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Microsponge: An adaptable topical drug delivery system

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Abstract

Microsponge a drug delivery system, possesses the versatility to load a wide range of active ingredients due large surface area. it facilitates controlled release of active ingredients and reduces systemic exposure and adverse effect. microsponges are polymeric sponges that consist of interconnecting voids with a flexible structure with a porous surface. Microsponge delivery techniques provides extended product stability, enhanced safety, enhanced formulation flexibility, product efficacy and aesthetic appeal with reduced adverse effects. It is regarded as safe, due to less bacterial contamination as it doesn't require preservatives in the formulation. Therefore it is used in various sterile formulations like ophthalmic, parenteral etc. This review provides an overview of microsponge technology with its methodology, mechanism, programmable release, characterization and recent data on marketed formulations, their applications, and the list of patents, evaluation and application of microsponges in various aspects. Microsponge are frequently used for topical application but recently used for oral also.

Keywords: Microsponge; Sustain release; Stability; Drug delivery; Preservative; Anti-fungal

1. Introduction

A microsponge delivery system (MDS) is, highly cross-linked, porous, polymeric system consisting of porous microspheres that can entrap wide range of active ingredients such as fragrance, sunscreen, emollient, anti-fungal, anti-infective and anti-inflammatory agents etc. [1] These are mostly used to prolong the topical administration of the drug.

Microsponges are tiny sponge-like spherical particles that consist of a myriad of interconnecting voids within a non-collapsible structure having a large porous surface and the size of these microsponges can be varied, usually from 5 to 300µm in diameter depending on the degree of smoothness [1]. Furthermore, they can improve stability, reduce side effect and favorably modify drug release and control their delivery rate, making them suitable for topical delivery. Therefore by optimizing formulation parameters such as drug: polymer ratio and agitation/ stirring rate it might be possible to manufacture optimized microsponge [1].Microsponges have many advantages which make it a adaptable drug delivery system.

Microsponges can suspend or entrap a wide variety of substances which can be formulated as a gel, cream, liquid, or powder for topical delivery [2]. When the formulation is applied to the skin, the MSD release the active ingredients on time and in response to the other stimuli (rubbing, temperature, pH). Recently it was investigated that microsponge also used for oral drug delivery system. Microsponge system has shown to increase the rate of solubilization of poorly water-soluble drugs by entrapping drugs in the microsponge system pores.

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The interior pore structure of 25µm particle have approximately 2,50,000 pores with internal pore structure equals to length of about 10ft, which allowing 1ml/g pore volume for huge drug retention. The surface varies from 20-500m^2 /g. Pore volume of microsponge can varied from 0.1-0.3cm^3 /g. This feature provides large reservoir type system, which is then loaded with capable weight of drug. The size of pore diameter is small, it unables bacteria whose size range is 0.007-0.2 um to penetrate through the pore structure of microsponge, leaving the beads sterile after manufacturing and thus do not require addition of preservatives in the preparation. So, it is regarded as the safety concern of microsponges regarding bacterial contamination of material entrapped. since microsponges is reservoir type system, it potentially delivers large number of substances. [3]

2. Material and methods

2.1. Salient features of microsponge delivery system [5]

- Microsponge are stable over pH 1 to 11
- They are thermally stable upto 130^0 C
- It has Self sterilizing property due to average pore diameter of 0.25 um through which microbes cannot penetrate, so formulation does not require addition of preservatives.
- Microsponges are cost effective as compared to other drug delivery systems.
- It is compatible with most of the vehicles and additives.
- Microsponge have High payload capacity (50-60% by weight), though remain in form of superfine, free flowing powder.
- Good in oil control, as it can absorb oil up to 6 times its weight.
- Flexibility to develop novel product forms.
- Enhance thermal, physical, and chemical stability.

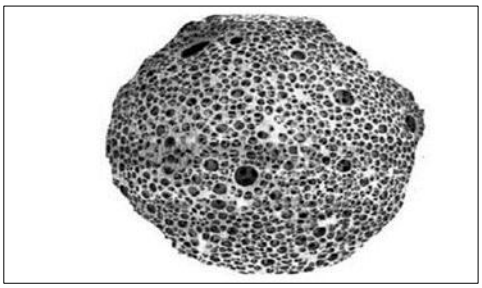

Figure 1 View of microsponge [2]

2.2. Drug requirements to be entrapped in microsponges [6]

For successful entrapment of active pharmaceutical agents within microsponges, certain conditions of the active pharmaceutical agents must be reached.

