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REVIEW ARTICLE

Small but Mighty: Micro Sponges Transforming Drug Delivery System

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ABSTRACT
Microsponges, an innovative drug delivery system, have garnered significant attention in recent years. This review presents an in-depth analysis of the manufacturing, evaluation parameters, and characterization techniques employed for microsponges as a drug delivery system. Manufacturing microsponges involves various methods, including quasi-emulsion solvent diffusion and precipitation polymerization. The choice of manufacturing technique significantly influences the microsponge characteristics, such as particle size, drug-loading capacity, and release kinetics. Key parameters during manufacturing include the choice of polymers, cross-linking agents, and solvents, which can be tailored to meet specific drug delivery requirements. this review provides a comprehensive overview of microsponges as a drug delivery system, highlighting the manufacturing techniques, evaluation parameters, and characterization methods. Microsponges offer a versatile platform for controlled drug delivery, with the potential to enhance drug solubility, stability, and bioavailability. The insights presented here aim to aid researchers and pharmaceutical scientists in developing effective drug delivery strategies utilizing microsponges.
Keywords: **Drug Delivery System**, *drug-loading capacity, Microsponges*

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INTRODUCTION

Conventional formulations such as gel, ointment, etc. release drugs upon application of dosage form and produce a highly concentrated layer of API which is rapidly absorbed but may cause irritation and less localization. In this topical dosage form, drugs fail to reach systemic circulation, more over these stickiness, unpleasant odor, and greasiness result in poor patient compliance which can be overcome by novel drug delivery discovered by Won in 1987 which is named as Microsponges [1-4]. Microsponges consist of porous microsphere with small sponges-like particles that connects with countless interconnecting voids within non-collapsible structure with large porous surface where the release of drug from these large porous surfaces in a sustained release manner. In comparison with other dosage forms such as liposomes, microencapsulated dosage forms. Microsponges have advantages such as stability over pH from 1 – 11 and temperature conditions up to 130 °C, It has compatibility for most of vehicles as well as ingredients [5].

Microsponges are applicative in various formulations such as sunscreens lotion, anti–acne preparations, anti–inflammatory formulations, etc. along with these formulations, Microsponges are also used in Food Industry, Chemotherapy etc [6]. The objective of this review is to enable the reviewer to the information about the Novel Delivery of Microsponges, its information about its characteristics, advantages, disadvantages, method of preparations and excipients, evaluation tests, stability studies, and case studies related to Microsponges.

Microsponges: as novel drug delivery system:

Microsponges is the patented polymeric system that consist of microsphere in through which wide range of APIs can entrapped and used for the topical application system. These micro sponges are further incorporated into other semisolid formulations such as gel, ointment, creams, lotion etc [7].

Table 1: Application of Microsponges [8]

Sr. No.	Marketed preparation	Applications
1.	Retin A Micro	Acne vulgaris
2.	Line Eliminator Dual Retinol Facial Treatment	Anti wrinkles
3.	Glycolic Acid Moisturizer w/ SPF 15	Anti Wrinkles, soothing
4.	Ultra Guard	Protects baby's skin
5.	EpiQuin Micro	Hyper pigmentation
6.	Retinol 15 Night cream	Antiwrinkle

Advantages of Microsponges drug delivery system[-9-11]:

1. They are stable over pH range of 1 to 11 and can withstand high degrees of temperature such as 130 °C.
2. It bypasses first pass metabolism through hepatic route.
3. It has high loading efficiency.
4. It has relatively longer half – life.
5. It does not undergo any further unwanted reaction.
6. They are thermally, physically as well as chemically stable.
7. It has several advantages such as non allergic, non toxic, non irritant also non mutagenic.
8. It offers wide range of drugs for entrapment and can enhance formulation flexibility.
9. Free flowing properties, economic during its productivity.
10. Release rate can be controlled in microsponges as compared to microencapsules and liposomes.
11. Reduces the irritation.
12. Improves efficacy, bioavailability of drug and extended release and action upto 12 hours.
13. It allows incorporation of immiscible products.
14. Microsponges improves oil control where it can absorb the oil upto 6 times of its weight without drying them.

Characteristics of Microsponges:[12, 15]

1. The spherical structure of microsponges should not be collapsed.
2. Microsponges should be water immiscible or slightly water soluble.
3. Microsponges should be inert with monomers where viscosity should be maintained during formulations.
4. NMT 10 to 12% w/w microsponges must be incorporated into the vehicle to avoid cosmetic problems.
5. Microsponge formulations have an average pore size 0.25µm through which bacteria can not be penetrated.
6. Microsponges should be stable with polymerization catalyst and polymerization conditions.
7. Optimization of payload and design of polymer for microsponges of active should be done which is required for release rate for a given period of time.

