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A REVIEW ON MICROSPONGE DRUG DELIVERY SYSTEM

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Abstract
The delivery method for microsponges is a highly cross-linked, porous, polymeric microsphere system that can entrap and release substances into the skin over time. It is a novel obtainment which offering many benefits for drug administration. The performance of medications delivered topically, parenterally, and orally is improved by the use of microsponges drug delivery systems. Microsponges with particle sizes between 10 and 20 microns in diameter can entrap a wide range of different components and release them at predetermined rates. Additionally, microsponges provide regulated medication release at a specific place while also allowing the drug to circulate throughout the entire body. Microsponges effects might last up to 12 hours. Microsponges are reliant on the physiochemical characteristics of the medication. MDS has made by various method utilization emulsion system or by suspension polymerization between a liquid-liquid system. Microsponges can be used in formulations including creams, powders, gels, and lotions to entrap different types of drugs. The formulations of microsponge are stable from pH 1 to 11; 130°c. Therefore, the development of microsponge drug delivery systems has great potential and is a rapidly developing topic that will require further future research.

INTRODUCTION

Comparing the Microsponge Drug Delivery System to other technologies like microencapsulation and liposomes reveals certain advantages. Typically, microcapsules are unable to regulate how quickly actives are released. The actives inside the microcapsules will be released once the wall is ruptured. Low payload, challenging formulation, limited chemical stability, and microbial instability are all problems for liposomes [1]. Controlling the rate of distribution of active chemicals to a specific human organ is one of the toughest issues addressed by pharmaceutical scientists. Various Systems that are trustworthy have been looked into for the transdermal a delivery method that uses the skin as the entry point for many [2]. Microsponges have the ability to sterilize themselves, and this thing is best about the Microsponges, multiple studies have shown that they are naturally non-mutagenic, non-irritating, non-allergic, and non-toxic, because this delivery systems is required high concentrations of active substances for optimal therapy. An active element in the composition of microsponges is delivered gradually. Small, inactive sphere formulations called "microsponges" used in medication delivery do not pass through the skin's membrane. Microsponges are proprietary polymeric delivery systems made of porous microspheres that can hold a variety of active substances, including sunscreen, emollients, perfumes, essential oils, and anti-infective, anti-fungal, and anti-inflammatory medications [3]. Microsponge technology on 1987 and assigned it to the polymer system. Their company created a variety of pharmaceutical and cosmetic items with slight modifications. Microspheres made of polymeric materials with pores make up microsponges. They have a spherical shape, are non-collapsible, and have a large porous surface. They are sponge-like structures made up of numerous interconnected voids. Microsponges have a high level of stability, few adverse effects, and the capacity to alter medication release. The microsponges have spherical particles with a size range of 5-150 m. Patented, highly cross-linked, porous polymeric microspheres used in the Microsponge Delivery System can entrap a variety of active ingredients and then release them at a controlled rate [4]. MDD System raise safety, and provide the high efficacy in the topically actives agents, extending product stability, and developed cosmetic characteristic.

Advantages [5-7]

Microsponges systems are non-irritating, non-mutagenic, non-irritating, non-allergic, and non-toxic.

- ❖ Developed product formulation flexibility.
- ❖ It allows the incorporation of immiscible products.

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- ❖ Microsponge drug delivery can be developed for increasing bioavailability of drug.
- ❖ Improves stability, thermal, physical and chemical stability.
- ❖ MDDS absorb oil secretions, which results in less greasy skin.
- ❖ Continuous activity for up to 12 hours after extended release.
- ❖ It can help to enhance the efficacy in treatment.
- ❖ Improves material processing like liquid can be converted to powders.

Limitation [8]

The formulation techniques involving the use of organic solvents as porogens, could be hazardous to the environment because of their high inflammable properties. Sometimes, find residues monomers can absorb which may be viperous and dangerous to human health. For monomers reactions it needed more time.

Potential features of microsponge drug delivery systems [9]

Some of the features are available in MDDS such as: -
Microsponges is a small in size their average pore size (0.25µm), it is not required any sterilization or addition of preservatives because it restrict the penetration of bacteria. Microsponges are naturally non-mutagenic, non-irritating, non-allergic, and non-toxic, because this delivery systems required high concentrations of active substances for optimal therapy. Microsponges have good compatibility with a range of mediums and substances. Microsponges has showing their stability at the high temperatures up to 130°Cover the pH ranging from 1 to 11. The best thing about the microsponges it's capable to sterilize themselves. Microsponges absorb the oil up to six times their weight without drying.

