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A Comprehensive Review on Microsponges Drug Delivery Systems

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ABSTRACT

The special qualities of microsponges are making them a promising drug delivery system. These cross-linked, highly porous polymer particles have the capacity to encapsulate and release medications in a regulated fashion. Microsponges can effectively entrap both hydrophilic and hydrophobic drugs, improving their stability and preventing drug degradation, thanks to their large internal surface area and adjustable pore sizes. Innovative drug delivery devices known as microsponges have drawn a lot of interest from the pharmaceutical industry. The controlled and sustained release of medications is made possible by these porous, polymeric structures, which also minimise side effects and increase patient compliance. These systems also provide regulated release kinetics, which enhance bioavailability and minimise adverse effects. Because microsponges can be used topically or orally, they can be used for a wide range of therapeutic purposes. The potential of microsponges as adaptable drug delivery devices that could completely change the pharmaceutical formulation industry.

***Keywords*-** NDDS, Micro sponge, Bioavailability.

I. INTRODUCTION

Microsponges are novel drug delivery systems that have gained significant attention in the field of pharmaceuticals science. They are tiny particles composed of a highly porous material that can absorbed and release drug in a controlled manner. These unique particles have revolutionized the way drugs are administered offering numerous advantages over conventional drug delivery system. The structure of microsponges is characterized by a large number of interconnected pores which give them their sponge-like appearance. The porous nature of these particles allows them to efficiently entrap drug within their structure. The size of the pores can be customized according to the desired drugs release rate making them highly versatile in terms of drug delivery application furthermore the particles can be easily surface modified to enhance their stability and control release. [1] One of the key advantages of microsponges is their ability to protect drugs from degradation. The porous structure of these particles acts as a barrier against external factor such as light, heat and PH which can negative affect the active pharmaceutical ingredients is significantly reduced ensuring better drug efficacy and improved patient outcomes. The porous structure of these particles allows for a sustained and controlled release of drugs over an extended period of time. This feature is particularly advantageous when dealing with drugs that have a narrow therapeutic window of required frequent dosing. By modulating the pore size and surface properties of the microsponges the release rate of the drugs can be finely tuned to achieve the desired therapeutics effect.[2] Microsponges improved patient compliance compared to conventional drug delivery systems. The controlled release of drugs from these particles reduces the frequency of dosing making it more convenient for patients. This feature is particularly beneficial for individuals who require long term medication or have difficulty adhering to complex dosing regimens.

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Additionally, the localized and targeted delivery of drugs by microsponges can minimize improving patients' tolerability. Microsponges have demonstrated potential in a wide range of therapeutics applications. They can efficiently encapsulate both hydrophilic and hydrophobic drugs allowing for the delivery of a diverse range of pharmaceuticals compounds. Additionally, the particles can be easily formulated into various dosage forms including cream, gels, ointments and tablets furthers expanding their applicability.[3] Microsponge systems can enhance the rate of dissolution of water-insoluble drugs. In oral applications, the microsponge system has been shown to increase the rate of solubilization of poorly water-soluble drugs by entrapping such drugs in the microsponge system's pores. Because these pores are very small, the drug is in effect reduced to microscopic particles and the significantly increased surface area thus greatly increases the rate of solubilization. An added benefit is that the time it takes the microsponge system to traverse the small and large intestine is significantly increased thus maximizing the amount of drug that is absorbed. Microsponges has capacity to adsorb or load high degree of active ingredients into the particles or onto the surface.[4]

II. DEFINING MICROSPONGES

Microsponges are ting sponge-like particles that are typically made from natural or synthetic polymers. Microsponges can be used in various applications including drug delivery cosmetics cleaning products and environmental remediation.

History of microsponge[4]

The microsponge technology was developed by Won in 1987 and the original patents were assigned to Advanced Polymer Systems, Inc. This Company developed a large number of variations of the technique and applied those to cosmetic as well as OTC and prescription pharmaceutical products. At the present time, this interesting technology has been licensed to Cardinal Health, Inc. for use in topical products.