- It should be completely soluble in monomer or become soluble after a small amount of water insoluble solvent is added.
- Monomer inertness must be demonstrated.
- It must be insoluble in water.
- The viscosity of the mixture should not get increased during the formulation.
- It must have limited solubility in vehicle for avoiding cosmetic issues.
- Spherical structure of microsponge must be preserved.
- It should have stability with polymerization catalyst as well as with polymerization conditions.
- Half-life of the API should be 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 microsponge.

- Due to solubility or miscibility with external phase, only hydrophilic polymers cannot be employed.

Table 1 List of drug used in the preparation of microsponges [6] [7]

Sl. No.	Drug name	Sl. No.	Drug name
1.	Paracetamol (NSAID)	16	Indomethacin (NSAID)
2	Curcumin (Anti-inflammatory)	17	Dicyclomine (Anti-microbial)
3	Flurbiprofen (NSAID)	18	Etodolac (Anti-inflammatory)
4	Benzoyl peroxide (Anti-acne)	19	Diclofenac (NSAID)
5	Ketoprofen (NSAID)	20	Lornoxicam (NSAID)
6	Fluconazole (Anti-fungal)	21	Luliconazole (Anti-fungal)
7	Acyclovir sodium (Anti-viral)	22	Clindamycin (Anti-biotic)
8	Retinol (Vitamin – A)	23	Diacerein (Anti-bacterial)
9	Erythromycin (Anti-biotic)	24	Oxiconazole (Anti-fungal)
10	Mupirocin (Anti-Bacterial)	25	Tioconazole (Anti-fungal)
11	Miconazole nitrate (Anti-fungal)	26	Trolamine (Analgesic)
12	Itraconazole (Anti-fungal)	27	Mometasone furoate (Corticosteriod)
13	Tretinion (NSAID)	28	Fluocinolone acetonide (Corticosteriod)
14	Ibuprofen (NSAID)	29	Acetazolamide
15	Prednisolone (Corticosteriod)		

Table 2 List of polymers used in the preparation of microsponges [8]

Sl.No	Polymer Name
1	Ethyl cellulose
2	Eudragit RSPO
3	Eudragit EPO
4	Eudragit RS 100
5	Eudragit RL 100
6	Eudragit S 100
7	Eudragit L100
8	HPMC E15
9	Sodium alginate
10	Carbopol 934
11	Carbopol 940
12	Propylene glycol
13	Polystyrene
14	Acrylic polymers
15	PHEMA

2.3. Advantages of microsponges technology [9] [10]

- It Improves product elegance.
- Microsponges Reduced toxicity
- Improved drug solubility and stability
- Microsponges Improves bioavailability of active pharmaceutical ingredients.
- Microsponges Enhances product performance.
- Microsponges sustain the release of medicaments and gives continuous action up to 12hrs.
- They have High surface area so higher entrapment efficiency.
- Microsponges are hypoallergenic, irritant free, mutagenic-free and non-toxic.
- Physical, chemical and thermal stability can be improved.
- New product forms can be generated quickly and easily.
- Drug can be directly applied to target organs.
- Capability of absorbing oily skin secretions there by giving shiny look to the skin.
- Material processing is more efficient.
- Microsponge can easily entrap immisible product.

2.4. Preparation methods of microsponges [11] [12]

According to physico – chemical properties of drug, the process of loading of drug in microsponges are is shown in fig.2

2.4.1. One step process

An inert, non-polar drug is loaded through this process. This type of drug produces porogen which is in porous structure. Polymerization process neither affects nor activates the porogen drug and it is stable to free radicals.

2.4.2. Two-step process

This process is employed when the drug is susceptible to polymerization environment. In this method substitute porogen is used during polymerization and is replaced with active substance under mild experimental environment.

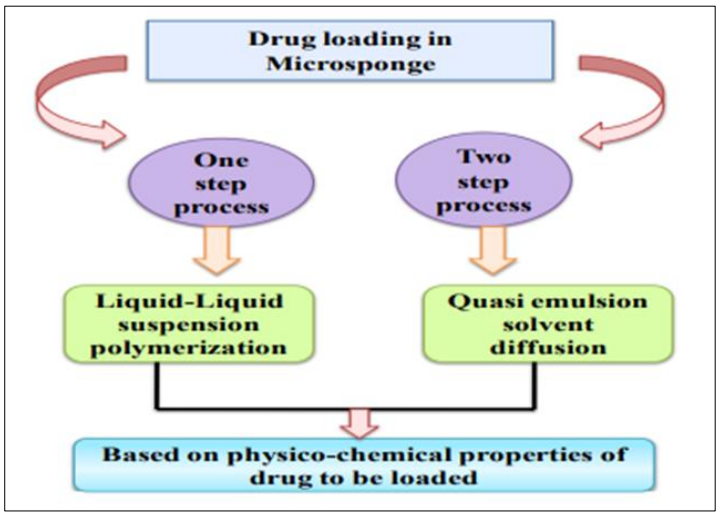

Figure 2 Process of drug loading in microsponge

Following are some preparation methods of microsponges. [13] [18]

