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A BRIEF REVIEW ON MICROSPONGES DRUG DELIVERY SYSTEM

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ABSTRACT

Microsponges are polymeric delivery systems prepared of porous microspheres. They're tiny sponge- suchlike spherical molecules with a large porous surface. also, they may improve stability, reduce side effects and modify drug release positively. Microsponge technology has multiple favorable characteristics, which form it a versatile drug release vehicle. Microsponge Systems are based on atomic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can also be incorporated into a formulated product similar as a gel, cream, liquid or powder. The external surface is generally porous, allowing a sustained inflow of substances out of the sphere. Microsponges are porous, polymeric microspheres that are used primarily for topical Sactive component efficiently at the minimum dose and also to enhance stability, reduce side effects, and modify drug release.

KEYWORDS: Microsponges, Topical Formulation, Over-the Counter (OTC), Controlled Release, Oral Administration.

INTRODUCTION

Microsponges is polymer drug delivery devices based on porous microspheres. The microsponge system consists of microscopic polymer-based microspheres that can trap a variety of compounds before mixing into the manufactured product such as gel, cream, liquid, or powder. They are round, a sponge-like particle with a large porous surface area. They can also improve stability, minimize side effects, and positively alter drug release. This technology has several advantages that make it useful drug delivery mechanism.[2,4]

The geography of drug delivery technologies has largely become competitive and is evolving rapidly. Increasingly advanced developments in delivery systems are being incorporated to optimize the effectiveness and cost-effectiveness of remediation. DNA-based peptides, proteins, and rectifiers cannot be delivered effectively by conventional means. New drugs and biopharmaceuticals (peptides, proteins, and DNA-based orthomers) are driving the rapid development of drug delivery technology. Micro-sponge delivery system(MDS) is "widely patented, cross-linked, permeable polymer microspheres, a tailored polymer system of permeable microspheres that can trap a variety of active ingredients and also release them into the skin in a timing and response to sensors." 10 to 25 microns at the periphery.[1,2]

In recent times, considerable emphasis has been placed on the development of novel microsponge-based drug delivery systems, aimed at modifying and controlling drug release. Thanks to objectification in the delivery system, it is possible to modify the medicinal index and duration of action of the drug. Growing consumer interest in skin care and treatment products is driven by the widespread use of ingredients such as α-hydroxyl acids and vitamins in topical products, which can delivers notable and demonstrable benefits, especially in cases of print damage or growth. Skin. Although relatively helpful, in many cases these ingredients can cause irritating effects; Similar irritation can be perceived as burning, burning or bluish and occurs especially in people with sensitive skin. Faced with this problem, inventors tried. To determine this problem in two ways. They reduced the concentration of these ingredients but sacrificed their effectiveness. They also modified the carrier to make the product more supple and skin-friendly.[5]

The microsponge drug delivery system offers advantages over other technologies such as microencapsulation and liposomes. Microcapsules are generally unable to control the rate of drug release. After breaking through the wall, the active ingredients contained in the microcapsules are released. The liposome has lower loading capacity, difficult formulation, limited chemical stability, and microbiological instability.[4]

Controlling the release rate of active substances at a specific site in the human body has been one of the greatest challenges for pharmaceutical scientists. Several predictable and reliable systemic drug delivery systems have been developed under the name transdermal delivery system "TDS"; Use the skin as an entry point. It has improved the effectiveness and safety of many medications that can be better delivered through the skin. However, TDS is not possible when providing materials whose ultimate target is the skin itself (Kydonieus and

Berner). The controlled release of the drug into the epidermis while ensuring that the drug remains primarily localized and does not enter the systemic circulation in significant quantities is a challenging area of research.[7]

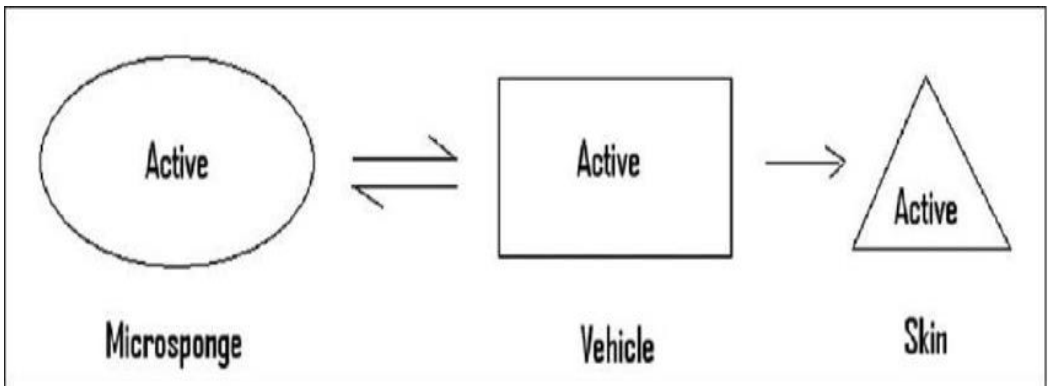

Figure 1: Schematic representation of the distribution of the loaded material (active) on skin.

