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Microsponge technology for novel topical drug delivery and oral drug delivery system: An overview

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ABSTRACT

Microsponge is unique drug delivery technique used for topical controlled drug delivery system as well as oral controlled drug delivery system. Microsponges are highly porous surface polymeric microspheres. A well typical Microsponges (25 µm) can have up to 250000 pores approximately, due to they also give prolonged release of active ingredients with continuously and reduce side effect, enhanced the stability of active ingredients. Mostly liquid – liquid suspension polymerization and quasi-emulsion diffusion methods are used for preparation of microsponges with different polymer such as Ethyl cellulose, Eudragit RS- 100, Eudragit S-100 and Eudragit E-100, Eudragit L-100, acrylic polymer etc used as formulation. Various therapeutics agents are loaded into Microsponges and then consolidate into different formulation like as gel, cream, and tablets. Drug is released from microsponges by different trigging system such as pressure system, solubility system, temperature change and pH triggered system. Various process parameters like concentration of drug and polymer, concentration of surfactants, volume of internal and external phase etc. affect the particles size, production yield, encapsulation efficiency and release of drug. In market different Microsponges based product are available such as NeoBenz®Micro, Neo®MicroSD, NeoBenz®Microwash, Retin A Micro, Retinol 15 Night cream, EpiQuin Micro and Retinol cream etc.

Keywords: Controlled release, drug delivery, healthcare systems and Microsponges.

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INTRODUCTION

Microsponges are highly porous surface polymeric microspheres, due to having highly porous surface they are look like tiny sponges, microsponges may enhance stability and reduce the side effect of active ingredients[1]. Polymeric base microsponges can entrap peptide, protein, DNA-based therapeutics and another wide variety of active substances, so these properties make it a versatile drug delivery vehicle and drug loaded microsponges can consolidate into different formulation like as gel, cream, liquid powder, tablets. The size of the microsponges ranges 5 to 300 µm in diameter and a well typical microsponges (25 µm) can have up to 250000 pores approximately and internal pore structure equivalent to 10 feet in length which provide a total pore volume of about 1ml/g for spacious drug retention microsponges can entrap of active ingredients up to three times of their weight.[2] Delivery of active substances in controlling manner for targeting of the human body has been major challenges faced by pharmaceutical scientist. Microsponges technology was developed by Won R in 1987 (Palo Alto, CA) and Advanced polymer systems inc. company were assigned first original patent, the microsponges technology were used by this company for cosmetic as well as pharmaceutical products, On September 8/1992, Won R. (Palo Alto, CA) 'Advanced Polymer Systems Inc. (Redwood City, CA) were received US patent for controlled release microsponges formulation developing by two-step method, On March 31/1992 Dean Jr. et. al. 'Verox Corporation Hanover' received a patent for the development of collagen microsponges, Retinoid loaded microsponges reduced irritation and enhanced stability; it was developed by bFroix et al. "Advanced Polymer Systems, Inc." (Redwood City, CA); On December 22-1998 they received US patent for developing retinoid Microsponges. Microsponges technology is used as topical formulation but researchers also developed MDDs for oral drug delivery, conventional topical formulation produce several side effects such as skin irritation, allergic reaction and they produce greasiness, stickiness, unpleasant and they lack of patient compliance, However microsponge technology reduce these problem and release drug continually by controlling manner, the active ingredients may release from microsponges into skin by a different trigger mechanism such as rubbing , higher then ambient skin temperature, moisture, pH and diffusion mechanism. MDDs in oral application increase the rate of solubility of poorly water drugs by entrapment of active ingredients into small pores of microsponges and they reduce the chances of dose dumping, it also used in bone and tissue engineering .[3]

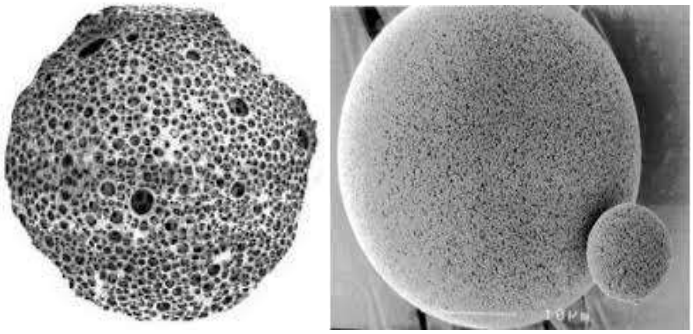

Figure 1: View of Microsponge

Table 1: List of Marketed Products based on Microsponges [4, 5]