- Quasi emulsion solvent diffusion technique
- Liquid -liquid suspension polymerization.
- w/o/w emulsion solvent method
- o/w emulsion solvent diffusion
- addition of porogen method
- lyophilization method

- vibrating orifice aerosol generator method
- ultrasound assisted production method
- electro hydrodynamic atomization method

Quasi emulsion solvent diffusion technique [20] [22]

When the picked drug is sensitive to the polymerization condition, two-step process is used. In this two-step process the different amounts of polymers are used. It is top to down approach which starts by using designed polymer. The method produces matrix type of porous microsponges. It requires development of quasi emulsion of two different inner phase and external phase. Inner phase consists of active therapeutic agent, polymer, volatile solvent and plasticizer. Triethyl citrate is used about 20% in the formulation as plasticizer which gives plasticity. External phase consists of polyvinyl alcohol in distilled water.

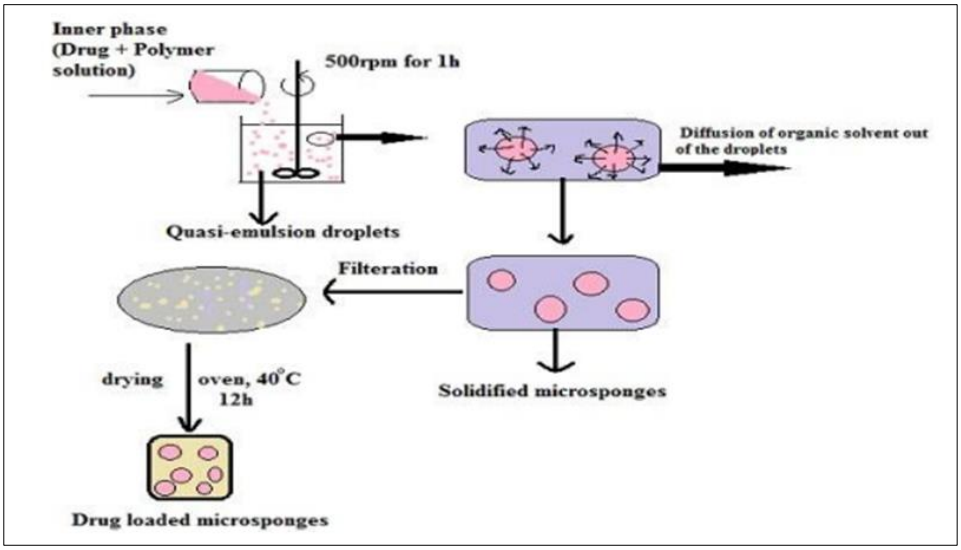

Figure 3 quasi emulsion solvent diffusion method

Steps involved in preparation can be described as: [24]

- Preparation of internal phase by dissolving polymer in volatile solvent like ethyl alcohol, acetone or dichloromethane.
- Slow addition of drug to above solution and dissolving of drug.
- Outer phase is prepared by dissolving PVA in water.
- Inner phase pouring in an outer phase with vigorous stirring which for 60 minutes at particular RPM.
- Vigorous stirring results in development of distinct globules are called as quasi emulsion globules.
- Extraction of solvent from globules to form insoluble, rigid microsponges.
- The formed microsponges are separated by filtration.
- Washing of microsponges with suitable solvent.
- Drying of microsponges in an oven at 40 ^{0}C upto 12 hrs.
- Weighing to determine Percentage yield.

Liquid-liquid suspension polymerization method [25] [26]

Porous microspheres are created in a liquid-liquid environment in this method. It is a one-step technique that begins with monomer. To begin, an appropriate solvent is chosen, and monomers and active components are dissolved in it. With agitation, this solution is disseminated into external phase containing surfactant and suspending agents. Polymerization begins when preferred sized separate droplets are observed, whether by the addition of catalyst, irradiation, or a change in temperature. The liquid is withdrawn after the polymerization process is completed. This technology creates a reservoir-type system that opens out to the outside via pores. In some circumstances, an inert liquid that is not miscible with water but throughout the polymerization process. When the polymerization process is finished, the solvent is removed, leaving behind microsponges that can be combined with different types of active

ingredients and used as topical carriers. In this conditions, a solvent is utilized to ensure that active ingredients are incorporated efficiently and quickly.