History Of Microsponge

The microsponge technology existed Developed by Won in 1987 and the original Brands was delegated to Advanced Polymer Systems, Inc. This Troop Developed interpretations of the system and appertained them to cosmetic as well as non-convention drugs(OTC) and convention medicine products. Presently, this immersing technology has existed certified to Cardinal Health, Inc. for employment in topical products.[10,19]

Defination of Microsponge

A assemblage of very negligible, spongelike molecules, having a bulky porous surface, applied for drug release. The Microsponges Delivery System(MDS) is apatented polymeric complex consisting of porous microspheres. They're bitsy sponger like globular molecules that consist of a myriad of interlinking voids within anon- collapsible structure with a bulky porous surface asshown in figure 2 through which functioning component are released in a controlled proprieties.[18]

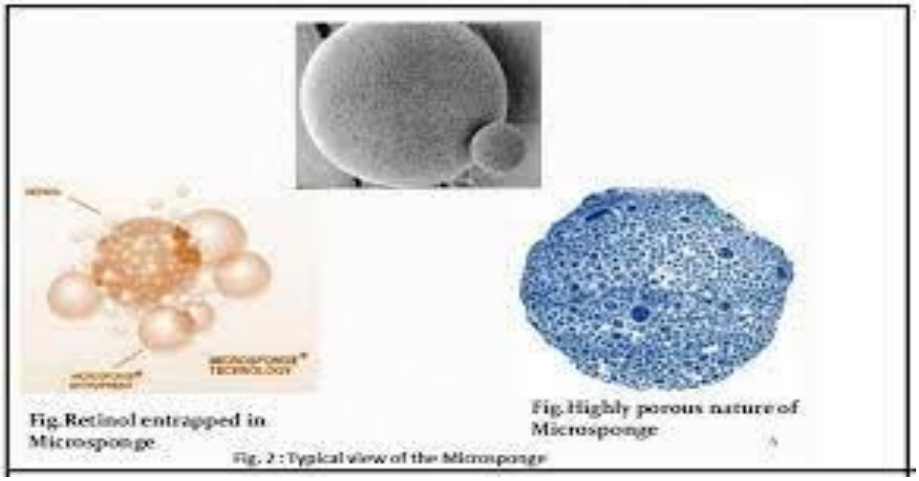

Figure 2;- Topical view of the Microsponge.

Potential features of microsponge drug delivery systems

- MDS have stability in pH extending from 1 to 11.
- It should have stability at high temperatures up to 130°C.
- MDS have self-sterilization due to pore size 0.2 5μm which prevents penetration of bacteria, thus they not require addition of a preservative.
- MDS have high loading capacity ranging from 50 to 60%.
- It should have Free flow properties and can be productive in relation toits cost.
- MDS Offer good compatibility with different vehicles and ingredients.
- Microsponges can absorb oil up to 6 times its weight without drying
- Microsponge particles themselves are too large so they are difficult to be absorbed into the skin and this adds a measure of safety to these microsponge materials by avoiding the side effects of the microsponge adjutants.
- Microsponges formulations can be cost effective even for the cosmetic mass market use where the cost of the materials is important.
- Microsponges are non-allergenic, non-irritating, non-mutagenic and non-toxic.
- Microsponges are characterized by free flowing properties.
- The average pore size of microsponges is small (0.25 μm) in a way to prevent the penetration of bacteria, thus they do not need sterilization or addition of preservatives.
- It provides continuous action up to 12 hours i.e. extended release.
- They have superior formulation flexibility.[3,6,8]

Characteristics of materials that are entrapped in Microsponges

Active ingredients which can be entrapped in microsponge can be incorporated into different products such as powders, creams, lotions, gels and soaps.

Some requirements must exist in material that will get entrapped in microsponge such as

- It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers.
- It should be stable in contact with polymerization catalyst and conditions of polymerization.
- It should be inert to monomers and should not increase the viscosity of the mixture during formulation.
- The spherical structure of the microsponges shouldn't collapse.
- Materials that are entrapped in the vehicle must be of restricted solubility to avoid problems in cosmetic preparations. The vehicles might consume micro sponges before the application, if solubility is not restricted.
- Half-life of the API should be less than 5hrs to provide sustained action.
- Molecular weight of drug should be less than 600g/mole so that it can penetrate easily.
- Design of polymer and payload of drug must be optimized to get desired release rate for a specified time period.
- Only 10-12%w/w microsponge should be used in the vehicle. If this concentration is not obtained, the vehicle's microsponge will be reduced before it is applied.
- Both hydrophilic and hydrophobic can be incorporated into the microspon.[9,19]

❖ **Benefit of MDS**

- Enhanced product performance.
- Extended release.