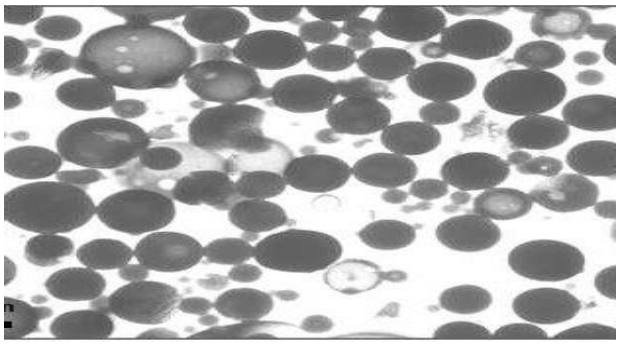

Fig: 1 SEM of Microsponges

In drug delivery microsponges can be loaded with therapeutic drugs and applied topically to deliver them to the desired target site. Their porous structure allows for controlled and sustained releases of the drug improving its efficacy and minimizing size effects. Microsponges can also be used to encapsulated volatile substances such as fragrances or flavours in items like perfumes or food products providing a slow and continuous release over time. In cosmetics microsponges are often incorporated into skincare and beauty products. They can help control oily skin by absorbing excess oil and sebum clearing the skin looking and feeling matte. Microsponges can also be used in sun-scream to enhance the products protection by absorbing and scattering UV-Radiation reducing its penetrating into the skin. Overall microsponges offer a versatile and efficient means of absorbing delivering and controlling the release of various substances in different applications. Their unique properties make them valuable tools in industries ranging from healthcare to cosmetic to cleaning and beyond.

Advantages and Limitation[2]

Advantages

1. Microsponges can absorb oil up to 6 times its weight without drying.
2. It provides continuous action up to 12 hours i.e. extended release.
3. Improved product elegancy.
4. Lessen the irritation and better tolerance leads to improved patient compliance.
5. It can also improve efficacy in treatment. improved performance of the product.
6. Reduce irritation, resulting in improved patient compliance; extended release.
7. Enhanced product class.
8. Better oil control due to its ability to absorb up to six times its weight in oil without drying.
9. Makes room for innovative product forms.
10. Enhances the effectiveness of treatment.
11. More quickly confirm the cure or control.
12. Enhance condition management.
13. Increased bioavailability of the same medications

Limitation

The preparation methods usually use organic solvents as porogens, which pose an environmental hazard, as some may be highly inflammable, posing a safety hazard. In some cases, the traces of residual monomers have been observed, which may be toxic and hazardous to health.

III. CHARACTERISTIC OF MICROSPONGES

1. Tiny size: Microsponges are frequently extremely tiny, measuring only a few micrometers to a few millimeters. This makes it simple for them to interact and penetrate various substances.

2. Highly porous structure: Microsponges have a structure made up of a lot of interconnected "pores" or voids. Due to their large surface area for substance

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adsorption and absorption due to their porous structure, they are extremely effective in a variety of applications.

3. Versatile material: Polymers, metals, ceramics, and even biological materials can be used to make microsponges. Due to their adaptability, microsponges can be customized to have particular traits or functionalities to suit various applications.

4. Controlled release capabilities: Microsponges can be made to release chemicals gradually and under control. They can be used in drug delivery systems because of this. when a specific medication dosage must be released gradually over time.

5. High Stability: Microsponges are renowned for their high stability, which makes them resistant to deterioration and able to retain their structure and properties for lengthy periods of time. They can be used in a variety of harsh environments because of this.

6. Capabilities for both absorption and adsorption: Microsponges are able to both absorb and adsorb substances. While adsorption refers to the surface of the microsponges, absorption describes the uptake of substances within the pores of the nanosponges. The ability to remove impurities or contaminants from liquids or surfaces using microsponges is a result of this.