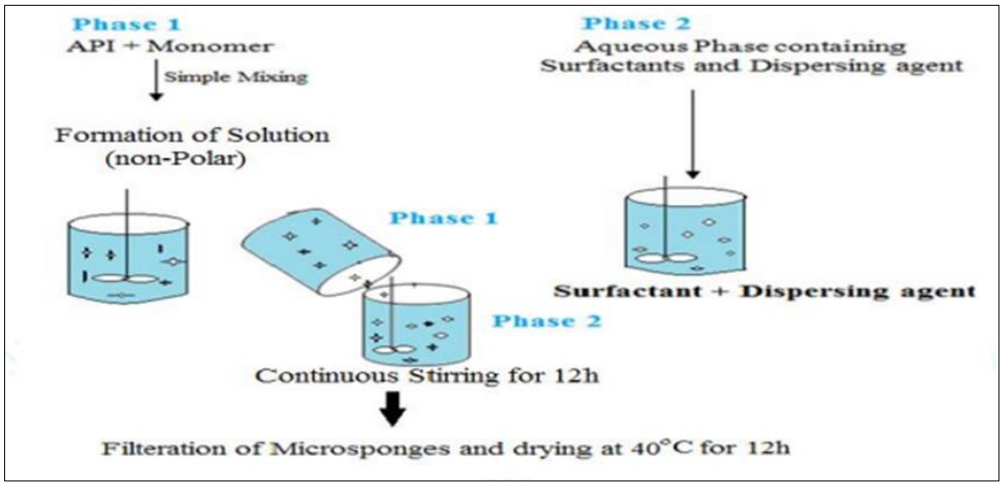

Figure 4 suspension polymerization method

Steps involved in suspension polymerization method can be described as follows: [27]

- Monomer selection (single or numerous).
- As the polymerization begins, chain monomers form.
- The formation of a ladder as a result of cross-linking between chain monomers.
- Formation of spherical particles (microspheres).
- Formation of bunches as a result of agglomeration of spherical particles.
- Microsphere clusters join together to generate microsponges.

Water in oil in water (w/o/w) emulsion solvent diffusion method

This is new approach for making biodegradable microspheres in which the emulsifier in the inner aqueous phase is dispersed in the organic polymeric phase. It can be prepared in the absences of an emulsion. The emulsion is then dispersed in an external aqueous phase of polyvinyl alcohol solution, resulting in a double emulsion. This method is applicable to both hydrophillic and hydrophobic drug. This type microsponge preparation can also entrap thermolabile medicines like proteins.

Addition of porogen

It is modified w/o/w double emulsion evaporation method that uses porogen instead of the internal aqueous phase (w/o) porogens, such as hydrogen peroxide or sodium bicarbonate, are gas-liberating agents that degrade into water oxygen under the influence of a catalyst, and oxygen bubbles produce internal pores within microsponges. The polymer was dissolved in organic solvent, and the porogen was disseminated within that polymeric solution, resulting in a w/o emulsion that was homogenized and transferred into an aqueous PVA phase, where it was re-emulsified for 4hrs using an overhead propeller. The organic solvent is then evaporated, leaving behind microsponges that have been cleaned and lyophilized in a freeze drier.

Oil in oil (O/O) emulsion solvent diffusion method

This method involves dissolving a given amount of polymer in a dispersing solvent such as acetone or dichloromethane to generate a clear solution, adding a deflocculating agent such as Mg stearate, and ultrasonically mixing the mixture to obtain a homogeneous dispersion. The mixture was then introduced to a continuous oil phase, similar to liquid paraffin, and stirred continuously for 45minutes. This was then heated to 35^0c and stirred for 30 min. diffusion and evaporation were used to remove the solvent at this point. The hardened microsponges were than filtered, cleaned, air dried, and stored in a desiccator. Pore inducers such as sucrose and pre-gelatinized starch were occasionally used.

Lyophilization technique

The gelation process is used to create microspheres in this case. Using the lyophilization procedure, this microsphere can be transformed into porous microsponges. microspheres were incubated and lyophilized in this experiment. Chitosan hydrochloride solution was utilized for incubation. During lyophilization, the solvent is removed resulting in the creation of porous microsponges.

Advantages: The process is quick easy. As a result of the quick elimination of the solvent, the particles become broken and shrunken.

Vibrating orifice aerosol generator technique

This approach was first described in the context of creating lipid bilayered mesoporous silica particles. A polymeric solution was prepared by dissolving polymers in an organic solvent and then adding the drug to it. Following that, the polymeric solution was poured into the syringe of the VOAG apparatus at the proper flow rate. Vibrating frequencies resulted in a continuous stream of monodisperse droplets. Droplets were then collected into a PVA aqueous solution and agitated for 24hrs to allow the solvent to evaporate. Finally, solidified micro particles were obtained through filtration, washing, centrifugation, and drying.

