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Microsponge: An Aeon in Therapeutics

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ABSTRACT

The drug delivery technology has become vastly competitive and rapidly evolving. More and more developments in delivery systems are being assimilated to elevate the efficacy and cost-effectiveness of the therapy. To govern the delivery rate of active pharmaceutical agents to a predetermined site inside the body has been one of the biggest challenges faced by the drug industry. Microsponge releases its active pharmaceutical ingredient in a time mode and also in response to other stimuli (rubbing, temperature, pH, etc.). Microsponge drug delivery technology offers entrapment of active pharmaceutical ingredients and is believed to contribute towards reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. In addition, number of studies have confirmed that microsponges systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic. Microsponge technology is being used currently in a wide range of formulations.

KEYWORDS: *Microsponge Delivery System, Controlled release, Quasi- emulsion solvent diffusion, Recent Advances*

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INTRODUCTION

The most convenient and commonly employed route is the oral route. Drugs that get easily absorbed from the gastrointestinal tract and has a short half-life gets eliminated rapidly from the blood circulation. [1]The control, effective, targeted drug delivery systems have been a dream for a long time, but it has been largely frustrated by the intricacy that is involved in the formulation development of new systems. [2]Drug Delivery Systems that control the release rate and target to a specific site of the body has an immense impact on the health care system. [3]

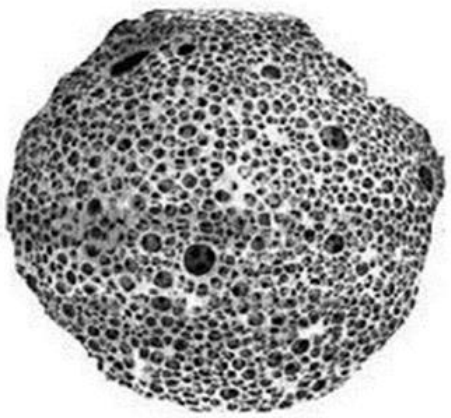

Figure 1: Porous structure of microsponge (Engineering of Microsponges)

The invention of microsponges has become a major step toward overcoming these problems. Microsponges offer the action at a particular target site and stick on the surface and initiate to release the drug in a very controlled and predetermined manner for drugs with poor solubility. [4]

The various drug delivery systems are being assimilated to optimize the efficacy and cost-effectiveness of the therapy with increasing competition necessity customer friendliness. In recent years, there has been huge emphasis given to the development of novel microsponges based drug delivery systems, to modify and control the release behavior of the drugs. By incorporation into a carrier system, it is possible to modify the therapeutic index and duration of the activity of drugs. [5]

The microsponge technology was developed by Won in 1987, and hence the original patents were assigned to Advanced Polymer Systems, Inc. This firm developed an enormous number of variations of the technique and applied it to the cosmetic as well as over the counter products. At present, this technology has been licensed to Cardinal Health, Inc., to be used in topical products. [6]

Microsponges are polymeric delivery systems formed of porous microspheres. They are tiny sponge-likespherical particles that involve a myriad of interconnecting voids within a non-collapsible structure with an enormous spongy surface. [7] Moreover, they may enhance stability, lessen side effects, and improve drug release well. [8]The hollow sphere polymers vary in diameter from 5 to 300µm. A 25µm sphere can have pore length up to 3000 mm, given that a total pore volume of about 1 ml/g. Depending upon their particle size,

these porous systems can be divided into microporous microbeads (particle size below 50µm) and microporous macro beads (particle size range of 100-200µm). [9]Microsponges release their active ingredients upon application, generating a highly concentrated layer of active ingredient which is quickly absorbed. The significance of topical drugs suffers from various complications like greasiness, stickiness associated with the ointments, and so on, which often result in a lack of patient compliance. To overcome the drawback of the ointment microsponge delivery system uses the development of mucoadhesive microspheres of acyclovir with enhanced bioavailability. [10] Microsponges extensively look upon as a leading technology for addressing skin conditions like acne, hyper pigmentation, keratosis, aging, and photo damage. [11]