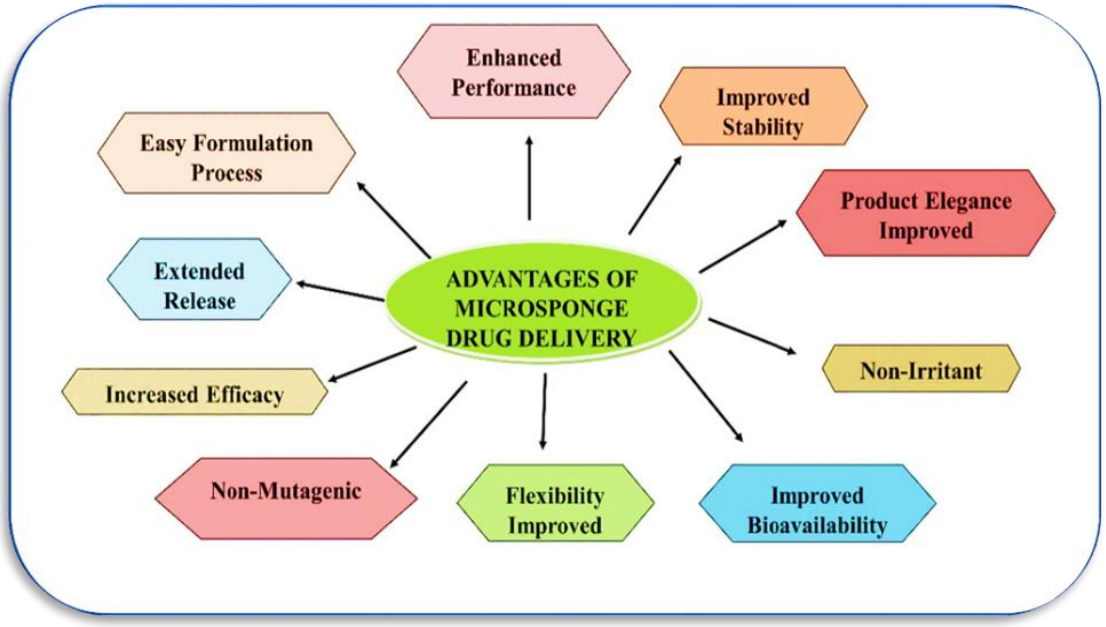

Figure 3:- Benefit of MDS.

- Reduced vexation and hence bettered patient Compliance.
- Bettered product classiness.
- Advanced oil control as it can absorb oil up to 6 times its weight without drying.
- Enhanced formulation inflexibility.
- Developed thermal, physical, and chemical stability.
- Inflexibility to develop new product forms.
- Microsponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic
- MDS allows the objectification of immiscible products.
- Allows new product form.
- Enhanced product aesthetics.
- Extended release, nonstop action up to 12 hours Reduced irritation, better forbearance means wide consumer acceptance enhanced product aesthetics, gives product an elegant sensation.
- Allows objectification of immiscible products.
- Improves material processing.
- liquid can be converted to maquillages.
- Improves efficacy in treatment.
- Cure or control confirm more instantly.
- Ameliorate control of condition Ameliorate bioavailability of same medicines.[1,3,6]

❖ **Limitations**

- The medication techniques generally use organic solvents as porogens.
- An environmental hazard.
- Highly combustible.
- Posing a safety hazard.
- In some cases, the traces of residual monomers have been observed, which may be poisonous and dangerous to health.[1,10]

❖ **Release Mechanism**

MDS consists of a multitude of porous microsphere that Forms a complex network of interconnecting voids with a Non-collapsible structure. The rate of release of active Ingredients depend on several factors like pore diameter, The extent of cross linking of the polymers, differences in Concentration of the active ingredient between the Microspheres and vehicle. Microsponge can be designed To release active ingredients over time in response to one Or more external triggers. The release mechanisms from MDS are accelerated or triggered by the following system and shown in figure 4.