Manufacturer	product name	Therapeutics Uses
Dermik Laboratories, Inc.	Carac Cream	Actinic keratoses
AMCOL Health & Beauty Solution	Glycolic Acid Moisturizer w/SPF 15	Soothing, Anti-Wrinkles
Intendis Inc. Morristown NJ07962 USA	NeoBenz®Micro, Neo®MicroSD NeoBenz®Microwash	provide gradual release of active ingredient into skin and absorb natural skin oils. Benzoyl peroxide is an oxidizing agent that posses antibacterial properties.
Avon	Line Eliminator Dual Retinol Facial Treatment	Anti wrinkle
Ortho-McNeil Pharmaceutical, Inc	Retin A Micro	Acne vulgaris
Sothys	Retinol 15 Night cream	Anti-wrinkles
SkinMedica Inc	EpiQuin Micro	Hyper pigmentation
Biomedic	Retinol cream	Helps maintain healthy skin
John and Ginger Dermalogica Skin Care Products	Dermalogica Oil Control Lotion	Skin protectant
Dermalogica	Oil free matte block SPF 20	Sunscreen
Embil Pharmaceutical Co. Ltd	Sports cream RS and XS	Anti-inflammatory
Biophora	Salicylic Peel 20	Excellent exfoliation
SDR Pharmaceuticals, Inc	Lactrex™ 12% Moisturizing Cream	Moisturizer
Scott Paper Company	Ultra Guard	Protects baby's skin

APPLICATION OF MICROSPONGES TECHNOLOGY

Microsponges technology for topical delivery[6]

The Microsponge can entrap different category of drug which is use for different topical disease, once drug loaded microsponges is prepared then it is easily consolidated into different final product such as a gel, cream, powder or liquid, polymer used for topical microsponges

formulations should be non-irritating , non-allergenic, non-mutagenic, non- biodegrable and non-toxic.

Advantage of microsponges over other conventional topical dosage form[6]

The topical drug delivery of Microsponges gel, cream, lotion, ointment is greater therapeutic activity than other conventional topical dosage form because conventional topical dosage form are easily evaporate from skin and cannot deliver the drug continuously for long time, while microsponges based gel, cream, lotion etc. Can absorbed oil from skin up to 6 times its weight, without drying it can continuously release the drug up to 12 hours. The other disadvantage of conventional topical dosage form is release high concentration of active ingredients on the skin or epidermis and produce several side effects such as skin irritation, allergic reaction and they produce greasiness, stickiness, unpleasant and they lack of patient compliance, while microsponges topical formulation give sustained release drug delivery and reduce the accumulation active ingredient within the epidermis and dermis. Microsponges based Sunscreens reduced irritancy and sensitization and enhanced protection against suns burn with long lasting product efficacy. Benzyl peroxide is used as anti-acne, conventional formulation of Benzyl peroxide produce skin irritation and sensitization while benzyl peroxide loaded microsponges gels reduce that problem, Antifungal loaded Microsponge produce sustained release of active ingredients.[18] A new formulation of 4% hydroquinone with 0.15% retinol loaded microsponges is used to treatment of melasma and post inflammatory hyper pigmentation, it reduce the skin irritation due to gradually prolong exposure to treatment. Mupirocin loaded microsponges were prepared by an emulsion solvent diffusion method and consolidated into an emulges base, cellulose dialysis membrane were used as drug release study which showed diffusion controlled release pattern and abdominal skin of Rate is used as drug deposition studies which showed significant retention of active in skin from microsponges formulation by 24 hrs and Druze patch test demonstrated that optimized formulation were stable and non-irritant to skin.