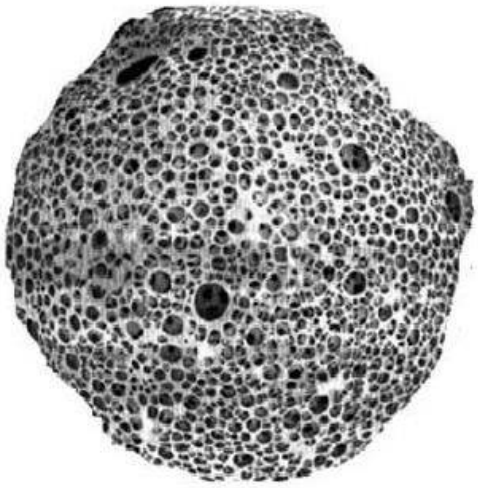

Fig 1: Highly porous structure of microsponges [16]

Size of Microsponges:

The size of microsponges 5 to 300 µm in diameter, 25 µm sized a typical sphere has up to 250000 pores with about equivalent to 10 feet (in length) of internal pore structure where total drug pore volume with 1ml/g for extensive drug retention. Microsponges are typically provided with the surface of range 20 – 500 m2/g and a pore volume of 0.1 to 0.3 cm^3/g. This provides a large reservoir within each Microsponge which is loaded with up to its own weight of active agents.

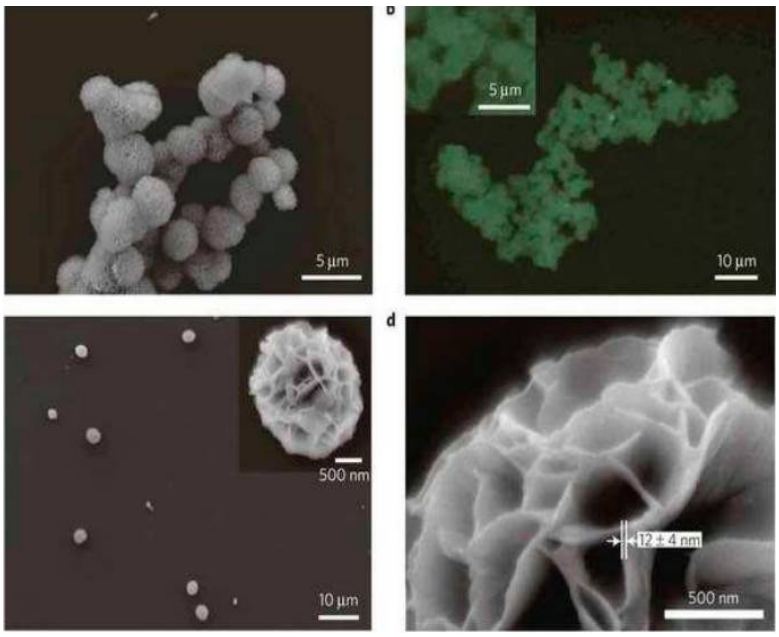

Fig 1: Different sizes of Microsponges[17]

Formulation of Microsponges:

The Microsponges drug delivery systems are generally formulated using API, Polymer, Vehicle, and plastisizer. For the fabrication of microsponges, various cage-forming polymers are used like Eudragit, styrene, ethyl vinyl benzyl, polylactide-co-glycolic acid, etc. Triethyl citrate a plasticizer that help to stabilize the resilient property of the microsponges, various APIs used in microsponges formulations are Domperidone, Pantoprazole, Diclofenac sodium, Fluconazole, Benzoyl peroxide, Indomethacin etc. vehicles such as ethyl alcohol. Plasticizers are PVP, PVC, etc.

Preparation methods of Microsponges:

Microsponges are prepard by the following methods(as per table no.1)[18]:

Table 2: Preparation methods of microsponges: its active components, Advantages, and disadvantages.