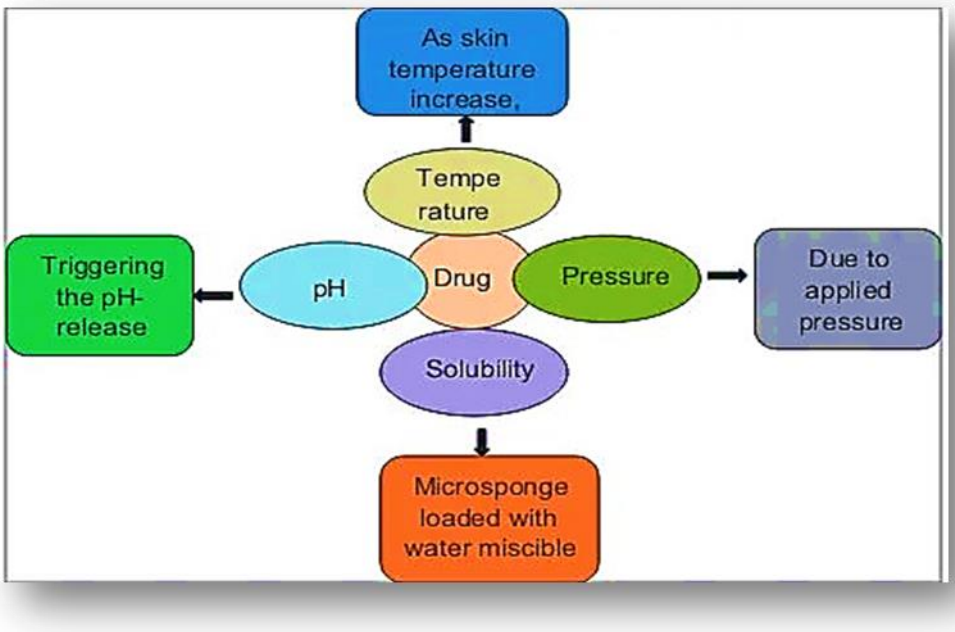

Figure 4:- Release Mechanism of MDS.

❖ **Solubility**

The release can be obtained by diffusion, taking into account the sharing coefficient of the active ingredients between the microsponges and the external system.

In the presence of water, microsponges containing water-soluble compounds such as antiperspirants and antiseptics release chemicals.

The release can also be triggered by diffusion, taking into account the partition coefficient of the component between the microsponges and the rest of the system.

It is also possible to create microsponges with long release times. Here are some factors to consider when developing such formulations: Physical and chemical properties of retained active ingredients. Pore diameter, pore volume, elasticity and other physical properties of the microporous system. Characterization of the medium in which microsponges are diffused. Micro-sponges can be made to release one

- **pH triggered system:** The alteration In coating of microsponges can be used to achieve the pH- based medicament release.
- **Pressure:** The release of drug from micro sponges can be Achieved by applying the pressure or by rubbing.
- **Temperature triggered system:** The inflow rate and delivery of The actives which are viscous at room temperature can be increased By increasing the skin temperature.[3,11]

METHOD OF PREPARATION OF MICROSPONGE DRUG DELIVERY SYSTEM

A Porogen drug is entrapped with a one- step procedure and neither hinders nor activates the polymerization process. It's also stable to free radicals(liquid liquid suspension polymerization). The following procedures are suitable for preparing microsponges and shown in figure 5.

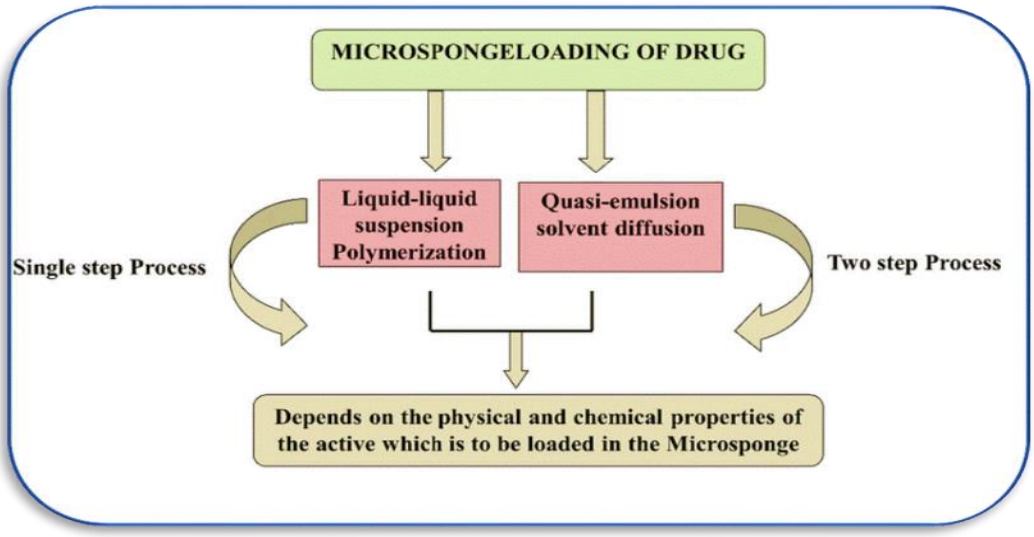

Figure 5:- Methods of preparation of microsponge drug delivery system.

1 Liquid-liquid suspension polymerization

In liquid- liquid systems, suspension polymerization is used to form porous microspheres. In this process, immiscible monomers are first dissolved with active ingredients in a capable solvent monomer, and also dispersed in waterless phases containing complements similar as surfactants and suspending agents to aid suspension formation. The polymerization is also touched off by raising the temperature, irradiating it, or adding a catalyst. The polymerization process continues to make a force-like system with a globular shape. The solvent is removed after the polymerization process, leaving globular structured porous microspheres, or microsponges and this process is shown in figure 6.

