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Review Article

Review on Microsponges As a Novel Drug Delivery System

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ABSTRACT
Microsponge can be effectively incorporated into oral delivery of drugs using bio erodible polymer's especially for colon specific delivery and also use for topical drug delivery system for retention of dosage form on skin and controlled release drug delivery system thus improving patient compliance by proving site specific drug delivery system and prolonging dosage intervals. The microsponge consists of myriad of interconnecting voids within non- collapsible structures with a large porous surface. The size of Micro sponges can be varied usually from 5-300 µm in diameter. The outer surface is typically porous, allowing the sustained flow of substances out of the sphere. Microsponge delivery system (MDS) can provide increased efficacy for topically active agents with enhanced safety, extended product stability, enhanced formulation flexibility , reduced side effects and improved aesthetic properties in an efficient and novel manner In addition these are non-mutagenic, non allergic, and non-toxic . The present review introduces Microsponge technology along with its synthesis, characterization, programmable parameters and release mechanism of MDS

Keywords: Microsponge, controlled release, oral drug delivery, topical drug delivery.

INTRODUCTION

The Microsponge technology was developed by Won in 1987 and the original patents were assigned to advanced polymer system[1]. Microsponge delivery system (MDS) is unique technology for controlled delivery of drug. MDS technology has been introduced in topical drug products to facillate the controlled release of active drug into the skin in order to reduce the systemic exposure and minimise local cutaneous reaction to active drug. A Microsponge delivery system is patented, highly cross linked, porous, polymeric microspheres polymeric system consisting of porous microspheres that can entrap wide range of actives and then release them onto skin over a time and in response to trigger[2]. The application of topical preparation suffers from many problems such as, ointments which are greasy and sticky nature, and also aesthetically unappealing, this results into lack of patient compliance. Thus, for effective formulation require high amount of active ingredient because of their low efficiency of delivery system which results into irritation and allergic reaction. Hence a need of such delivery system which can overcome those problems and thus Microsponges delivery system can be used in this case.

Microsponges are uniform, tiny, micro-porous polymeric beads and special in shape. It has the interconnected voids of particle size ranges between 5- 300µm. Microsponges Have the network of pores which holds the active ingredients is released in controlled manner due to the porous surface of non-collapsible structure. The Microsponge system has the high degree of cross linking which results in particle that is insoluble, inert and of sufficient strength to withstand the high shear[3].

The microsponge delivery system is designed to:

- Deliver a pharmaceutically active ingredients efficiently at minimum dose,
- Enhance the stability,
- Reduce side effects.

Microsponges are capable of absorbing skin secretions which reduces the oiliness from skin. It has the ability to load a wide range if actives which provide the benefit of enhanced product efficiency, tolerability, mildness etc. These Microsponges are further incorporated into the formulation like gels, lotions, creams, ointments, tablet, capsule and powder[4,5].

Characteristics of Microsponges

- MDS are stable over range of pH 1 to 11
- These are stable at the room temperature up to 130^0c
- Microsponge's formulations are compatible with the majority of vehicles and ingredients.
- Self- sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate.
- These system have higher payload up to 50 to 60 % still free flowing and can be cost effective[6,7,8].

Benefit of Microsponge drug delivery system:

- Enhanced product performance
- Extended release.
- Reduced irritation and hence improved patient compliance
- Improved product elegancy

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- Improved oil control as it can absorb oil up to 6 times its weight without drying.
- Improved formulation flexibility.
- Improved thermal, physical and chemical stability.
- Flexibility to develop novel product forms.
- Microsponge system are non-irritating, non- mutagenic and non- toxic[9,10]

Advantages of Microsponge

Microsponge delivery system has three main advantages, which includes:

Advantages over conventional topical preparation

Conventional topical preparation releases their active ingredient upon application and produces highly concentrated layer of drug which is rapidly absorbed. While Microsponge delivery system can prevent the accumulation of active ingredient and reduces the irritation at site of application and also helps in maintaining the efficacy of drug.

Advantages over liposomes and microencapsulation

Microsponge delivery system can control the release rate of actives which is not possible in case of microcapsules, where once the wall is ruptured the active ingredient will be released .Liposome formulations suffer from the problem like lower payload ,formulation difficulty, limited chemical stability an microbial instability. Microsponge delivery system can help to overcome these problems.