Ultrasound assisted method

This method is modification of liquid-liquid suspension polymerization. Microsponges are produced by using monomers and cross-linking agents. the monomer is beta-cyclodextrin, while the cross linker is diphenyl carbonate. The resulting mixture was allowed to cool after heating and sonication. After that, porous, irregular microparticles were created by crushing the resultant product.

- Advantages: There are no solvent residues, and the results are achieved promptly and consistently.
- Disadvantages: Toxic cross linking agent residues become entrapped; irregular structure may result.

Electro hydrodynamic atomization method

The porous microspheres of chitosan were made using this method. The chitosan solution was retained for sonication in order to generate bubbles. The suspension was then placed in a syringe, perfused through a capillary, and electro hydrodynamically atomized. microparticles were made via ion induced gelation. During setup, the proper flow rate and voltage were supplied. The solution of aqueous NaOH was made and maintained in a beaker. When a beaker in put on a magnetic stirrer and constantly agitated during the electro spraying of chitosan solution, the electro sprayed chitosan gels are formed. The chitosan droplets collected in NaOH solution which acquired a spherical in shape after an hour.

2.5. Effect of formulation variable on microsponges [28]

2.5.1. Effect of composition of internal and external phase

The particle size of microsponge were directly proportional to the apparent viscosity of the dispersed phase. if more difference between apparent viscosity of dispersed and continuous phase, larger the mean particle size of the microsponge. when the dispersion phase is more viscous is poured into the continuous phase (external phase), the globules of the formed emulsion can hardly be divided into smaller particles and bigger droplets are found resulting in an increase in mean particle, due to the higher viscosity of the internal phase.

Best microsponges can be produced only when 3 to 5ml of internal phase is used. When the internal phase is increased from 5 to 15ml, the production yield and drug content of microsponges is found to be decreased. This is due to the higher concentration of internal phase with lower concentration of drug.

2.5.2. Effect of drug to polymer ratio:

The parameter which affected from the drug: polymer ratio change is particle size. When the amount of drug is increased, particle size of the microsponge is also increased. When the amount of polymer concentration is kept in constant but the ratio of drug to the polymer is varied , the loading capacity is not much affected but the production yield can be considerably changes from minimum ratio to maximum one .

2.5.3. Effect of stirring rate:

Microsponges of lesser size are obtained as the stirring rate is raised. When the stirring rate is increased, the production yield is reduced, but the drug content increases, indicating that drug loss is reduced when the stirring rate is increased. This is due to the turbulence induced in external phase, which causes the polymer to stick to the paddle and reduces manufacturing yield.

2.6. Physical characterization of microsponges [29]

2.6.1. Particle size and shape

Laser light diffractometry or any other relevant approach, such as scanning electron microscopy, can be used to determine the particle size of loaded and empty microsponges. For all formulations, the values (d 50) can be represented as a mean size range. By controlling the size of the particles during polymerization, free-flowing powders with sensitive aesthetic qualities can be created. Percentage overall to investigate the effect of particle size on drug release, the graph is plotted against particle sizes versus time.

Traditional light microscopy (LM) and scanning electron microscopy (SEM) are the two most used methods for visualizing microparticles (SEM). Both of these methods can be used to determine the microparticles size, shape, and exterior surface. Because particles are bigger than 30um can cause a gritty feeling, topical formulations should use particles between 10 and 25um.

2.6.2. Morphology and surface topography

Various techniques, such as photon correlation spectroscopy, are utilized in the morphological investigation of microsponge topography. Scanning electron microscopy (SEM), transmission electron spectroscopy (TEM). The surface morphology of the prepared microsponges can be explored using scanning electron microscopy after it has been coated with gold-palladium in an argon environment at room temperature (SEM). SEM can be used to examine the ultrastructure of a fractured microsponge particle.

2.6.3. Determination of loading efficiency

Drug loading in microsponges is determined by the drug's physicochemical properties. Drug loading can be done in 2ways: actively or passively. The passive loading is the most efficient loading method. Drug loading efficiency is increased when the drug-to-polymer ratio is rised.

The loading efficiency (%) of the microsponges can be calculated according to the following equation: LE = practical drug loading / theoretical drug loading X 100

2.6.4. Determination of production yield [40]

The drug polymer ratio also affects production yield, an increase in drug: polymer ratio leads to increase in production yield.

The production yield of the microsponges can be calculated by using this formula:

Production yield= practical quantity/ theoretical quantity X 100

2.6.5. Compatibility studies:

Thin layer chromatography (TLC) and Fourier transform infrared spectroscopy can be used to determine the drug's compatibility with reaction additives (FT-IR). The crystallinity of medication depending on polymerization is detected by differential scanning colorimetry (DSC) and powder X-ray diffraction (XRD).