Engineering of Microsponges:

Active pharmaceutical ingredients can have entrapped in microsponge polymers either at the time of synthesis[12] or if the material is too labile to withstand polymerization condition, they can be post loaded after the formation of sponge structure.[13] The post-loading is most preferred mode since so many cosmetic ingredients and most pharmaceutical ones would decompose at the temperatures of polymerization. Microsponge particles loaded by diffusion in a way quite similar to a regular sponge and can then be progressively released when the polymer is placed in contact with the skin. [14]

Benefits/ Advantages of Microsponge Technology:

1. Enhanced product performance with extended-release. [15]
2. Reduced irritation and hence to improved product elegancy, patient compliance. [16]
3. Compare to other technologies like microencapsulation and liposome, microsponges has a wide range of chemical stability, higher payload, and ease in the formulation. [17]
4. Improves materials processing as liquid converted into solid forms.
5. Improved formulation flexibility. [18]

Characteristic of Microsponge Drug Delivery Systems:

1. Micro sponges are stable over the extended pHrange from 1 to 11 and constant up 130^{0}c. [19]
2. Microsponge formulations have a higher payload (50 to 60%) and can be cost-effective. [20]
3. Micro sponges are friendly with many of excipients and no require of sterilization.
4. These are still molecules without any allergy, irritation, and toxicity.
5. It must be either fully miscible in a monomer or capable of being made miscible by the addition of a small amount of a water-immiscible solvent.
6. It must be water-immiscible or at most only slightly soluble.
7. It must be inert to monomers and should not increase the viscosity of the mixture throughout formulation. [21]
8. They are non-irritating, non-mutagenic, no allergenic, and non-toxic.
9. They can absorb oil up to 6 times its weight without drying.
10. They show good compatibility with various vehicles and ingredients. [22]
11. Microsponges formulations are self-sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate. [23]

Characteristics of Material Entrapped in Microsponge.

1. Most liquid or soluble ingredients can be entrapped in the particles. Actives that can be entrapped in microsponges must meet the following requirements. [24]
2. The active ingredient must show limited solubility with the carrier vehicle to avoid cosmetic problems.
3. It should be water-immiscible or at most only slightly soluble. [25]
4. Polymer design and payload of the microsponges for the action must be optimized for the required release rate for a given period.
5. It should be stable in contact with polymerization catalysts and conditions of polymerization. [26]

Advantages of microsponges

1. They offer entrapment of numerous ingredients and are believed to contribute elegance and enhanced formulation flexibility.
2. Microsponges are thermal, physical, and chemically stable.
3. These are compatible with the majority of vehicles and ingredients.
4. They are self-sterilizing as the average pore size is 0.25 µm where bacteria cannot penetrate. [27]
5. Provides Modified release drug delivery and Site targeting delivery for improved treatment.
6. The drug releases from microsponges by external stimuli like pH, temperature, pressure, and rubbing.
7. It provides gradual release up to 12 h. and improves product elegance, efficacy, and bioavailability.
8. They facilitate accurate delivery of small quantities of the potent drug and reduced concentration of drug at a site other than the target organ or tissue. [28] [29] [30]

Advantages over conventional formulation:

The existing formulations in the market are having huge side effects and adverse effects in the treatment. Conventional formulations of topical drugs are intended to apply to the outer layers of the skin. Such products release their active ingredients upon application. When compared to the Microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis. Potentially, the Microsponge system can reduce significantly the irritation of effective drugs without reducing their efficacy. For example, Jelvehgariet al. prepared the microsponges of Benzoyl peroxide formulations which have excellent efficacy with minimal irritation. [31][32]

Advantages over microencapsulation and liposomes:

The Microsponges has advantages over other technologies like microencapsulation and liposomes. Microcapsules cannot control the release rate of actives as once the wall is ruptured the actives contained within microcapsules will be released disorderly. Liposomes suffer from the lesser payload, challenging formulation, partial chemical stability, and bacterial instability. While the microsponge system in contrast to the above systems is stable over a range of pH 1 to 11, temperature up to 130C, compatible with most vehicles and ingredients, higher payload (50 to 60%), free-flowing and can be cost-effective.[33][34]