Microsponges technology for oral delivery[6]

The microspong for oral drug delivery has been shown to increase the solubility of poorly water soluble drug by entrapment of drug into the small pores structures of microsponges. Microsponges technology is used as oral control drug delivery such as GRDDS and colon target drug delivery system. Osmani R.A.M. et.al, formulated and evaluated Microsponge based drug delivery system for augmented gastroparasis therapy using Domperidone drug, They employed Eudragit RS-100 with various drug polymer ratios and concluded that microspong with drug polymer ratios of 1: 2 were more proficient to give extended drug release of 76.38% at the end of 8 hours. Shah H.et.al.,

formulated and evaluated of controlled release colon target microsponges using Aceclofenace drug, the Aceclofenace loaded Microsponges were prepared by using different polymer ethyl cellulose , eudragit RS-100, eudragit S-100, eudargit RL-100, in different concentration and they observed that microsponges with drug polymer ratio (1:12) were showed 97.55% drug released at 24 hours.

Advantage of Microsponges over microcapsule, liposome and other microparticles [6]

Microsponges has similar advantage like microcapsule or other micro particle but the drug controlled release properties is greater than microcapsule as well as other micro particle, due to high porous surface of microsponges through which drug is release by controlled manner, on the other hand once the wall of microcapsule or other micro particle is rupture they release high concentration drug substances and chance of dose dumping while microsponges may reduces these problems. Liposome required for specific condition to maintain physicochemical and stability of active ingredients as well as maintain microbial growth while microsponges is self sterilization system they do not require sterilization or addition of preservative due to having 0.25µm pore size which act as barrier for penetration of bacteria.

Importance of Microsponges technology in Bone and Tissue Engineering/ Bone-substitute[7]

Microsponges were prepared by mixing of polymetha methacrylate and pre polymerized powder of poly methyl metacrylate with two aqueous calcium deficient hydroxyapatite powder and tricalcium phosphate grains, the final mixture is appeared as porous microsponges. Basic fibroblast growth factor (bFGF) consolidated into a sheet of collagen sponges, that fixed in the mouse sub-cutis which give sustained release with local angiogenic activity and (bFGF) incorporated microsponges injection induce blood flow.[3]

Recent advantages of Microsponges drug delivery system[7]

The nanosponge, nano ferrosponges and porous micro beads are modified method of Microsponges. β-cyclo dextrin nanosponge developed for the delivery of hydrophilic and hydrophobic drug. Oral administration of dexametasone, flurbiprofen, doxorubicin Hcl, itraconazole and serum albumin are studied as microsponges delivery system. Developer also observed drug which is used for cancerous, can increased the potency of the drug for targeting the cancerous cell by microsponges delivery.

Table 2: Application of Microsponges technology[7, 8]

Therapeutic agents	Application
Anti-dandruffs e.g. zincpyrithione, selenium sulfide	Extended efficacy and safety with reduced irritation and reduced unpleasant odor.
Anti-inflammatory e.g. hydrocortisone	Reduced allergic response and dermatoses with Long lasting activity.
Skin depigmenting agents	Improved efficacy and aesthetic appeal with Improved stabilization.
Antipruritics	Extended with improved activity.
Anti-fungal	Sustained release of actives.
Skin depigmenting agents e.g. hydroquinone	Improved efficacy and aesthetic appeal with reduce oxidation.
Rubefacients	Reduced irritancy and greasiness with Prolonged activity.
Sunscreens	Improved protection against sunburns and sun related injuries with Long lasting product efficacy.
Maintaining the skin's youthful appearance. Eg. vitamin A	Reduce the skin irritation with enhance skin shining
Anti actinic keratosis Egg. -Fluorouracil (5-FU)	treating actinic keratosis, reduce irritating

Silent feature of Microsponges drug delivery system [9,10, 11]

- Microsponges are stable over pH range 1 to 10 and can stable at up to 130 °C.
- Microsponges exhibit good compatibility with various vehicles and ingredients.
- They have free flowing properties
- Microsponges do not required sterilization or addition of preservative because the pore size of microspong is 0.25µm, due to small porous properties the bacteria cannot penetrate.
- Microsponges can absorbed oil up to 6 time weight without drying.
- It enhances the solubility of poorly water soluble drug.