7. Customized surface characteristics: Microsponges' surface characteristics can be modified to improve their interactions with particular substances. To increase compatibility or selectivity, surface modifications such as charging or other surface additions may be used.

IV. EVALUATION PARAMETERS OF MICRO SPONGES[5]

1. Particle size determination

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

2. 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.

3. Determination of loading efficiency and production yield

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

4. 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 determinations [17].

5. 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 intrusion porosimetry can be employed to study effect of pore diameter and volume with rate of drug release from microsponges. Porosity parameters of microsponges such as intrusion–extrusion isotherms pore size distribution, total pore surface area, average pore diameters, shape and morphology of the pores, bulk and apparent density can be determined by using mercury intrusion porosimetry.

6. 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 aluminum pans and sealed and can be run at a heating rate of 15oC/min over a temperature range 25–430oC in atmosphere of nitrogen.

7. Resiliency (Viscoelastic properties)

Resiliency of microsponges can be modified to produce beadlets that are softer or firmer according to the needs of the final formulation. Increased cross-linking tends to slow down the rate of release.

8. Dissolution studies

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

V. APPLICATIONS OF MICROSPONGES[6]

Microsponge for topical delivery The Micro sponge systems are based on microscopic, polymer-based microspheres that can bind, suspend or entrap a wide variety of substances and then be incorporated into a formulated product, such as a gel, cream, liquid or powder. A single Micro sponge is as tiny as a particle of talcum powder, measuring less than one thousanth of an inch in diameter.

Micro sponge for oral delivery In oral applications, the micro sponge system has been shown to increase the rate of solubilisation of poorly watersoluble drugs by

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entrapping such drugs in the micro sponge system's pores. As these pores are very small, the drug is in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increases the rate of solubilisation.

Micro sponge for Bone and Tissue Engineering Bone-substitute Compounds were obtained by mixing pre polymerized powders of polymethyl methacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium deficient hydroxyapatite powders. The final composites appeared to be porous and acted as micro sponges.

Recent advances in micro sponge drug delivery system: Various advances were made by modifying the methods to form Nan sponges, nan of errosponges and porous micro beads. β - CD nanosponges were also developed that can be used for hydrophobic as well as hydrophilic drugs, in contrast to polymeric micro or nanosponges. These advanced systems were studied for oral administration of dexamethasone, Flurbiprofen, doxorubicin hydrochloride, itraconazole and serum albumin as model drug

Micro sponges for biopharmaceuticals delivery The micro sponge delivery system (MDS) is employed for both in the delivery of biopharmaceuticals as well as in tissue engineering.

VI. METHODS OF PREPARATION OF MICROSPONGES [7]

Initially, drug loading in micro sponges is mainly take place in two ways depending upon the physicochemical properties of drug to be loaded. If the drug is typically an inert non-polar material which will generate the porous structure, then, it is known as porogen. A Porogen drug neither hinders the polymerization process nor become activated by it and also it is stable to free radicals is entrapped with one-step process (liquid-liquid suspension polymerization). Microsponge are suitably prepared by the following methods.

1. Liquid-liquid suspension polymerization

Microsponge is prepared by suspension polymerization process in liquid-liquid systems (one-step process). Firstly, the monomers are dissolved along with active ingredients (non-polar drug) in an appropriate solvent solution of monomer, which are then dispersed in the aqueous phase with agitation. Aqueous phase typically consists of additives such as surfactants and dispersants (suspending agents) etc in order to facilitate the formation of suspension. Once the suspension is established with distinct droplets of the preferred size then, polymerization is initiated by the addition of catalyst or by increasing temperature as well as irradiation. The polymerization method leads to the development of a reservoir type of system that opens at the surface through pores. During the polymerization, an inert liquid immiscible with water however completely miscible with monomer is used to form the pore network in some cases. Once the polymerization process is complete, the liquid is removed leaving the micro sponges which is permeate within preformed micro sponges then, incorporates the variety of active substances like anti-fungal, rubefacients, anti-acne, anti-inflammatory etc and act as a topical carrier. In some cases, solvent can be used for efficient and faster inclusion of the functional substances. If the drug is susceptible to the condition of polymerization, then, two-step process is used and the polymerization is performed by means of alternate porogen and it is replaced by the functional substance under mild conditions.