Limitations:

The principal limitation of microsponge technology is the use of several organic solvents in formulations. The use of organic solvents poses threats like a toxicity and flammability. Traces of residual monomers in the bottom-up approach can be toxic and hazardous to health. But these limits can be overcome by quality control measures, optimization, and standardization of procedures e.g, post-manufacture washing.[35][36]

DRUGS EXPLORED IN THE MICROSPONGE DELIVERY SYSTEM:-

Polymers used for the preparation of microsponges:

Eudragit RS 100, Eudragit RL 100, Ethylcellulose, Polystyrene Acrylic polymer, Carbopol 934. [37]

Microsponge Delivery Systems	Drug	Disease
Gels	Tazarotene, Tretinoin	Facial acne vulgaris[38]
	Metronidazole	Surgical wounds[39]
	Oxiconazole nitrate	Antifungal[40]
	Miconazole	Diaper dermatitis[41]
	Benzoyl peroxide	Anti-Acne Treatment[42]
	Nebivolol	Diabetic wound[43]
	Fluconazole	Inflammation[44]
	Mupirocin	Antibacterial activity[45]
	Silver sulfadiazine	Burn wounds[46]
	Oxybenzone	Sunscreen agent[47]
	Diclofenac sodium	Inflammation[48]
	Acyclovir	Viral infections[49]
	Hydroxyzine HCl	Urticaria,dermatitis[50]
	Terbinafine HCl	Anti-fungal[51]
Lotions	Benzoyl peroxide	Anti-Acne Treatment[52]
Oil	Babchi oil	Antimicrobial[53]
Cream	Hydroquinone and Retinol	Hyperpigmentation[54]
Capsule	5-fluorouracil	Colorectal cancer[55]
Powder	Calcium phosphate	Bone substitute[56]
Tablets	Indomethacin	Inflammation[57]
	Nicorandil	Cardiovascular uses[58]
	Piroxicam	Rheumatoid arthritis[59]
	Paracetamol	Anti-pyretic[60]
Implants	Polylactic-co-glycolic acid	Tissue engineering[61]
Grafts	Polylacticglycolic acid	Cardiovascular uses[62]
Injection	Fibroblast growth factor	Growth factor[63]

Table No.1:- Examples of microsponge drug delivery with their formulations

APPLICATIONS OF MICROSPONGES:

Oral drug delivery:

The microsponge drug delivery provided that the enhancement of solubility, efficacy of the poorly aqueous soluble drug. The Kawashima achieved the controlled and effective oral delivery of ibuprofen microsponges by changing their intraparticle density. The Microsponge system has been shown that the upturn in the rate of solubilization of poorly water-soluble drugs by trapping such drugs in the microsponge pores.[64] *In vitro* studies showed that compression-coated colon-specific tablet formulations started to release the drug at the eighth hour while the drug release from the colon-specific formulations prepared by pore plugging the microsponges showed an increase at the eighth hour, The Orlu and team prepared a novel colon-specific drug delivery system containing flurbiprofen microsponges which shows controlled release of flurbiprofen with colon targeting. Microsponge with less than 200 µm may competently be taken up by the macrophages present in the colon, thus exhibiting effective localized drug action at the desired site. They can also increase the lag time for the absorption of the drug as these get entrapped on the surface of the colon and thus have the potential for being developed as a colon-targeted drug delivery system.[65]

Ophthalmic drug delivery:

As formulators think novel and innovative ways to deliver actives, they can understand the full capability of these sole material providing better safety, enhanced stability, reduced side effects from actives, better multi functionality, and enhanced ingredient compatibility. [66]The ophthalmic drug delivery systems have rapid and extensive precorneal loss caused by the drainage and the high tear fluid turnover. To overcome these problems an increase in the contact time between drug and the corneal surface is required. In situ, gelling systems are viscous liquids, which undergo a sol to gel transition, when applied to the human body, due to change in a physicochemical parameter such as temperature, pH or ionic strength. In situ, gelling systems allow accurate and reproducible administration of drugs unlike the preformed gels, and are capable of prolonging the residence time to the mucosal surfaces. Obiedallah and team formulate novel acetazolamide loaded microsponges and formulating them into in situ gel for ocular drug delivery, to decrease the systemic side effects of acetazolamide and increase patient compliance with the demand for a novel and extremely competent pharmaceutical as well as beauty products, the market holds considerable potential for microsponges and the flexibility they offer. the formulation showed higher therapeutic efficacy compared to a free drug in the gel. It was

nonirritant as it passes the safety parameters. These results indicated that microsponges in situ gel have the potential ability for ophthalmic delivery. [67]

Microsponge Based Delivery System for Cardiovascular:
Iwai et al., Prepared the poly lactic-co-glycolic acid collagen microsponge patch which showed well in situ cellularizations and synthesis of extracellular matrix in a dog model for the reconstruction of the pulmonary artery. The PLGA-collagen patch has promise as a bioengineered material for the reconstruction of autologous tissue in cardiovascular surgery. [68] A biodegradable material with autologous cell seeding requires a complicated and invasive procedure that carries the risk of infection. To escape these difficulties, a biodegradable graft material containing collagen microsponge that would permit the renewal of autologous vessel tissue has developed. The capability of this material to quicken in situ cellularizations with autologous endothelial and smooth muscle cells was tested with and without recellularization. Poly (lactic-co-glycolic acid) as a biodegradable scaffold was compounded with a collagen microsponge to form a vascular patch material. These poly (lactic-co-glycolic acid)-collagen patches with (n =10) or without (n = 10) autologous vessel cellularization were used to patch the canine pulmonary artery trunk. Histologic and biochemical assessments were performed 2 and 6 months after the implantation. There was no thrombus formation in either group, and the poly (lactic-co-glycolic acid) scaffold was almost completely absorbed in both groups. Histologic results showed the formation of an endothelial cell monolayer, a parallel alignment of smooth muscle cells, and a reconstructed vessel wall with elastin and collagen fibers. This patch shows promise as a bioengineered material for promoting in situ cellularizations and the regeneration of autologous tissue in cardiovascular surgery. [69] [70]

Topical drug delivery:
The microsponge 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 microsponge is as tiny as a particle of talcum powder and it's like a true sponge, each sponge consists of a myriad of interconnecting voids within a non-collapsible structure that can accept a wide variety of substances. The outer surface is typically porous, allowing the controlled flow of substances into and out of the sphere. Several primary characteristics, or parameters, of the microsponge system, can be defined during the production phase to obtain spheres that are tailored to specific product applications and vehicle compatibility. microsponge systems are made of biologically inert polymers. Broad safety studies have demonstrated that the polymers are non-irritating, non-mutagenic, non-allergenic, non-toxic, and non-biodegradable. [71] Bothiraja et al. prepared ethyl cellulose-based microsponges of eberconazole and incorporated it into a gel for topical delivery. The characterization of microsponges and skin irritation studies were conducted to demonstrate controlled release and non-irritancy. Further, antifungal activity was carried out on the microsponge gel. Results of the in vivo skin deposition study demonstrated four times higher drug retention in the stratum corneum when compared to commercial cream. Results signified that the prepared eberconazole microsponge gel may be a potential topical delivery system for antifungal therapy. [72]

