivery. This shows advantageous over other products by non mutagenic, non toxic, non irritant. So microsponge drug delivery system has got a lot of potential and is a very emerging field which is needed to be explored in the future with most research study.

REFERENCES

1. Microsponge: A Prominent Strategy to Accelerate Performance of Topical Formulation. Sanket Gandhi, Hemalata Dol, Sagar Ghorpade. International journal of pharmacy and pharmaceutical research, 2016; 7(3): 272-282.
2. Bezawada S., Charanjitha, Reddy V.M., Naveena, Gupta V.R., “Nanosponges: A Concise Review For Emerging Trends”, International Journal of Pharmaceutical Research and Biomedical Analysis, 2014; 3: 1-6.

3. David F., Nanosponge drug delivery system more effective than direct injection, 2010, www.physorg.com, accessed on 20.12.2011.
4. Jenny A., Merima P., Alberto F., Francesco T., Roleof β- cyclodextrin nanosponges in polypropylene photooxidation. Carbohydrate Polymers, 2011; 86: 127– 135.
5. Selvamuthukumar Subramanian, Anandam Singiredd, Kannan Krishnamoorthy, and Manavalan Rajappan, Nanosponges: A Novel drug delivery system-Review, J Pharm Pharmaceut Sci (www.cspsCanada.org), 2012; 15(1): 103 -111.
6. Jilsha G., Vidya Viswanand., Nanosponge A Novel Approach of Drug Delivery System International Journal of pharm. Science Review And Research, 2013; 19(2).
7. Nilesh J., Ruchi J., Navneet T, Braham Prakash G., Deepak Kumar J., Nanotechnology: A Safe and Effective Drug Delivery Systems, Asian Journal of Pharmaceutical and Clinical Research, 2010; 3(3): 159-165.
8. Won R: Method for delivering an active ingredient by controlled time release utilizing a novel delivery vehicle which can be prepared by a process utilizing the active ingredients as a Porogen. 1987; US Patent No. 4690825.
9. Aritomi H., Yamasaki Y., Yamada K., Honda H, Koshi M. Development of sustained release formulation of chlorpheniramine maleate using powder coated microsponges prepared by dry impact blending method. Journal of Pharmaceutical Sciences and Technology, 1996; 56(1): 49-56.
10. D"souza J.I., Masvekar R.R., Pattekari P.P., Pudi S.R., More H.N. Microspongic delivery of fluconazole for topical application. Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech., 2004; 76.
11. Parthiban K.G., Manivannan R., Krishnarajan D., Chandra S., Nidhin R. Microsponge role in novel drug delivery system. Intl. J. Pharm. Res. Devel., 2011; 3(4): 117-125.
12. Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Gary P, Martin, Nokhodchi A: The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies. International Journal of Pharmaceutics, 2006; 308: 124-132.
13. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity. Chemical and pharmaceutical bulletin, 1992; 40(1): 196-201.
14. Vyas L.K., Tapar K.K., Laddha B.H., Lahoti A.O., Nema R.K. Formulation and development of anti-blemish preparation using microsponge technology. J. Chem. Pharm. Res., 2010; 2(5): 562-571.

15. Chadawar V., Shaji J. Microsponge Delivery System. Current Drug Delivery, 2007; 4: 123-129.
16. Grochowicz M, Bartnicki A, Gawdzik B. Preparation and characterization of porous polymeric microspheres obtained from multifunctional methacrylate monomers. J Polymer Sci., 2008; 46: 6165-74.
17. Patrick B., Deasy ed. Microencapsulation and related drug processes. In: Drugs and Pharmaceutical sciences series. Vol. No. 20. Marcel Dekker Inc.: N.Y., 1984; 195.
18. Comoglu T, Gonul N, Baykara T. Preparation and in vitro evaluation of modified release ketoprofen microsponges. ll Farmaco, 2003; 58: 101-6.
19. Martin A., Swarbrick J., Cammarrata A. In: Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences. 3rd Ed., 1991; 527.
20. Emanuele A.D., Dinarvand R. Preparation, characterization and drug release from thermo responsive microspheres. Int. Journal of Pharmaceutics, 1995; 237-242.
21. Jones D.S., Pearce K.J. Investigation of the effects of some process variables on microencapsulation of propranolol HCl by solvent evaporation method. Int J. Pharm., 1995; 118: 99-205.
22. Anderson D.L., Cheng C.H., Nacht S. Flow characteristics of loosely compacted macroporous microsponge polymeric systems. Powder technology, 1994; 78: 15-18.
23. Ford J.L., Timmins P. Pharmaceutical Thermal Analysis- Techniques and Applications. Ellis Horwood Ltd.: Chichester, 1989.
24. Jayaweera D.M. Medicinal Plants (Indigenous and exotic) used in Ceylon. Part-II. A Publication of the Natural Sciences Council of Sri Lanka: Colombo, 1980.