Microsponge As Emerging Drug Delivery System

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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. Microsponge Systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as a gel, cream, liquid or powder. The outer surface is typically porous, allowing a sustained flow of substances out of the sphere. Microsponges are porous, polymeric microspheres that are used mostly for topical use and have recently been used for oral administration. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects, and modify drug release.*

Keywords- Controlled release, drug delivery, healthcare systems, microsponges

I. INTRODUCTION

In recent years, there has been considerable emphasis given to the development of novel microsponge base drug delivery systems, in order to modify and control the release behavior of the drugs. By incorporation into a carrier system, it is possible to alter the therapeutic index and duration of the activity of drugs. The ever-increasing interest among consumers with regard to skin care and skin treatment products has been fostered by the widespread use of ingredients like α-hydroxy acids and vitamins in topical products, which can induce perceivable and demonstrable benefits – especially in aging or photo-damaged skin. Although quite useful, in many instances, these ingredients may produce irritancy; such irritancy can be perceived as burning, stinging or redness and particularly occurs in individuals with sensitive skin. Recognizing this problem, the formulators have attempted to deal with this problem in one of the two methods. They have reduced the concentration of such ingredients, but in the process, sacrificed efficacy. They have also modified the vehicle in order to make the product more emollient or skin-compatible.[1] However, this approach, in many cases, also reduces the beneficial effects of the final product. The expanding arena of emerging drugs, increased sensitivity to clinical outcomes, and healthcare costs are driving the need for alternative drug delivery methods and devices. Drug delivery systems that can precisely control the release rates or target drugs to a specific body site have had an enormous impact on the healthcare system. Several predictable and reliable systems been developed for systemic drugs under the heading of transdermal delivery systems (TDS) using the skin as a portal of entry.[2] It has improved the efficacy and safety of many drugs that may be better administered through skin. However, TDS is not practical for delivery of materials whose final target is the skin itself. Controlled release of drugs onto the epidermis with an assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts, is an area of research that has only recently been addressed with success. No efficient vehicles have been developed for controlled and localized delivery of drugs into the stratum corneum and underlying skin layers and not beyond the epidermis. Moreover, the application of topical drugs has many problems, such as, ointments that are often aesthetically unappealing, greasiness, stickiness, and so on, that often results in lack of patient compliance. These vehicles require a high concentrations of active agents for effective therapy because of their low efficiency of delivery system, resulting in irritation and allergic reactions in significant users. Other drawbacks of topical formulations are uncontrolled evaporation of the active ingredient, unpleasant odor, and the potential incompatibility of the drugs with the vehicles. Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Typically, such products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. Thus the need exists for a system to maximize the amount of time that an active ingredient is present either on the skin surface or within the epidermis, while minimizing its transdermal penetration into the body. Microsponges are microscopic spheres capable of absorbing skin secretions, therefore reducing oiliness and shine from the skin. Spherical particles composed of clusters of even tinier spheres are capable of holding four times their weight in skin secretions. Microsponge particles are extremely small, inert, indestructible spheres that do not pass through the skin. Rather, they collect in the tiny nooks and crannies of the skin and slowly release the entrapped drug, as the skin needs it. The microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis.

Potentially, the microsponge system can significantly reduce the irritation of effective drugs without reducing their efficacy. The empty spheres are then washed away with the next cleansing. The microsponge delivery system fulfills these requirements and has resulted in a new generation of very well-tolerated and highly efficacious, novel products. These products are typically presented to the consumer in conventional forms like creams, gels or lotions and they contain a relatively high concentration of active ingredients.

Microsponges are patented polymeric delivery systems consisting of porous microspheres that can entrap a wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens, and anti-infective, anti-fungal, and anti-inflammatory agents.[3] Like a true sponge, each microsphere consists of a myriad of interconnecting voids within a non-collapsible structure, with a large porous surface. The microsponge technology was developed by Won in 1987, and the original patents were assigned to Advanced Polymer Systems, Inc.[4] This company developed a large number of variations of the technique and applied those to the cosmetic as well as over-the-counter (OTC) and prescription pharmaceutical products. At the present time, this interesting technology has been licensed to Cardinal Health, Inc., for use in topical products. The size of the microsponges can be varied, usually from 5 – 300 μm in diameter, depending upon the degree of smoothness or after-feel required for the end formula. Although the microsponge size may vary, a typical 25 μm sphere can have up to 250000 pores and an internal pore structure equivalent to 10 ft in length, providing a total pore volume of about 1 ml/g. This results in a large reservoir within each microsponge, which can be loaded with up to its own weight of active agent. The microsponge particles themselves are too large to be absorbed into the skin and this adds a measure of safety to these microsponge materials. Another safety concern is the potential bacterial contamination of the materials entrapped in the microsponge. As the size of the pore diameter is smaller, the bacteria ranging from 0.007 to 0.2 μm cannot penetrate into the tunnel structure of the microsponges [Figure 1].[3]

Advantages of Microsponge Drug Delivery System:-, 6

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 120oC.

MDDS well-matched with most of vehicles and ingredients.

MDDS improves product elegancy.

MDDS can improve bioavailability of the drugs.MDDS have superior formulation flexibility.

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 polymerization:-** 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 microsponge and infuse within preformed microsponge 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.
2. **Quasi-emulsion solvent diffusion:** Microsponges are also prepared by quasiemulsion 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 phaseEudragit 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 microsponge. Microsponges are then dried in an hot air oven at 40 0C for 12hr. and calculate the weight.
3. **Characterization of Microsponge**
4. **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 pyanometer under helium gas.

2.Surface Topography of Microsponges: Various techniques can b 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,

Actual drug content of microsponges X 100 Theoretical Drug Conten

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

Production Yield= Practical Mass of Microsponges X 100 Theoretical Mass

4.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 microsponge to vehicle. Pore surface area, average pore diameter, shape, morphology, bulk, density can b measured by intrusion porosimetry. The pore diameter of microsponge can be measured by Washburn equation,

Production Yield D= - 4 Y cos Θ P

Where, D is the pore diameter (μm); γ the surface tension of mercury (485 dyn cm−1); θ the contact angle (130o); and P is the pressure (psi). Total pore area (Atot) 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 microsponge 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 microsponge 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 where analyzed by suitable analytical techniques.

10. Kinetics of release: For study of drug release mechanism the different mathematical models were used to analyze release data.

II. CONCLUSION

Microsponge drug delivery system holds a promising opportunity in various pharmaceutical applications in the upcoming future as it has unique properties like enhanced product performance and elegancy, extended release, improved drug release profile, reduced irritation, improved physical, chemical and thermal stability which makes it flexible to develop novel product forms.

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