Advantages over ointments

Generally, the ointments are greasy and sticky in nature; these vehicles require the high concentration active drug because of their low efficiency which results into irritation and allergic reactions. It also suffers from other drawbacks such as uncontrolled evaporation of actives, unpleasant odour etc. Whereas Microsponge system increases the amount of time foe which the actives remains present on skin surface and reduces its transdermal penetration[11].

Formulation Consideration

After entrapment of actives, the Microsponges can be incorporated into dosage form like lotions, creams, powder, capsule, tablet, and soaps. To the desired characteristics product, certain considerations are taken into account during the formulation of vehicle. These are:

- The solubility of active in the vehicle must be limited to avoid the depletion of Microsponges before the application
- Only 10-12% Microsponges must be incorporated into vehicle to avoid the cosmetics problem.
- The optimized polymer design and payload of the Microsponge for active must be there for required release rate for given time period.

Criteria of the actives to be entrapped into Microsponge

The active ingredient which can be entrapped into Microsponges must meet the following requirements,

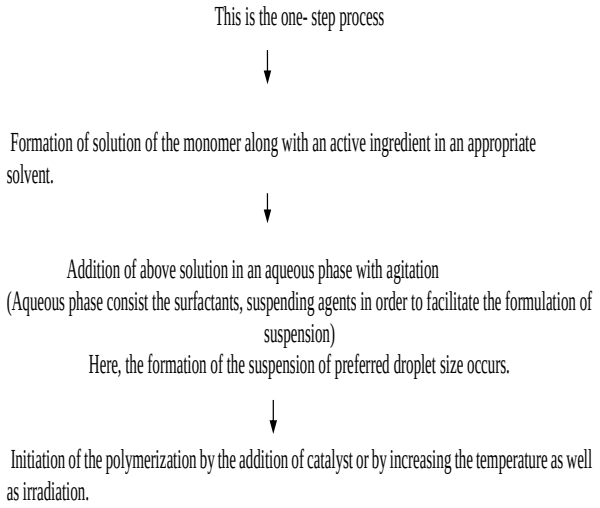
- The active ingredient should be inert to monomer and should not increase viscosity of formulation.
- The active ingredient should be either fully miscible in monomer or miscible by addition of small amount of water immiscible solvent.
- The active should be water immiscible or at most only slightly soluble.
- It should be stable in condition of polymerization condition and in contact with polymerization catalyst[12].

Method of preparation for Microsponge

Depending upon the physicochemical properties of the drug Microsponges can be prepared by two methods,

- Liquid-liquid suspension polymerization
- Quasi-emulsion solvent diffusion.

Liquid –liquid suspension polymerization



The method of polymerization leads to development of reservoirs type of system which opens at the surface through pores. During the polymerization, an inert liquid which is immiscible with water but completely miscible with monomer is used to formation of pore like network. After completion of polymerization process the liquid is removed leaving the porous Microsponge which incorporate the variety of the actives and act as topical carrier.

Quasi- emulsion solvent diffusion

The is the two-step process and used when the drug is sensitive to polymerization reaction. In this method the Microsponge are prepared by using different polymer amount.

This method consists of two phases:

External phase

It includes the 40 mg polyvinyl alcohol in 200 ml distilled water.

Internal phase

The internal phase consists of drug, ethyl alcohol, tritely citrate and polymer. Triethyl citrate is used as the plasticizer and it is added in an amount of 20% of the polymer.

Steps involved in preparation of Microsponges by quasi-emulsion solvent diffusion techniques

Step 1: Preparation of internal phase by addition of polymer in ethyl alcohol

Step2: Addition puff drug to above solution under ultra-sonication at 35^0c

Step3: Addition of internal phase into external phase carried out by continuous stirring for 3hrs

Step4: Filter the mixture to separate Microsponge

Step5: Dry in an oven for 12 hrs. At 40^0cand weigh to determine the production yield[13,14].