Microsponge Based Delivery System for Bone Substitute:
The bone substitutes are plays important in arthritis as the microsponge may lead to form trabecular bone. Compounds were gained by mixing pre polymerized powders of polymethylmethacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium-deficient hydroxyapatite powders. The final composites appeared to be spongy and acted as microsponges. Beruto et al. prepared bone-substitute compounds that were gained by mixing pre-polymerized powders of polymethylmethacrylate and liquid methylmethacrylate monomer with two aqueous dispersals of alpha-tricalcium phosphate (alpha-TCP) grains and calcium-deficient hydroxyapatite (CDHA) powders. The ending composites seemed to be porous. The water, which was the pore-forming agent, vaporized after the polymerization process, leaving behind unfilled spaces in the polymeric matrix. Both the penetrability and shape of the pores shown to be a function of the total open porosity. They verifiedosteoconductivity and osteoinductivity of the final composites by in vivo implantation in rabbits. The formation of new trabecular bone was detected inside the pores where the inorganic powders had been positioned.[73][74]

HYPOTHETICAL MECHANISM OF MICROSPONGES:
The microsponge particles have an open structure as there is no continuous membrane surrounding them and active is free to move in and out from the particles and into the vehicle until equilibrium is grasped. When the vehicle becomes saturated. Let's take an example of topical delivery, once the complete product is applied to the skin, the activity that is already in the vehicle will be immersed into the skin, depleting the vehicle, which will become unsaturated, therefore, disconcerting the equilibrium. This will jerk a flow of the active from the microsponge particle into the vehicle, and from it, to the skin until the vehicle is either dehydrated or absorbed. The steady release of the active to the skin providing prolonged release over time. This suggested mechanism of action highlights the importance of formulating vehicles for use with microsponge entrapments. If the active is too soluble in the chosen vehicle during compounding of the finished products, the products will not provide the desired benefits of gradual release. Instead, they will work as if the active was added to the vehicle in a free form. When using microsponge's entrapments, some solubility of the active in the vehicle is suitable, because the vehicle can provide the preliminary loading dose of the active until release from the microsponge is triggered by the shift in equilibrium from the polymer into the carrier. Another way to sidestep unwanted premature leaching of the active from the microsponge polymer is to formulate the product with some free and some entrapped active, so the vehicle is pre-saturated. The rate of active release will eventually depend on the partition coefficient of the active ingredient between the polymer and the vehicle, surface area, mean pore diameter, and some other triggers such as moisture, pH, friction, or temperature. [75][76] This principle is contrary to the conventional formulation principles usually applied to the topical products. For this conventional system, it is normally recommended to maximize the solubility of the active into the vehicle. [77]

FORMULATION CONSIDERATION:
When formulating the microsponge, certain consideration is taken into account in order to achieve the desired product

characteristics .the aqueous solubility must be limited otherwise, the continuous phase will deplete the microsponge during formulation, and polymer design and payload of microsponges for the action must be optimized for required release after a given time period the solubility of actives in the vehicle is must be limited .otherwise the vehicle will deplete the active ingredient before the application.[78]To avoid cosmetic problems; not more than 10 to 12% w/w microsponges must be incorporated into the vehicle.[79]

Method of preparation: Drug loading in microsponges can take place in two ways, one-step process or by two-step process as discussed in liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques which are based on physicochemical properties of the drug to be loaded. If the drug is typically an inert non-polar material, it will create the porous structure it is called porogen. [80] A Porogen drug neither hinders the polymerization process nor become activated by it. [81]

Liquid-liquid suspension polymerization:
The porous microsponges are prepared by the suspension polymerization method in a liquid-liquid system. The liquid-liquid suspension polymerization method is carried out by using a round bottom flask which is prepared by adding monomer to the non-polar active ingredient and this is added to the aqueous phase. Usually containing surfactant and dispersant as the additives and suspension are formed. Polymerization is initiated by adding catalysts or by increasing the temperature. [82] The polymerization process lasts the formation of a reservoir type of system with a spherical structure. After the polymerization process, the solvent is removed leaving the circular structured porous sponge, i.e., microsponges. The various steps involved in the preparation of microsponges. [83] [84]

The various steps to summarize:
1. Selection of monomer or combination of monomers
2. Formation of chain monomers as polymerization begins
3. Formation of ladders as a result of crosses linking between chain monomers
4. Compact of monomer folding ladder to form spherical particles
5. Agglomeration of microspheres, which give rise to the formation, bunches of
6. microspheres
7. Binding of bunches to form microsponges.[85][86]

