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MICROSPONGE DRUG DELIVERY: A REVIEW

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ABSTRACT

Microsponges is a novel approach which offers numerous advantages for drug delivery. Microsponges drug delivery system is employed for the improvement of performance of orally, parenteral and topical administered drugs in various diseases. Microsponges also offers release of drug at specific site in can circulate into the whole body and release the drug at a specific site in a controlled manner. Microsponges consists of macroporous beads, typically 10-25 micron in diameter, loaded with active agent. Microsponge drug delivery can provide increased efficacy for topically active drugs with enhanced safety, improved product stability and improved aesthetic properties in an efficient and novel manner. Microsponges mostly used for topical use and have recently been used for oral administration. So microsponge drug delivery system has got a lot of prospective and is a very emerging field which is needed to be explored in the future with most research study.

Key words: Pharmacosomes, Amphiphilic Compounds, Carrier Mediated Drug Delivery, glycerylmonooleate, lipid crystal.

INTRODUCTION

The Won developed microsponge technology in 1987 & filled original patent for the same and it is assigned to polymer system. Their company developed with variations various products for pharmaceutical and cosmetic use. Microsponges consist of polymeric drug delivery system porous microspheres. They are sponge like structure consisting of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface and spherical in shape. Microsponges are highly stable with less side effects and having ability of modifying drug release. The microsponges are spherical in nature and having particle size ranging from 5-150 μm .¹

Microsponges are the cross-linked, porous, polymeric microspheres which acquire the

flexibility to entrap variety of active ingredients. They are mostly used for topical & oral administration with altering release rate.

The microsponges i.e. microsphere drug delivery system (MDDS) consist of size 5 -150 μm in diameter & with a typical 25 μm sphere can up to 250000 pores and an internal structure of pore equivalent to 10 ft. in length which provides a total pore volume of 1ml/gm. This kind of system exhibits large reservoir within microspionic structure which can be loaded with the same weight of active ingredient.^{2, 3, 4}

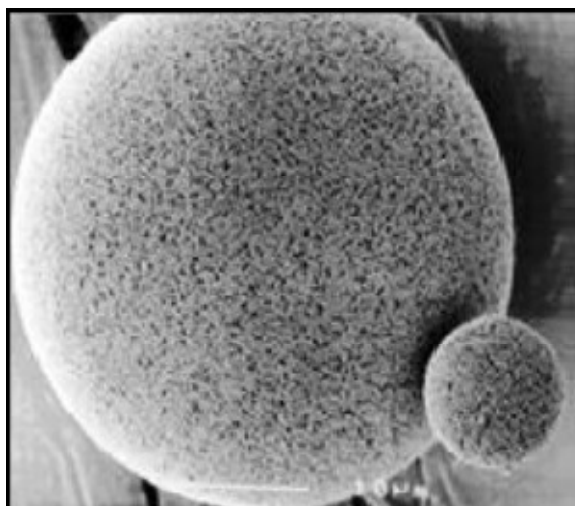


Fig: View of Microsphere

Advantages of Microsphere Drug Delivery System^{5, 6, 7, 8}

MDDS prevent accretion of active ingredient in the epidermis and dermis.
MDDS reduces irritation of effective drug by maintaining their effectiveness.
MDDS has patient compliance.
MDDS increases residential time of a drug on skin surface or in epidermis.
MDDS stable over range of pH 1 to 11, temperature up to 120°C.
MDDS well-matched with most of vehicles and ingredients.
MDDS improves product elegance.
MDDS can improve bioavailability of the drugs.
MDDS have superior formulation flexibility.

Limitations⁹

The formulation methods consisting of use of organic solvents as porogens which may cause an environmental hazard due to their highly inflammable properties. Some time traces of residual monomers can be absorb which may be toxic and hazardous to human health.

Methods of preparation

The Drug loaded microsponges can be prepared by two ways, one step or two step process based on their physicochemical properties of the drug to be incorporated. The active drug which is stable to free radicals is entrapped by one – step process.

1. **Liquid-liquid suspension polymerization¹⁰:** The microsponges are formulated by liquid liquid suspension polymerization method in one step. In this method the monomers are dissolved with active drug (non polar) in suitable solvent of monomer, which further disperse in aqueous phase with agitation. In this aqueous phase addition of surfactants and suspending agents are added to facilitate the formation of suspension. The suspension is formed with distinctive droplets of favored size then polymerization is stated by addition of catalyst or by increasing temperature. A reservoir type of system that opens at the surface through pores because of polymerization. An inert liquid immiscible with water and miscible with monomer is used to form pore network. After completion of polymerization process the liquid is removed from the microsphere and infuse within preformed microsphere and then fit in various active ingredients that acts as a topical carrier. For the efficient and earlier insertion of functional substances solvent can be used. Two-step processes are used and polymerization is perform by means of porogen and that is replaced by functional group if the drug is susceptible to polymerization.

2. **Quasi-emulsion solvent diffusion¹¹:** Microsponges are also prepared by quasi-emulsion solvent diffusion method by using the different polymer. Two phases involved in this i.e. one is inner phase and another one is outer phase. Inner phase- Eudragit RS 100 was dissolved in ethyl alcohol. Drug is added in this solution and dissolved by means of ultrasonication at 35⁰C. Outer phase- PVA solution is added water. The inner phase was poured into outer phase continuing 60 min of stirring, after completion of stirring process, solution is filtered to separate the microsphere. Microsponges are then dried in an hot air oven at 40⁰C for 12hr. and calculate the weight.