Advantage of Microsponges drug delivery system [9,10, 11]

- Microsponges enhance the product performance.
- Microsponge technology is used as extended released formulation.
- In external application it reduces the skin irritation & improved the patient compliance.
- It maintained the physiochemical properties of drug.
- Microsponges have batter thermal stability.
- It Reduce dose frequency.
- It enhance solubility of poorly water soluble active ingredients

- It Reduce side effect and formulation flexibility is well, due to formulation flexibility it developed as another product form.
- Bioavailability of drug can improve by MDDs.

Disadvantages of Microsponges

- Difficult to optimize the accurate dose and dosing interval.
- Patient variability effect the release rate like GI emptying rate, fasting or non fasting condition.
- Time consuming during manufacturing.
- Required high quantity of drug for encapsulation.
- Large particle size may produce greasiness on to skin.

The following characteristic should be active ingredient [11]

- The active ingredient should be stable with during polymer catalysis and polymerization.
- It should be miscible with monomer.
- The physiochemical properties of drug should not changes when microsponges loaded drug convert into another form like gel, lotion, cream, tablets etc.
- The active ingredients should not soluble with the external phase during Microsponges formulation.

Formulation of microspong[12'13]

Microsponges drug delivery system contains drug, polymer, vehicle, plasticizer, emulsifier and solvents.

Polymer use [12,13,14,15]- Microsponges can prepared various polymer like, ethyl cellulose, Eudragit RS- 100, Eudragit S-100 and Eudragit E-100, Eudragit L-100, acrylic polymer, polystyrene and PHEMA, HPMC K4M, Carbopol 934 and Eudragit RL100 etc.

Drug release mechanism

Pressure system[16] - by application of rubbing and pressure, the drug is release from Microsponges on the skin.

Solubility system[16]- water soluble active ingredient is released from microsponges by diffusion, the partition coefficient of active between Microsponges and outside system affects drug release mechanism.

Temperature change[17] - some entrapped active ingredient have too viscous properties at room temperature but during the contact with physiological temperature the flow rate of drug may increase and it release easily .

pH triggered system [17]- the active ingredients release from microspores by pH dependent solubility, Triggering the pH-based release of the active can be achieved by modifying the coating on the Microsponges.

Method of preparation of Microsponges

Microsponges prepared is by following two method

1-liquid – liquid suspension polymerization method

2- Quasi-emulsion solvent diffusion method

Liquid–liquid suspension polymerization method[18,19,20,21]**-**

Microsponges is prepared by liquid- liquid suspension polymerization method, in this technique first the monomer and active ingredient mixed into a suitable solvent after that the mixture solution is dispersed in the aqueous phase containing (surfactants) with the agitation. During the polymerization process the solvent is removed and spherical porous Microsponges are formed.

The following step by which Microsponges is formed:

1- Selection of monomer.
2- Mixed monomer with drug into suitable solvents.
3- Poured the mixed solution into external phase and stirring continuously.
4- Polymerization starts by formation of chain monomer.
5- By crosses linking between chain monomer the ladder is formed.
6- After formation of ladder the spherical particles is formed by folding of monomer ladder.
7- The bunch of microspheres is formed from agglomerization of microspheres.
8- Finally the Microsponges are formed by binding of bunch.

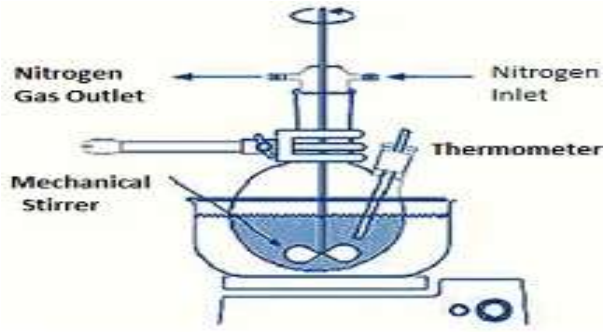

Figure 2: Reaction Vessel for Microsponges Preparation by Liquid-Liquid Suspension method

Quasi-emulsion solvent diffusion method [20,21,22,23,24]**-**

In this method first two phases (external and internal phase) is prepared.