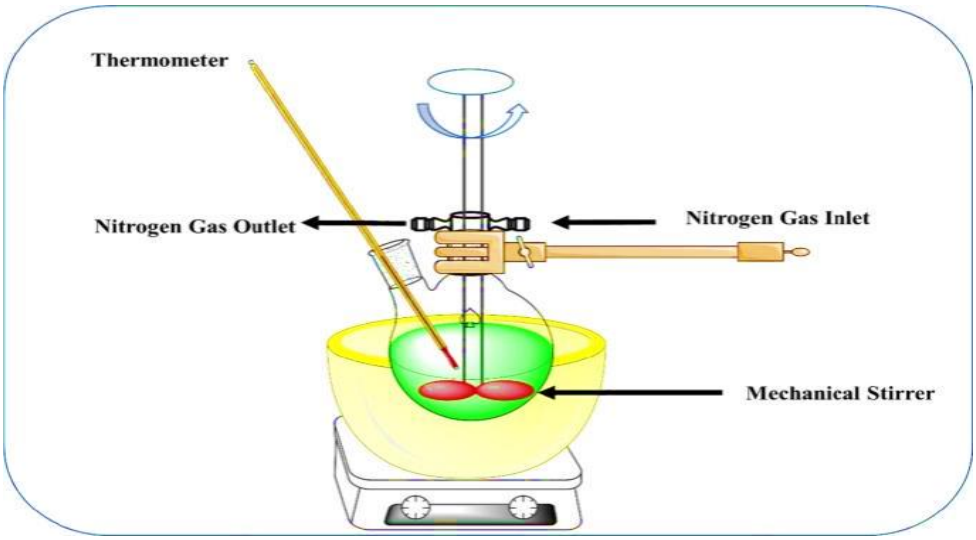

Figure 6: liquid-liquid suspention polymerization.

The following are the numerous way involved in

the medication of microsponges.

Step 1 :- Choose a monomer as well as a monomer combination.

Step 2 :- As polymerization begins, chain monomers form.

Step 3 :- Graduation conformation caused bycross-linking between chain monomers.

Step 4 :- The monomer graduation is folded to Form globular patches.

Step 5 :- Agglomeration of microspheres results in the conformation of microsphere bunches.

Step 6 :- Creating microsponges by clinging bunches together.[1,26]

❖ **Quasi-Emulsion Solvent Diffusion**

(Mine et.al, 2006).

In this quasi-emulsion solvent diffusion system, it is a two-dimensional process where microsponges can be prepared by quasi-emulsion solvent diffusion system using different

amounts of polymer. To prepare the internal phase, Eudragit RS 100 is dissolved in ethyl alcohol. In addition, the drug can be added to the solution and dissolved under ultrasound at a temperature of 35°C.

The internal Phase was poured into the PVA solution in water (external phase). After 60 minutes of waiting, the mixture was filtered to separate Microsponges. Microsponges were dried in an air-heated oven at 40°C for 12 h and counted to determine production yield (PY). When the drug is sensitive to polymerization conditions, a two-step process is used. The microsponges were prepared by the water emulsion solvent diffusion method using different amounts of polymer. In emulsion solvent diffusion, the affinity between the drug and the good solvent is stronger than the affinity between the good solvent and the bad solvent. Drug is soluble in good solvents and the dispersion in bad solvents produces (quasi-) emulsion droplets, although the pure solvent is miscible.

The good solvent gradually diffuses out of the emulsion droplets into the surrounding phase.