Optimum Values for Microsphere Formulation^{12, 13}

Sr. No	Specification	Optimum value
1	Drug and polymer ratio	1:1 , 1:2 , 1:3 , 2:1 , 3:1
2	Amount of drug (mg)	100 – 300
3	Polyvinyl alcohol(mg)	100
4	Inner phase solvent (ml)	Ethyl alcohol
5	Amount of inner phase solvent	10
6	Amount of water in outer phase (ml)	100
7	Temperature of inner phase	25°C
8	Types of process	Magnetic stirrer & Bath sonicator
9	Magnetic stirrer speed	100 rpm

Mechanism of Microsponge^{14, 15}

The microspionic particles consist of open structure that is they don't have continuous membrane, the active drug is free to move in and out. The active component that exists in vehicle will be absorbed in skin. After this the microspionic particles which are retained on surface of stratum corneum continue the release of the drug to the skin by prolonged release over the time.

The mechanism of action highlights the importance of carrying vehicles, if the active ingredient is more soluble in vehicle during formulation, the finished product will not be able to produce desired effect of gradual release. Hence in formulation of microsponge with entrapped drug it becomes necessary to design vehicle which have minimum solubilising power.

Release mechanism of microsponge^{16, 17}

Release of active ingredients from microsponge is depends on following factors-

- i. Pressure – for topical preparation of microsponges rubbing or pressure applied can release the drug on the skin.
- ii. Solubility- water soluble ingredient, microsponges releases the drug in presence of water.
- iii. Change in temperature – if drug incorporated in microsponge is too viscous to flow on the skin, then increase in temperature of the skin increases flow and release rate. for drug release study Franz – diffusion cell is used.
- iv. pH dependant systems : by coating of microsponges pH triggered release can be obtained.

Characterization of Microsponge^{18, 19}

1. Physicochemical properties

- a) **Particle size distribution:** Optical microscope or electron microscope can be used for particle size and size distribution. The particle size affects the texture and stability of formulation. Particle size analysis of loaded or unloaded microsponge can be done by using diffractometry or other suitable methods. Effect of particle size on drug release can be obtained by plotting graph particle size against time.
- b) **Determination of pH:** Microsponge containing gel or other topical formulation Ph can be determined by sophisticated Ph meter.
- c) **Determination of true density:** It is measured by using ultra pycnometer under helium gas.

2. Surface Topography of Microsponges: Various techniques can be used such as photon correlation spectroscopy (PCS), SEM, TEM for study of surface topography of microsponges.

3. Determination of Loading Efficiency and Production Yield: The percentage loading efficiency of microsponges is calculated by following formula,

$$\frac{\text{Actual drug content of microsponges}}{\text{Theoretical Drug Content}} \times 100$$

4. **Production yield:** The production yield of microsponges can be determined by following equation.

$$\text{Production Yield} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical Mass}} \times 100$$

5. **Characterization of Pore Structure:** The pore volume and diameter plays important role in releasing amount of active drug. It is also responsible for movement of drug from microsphere to vehicle. Pore surface area, average pore diameter, shape, morphology, bulk, density can be measured by intrusion porosimetry. The pore diameter of microsphere can be measured by Washburn equation,

$$\text{Production Yield } D = \frac{-4 \gamma \cos \theta}{P}$$

Where, D is the pore diameter (μm); γ the surface tension of mercury (485 dyn cm^{-1}); θ the contact angle (130°); and P is the pressure (psi). Total pore area (A_{tot}) is calculated by using equation, Pore morphology can be characterized from the intrusion–extrusion profiles of mercury in the microsponges.

6. **Compatibility studies:** The compatibility of active ingredient i.e. drug can be checked by TLC and FT-IR. Polymerization effect on crystallinity is examined by Powder X-ray diffraction (XRD) & DSC.
7. **Polymer/monomer composition²⁰:** Polymer composition study is necessary for calculating the release rate of microsponges. Polymer composition may affect partition coefficient between entrapped drug vehicle and microsphere system, hence influences release rate. It can be studied by plotting cumulative % of drug release against time.
8. **Viscoelastic properties:** Viscoelastic properties can be altered according to need of final product. As cross linking increases the rate of release decreases.
9. **Dissolution tests²¹:** For dissolution study of microsphere dissolution test apparatus USP XXIII is used along with modified basket. The dissolution medium is selected according to solubility of active ingredient. The samples withdrawn at suitable intervals were analyzed by suitable analytical techniques.
10. **Kinetics of release²²:** For study of drug release mechanism the different mathematical models were used to analyze release data.

Microsphere Patents²³

Patent Number	Patent Name
5100783	Weighted microsphere for immobilizing bioactive material
1288370	Weighted collagen microsphere
4997753	Weighted collagen microsphere for immobilizing bioactive material
1275955	Weighted microsphere

4863856	Weighted collagen micro sponge for immobilizing bioactive materials
4861714	Weighted collagen micro sponge for immobilizing bioactive material
0217917	Weighted micro sponge for immobilizing bioactive material
1986056694	Weighted micro sponge for immobilizing bioactive material
WO/1986/005811	Weighted micro sponge for immobilizing bioactive material
4092381	Methods of fabricating micro sponge denudated hydrocarbon polymer targets which emit neutrons when irradiated by high energy beams

FUTURE SCENARIO

MDDS have a promising scope in various pharmaceutical applications due to their unique properties like elegance in appearance, performance and pattern of release profile. Also they have good kind of physical, chemical and thermal stability which allows flexibility in manufacturing dosage form. The real future challenge is to prepare safe drug delivery system of drug by using various polymers.

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