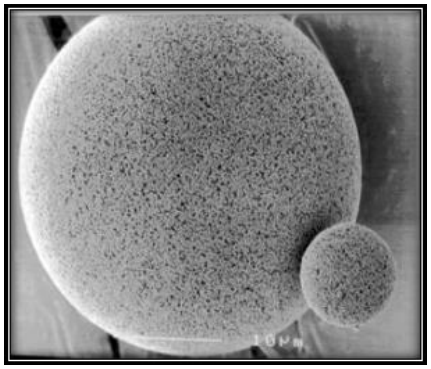


Figure 1: Microsponge

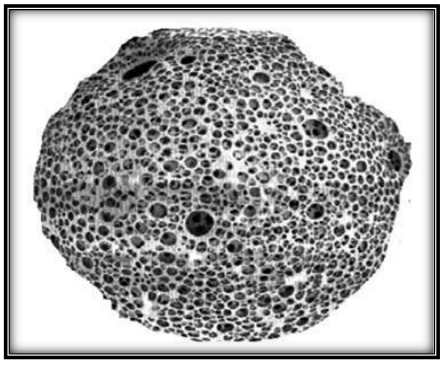


Figure 2: Porous nature of microsponge[23]

Table 1: Commonly used Drugs, polymers and excipient in microsponge formulation[23,24]

Drugs	Polymers	Excipients
Benzoyl Peroxide, Dicyclomine, Fluconazole, Flurbiprofen,Ibuprofen, Ketoconazole, Ketoprofen, Paracetamol, Retinol.	Dimethacrylate, Ethyl cellulose, Eudragit RS 100,Poylstyrene,Polyhydroxyethylmethacrylate	Triethyl citrate.

Mechanism of drug release through Microsponge

The release of drug through Microsponge can be determined by following triggers

Solubility

Release can be achieved by diffusion taking into consideration the partition coefficient of the actives into Microsponges and outside system .Microsponges of water soluble ingredients release the drug in presence of water. Presence of 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 Microsponge network.

pH triggered system

The modification in coating of Microsponge can be used to achieve the pH based drug release.

Pressure

In Microsponges release of the drug can be achieved by applying pressure or rubbing.

Temperature triggered system

The flow rate and release of the actives which are too viscous at room temperature can be achieved by increasing the skin temperature[15].

Characterization of Microsponge

Particle size Determination

Particle size analysis of Microsponge was determined using Motic microscope (Motic DMB series). To determine the particle size, small amount of Microsponges were taken on glass slide and slide was placed on stage of microscope. Then the course and fine adjustment was done to obtain the clear image. The reading of particle size was displayed on the display of computer. Same procedure was repeated for all batches.

Particles larger than 30µm can impart gritty feeling and hence particles of sizes between 10 and 25µm are preferred to use in final topical formulation.

Morphology and Surface Topography of Microsponges

For morphology and surface topography, Microsponges can be coated with gold palladium under an argon atmosphere at room temperature and then the surface morphology of the Microsponge can be studied by scanning electron microscopy (SEM) SEM of a fractured Microsponge particle can also be taken into illustrate its ultra-structure[16].

Loading efficiency and production yield

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

Loading efficiency (%) =

$$\frac{\text{Actual drug content in Microsponge x 100}}{\text{Theoretical Drug content}} \quad \text{....Equation no.1}$$

Production yield of the microparticles can be determined by calculated by calculating accurately the initial weigh of the raw materials and the last weight of the Microsponge obtained

Production yield (PY) =

$$\frac{\text{Practical mass of Microsponges} \times 100}{\text{Theoretical Mass}} \quad \text{...Equation no.2}$$

Characterization of pore structure

Pore volume and diameter are vital in controlling the intensity and duration of effectiveness of the active ingredient .Pore diameter also affects the migration of active ingredients from Microsponge into the vehicle In which the material is dispersed .Mercury intrusion porosimetry can be employed to study effect of pore diameter and volume with rate of drug release of drug from Microsponges .Porosity parameter of Microsponges such as intrusion- extrusion isothermal pore size distribution , total pore surface area ,average pore diameter ,shape and morphology of the pores, bulk and apparent Density can be determined by using mercury intrusion[17].