2.6.6. Resiliency

Microsponges' Viscoelastic qualities (resiliency) can be tweaked to produce softer or stiffer bead lets, depending on the final formulations' requirements. The rate of release is slowed by greater cross-linking.

2.6.7. Release evaluation:

Diffusion or other triggering mechanisms such as moisture, pH, friction and temperature can be used to control drug release from microsponges. This release method is utilized to improve the performance of the product.

2.6.8. Dissolution study

Microsponges in vitro dissolution data is obtained using a modified USP XXIII basket dissolution device with a 5um stainless steel mesh. The temperature is maintained at 37^0 C and 150rpm, dissolution media is chosen based on the solubility of the active components. The samples are taken out of the dissolution media at specific time intervals and analyzed using the appropriate analytical procedure. Various apparatus and media are employed to analyze the permeation profile and drug release from MS, which are presented in table dissolving medium selected according to the solubility of active ingredients for maintaining proper sink conditions.

Table 3 Various apparatus and media used in dissolution study

Apparatus	Medium used	Dosage form
USP apparatus I	Simulated fluid	Tablet
	Phosphate buffer 7.4	Hydrogel
USP II	0.1 N HCL	Capsule, tablet, floating systems
Vertical diffusion cell	Phosphate buffer of pH 7.4 ,6.8 ,5.4 water + acetone	Hydrogel
		Lotion, cream
Modified rossett -rice cell	Phosphate buffer 7.4 + tween 80	Floating system

3. Drug release mechanism from microsponges [30] [31]

One or more external stimuli or triggers can release the active component enclosed in microsponges gradually.

3.1. Temperature triggered release

In this process, the active substance is released into the system when the temperature changes. At room temperature some medications are too viscous to flow without interacting with the porous system. When applied to the skin, however, an increase in skin temperature causes an increase in flow rate and hence a continuous release of the medicine.

3.2. Pressure triggered release

In this technique, the entrapped medicine is released by microsponges when the dosage form is brushed across the skin. The amount of medicine released is determined by a variety of microsponges features, including process factors, robustness, and the type of material utilized.

3.3. Solubility triggered release

Porous systems containing a water-soluble excipient release the medicine when exposed to water. Diffusion mechanisms, which involve the partition coefficient between the drug and external system, can sometimes cause release.

3.4. PH triggered release

A change in pH initiates medication release in this method, which is achieved by changing the coating on microsponges for pH-based actives.

4. Hypothetical drug release mechanism [32]

The Drug is encapsulated and added to the vehicle. Drug can freely flow in and out of the microsponge system as well as the vehicle due to the open structure until equilibrium is reached. This results in drug saturation of the vehicle. When a formulation is applied to the skin it results in unsaturation of the vehicle and a loss of equilibrium. To re-establish this balance, the medicine will flow from the vehicle to the skin, until the vehicle has dried or absorbed. The active medicine is then progressively released over time via microsponge particles retained on the stratum corneum surface. Vehicles play an important role in the formulation of microsponges because they allow for the slow and continuous release of active ingredients. As a result vehicle should be chosen such that the active ingredients solubilizing power is minimal. To avoid early drug leaching from the polymer, the dosage form can contain both free and entrapped drug moieties.

Factors affecting drug release from microsponges:

- Physicochemical characteristics of entrapped API.
- Physical parameters of microsponges such as pore diameter, volume, particle size, resiliency.
- Characteristics of vehicle that is used for dispersing microsponges.
- Factors like pore characteristics, monomer composition.

Table 4 Comparision between microsponge, microcapsules and liposomes [33] [34]

Microsponges	**Microcapsules**	**Liposomes**
porous in structure	Shell like structure	Bilayer vesicles
size range 5 to 300um	size range 50nm to 2mm	size range 40-180nm
both hydrophilic and hydrophobic drugs can be entrapped	solid or droplets of liquids and dispersion can be entrapped	can entrap both hydrophilic and hydrophobic drugs
controlled drug release	no controlled drug release	Controlled drug release
drug entrapment is about 50-60%	drug entrapment is about 30%	drug entrapment is about 50%
preservatives are not required in the formulation	Preservatives are required in the formulation.	Preservatives are required in the liposome formulation.
chemically inert across temperature and pH	Chemically and thermally stable.	Chemically unstable.

4.1. Advantages over conventional formulation [35] [36]

Topical medicines in their traditional formulations are designed to function on the skin's outer layers. Upon application, these products release their active ingredients, resulting in a concentrated layer of active substances that is quickly absorbed. In contrast to the microsponges system, it can prevent excessive component accumulation in the epidermis and dermis. The microsponges technology has the potential to dramatically minimize the irritation of effective medications while maintaining their potency.

