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Approaches of Microsponges Review

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ABSTRACT: During the last few decades, pharmaceutical industry gave more importance to the controlled release of dosage forms like solid formulation, semi solid formulation, and topical preparation due to efficacy and patient compliance. Normal topical preparations have some disadvantages like unpleasant odour, greasiness, and skin irritation reported in study cases. Also many topical preparations fail to reach the systemic circulation in sufficient amounts in few cases. This problem is achieved by the present formulation as microsponge in the areas of research. MDS is a microscopic sphere capable of absorbing skin secretions, therefore reducing the oiliness of the skin. Microsponge having particle size of 10-25 microns in diameter, have wide range of entrapment of various ingredients in a single microsponges system and release them at desired rates. Drug release in microsponge is done by the external stimuli like (pH, temperature, rubbing). It has several advantageous over the other topical preparations are non allergenic, non toxic, non irritant, non mutagenic. These MDS's are closely related to microspheres, and used in the sun screens, creams, ointments, (OTC) over- the-counter skin care preparations, recently used in oral drug delivery and also in biopharmaceuticals.

KEY WORDS: Microsponge; microspheres; control release, Biopharmaceuticals.

I.INTRODUCTION

Topical drug delivery systems are formulated to enter in to the systemic circulation, where skin serves as the portal of entry to the drug and various formulations made available in the market are creams, lotions, ointments, TDS etc. Main drawbacks of former topical preparations are the drug doesn't reaches the systemic circulation in sufficient amounts and they are topically localized and no such vehicles and ingredients are incorporated for the controlled release of active medicament. The effective therapy of the disease often seen high concentration of active medicament and produces the skinirritation problems reported in some research studies and also uncontrolled evaporation of active agents, potential incompatibility of drug with vehicles. Thus the microsponge should remain maximum time at the skin and below the epidermis and release the medicament slowly. For these reasons microsponge should meet the following characteristics:

- Microsponges should be uniform, spherical having the cross linked polymeric system, noncollapsible structure consisting of porous void space for the large entrapment of various active ingredients in the spaces and it offers higher shear strength which are commonly used in the area of creams, lotions, powders, having maximum payload of (50% to 60%), and inter connected avoid space of particle size range5-500µm.[2]
- It should be non irritant, non mutagenic, non toxic, non greasy.
- It should be Stable at high temperature, and high shear.
- It should shows improved stability.
- It should have advanced Oil control i.e. Absorbs up to 6 times its weight without drying.
- It should show extended release up to 12 hours.

These formulation are advantageous over the other microcapsules. In microcapsule formulation controlled release of medicament is not possible and when the capsule wall raptures the entire medicament release at a same time where as Microsponge formulations are stable at the temperature of about 130°c.

- This is advantageous over liposomes, because liposomes suffer lower load, difficult informulation, limited chemical stability, microbial instability and in microsponges having average pore size of 25µm, in this pore size even bacteria cannot penetrate through this, i.emicrosponge are self sterilizing.

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- This drug delivery is advantageous over ointments, they produce unpleasant odour, greasiness, skin irritation, they require high concentration of the active medicament which produce skin irritation which is localized on the surface of the skin and uncontrolled evaporation of active medicament, also be there where in microsponges it is slightly water miscible avoids greasiness.

A. Microsponges must meet following requirements:

- If the drug is typically non-polar material, it should create the porous structure this is called porogen.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers and polymers.
- It should be stable in contact with polymerization catalyst and conditions of polymerization.
- Release can be controlled through diffusion or other triggers such as moisture, pH, friction,or temperature.

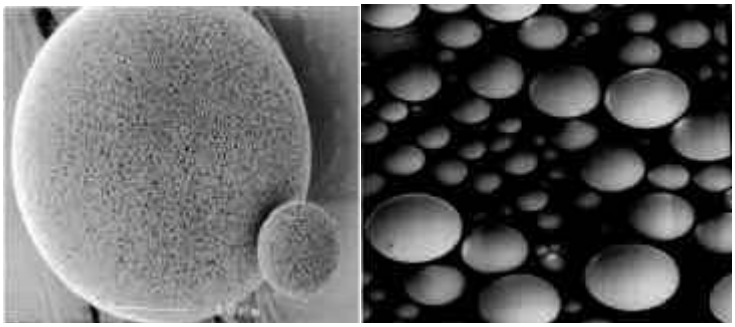

Fig:1 microsponge

The advantages of hollow microspheres include[6]:

1. Improves patient compliance by decreasing dosing frequency.
2. Bioavailability enhances despite first pass effect because fluctuations in plasma drug concentration is avoided, a desirable plasma drug concentration is maintained by continuous drug release.
3. Better therapeutic effect of short half-life drugs can be achieved.
4. Gastric retention time is increased because of buoyancy.
5. Drug releases in controlled manner for prolonged period.
6. Site-specific drug delivery to stomach can be achieved.
7. Enhanced absorption of drugs which solubilise only in stomach.
8. Superior to single unit floating dosage forms as such microspheres releases drug uniformly and there is no risk of dose dumping.
9. Avoidance of gastric irritation, because of sustained release effect, floatability and uniform release of drug through multiparticulate system.

Disadvantages[7]

1. They are not suitable candidates for drugs with stability or solubility problem in stomach.
2. FDDS require sufficiently high level of fluid in stomach so that the system can float and thus sufficient amount of water (200-250 ml) of water to be taken together with FDDS.
3. Drugs having irritant effect on gastric mucosa are not suitable candidates for FDDS.
4. Drugs which are absorbed along the entire GIT and which undergo first pass metabolism may not be desirable e.g. nifedipine.

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B. Characteristics of actives moieties that is entrapped into microsponges:

1. Active ingredients that are entrapped in microsponge can then be incorporated into manyproducts such as creams, gels,powders, lotions and soaps.
2. Certain considerations are taken into account while, formulating the vehicle in order to achieve desired productcharacteristics:
3. It should be either fully miscible in monomer as well as capable of being made miscibleby addition of small amount of awater immiscible solvent.
4. It should be inert to monomers and should not increase the viscosity of the mixture during formulation.
5. It should be water immiscible or nearly only slightly soluble.
6. It should not collapse spherical structure of the microsponges.
7. It should be stable in contact with polymerization catalyst and also in conditions of Polymerization The solubility of actives in the vehicle must be limited.
8. If not, the vehicles will deplete the microsponges before the application.
9. Not more than 10 to 12% w/w microsponges must be incorporated into the vehicle order to avoid cosmetic problems.
10. Payload and polymer design of the microsponges for the active must be optimized for required release rate for given period of time [17, 18]Microsponge formulations are

Stable over range of pH 1 to 11;

- Microsponge formulations are stable at the temperature up to 130oC
- Microsponge formulations are compatible with most vehicles and ingredients
- Microsponge formulations are self sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate
- Microsponge formulations have higher payload (50 to 60%), still free flowing and can be Cost effect.

II. Method of preparation of microsponge:

Micro sponge's drug delivery system can be prepared in two ways, one-step process or by two-step process that is liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques based that is based on physicochemical properties of drug to be loaded.

A. Liquid-liquid suspension polymerization:

The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems. In this method the monomers which are immiscible are first dissolved along with active ingredients in a suitable solvent monomer and are then dispersed in the aqueous phases which consist of additives like surfactant, suspending agents to facilitate formation of suspension. The polymerization is then activated by increasing temperature or irradiation or by addition ofcatalyst. The polymerization process continues the formation of a reservoir type of system with spherical structure. After the polymerization process the solvent is removed leaving the spherical structured porous microspheres, i.e., microsponges.