Compatibility studies

Sr no.	Active agents	Application
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-inflammatory e.g. hydrocortisone	Long lasting activity with decreased skin allergic response and dermatoses.
3.	Acti acne e.g.Benzoyl peroxide	Maintained efficacy with decreased skin irritation and sensitization.
4.	Anti- fungal	Sustained release of actives
5.	Anti-dandruffs e.g. zinc pyri-thione,selenium sulfide	Reduced unpleasant odour with lowered irritation with extended safety and efficacy
6.	Antipruritics	Extended and improved activity
7.	Skin depigmenting agents e.g. hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.
8.	Rubefacients	Prolonged activity with reduced irritancy greasiness and odor.

Compatibility of drug with rejection adjuncts can be studied by thin layer chromatography (TLC) and Fourier Transform Infra- red spectroscopy (FT-IR). Effect of polymerization on crytallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC)[18].

Determination of true density

The true density of microparticles is measured using an ultra-pycnometer under helium gas and is calculated from a mean of repeated determination.

Polymer/ Composition

Factors such as microsphere size, drug loading, and polymer composition govern the drug release from microspheres polymer composition of the MDS can affect partition coefficient of the entrapped drug between the vehicle and the Microsponge system and hence have direct influence on the release rate of entrapped drug. Release of the drug Microsponge system of different polymer composition can be studied by plotting cumulative % drug release against time.

Resilliency (viscoelastic properties)

Resiliency (viscoelastic properties) of Microsponge can be modified to produce beadlets that is softer or firmer according to the needs of the final formation. Increased crossed –linking tends to slow down the rate of release.

Dissolution studies

Dissolution profile of Microsponge can be studied by use of dissolution apparatus USP XXIII with modified basket consisted of 5 µm stainless steel mesh. The speed of the rotation is 150 rpm. The dissolution medium is selected while considering solubility of actives to ensure sink condition. Samples from the dissolution medium can be analyzed by suitable analytical method at various intervals[19].

Kinetics of release

To determine the dug release mechanism and to compare the release profile differences among Microsponges, the drug released amount versus time was used. The release data were analyzed with the following mathematical models:

$Q= k_1t^n$ or $\log Q = \log k_1 + n \log t$..... (3)

Where Q is the amount of the released at time (h), n is a diffusion exponent which indicates the release mechanism, and k1 is a constant characteristics of the drug- polymer interaction.

From the slope and intercept of the plot of log Q versus log t, kinetic parameters n and k1 were calculated.

From comparison purposes, the data was also subjected to Eq. (4), which may be considered a simple, Higuchi type equation.

$Q= k_2t^{0.5} + C$..... (4)

Eq. (4) ,for release data dependent on the square root of time, would give a straight line release profile, with k_2 presented as a root time dissolution rate constant and a constant.

Application of Microsponge Systems

Microsponge are porous, polymeric microspheres that are used mostly for topical and recently for oral administration. It offers the formulation a range of alternatives to develop drug and cosmetic products. Microsponges are designed to deliver a pharmaceutical active active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects and modify drug release.

- Microcpsules cannot usually control the release rate of the active pharmaceutical ingredients (API). Once the wall is ruptured the API contained within the microcapsules will be released
- Pay load is up to 50-60%.
- Free flowing and cost effective
- Microsponges are microscopic spheres capable of absorbing skin secretions, therefore, reducing oiliness and shine from the skin.

Product under development or in the market place utilizes the topical Microsponge system in three primary ways

- As reservoirs releasing active ingredients over an extended period of time
- As receptacles for absorbing undesirable substances, such as excess skin oils or
- As closed containers holding ingredients away from conventional topical formulation over an extended period of time is quite difficult[8,20,21,22].

CONCLUSION

MDS has become highly competitive and rapidly evolving technology more and more research is carrying out for cost-effective therapy. MDS holds a promising future in various pharmaceutical applications in the upcoming years as they have unique properties like small size, enhanced product performance and elegancy. Microsponge can be effectively incorporated into topical drug delivery system for retention of dosage form on skin and also use for oral delivery of drugs using bio erodible polymers, especially for colon specific delivery and controlled release drug delivery system thus improving patient compliance by providing site specific drug delivery system and prolonging dosage intervals. New classes of pharmaceuticals, biopharmaceutical (peptides, protein and DNA- based therapeutics) are fueling the rapid evolution of drug delivery technology. Thus, MDS is a very emerging field which is needed to be explored.