4.2. Advantages over ointments [37]

Ointments are typically cosmetically unpleasant due to greasiness, stickiness, and other factors, patients are less likely to comply. Due to its ineffective distribution technique which causes discomfort and allergic reactions in significant number of users, these vehicles require high concentration of active drugs for effective therapy. When a microsponges system maximizes the duration of active substances on the skin surface within the epidermis while decreasing its transdermal penetration into the body, another disadvantage of topical formulations is uncontrolled evaporation of active ingredient, unpleasant odor, and potential incompatibility of drugs with the vehicle.

Table 5 Different microsponge drug delivery system with their formulations [38] [39] [40]

Sl.No.	**Microsponge drug delivery**	**Drug**	**Disease**
1	Gels	Benzoyl peroxide Fluconazole Mupirocin Diclofenac sodium Acyclovir Hydroxyzine HCL Terbinafine HCL	Anti-acne treatment Inflammation Antibacterial activity Inflammation Viral infection Urticaria and atopic dermatitis Anti-fungal
2	Lotions	Benzoyl peroxide	Anti-acne treatment
3	Creams	Hydroquinone and retinol	Melanoma
4	Tablets	Indomethacin	Inflammation

		Paracetamol Chlorpheniramine maleate Ketoprofen Fenofibrate meloxicam	Anti-pyretic Hay fever Musuloskeleton pain Gout Arthritis
5	Capsule	Curcumin	Anti-inflammatory
6	Implants	Poly(DL-lactic-co-glycolic acid)	skin tissue engineering
7	Grafts	Poly(lactic-co glycolic acid)	Cardiovascular surgery
8	Injections	Basic fibroblast growth facto Acyclovir Benzoyl peroxide Diclofenac sodium	Growth factor Viral infections Anti-acne treatment Inflammation
9	Ocular	Acetazolamide Atenolol	Glaucoma Anti-hypertensive

Table 6 Various marketed formulation based on microsponge delivery technique for topical application **[**41] [42] [43]

Sl.no.	**Ms Delivery System**	**Drug**	**Name Of Product**	**Treatment**
1	Cream	Tretinoin	Retin-A-Micro	Acne vulgaris
2	Cream	Fluorouracil	Carac Cream 0.5%	Actinic keratoses
3	Cream	Retinol	Line eliminator dual retinol facial treatment	Anti-wrinkle
4	Cream	Retinol	Retinol 15-night cream	Anti-wrinkle
5	Sunscreen	Green tea	Oils free matte block spf-20	Sunscreen
6	Cream	Hydroquinone & Retinol	EpiQuin micro	Hyperpigmentation
7	Gel	Salicylic acid	Salicylic peel 20 & 30	Excellent Exfoliation
8	Moisturizing Cream	Lactic acid & ammonium Lactate	Lactex™ 12% Moisturizing Cream	Moisturizer
9	Lotion	Natural antibiotics	Oil control lotion	Tightness to promote healing, acne-prone, oily skin conditions
10	Spray		Aramis Fragrances	Antiperspirant spray gives sustained release fragrance
11	Lotion impregnated wipes	Dimethicone	Ultra-Guard	Protect babies-skin
12	Cream	Benzyl peroxide	Neo Benz	Anti-acne treatment
13	Cream	Rubefacients	Capsaicin	Anti-allergy
14	Lotion	Salicylic acid	Dermalogica oil control	Skin protectant
15	Lotion	Salicylic peel 20	Salicylic peel 20	Excellent exfoliation

Table 7 Patents filed on microsponge [44] [45]

Sl.no.	Patent number	Patent name
1	US5100783	Weighted microsponge for immobilizing bioactive material
2	1288370	Weighted collagen microsponge
3	US4997753	weighted collagen microsponge for immobilizing bio-active material
4	1275955	weighted microsponge
5	4863856	Weighted collagen microsponge for immobilizing bioactive material
6	4861714	Weighted collagen microsponge for immobilizing bioactive material
7	0217917	Weighted microsponge for immobilizing bioactive material
8	1986056694	Weighted microsponge for immobilizing bioactive material
9	WO/1986/005811	Weighted microsponge for immobilizing bioactive material
10	4092381	Methods of fabricating microsponge deuterated hydrocarbon polymer targets which emit neutrons when irradiated by high energy beams

5. Microsponges in pharmaceutical applications [46]

Topical prescription, over-the-counter, and personal care products use microsponges delivery systems to improve their effectiveness, safety, and aesthetic quality. Microsponges have a wide range of applications, it's usually used topically, although it's also been taken orally recently. Due to its high loading capacity and prolonged release capabilities, it has been stated in several patents that it can be utilized as an excipient.