Quasi-emulsion solvent diffusion:
Porous microsponges were also formulated by a quasi-emulsion solvent diffusion method (two-step process) 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 plasticizers such as triethyl citrate (TEC) were added to aid the plasticity. The inner phase is then poured into the external phase containing polyvinyl alcohol and microsponges. microsponges were washed and dried in an air- heated oven at 40°C for12 h. [87] [88]

RELEASE MECHANISM:
Microsponges can be designed to release a given amount of active ingredients over time in response to one or more external triggers. In general, microsponges retard drug release. Some studies have revealed a better rate of release by cumulative the active/polymer ratio and lowering the polymer wall thickness; however, these results are not supported by another set up of studies. Thus, there appear to be lots of other factors affecting the release of the drug from the microsponges. Another significant parameter that regulates the release seems to be the pore diameter, however; another study has shown that even the overall porosity (including the pore diameter and the number of pores) also affects the drug release. [89]

Temperature-triggered systems: at room temperature, few entrapped active ingredients can be too viscous to flow suddenly from microsponges onto the skin. With an increase in skin temperature, the flow rate is also increased, and therefore release is also enhanced. [90]

Solubility: Solubility: Microsponges loaded with water-miscible ingredients like antiseptics and antiperspirants will release the ingredient in the presence of water. The release can also be triggered by diffusion but taking into attention, the partition coefficient of the ingredient between the microsponges and the external system. [91]

pH: The pH-responsive microsponges involve the coating of Conventional Microsponge delivery systems with the enteric-coating type of material, which imparts pH responsiveness to this delivery system. The studies were performed by using highly water-soluble dye. The pH response studies were carried out in the USP spindle dissolution apparatus. At acidic pH of around 3, there was no remarkable release but when the pH was increased to 8 the release of up to 80% was obtained. So it was found that at lower pH the release was less but by increasing the pH the release rate was increased. So the rate of drug release is to be modulated as per the requirements. [92] Triggering the pH-based discharge of the active can be achieved by adapting the coating on the microsponge. [93]

Pressure: Pressure/ Rubbing applied can release active ingredients from microsponge onto the skin in a controlled manner. The pressure triggered 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. When compared with mineral oil containing microcapsules, mineral oil containing microsponge showed a much more softening effect as the microcapsules show irritancy effect. [94]

Safety Parameters:
As such Microsponge delivery systems are made up of biologically inert polymers, the substantiation of safety required insight of more than the 30 safety parameters.: Safety studies of microsponges can be confirmed by:
Allergenicity in guinea pigs.
Eye irritation studies in rabbits.
Mutagenicity in bacteria.
Oral toxicity studies in rats.
Skin irritation studies in rabbits. [95] [96]

EVALUATION PARAMETER OF MICROSPONGES:
Various factors are affecting the drug release from microsponges. So it can be evaluated by the following factors.

Preformulation studies:
Preformulation parameters are considered to identify those physicochemical properties, melting points, and excipients that may affect the formulation design, method of manufacture, pharmacokinetic and biopharmaceutical properties. Organoleptic property as a chemical state, taste, odor, and color of the drug are studied out. [97]

Particle Size and shape: Free-flowing powders with fine aesthetic attributes are likely to obtain by directing the size of particles during polymerization. Particle size analysis of loaded and unloaded Microsponges can be performed by laser light diffractometry or any other appropriate method. The values (d50) can be expressed for all formulations as a mean size range. Cumulative percentage drug release from microsponges of different particle sizes will be plotted against time to study the conclusion of particle size on drug release. A particle larger than 30 µm can impart grittily.[98]

Polymer/ monomer composition:
The selection of monomer is dictated both by characteristics of active ingredient ultimately to be entrapped and by the vehicle into which it will be dispersed. Polymers with varying electrical charges or degrees of hydrophobicity or lipophilicity may be prepared to provide flexibility in the release of active ingredients. Various monomer mixtures will be screened for their suitability with the drugs by studying their drug release profile. [99]