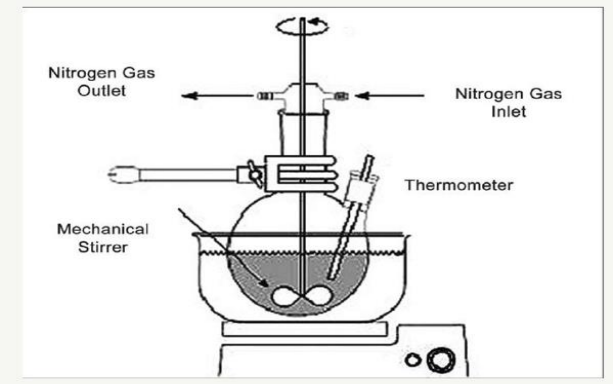

Fig:- 2 Liquid-liquid suspension polymerization

Quasi-Emulsion Solvent Diffusion:

In liquid-liquid systems, the suspension polymerization method is used to create the porous microspheres. In order to prepare them, the active ingredients and monomers are first dissolved in an appropriate monomer solvent solution. Then, the additives surfactant, suspending agents, etc. are dispersed throughout the aqueous phase. Next, a catalyst is added, the temperature is raised, or the rate of irradiation is increased for a predetermined amount of time to start the polymerization. After choosing a monomer or combinations of monomers, polymerization starts to form chain monomers because ladders of cross-linking form between the monomer chains. Folding of the monomer ladder results in spherical particles, or the agglomeration of microspheres, which in turn forms microsphere bunches. bunches binding together to create microsponges, a reservoir-style system, which uses pores to open at the surface. Occasionally, an inert liquid that is entirely miscible with monomer but immiscible with water is employed in the polymerization process to create the pore network. Liquid is removed from the porous microspheres, or microsponges, following polymerization. A solvent can be used to incorporate the drug ingredients more quickly and effectively. the process of polymerization Reaction vessel used to prepare liquid-liquid suspension microsponges.

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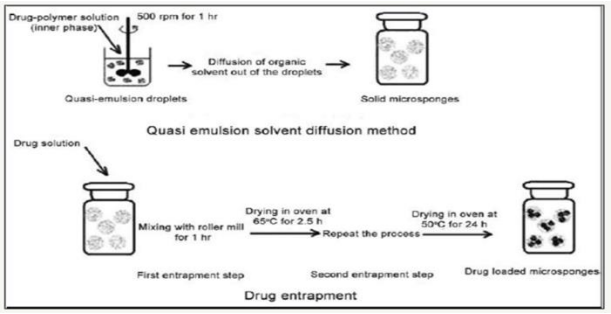

Fig:-3 Method Of Quasi-Emulsion Solvent Diffusion

VII. RELEASE MECHANISM

1. Programmable drug release: Microsponges can be designed to release given amount of active ingredients over time in response to one or more external triggers.

2. Pressure triggered systems: Microsponges system releases the entrapped material when pressurized/rubbed; the amount released depends upon various characteristics of the sponge. By varying the type of material and different process variables, the microsponge best suited for a given application may be optimized. When compared with mineral oil-containing microcapsules, mineral oil containing microsponge showed much more softening effect. The duration of emolliency was also much more for the microsponge systems. [52]

3. Temperature-triggered systems: Some entrapped active ingredients can be too viscous at room temperature to flow spontaneously from microsponge onto the skin. Increased in skin temperature can result in an increased flow rate and hence release. So it is possible to modulate the release of substances from the microsponge by modulation of temperature. For example, viscous sunscreens were found to show a higher release from microsponge when exposed to higher temperatures; thus a sunscreen would be released from a microsponge only upon exposure to the heat from the sun [53]

4. pH triggered systems: Triggering the pH-based release of the active can be achieved by modifying the coating on the microsponge. This has many applications in drug delivery.