5.1. Long lasting-coloured cosmetics [50]

Microsponges can entrap the colours in a variety of coloured cosmetics items, such as rouge and lipsticks, to help them to remain for longer period of time. Microsponge, as previously indicated, aids in consistent spreading and improved covering power. Colored cosmetics created with microsponges would be extremely exquisite as a result.

5.2. In topical administration [51]

Table 8 List of topical drug delivery using microsponge technology [52] [54]

Sl.no.	Category	Drugs	Applications
1	Anti-fungal	Fluconazole, miconazole, clotrimazole, econazole	Give sustained release of drugs
2	Anti-dandruff	Selenium disulfide, zinc pyrithione	Enhanced safety and efficacy of drugs with reduced irritation and odor
3	Anti-acne	Tretinoin, benzoyl peroxide	Reduce skin irritation and sensitization
4	Anti-wrinkle	Retinol	Time released delivery into the skin
5	Anti-inflammatory	Piroxicam, hydro-cortisone	Extended drug release with reduced dermatoes and allergy
6	Anti-actinic keratoses	5-fluorouracil	Treat actinic keratoses with reduced dosage form.
7	Skin depigmentation	Hydroquinone	Improve aesthetic appeal with reducing oxidation.
8	Moisturizer	Lactic acid and ammonium lactate	Moisturize dry, cracked and flaky skin.

Topical dosage forms such as cream, emulgel, powder, gel, and lotions contain various drug- loaded microsponges. It expands drug residence time in the epidermis and dermis, by lowering application frequency. The use of a biocompatible, inert, non-toxic polymer further reduces negative effects.

5.3. In oral administration [55] [56]

The Oral route is convenient, safe, and non-toxic, but it has drawbacks such as quick drug excretion due to short half-life and substantial first-pass metabolism in some formulations. As a result, numerous microsponges formulations are developed for controlled and targeted oral distribution, with a variety of uses. By trapping hydrophobic medicines in pores, the microsponges technology enhances their solubilization rate. The rate of solubilization is enhanced when the surface area is large for smaller particles. Ibuprofen microsponges were prepared for regulated drug distribution by modifying the intra particle density of eudragit RS. Powder coated microsponges of chlorpheniramine maleate are manufactured for prolonged release utilizing the dry impact mixing method. Microsponges of ketoprofen are produced and subsequently formed as tablets using the direct compression method for regulated oral delivery.

Table 9 List of oral drug delivery using microsponge technology

Sl.no.	Category	Drugs	Applications
1	Anti-inflammatory	Indomethacin	Reducing side effects like G.I. irritation with modified release
2	Anti-pyretic	Paracetamol	time-release dosage form with a pH-independent polymer coating.
3	Anticholinergic	Dicyclomine	Effective local action with prolonged drug release
4	Colon targeting	Paracetamol	time-release dosage form with a pH-dependent polymer coating
5	Musculoskeletal pain	Ketoprofen	Provided modified-release with reducing the severity of adverse effects.

5.4. In bone and tissue engineering [57] [58] [59]

When 2 acrylate derivative monomers were combined with two aqueous dispersions of tricalcium phosphate grains and hydroxyapatite powder, a porous microsponge was formed. Basic fibroblast growth factor (bFGF) was applied to a collage sponge sheet, which has a prolonged release within the mouse subcutis due to matrix biodegradation, and demonstrated limited angiogenic impact in dose-dependent manner. It revealed enhanced blood flow in the ischemic hind leg of mice, implying that type I collagen could be used as a bFGF reservoir for therapeutic purposes.

6. Conclusion

The microsponge delivery technology of controlled release system in which active pharmaceutical ingredient is loaded in the macro porous beads and initiates reduction in side effects with improved therapeutic efficacy. Microsponge can be effectively incorporated into topical drug delivery system for retention of dosage form on skin, and also use for oral delivery of drugs using bio erodible polymers, especially for colon specific delivery and controlled release drug delivery system thus improving patient compliance by providing site specific drug delivery system and prolonging dosage intervals. This technology is being used currently in cosmetics, over-the-counter skin care, sunscreens, and prescription products. This kind of drug delivery technology may lead to a better understanding of the healing of several diseases. Hence, the microsponge-based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future.

For the existing era and future prospects, sustained drug delivery by means of polymer based systems has been recommended to exist owing to frequent probable benefits for technical and cost effective grounds. The notion behind the development of polymer based microsponge delivery system was to release the active in a recurrent approach for wide time period to cut the dosing frequency and to improve bioavailability.

Compliance with ethical standards

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Disclosure of conflict of interest

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