Morphology and Surface Topography of Microsponges:
The occurrence of pores is an essential feature of microsponges, its internal and external morphology, and surface topography can be obtained by using scanning electron microscopy and transmission electronmicroscopy. studied microsponge of naproxen and observed microsponge were spherical and uniform with no drug crystal on the surface. The particle size, shape, and surface morphology of miconazole nitrate were examined by SEM and TEM found the porous, spherical shape in µm size.[100]

Determination of Production Yield and Loading Efficiency: [101] [102]
Production Yield The production yield of the microsponges can be determined by calculating accurately the initial weight of the raw materials and the last weight of the Microsponge obtained.

The production yield of the Microsponge can be determined by the following equation:

$$\text{Production Yield} = \frac{\text{Practical mass of Microsponge}}{\text{Theoretical mass (polymer + drug)}} \times 100$$

Loading efficiency-The loading efficiency (%) of the microsponges can be calculated by putting the value of Actual drug content and Theoretical drug content in the following equation.

The loading efficiency (%) is calculated using the following equation:

$$\text{Loading Efficiency} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100$$

Determination of True Density: True density can be measured by an ultra-pycnometer using helium gas, and calculated as a mean of repeated determinations. [103]

Characterization of Pore Structure: Pore volume and diameter are important in controlling the intensity and duration of the 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 the effect of pore diameter and volume with the 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. [104]

Resiliency: (viscoelastic properties) of microsponges can be modified to produce beadlets that is softer or firmer according to the needs of the final formulation. Increased cross-linking tends to slow down the rate of release. [105]

RECENT ADVANCES IN POROUS DRUG DELIVERY SYSTEMS:
Although the merits of microporous systems in dermatological preparations are well proven, in the current times when nanotechnology is dominating all the spheres of scientific endeavors, Nanosized porous systems are being approached as a further advancement to their microsized counterparts. Nanosponges are hyper cross-linked polymer-based colloidal structures, consisting of countless interconnecting voids within a collapsible structure with a porous surface. [106] These offer passive targeting of dermal agents to the skin leading to dosage form retention on the skin, total dose reduction, and systemic absorption avoidance. Very few research groups have attempted to investigate these nanoporous carriers for encapsulating dermally relevant moieties. Swaminathan et al. formulated cyclodextrin nanosponges for solubility enhancement of itraconazole, a poorly water-soluble drug. [107] The babchi oil loaded cyclodextrin nanosponges were also fabricated by our research group for solubility and photostability enhancement of entrapped essential oil. [108] Sharma and Pathak fabricated ethyl cellulose nanosponges as an alternative system for targeting econazole nitrate to the skin through hydrogel formulation. Hence, nanosponges can be looked upon as an emerging alternative for dermatological disorders. Because of the safety concerns associated with nanoscale particles, exploration of these nanoporous systems as carriers for dermatological agents demands a great deal of attention, and in-depth investigation. Veritably, this domain offers tremendous scope, and scientists looking to enter this field should give due consideration to the issues stated above. [109]

CONCLUSION AND DISCUSSION:
The formulators consider microsponge's technology as a new and creative way to deliver actives with enhanced safety, improved stability, reduced side effect and enhanced multi-functionality and improved ingredient compatibility. Microsponge delivery systems can be an attractive strategy for a new generation of Pharmaceutical and Cosmeceuticals. Microsponges have a distinct advantage over all types of

existing conventional formulation. It is an exclusive technology for the controlled, extended, and target release of topical agents, cardiovascular, ophthalmic, and oral as well as biopharmaceutical drug delivery. The microsponge products are non-mutagenic, non-toxic, and non-irritant. So the microsponge drug delivery system has got a lot of forthcoming and is an emerging field which is needed to be explored in the future for the attractive characteristics of microsponges with the revolutionized nanotechnology trend to enhance their performance.

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