Characteristics of materials that are entrapped in Microsponges [1, 10]

The ingredients which are entrapped in the particles they are mostly liquid or soluble Microsponges follows this thing such as: -

- When in contact with the catalyst for polymerization and under polymerization circumstances, it should be stable.
- It must either be completely miscible in monomer or have the ability to become miscible by adding a tiny amount of a solvent that is water immiscible.
- It must be immiscible in water and slightly soluble. It should be inert to monomers.
- The spherical structure of microsponges should not collapse.
- When in contact with polymerization catalyst it must be stable and conditions polymerization.

Drugs explored in Microsponge Delivery System [11,12]

- Ibuprofen
- Benzyl peroxide
- Paracetamol
- Flurbiprofen
- Retinol
- Fluconazole
- Ketoprofen
- Dicyclomine
- Ketoconazole

Evaluation Parameters of Microsponges [13]

- Particle size (Microscopy)
- Topography of surface and morphology
- Characterization of pore structure
- Loading efficiency and production yield
- Characterization of pore structure
- Compatibility studies
- Resiliency
- Release study of drug

Physical Characterization of Microsponges:

1. Particle Size Determination [14]

The analysis of the particle size of loaded and unloaded microsponges can be done using laser light diffractometry or any other appropriate technique. Particles between10 and 25 m in size are preferable for use in the final topical formulation because particles bigger than 30 m can give off a gritty feeling. The values can be expressed for all formulations as mean particle size range.

2. Scanning electron microscope study [15]

Prepared microsponges can be coated with gold palladium at room temperature in an argon environment to study their morphology and surface topography. SEM can then be used to examine the microsponges surface morphology (SME). SEM of a fractured microsponges particle can be taken its ultrastructure.

3. Determination of Loading Efficiency and Production Yield [16]

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

$$Loading\ efficiency = \frac{Actual\ DC}{Theoretical\ DC} \times 100$$

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.

$$Production\ Yield = \frac{Practical\ mass\ of\ microsponges}{Theoretical\ mass\ (Polymer + drug)} \times 100$$

4. Determination of True Density [17]

Utilizing an ultra-pycnometer and helium gas, the true density of microparticles is determined by averaging several measurements.

5. pH Triggered Systems [18]

By changing the coating on the microsponge, it is possible to initiate the pH-based release of the active. There are numerous uses for this in drug delivery.

6. Temperature Change [19]

Few encapsulated active substances can be too viscous at room temperature to flow abruptly from microsponges onto the skin. The rate of flow also increases with an increase in skin warmth, which improves release.

7. Solubility [20]

When there is water present, microsponges containing water-soluble compounds such as antiseptics and deodorants release the component. Diffusion can also be used to activate the release, but it must take into account how evenly the substance is distributed between the microsponges and the external system.

8. Compatibility Studies

Compatibility of drug with reaction adjuncts can be studied by thin layer chromatography (TLC) and Fourier Transform Infra-red spectroscopy (FT-IR) [21].Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and differential (XRD) and Differential Scanning Colorimetry (DSC) [22].

For DSC, samples can be precisely weighed into aluminum pans, sealed, and heated at a rate of 15°C/min throughout a temperature range of 25-430°C in a nitrogen atmosphere [23,24]

Mechanism of releasing [25, 26]

The mode of action emphasis the value of transporting vehicles; if the active ingredient is more soluble in the vehicle during formulation, the completed product will not be able to provide the intended effect of progressive release. Therefore, it becomes vital to create a vehicle with a low solubilizing power when creating a microsponge with an entrapped medication.

Since the microspongic particles don't have a continuous membrane, they have an open structure that allows the active substance to pass freely in and out. The vehicle's active component will be absorbed by the skin. Following this, the stratum corneum's surface-retained microspongic particles continue to distribute the medication to the skin over time through a sustained release.

Preparation of microsponge:

Depending on the physicochemical characteristics of the drug to be loaded, drug loading in microsponges can be accomplished in one step or two steps process as studied in the liquid-liquid suspension polymerization and quasi emulsion solvent diffusion procedures. If the medicine is normally a non-polar inert substance, it will produce the porous structure known as a porogen. Porogen medication that is stable to free radicals and neither slows down nor activates polymerization is trapped using a one-step procedure.

1. Liquid-liquid suspension polymerization [26-28]

In this liquid-liquid suspension polymerization process, porous microspheres are made using the liquid-liquid suspension polymerization method. In this approach, the monomers are dissolved in a suitable solvent together with the active ingredient (a non-polar medication), which is then dispersed in an aqueous phase while being stirred. Surfactants and suspending agents are applied during this aqueous phase to aid in the production of suspension. Then the polymerization is started by adding a catalyst, raising the temperature, or using radiation.

A spherical structure made up of tens of thousands of microsponges that are clustered like grapes and create interconnecting reservoirs is created as the polymerization process progresses. The microsponge products can be made using styrene and divinylbenzene or methyl methacrylate and ethylene glycol dimethacrylate as starting materials.