Sr. No.	Name of the Method	Components	Advantages	Disadvantages
1.	Liquid – liquid suspension polymerization.	Non – polar drugs, Monomers, surfactants, Dispersants, water insoluble pore forming diluents [19].	One or two step method for the purpose of drug loading.	Non uniform structure, More time consuming, Thermosensitive drugs requires two steps for the reaction of monomers.
2.	Quasi – emulsion solvent diffusion.	Drug – polymer solution with volatile solutions (ethanol, acetone, ethyl cellulose, dichloromethane), Polyvinyl alcohol as external phase [20].	High drug loading, no monomer entrapment, easy control on size of microsponges, spherical particles are obtained in this method.	Water soluble drugs cannot be loaded using this method.
3.	W/O/W emulsion solvent diffusion.	Emulsifying agents such as span, polyehyleneimine and sterylamine in polymeric solution, PVA [21].	Useful for thermolabile drugs such as proteins. Water soluble drugs can be efficiently loaded	Residues of water insoluble surfactants can be present in resultant microsponges.
4.	Addition of porogens.	Porogens like hydrogen peroxide or sodium bicarbonate, external phase as PVA [22].	Highly porous structure with nicely interconnected and distributed pores.	Disruption of structure may results.
5.	O/O emulsion solvent diffusion.	Volatile organic such as dichloromethane with polymer as polylactide glycolic acid with mixture of fixed oil , dichloromethane and span 85 [23].	Complete removal of surfactants.	Removal of organic compounds requires vigorous shaking.
6.	Lyophilization.	Chitosan hydrochloride [24].	Easy, quick and reproducible results.	Cracking or shrinkage may results.
7.	Vibrating Orifice Aerosol Generator method.	Tetraethylorthosilicate, ethanol, water, dilute hydrochloric acid [25].	Formulation of microsponges that used for targeted drug delivery system.	Reflux conditions are required.
8.	Ultrasound – assisted production methods.	B – Cyclodextrin, diphenyl carbonate [26].	Complete removal of solvents, Quick and reproducible results.	Irregular structures.
9.	Electrohydrodynamic atomization method.	Chitosan 4% w/v sodium hydroxide solution [27].	Quick and reproducible results.	Expertises are required for control size of pore and particles.

Characterization of Microsponges:

Microsponges are characterized for various properties such as particle size and its distribution, morphology as well as surface topography, pore structure, loading efficiency, production yield, true density, pore structure, drug – excipients compatibility studies, drug release, Polymer study, resiliency, etc.

Table 3: Characterization of Micro sponges [28, 29]

Sr. No.	Property	Methodology
1.	Particle size and its distribution.	Optical Microscope, Laser light diffractometry.
2.	Particle morphology and surface topography.	Photon correlation spectroscopy, Scanning electron microscopy, Transmission electron microscopy.
3.	Pore structure.	Mercury intrusion porosimetry.
4.	Entrapment efficiency.	UV – visible spectrophotometer.
5.	True density.	Ultra – pycnometer.
6.	Drug – excipients compatibility.	Differential scanning calorimetry, Infrared spectroscopy, Thin layer chromatography, X – ray diffraction.
7.	Drug release.	Dissolution apparatus USP XXIII.

Stability Studies of Microsponges:

Stability studies for the optimized gel formulation were carried out as per ICH norms. Gel was filled in clean collapsible aluminum tubes. Various replicates of these collapsible tubes were kept for 3 months at 40 ± 2 °C and 75 ± 5% RH in humidity chamber. This gel was assessed for change in physicochemical and in vitro release profile at an interval of 30, 60, 90 days. After three months if no significant changes observed then we can conclude that formulation has good stability studies [27].

For example, stability studies of Formulations of curcumin microsponges used for oral and topical drug delivery were conducted as per ICH norms and analyzed for physicochemical tests such as appearance, in vitro percentage release, FTIR spectrographically studies and showed that no significant changes and hence it results in to no signs of instability and have good shelf life [24].

Stability studies conducted on acetazolamide microsponges in situ gel formulations for ocular drug delivery at 25 °C for 6 months to study the effect on mean particle size and % Entrapment Efficiency. Formulations were stored for 3 and 6 months and observed for particle size and size distribution. Selected microsponge formulation (S2) in situ microsponge formulation and free drug were exposed to 4 °C for 8 weeks and evaluated for pH and drug content determination. From this stability studies it was observed that there were no significant changes in % entrapment efficiency and mean particle size of all the microsponges formulation and they conclude that these microsponges formulations were stable for 6 months at room temperatures (25 °C). The results of stability for selected formulation of microsponges (S2) was compared with free drug stored at 4 °C and they observed that the percent drug content was decreased by 12.7 % and 23.77 after the storage of 2 and 8 weeks respectively. From this they conclude that the incorporation of drug into microsponges increases the stability of the drug in gel at storage of 4 °C for upto weeks [29].

Stability studies for microsponges of Babchi essential oil was conducted as per ICH norms and was evaluated for physicochemical properties. They observed that no color changes were observed even no changes observed in drug content and hence concluded that microsponges formulation of Babchi oil was more beneficial than pure Babchi oil [30].

Stability studies as per ICH guideline was conducted on Atorvastatin loaded microsponges gel formulation. And stored for 1 and 3 months at 40 ± 2 °C/ 75 ± 5% RH where samples were withdrawn at 15 and 30 day time interval and observed for Physical properties such as appearance, pH, rheological properties and drug contents etc. and no significant change was observed in appearance, drug content upon storage [31] .

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