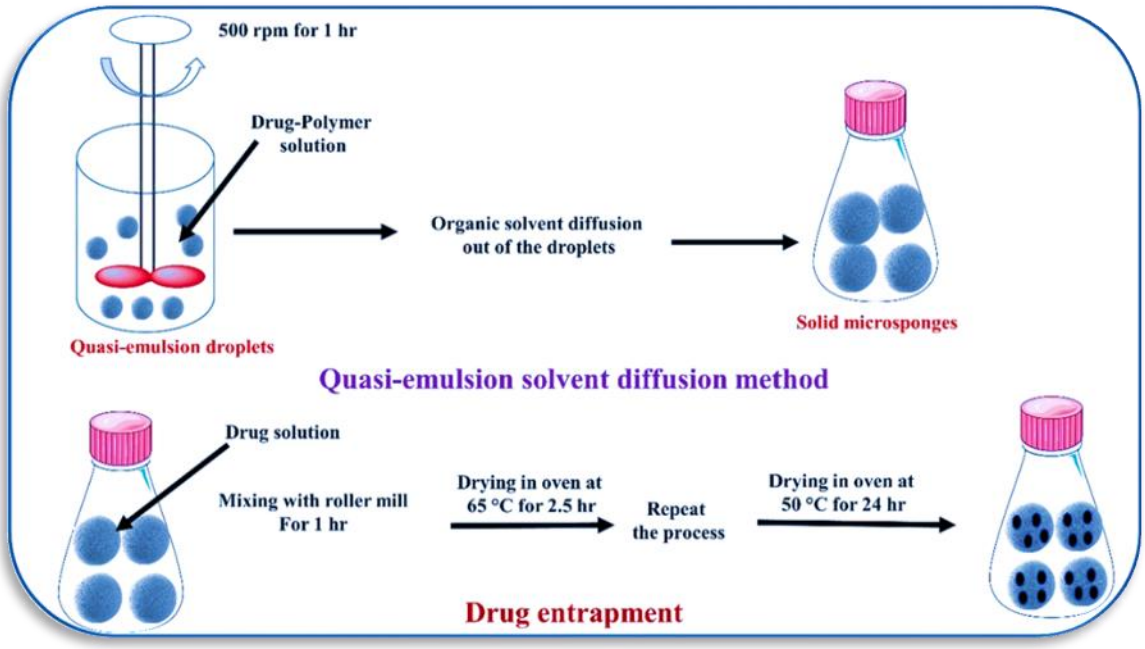

Figure 7:- Quasi-emulsion solvent diffusion method.

Poor solvent mixing and bad solvent diffusion into the droplets cause the drug to crystallize inside the droplets (Tansel and Omoglu, 2002).

This is a two-step process in which the polymer along with an active, plasticizing and diffusing agent (Porogen) is poured into an external aqueous phase, which typically includes

a stabilizer such as polyvinyl alcohol. After emulsification, the system was continuously stirred for 2 hours and kept at high temperature if necessary.

The diffusion of porogen into the external environment creates a very porous microparticle called "Microsponge". Then, next process is mixture was filtered and to separate micro sponges.

The product is washed and dried in a vacuum roaster at 50°C for 24 hours as shown in Figure 7.[2,4]

❖ **Ultrasound-Assisted Production**

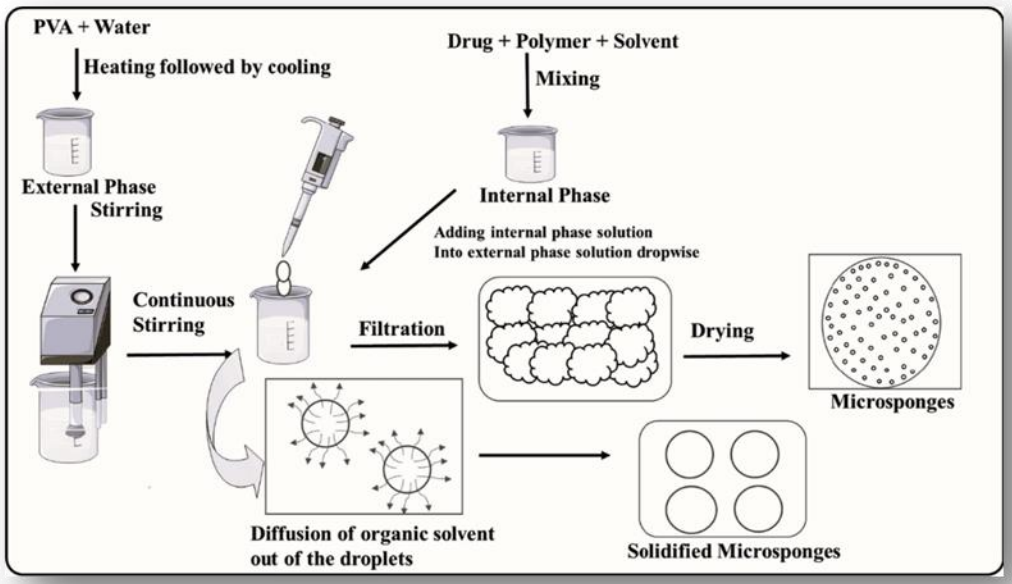

Figure 8:- Ultrasound-assisted production Method.

To produce nanosponges, the technique was modified to use alpha-cyclodextrin (beta-CD) as the monomer as well as diphenyl carbonate, as the cross-linker. The mixture is then heated and sonicated to control the size of the microparticles. The reaction mixture was allowed to cool, and the resulting product was ground into coarse particles which were then washed in distilled water and ethanol as shown in Figure 8. Beta-CD microparticles cross-linked with porous microparticles can be used as drug carriers. Additionally, this technique has the problem of retaining cross-linking residues, which can be dangerous.[14,7]

❖ **Evaluation parameters of microsponges**

- Particle size (Microscopy)

- Morphology and Surface topography
- Loading efficiency and production yield
- Resiliency
- Compatibility studies
- Drug release study

Particle size and shape

The most commonly used procedures to visualize microparticles are conventional Optical microscopy (LM) and scanning electron microscopy (SEM). Both can be used to determine the shape and external structure of microparticles.

The LM allows you to control coating parameters in the case of double-walled microparticles. The structure of the microparticles can be seen before and after coating and the changes can be measured under a microscope.