The various steps involved in the preparation of microsponges are summarized as: -

- Choosing a monomer or a mixture of monomers.
- Formation of chain monomers as polymerization begins.
- Formations of ladders as a result of cross linking between chain monomers.
- Binding of bunches to form microsponges.

Folding of monomer ladder to form spherical particles- Agglomeration of microspheres, which give rise to formation of bunches of microspheres

1. Quasi-emulsion solvent diffusion:

Microsponges are also made by quasi-emulsion solvent diffusion method by using the different polymer. The internal phase was made up of the drug, ethyl alcohol, polymer, and TEC, which was added to the polymer in the internal phase at a rate of 20% to help with plasticity. At first, the external phase was combined with the internal phase, which had been produced at 60 °C. The mixture

was continually swirled for two hours following emulsification. The mixture was subsequently filtered to remove the microsponges. The product was washed and dried by vacuum oven at 50°C for 24 hours [10].

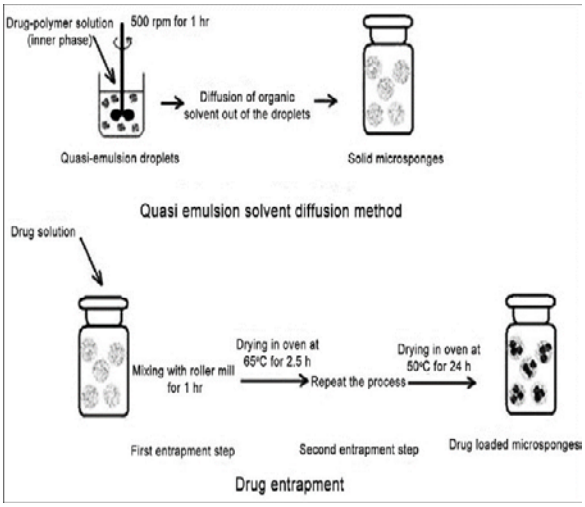

Figure 1: Preparation of microsponges by the quasi-emulsion solvent diffusion method

Table1: Applications of microsponge system [29]

Active agents	Applications
Anti-fungals	Sustained release of actives.
Anti-inflammatory	Long lasting activity with reduction of skin allergic response and dermatoses.
Anti-acne	Maintained efficacy with decreased skin irritation and sensitization
Anti-dandruffs	Reduced unpleasant odour with lowered irritation with extended safety and efficacy.
Rubefacients	Prolonged activity with reduced irritancy greasiness and odour.
Skin de-pigmenting agents	Improved stabilization against oxidation with improved efficacy and aesthetic appeal
Antipruritics	Extended and improved activity
Sunscreens	Enhanced defence against sunburns and other sun-related harm.

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Table 2: List of marketed products using microsponge drug delivery system [30]

Product name	Content	Uses	Manufacture
Salicylic Peel 20	Salicylic acid 20%,	Improve fine lines, pigmentation and acne concerns.	Biophora
Salicylic peel 30	Salicylic acid 30%	Freeing the skin of all dead cells while doing no damage to the skin.	Biomedic
NeoBenz®Micro	Benzoyl peroxide, methyl methacrylate/glycol	Antibacterial properties and is classified as keratolytic	Intendis Inc. Morristown NJ07962 USA
Retin-A-Micro	0.1% and 0.04% Tretinoin, methyl methacrylate/ glycol dimethacrylate, aqueous gel base.	Diminishment of fine lines and wrinkles, a noticeable improvement in the skin discolorations due to aging, and enhanced skin smoothness.	Biomedic, Sothys
Line eliminator dual retinol facial treatment	Vitamin A	Improve fine lines, pigmentation, and acne concerns	Biophora
Dermalogica Oil Control Lotion	Niacinamide, Zinc Gluconate, Yeast Extract, Caffeine, Biotin, Salicylic Acid, Enantia Chlorantha Bark Extract.	To reduce oily shine on skin's surface	John and Ginger Dermalogica Skin Care Products
Carac Cream	0.5% Fluorouracil, 0.35% methyl methacrylate / glycol dimethacrylate cross-polymer & dimethicone.	Visibly diminishes appearance of fine lines, wrinkles & skin discolorations Associated with aging.	Avon

CONCLUSION

Microsponge Delivery System is raised for topical delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, antipruritics, rubefacients etc it is loaded with active ingredients and consists of many microporous, for controlled release of topical agents MDDS is excellent technology. The microsponge Delivery technology highly eligible for the dermatological drug delivery products. MDD is improved the bioavailability of drug and maintaining their therapeutic efficacy and reduce the adverse effect the best thing about microsponge they have the ability to sterilize

themselves Therefore, the microsponge drug delivery system as an important tool for future inventions in controlled drug delivery system.

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