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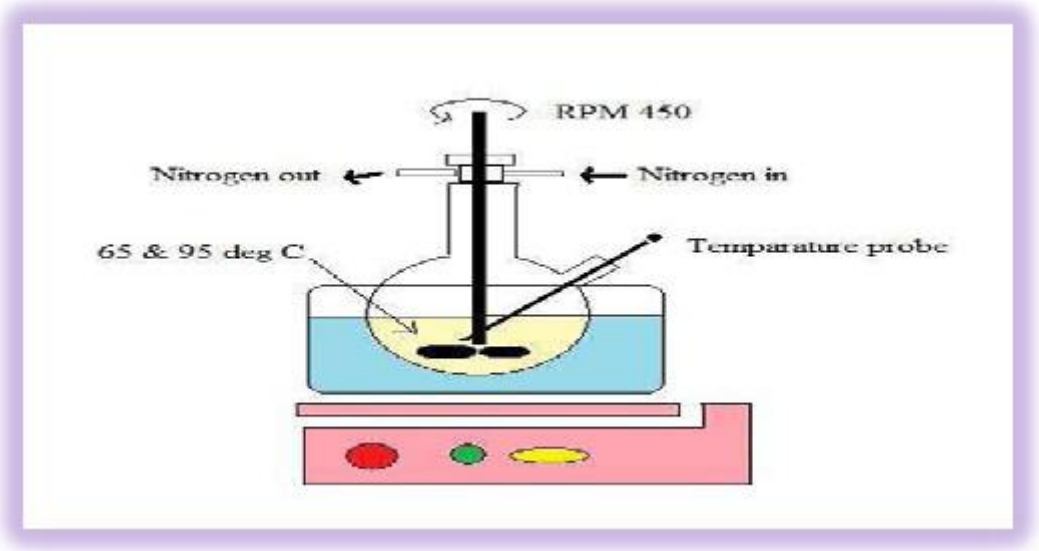

1. **Quasi-emulsion solvent diffusion[9]:**

Porous microspheres (microsponges) were also prepared by a quasi-emulsion solvent diffusion method (two-stepprocess) using an internal phase containing polymer such as eudragit which is dissolved in ethyl alcohol. Then, the drug is slowly added to the polymer solution and dissolved under ultra-sonication at 35°C and plasticizer such as triethylcitrate(TEC) was added in order to aid the plasticity. The inner phase is then poured into external phase containing polyvinylalcohol and distilled water with continuous stirring for 2 hours. Then, the 11 mixture was filtered to separate the microsponges. The product (microsponges) was washed and dried in an air- heated oven at 40°C for 12 hr.

III.EVALUATION OF MICROSPONGES:

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

Physical Characterization of Microsponges

A. Particle Size Determination:

Particle size analysis of loaded and unloaded microsponges can be performed by laser light diffractometry or any other suitable method. The values can be expressed for all formulations as mean particle size range. Cumulative percentage drug release from microsponges.

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different particle size will be plotted against time to study effect of particle size on drug release. 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.

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B. 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.

C. Determination of Loading Efficiency and Production Yield[10]

The loading efficiency (%) of the Microsponges can be calculated according to the following equation:
loading efficacy=$actual\ drug\ content\ in\ microsponges/theoritical\ drug\ content X100$

The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microsponge obtained. Practical Mass of Microsponges.
Production yield = practical mass of microsponges\theoretical mass (polymer +drug) X 100

D. Determination of True Density:

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

E. 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 microsponges into the vehicle in which the material is dispersed. Mercury intrusionporosimetry can be employed to study effect of pore diameter and volume with rate of drugrelease from microsponges. Porosity parameters of microsponges such as intrusion–extrusion isotherms, pore size distribution, total pore surface area, average pore diameters, interstitial void volume, percent porosity, percent porosity filled, shape and morphology of the pores,bulk and apparent density can be determined by using mercury intrusion porosity.

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F. 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 5mg 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.

G. Polymer/Monomer Composition:

Factors such as microsponge size, drug loading, and polymercomposition govern the drugrelease from microsponges. 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 drug from microsponge systems of different polymer compositions can be studied by plotting cumulative % drug release against time. Release rate and total amount of drug released from the system composed of methylmethacrylate/ethylene glycol dimethacrylate is slower than styrene/divinyl benzene system.

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H. Resiliency:

Resiliency (viscoelastic properties) of microsponges can be modified to produce beadletsthat is softer or firmer according to the needs of the final formulation. Increased cross-linkingtends to slowdown the rate of release. Hence resiliency of microsponges will be studied andoptimized as per the requirement by considering release as a function ofcross-linking withtime.

I. Dissolution Studies:

Dissolution profile of microsponges can be studied by use of dissolution apparatus (USPXXIII) with a modified basket consisted of 5µm stainless steel mesh. Speed of the rotationis150 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.

IV.CONCLUSION

The microsponge delivery technology of controlled release system in which active pharmaceutical ingredient is loaded in the macro porous beads and initiates reduction in side effects with improved therapeutic efficacy. 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. This technology is being used currently in cosmetics, over-the-counter skin care, sunscreens, and prescription products. This kind of drug delivery technology may lead to a better understanding of the healing of several diseases. Hence, the microsponge-based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future.

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