5. Solubility triggered systems: Presence of an aqueous medium such as perspiration can trigger the release rate of active ingredients. Ingredients such as antiseptics, deodorants and antiperspirants may be formulated in such types of systems. 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 [55]

VIII. FACTOR AFFECTING MECHANISM OF DRUG RELEASE[56]

Physical and chemical properties of entrapped actives.

1. Physical properties of Microsponge system like pore diameter, pore volume, resiliency etc. Properties of vehicle in which the microsponges are finally dispersed
2. .Particle size, pore characteristics, resiliency and monomer compositions can be considered as programmable parameters and microsponges can be designed to release given amount of actives in response to one or more external triggers like; pressure, temperature and solubility of actives.
3. Pressure Rubbing/ pressure applied can release active ingredient from microsponges onto skin.
4. Temperature change some entrapped actives can be too viscous at room temperature to flow spontaneously from microsponges onto the skin. Increased in skin temperature can result in an increased flow rate and hence release.
5. Solubility Microsponges loaded with water-soluble ingredients like antiperspirants and antiseptics will release the ingredient in the presence of water. The release can also be activated by diffusion taking into consideration the partition coefficient of the ingredient between the microsponges and the outside system

Characteristics of Materials that is Entrapped in Microsponges [35-39]:

Most liquid or soluble ingredients can be entrapped in the particles.Actives that can be entrapped in microsponges must meet following requirements, It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent[33]

1. It should be water immiscible or at most only slightly soluble.
2. It should be inert to monomers.
3. The solubility of actives in the vehicle must be limited to avoid cosmetic problems; not more than 10 to 12% w/w microsponges must be incorporated into the vehicle. Otherwise the vehicle will deplete the microsponges before the application.
4. The spherical structure of microsponges should not collapse.
5. Polymer design and payload of the microsponges for the active must be optimized for required release rate for given time period.
6. It should be stable in contact with polymerization catalyst and conditions of polymerization.

Release mechanism of active ingredient from microsponges[50]

1. Pressure

Microsponge system releases the entrapped material rubbing/ pressure applied can release active ingredient from microsponges onto skin. The amount released depends upon various characteristics of the sponge. By varying the type of material and different process variables, the microsponge best suited for a given application may be optimized. When compared with mineral oil containing microcapsules, mineral oil containing microsponge showed much more softening

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2. pH triggered systems

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3. Solubility

Microsponges loaded with water-soluble ingredients like anti-prespirants and antiseptics will release the ingredient in the presence of water. The release can also be activated by diffusion taking into consideration the partition coefficient of the ingredient between the microsponges and the outside system. Sustained release microsponges can also be developed. Various factors that are to be considered during development of such formulations includes, Physical and chemical properties of entrapped actives. Particle size, pore characteristics, resiliency and monomer compositions can be considered as programmable parameters and microsponges can be designed to release given amounts of actives in response to one or more external triggers like; pressure, temperature and solubility of actives.

Microsponges are innovative drug delivery systems designed to control the release of active ingredients. They are highly porous, polymeric particles that can absorb and encapsulate active ingredients within their structure. The release mechanism of the active ingredient from microsponges involves both physical and chemical processes.[48]

IX. CONCLUSION

In the conclusion, drug delivery systems utilising microsponges have shown great promise for transforming the drug delivery industry. Because of their special porous structure, these small polymeric spheres have many benefits, including targeted delivery, improved stability, and controlled release. Microsponges protect medications from deterioration by encasing them within their structure, guaranteeing maximum therapeutic efficacy. Furthermore, they hold great promise for personalised medicine due to their capacity to pierce deeply into tissues and release drugs selectively at the desired location. It is clear that as science develops, drug delivery systems utilising microsponges will be essential to enhancing patient outcomes and paving the way for a more promising future in the pharmaceutical sciences.

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