The SEM provides higher resolution than the LM.SEM allows the study of microparticle surfaces, and once the particles are sheared, it can also be used to study double-walled systems. A Confocal Fluorescence microscope was used to characterize the structure of the multi-walled microparticles. Laser light scattering and multiscale counters, which are not instrumental methods, can be used to characterize the size, shape, and morphology of microsponges

❖ **Morphology and surface topography of microsponges**

For surface morphology and topography, the prepared microsponges can be coated with palladium gold under an argon atmosphere at room temperature and then The surface morphology of microsponges can be studied using SEM.

SEM of a cracked microsponge particle can also be taken to illustrate its microscopic structure.[15,20]

❖ **Determination of loading efficiency and production yield**

$$\text{Loading Efficiency} = \frac{\text{Actual Drug Content in microsponges}}{\text{Theoretical Drug Content}} \times 100$$

Loading efficiency (%) is calculated by the following equation

Microparticle production will be analyzed by accurately calculating the weight initial weight of the raw material as well as the final weight of the resulting microsponge.

Production Yield

$$\text{Production Yield} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical Mass (Polymer + Drug)}} \times 100$$

❖ **Compatibility Studies**

The compatibility of drugs with reaction supports can be studied by thin layer chromatography (CMC) and pink spectroscopy Fourier transform (FT-IR).

The effect of polymerization on drug crystallinity can be studied by X-ray powder diffraction (XRD) and differential scanning calorimetry (DSC).

For DSC, approximately 5 mg of the sample can be accurately weighed into a tightly sealed aluminum pan and can be analyzed at a heating rate of 15 °C/min over a temperature range of 25 to 430 °C under a nitrogen atmosphere.[13,24]

❖ **Resiliency**

The ability of microsponges to bounce back (viscoelastic properties) can be changed to create bead lets that are more gentle. Or more solid to fit the requirements of the final mixture. The process of cross-linking more frequently results in a slowdown. The delivery rate of drug . Result, the resilience of microsponges will be examined and enhanced by the outcome. When assessing the need, one should take into account the release as a factor influenced by the duration of cross-linking.

❖ **Polymer/ Monomer composition (Barkai et al. 1990)**

Microsphere size and the composition of the drug-loading polymer were determining factors in the drug formulation of the microsphere series. The polymer composition of the MDS can affect the distribution of the drug between the vehicle and the microsponge system as measured by the partition coefficient. As a result, it directly affects the liberation of the trapped drug. The release of drugs from microsponge systems made of various types of polymers can be analyzed by graphing the percentage of drugs released over time. The rate at which the methyl methacrylate/ethylene glycol dimethacrylate system releases and the overall amount released is slower compared to the system consisting of styrene/divinylbenzene. The choice of monomer relies on both the properties of the active substance that will be trapped and the medium in which it will be distributed. Different types of polymers can be modified with different electrical charges or levels of water-repellence or oil-repellence to allow for flexibility in the way they release substances. Active ingredients are the substances in a

product that are responsible for its primary action or effect. Different combinations of monomers will be evaluated to determine their compatibility with the medications by analyzing how they release the drugs.[17,22,29]

Applications of micro sponges with respect to their advantages

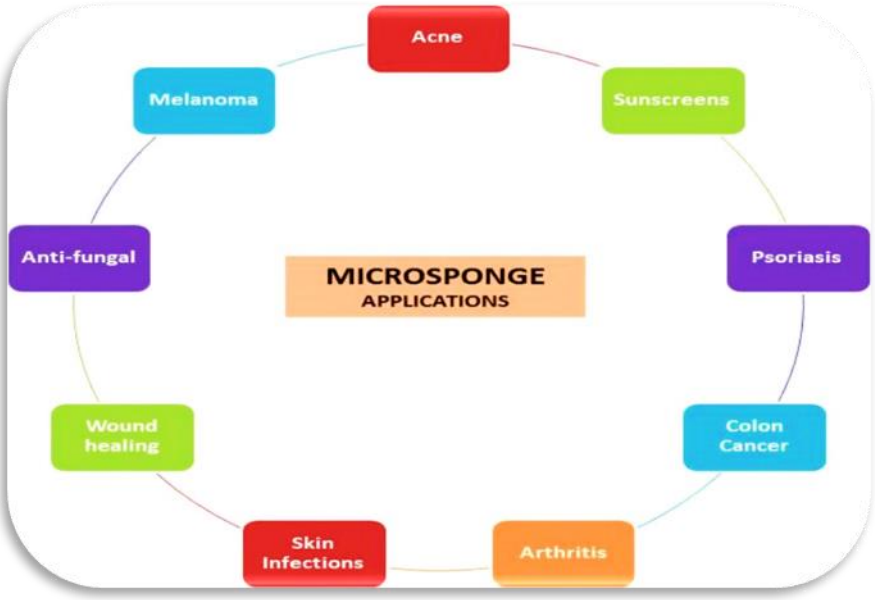

Figure 9:- Application of microsponge.