REFERENCES

1. Won R. Method for delivery, 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. Patent No.4690825. US: 1987.
2. Newton DW, Biotechnology Frontier: Targeted Drug Delivery, US Pharmacist, 1991; 16:38-39, 43-44, 46-48, 50-51.
3. Mandava SS, Thava V. Novel Approach: Microsponge Drug Delivery system. International Journal of Pharmaceutical Sciences and Nanotechnology, 2013; 60(1):1935.
4. Londhe KA, Gondkar SB, Saudagar RB, Preparation and Characterization of Diclofenac Sodium Loaded Microsponge for capsule, American Journal of Pharmatech Research 2014, vol 4(6):408-417.
5. Yerram C, Shaikh F, Rubia Y, Amravati V, Mahitha b, Aruna U. Microsponges: A Novel drug delivery system for controlled Delivery of Topical Drugs. International Journal of Pharmaceutical Sciences and Research, 2012:3(4):967.
6. Khopade A J, Jain S and Jain NK, The Microsponge, Eastern Pharmacist, March 1996: 49-53.
7. Vyas SP, Khar RK, Targeted and Controlled Drug Delivery –Novel Carrier System: New Delhi: CBS Publication, First edition; 20044:453.
8. Aritomi H, Yamasaki y, Yamada Honda and Koshi M. Development of Sustained release formulation of chlorphenaramine maleate using powder coated Microsponges prepared by dry impact blending method. J.Pharm.Sci. Tech., 1996; 56(1):49-56.
9. Aloorkar N.H, Kulkarni A.S, Ingale D.J and Patil R. A, Microsponges as Innovative Drug Delivery System, International journal of pharmaceutical Sciences and Nanotechnology, volume 5, Issue 1, April –June 2012.
10. D'souza J.I., More H.N (2008).Topical Anti-Inflammatory Gels of Fluocinolone Acetonide Entrapped in Eudragit Based Microsponge Delivery system .Res J Pharm. Tech 1 (4):502-506.
11. Pradhan SK, Microsponge as versatile tool for drug delivery system, IJRPC, 2011; 1(2).
12. Jadhav Patel V,Mungekar ,S,BhamareG, Karpe M Kadus V. Microsponge delivery system: An updated review ,current status ,future prospects .Journal Of Scientific And Innovative Research ,2013;2(6):1097-1110.
13. Jain N, Sharma PK, Banik A. Recent Advances on Microsponge Delivery system International Journal of Pharmaceutical Sciences Review and Research, 2011; 8(2).
14. Pandey P, Jain V, Mahajan SC. A Review: Microsponge Drug Delivery system. International Journal of Bio pharmaceutics, 2013; 4(3); 226-227.
15. Kilicarslan M, Baykara T, The effect of the drug /polymer ratio on the properties of Verapamil HCL loaded microsphere, Int. J. Pharm, 2013; 252:9-109.
16. Chndramaouli Y, Shaikh F, Rajalakshmi R, Amravati Rubia Y, Chakravarthi N, preparation and evaluation of microsponge loaded control release topical gel of acyclovir Sodium. International Journal of Bio pharmaceutics, 2012;3(2):96-102.
17. Deore M.B,Salunke K.S, Pawbake G.Microsponges As A Modified Drug Delivery System1, Word Journal of Pharmaceutical Research ,vol 4(3) 2015.657-667.
18. Saraf A, Dasani A, Pathan HK. Microsponge Drug Delivery System. As an Innovation in cosmetic word: A Review. Asian Journal of Pharmaceutical education and Research, 202:1(2):70, 75-77.
19. Franz TJ. Percutaneous absorption. On the relevance of in vitro date. J Investdermatol 1975; 45:498-503.
20. Kydonieus AF, Berner B. Transdermal Delivery of drug, CRC Press, Boca Raton, 1987.
21. Tansel C. Preparation and in vitro evaluation of modified release ketoprofen microsponge.|| Farmaco, 2003; 58:101-106.
22. Guyot M and Fawaz F. Microspheres- Preparation and physical characteristics. Int.J. pharmaceutics, 1998; 175:61-74.
23. http://www.pharmainfo.net/files/images/stories/article_images/ReactionVesselForMicrosponge.Preparation.jpg.
24. Chadawar V, Shivaji J. Microsponge delivery system. Current Drug Delivery, 2007; 4: 123-129.