Table 1: Applications of micro sponges with respect to their advantages.[14,26,28]

S.No	Application	Advantages
1	Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization
2	Anti-acne e.g. Benzoyl peroxide	Maintained efficacy with decreased skin irritation and sensitization.
3	Anti-inflammatory e.g. hydrocortisone	Long lasting activity with reduction of skin allergic response and dermatoses.
4	Anti-dandruffs e.g. zinc pyrithione, selenium sulfide	Reduced unpleasant Oduor with lowered irritation with extended safety and efficacy.
5	Antipruritics	Extended and improved activity.
6	Skin depigmenting agents e.g. hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.

Examples of micro sponge drug delivery with their formulations[12,4]

Table 2: Examples of micro sponge drug delivery with their formulations.

Micro sponge Delivery Systems	Drug	Disease
Gels	Benzoyl peroxide	Anti-Acne Treatment
	Fluconazole	Inflammation
	Mupirocin	Antibacterial activity
	Diclofenac sodium	Inflammation
	Acyclovir	Viral infections
	Hydroxyzine HCl	Urticaria and atopic dermatitis
	afine HCl	Anti-fungal
Lotions	Benzoyl peroxide	Anti-Acne Treatment
Creams	Hydroquinone and Retinol	Melanoma
Tablets	Indomethacin	Inflammation
	Paracetamol	Anti-pyretic
	Chlorpheniramine maleate	Hay Fever
	Ketoprofen	Musculoskeletal pain
	Fenofibrate	Gout
	Flurbiprofen	Metabolic ratio
	Dicyclomine	Anticholinergic
	Meloxicam	Arthritis
	Paracetamol	Colon targeting
Implants	Poly (DL-lactic-co-glycolic acid)	Skin tissue engineering
Grafts	Poly (lactic-co glycolic acid)	Cardiovascular surgery
Injection	Basic fibroblast growth facto	Growth factor
Others	Benzoyl peroxide	Anti-Acne Treatment
	Mefenamic acid	Rheumatoid arthritis
	Ibuprofen	NSAID

Table 3: List of Marketed Products based on Micro sponges.[4]

Product Name	Pharmaceutical Uses	Manufacturer
Glycolic Acid Moisturizer w/SPF 15	Anti-Wrinkles, soothing	AMCOL Health & Beauty Solution
Retin A Micro	Acne vulgaris	Ortho-McNeil Pharmaceutical, Inc.
Carac Cream, 0.5%	Actinic keratoses	Dermik Laboratories, Inc.
Line Eliminator Dual Retinol Facial Treatment	Anti-wrinkle	Avon
Retinol 15 Night cream	Anti-wrinkles	Sothys
Retinol cream	Helps maintain healthy skin	Biomedic
EpiQuin Micro	Hyper pigmentation	SkinMedica Inc
Salicylic Peel 20	Excellent exfoliation	Biophora
Sports cream RS and XS	Anti-inflammatory	Embil Pharmaceutical Co. Ltd
Oil free matte block SPF 20	Sunscreen	Dermalogica
Lactrex™ 12% Moisturizing Cream	Moisturizer	SDR Pharmaceuticals, Inc
Dermalogica Oil Control	Skin protectant	John and Ginger Dermalogica Skin

Lotion		Care Products
Ultra Guard	Protects baby's skin	Scott Paper Company

❖ **Patents Filed Related to Micro sponges[10]**

Table 4: Patents Filed Related to Micro sponges.

Patent no	Inventors	**Publication Date**
US4690825	Won, Richard	1987
US4863856	Dean RC Jr et al.	1989
US5292512	Schaefer et al	1989
US5135740	Katz et al.	1992
US5679374	Fanchon; Chantal et al	1994
US5316774	Eury, Robert P et al.	1994
US5725869	Lo; Ray J. R.	1996
US6395300	Straub et al.	1999
US6211250	Tomlinson et al	2001
US20030232091	Shefer et al.	2002

CONCLUSION

Microsponge drug delivery has become an evolving technology and research is underway to optimize the formulation cost and benefits of this therapy. Thanks to its high efficiency and advanced technology, it has numerous applications in the pharmaceutical and cosmetic sectors. There is significant market potential for microsponge technology and the associated flexibility. Formulators are exploring new and innovative methods of delivering active ingredients and can exploit the full potential of these active ingredients. unique ingredients for improved safety, improved stability, fewer active ingredient side effects, improved multiple functionality and better ingredient tolerability. Microsponge delivery systems could be a better strategy for the new generation of pharmaceuticals and cosmetics. Microsponges have an advantage over several conventional topical dosage forms for local diseases: they are a unique technique for the controlled release of topical active ingredients, which is also used when taking medications. oral and the use of biological drugs. This drug delivery has advantages over other products due to its non-mutagenic, non-toxic and non-irritating properties. Therefore, the microsponge drug delivery system has great potential and is a versatile delivery system that should be explored with maximum research in the future.

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