External phase distilled water containing with surfactants (PVA) and internal phase containing, drug, polymer, solvent and plasticizer

The following step by which Microsponges is formed:

1- Take required quantity of polymer and drug dissolved into volatile organic solvent.
2- The mixture solution of drug and polymer is then poured into aqueous solution of PVA by dropping method with stirring.
3- After emulsification the mixture continuously stirred until sphere particle of Microsponges are formed.
4- The Microsponges then filtered and washed with distilled water.
5- Then dry the Microsponges at 40°C for 12 hours.

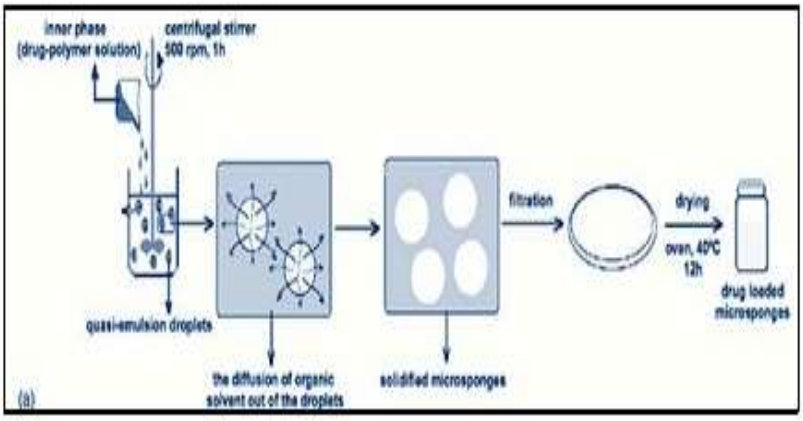

Figure 3: Preparation of Microsponges By Quasi-Emulsion Solvent Diffusion Method

Table-3: Review of prepared Microsponges [1-22]

Author	Drug uses	Polymer uses	Method of preparation	Result
Mehajan A.J. et.al., (20011)	Indomethacin	Eudragit RS-100	Quasi emulsion solvent diffusion	88.69 to 94.074 drug release at 12 hours
Rekha U. et.al., (2011)	Mometasone furoate	Eudragit RS-100	Quasi emulsion solvent diffusion	Increasing the ratio of drug and polymer (1:1 to 13:1) will decrease the release rate of drug.
Maiti S. et.al., (2011)	Diclofenac sodium	Ethyl cellulose	Quasi emulsion solvent diffusion	Increasing the drug and polymer ratio (0.4:1, 0.6:1, 0.8:1) will increase their release rate (78.1-88.55 %), followed Higuchi's diffusion kinetic.
swetha et,.al., (2011)	Etodolac	Ethyl cellulose, Eudragit RS-100	Quasi emulsion solvent diffusion	Formulation of Etodolac with Ethyl cellulose give the maximum drug release 99.3% within 8 hrs, while formulation of Etodolac with Eudragit RS-100 give 87.6% drug release within 8 hrs.
Yerram Chandramouli et.al., (2012)	Acyclovir sodium	Ethyl cellulose	Emulsion solvent diffusion method	50.85% of drug release at 8 hours.
Markand Mehta et.al.,(2012)	Clotrimazole	Ethyl cellulose, HPMC K4M, Carbopol 934, Eudragit RS100, Eudragit S100, Eudragit RL100	Emulsion solvent diffusion technique	The drug release from gel formulations follows zero order release.
Yerram Chandramouli et.al., (2012)	Acyclovir sodium	Ethyl cellulose	Emulsion solvent diffusion method.	Optimized F1 released 50.85% of drug at 8 hours and followed Zero order kinetics.
R. Ravi et.al., (2013)	Erythromycin	Ethyl cellulose	Quasi emulsion solvent diffusion	They concluded that erythromycin can be formulated as Microsponges gel and can release the drug up to 8hrs with reduced side effects.
Jaya raja Kumar et.al., (2013)	Ketotifen	Ethyl cellulose	Quasi-emulsion solvent diffusion	The optimized formulations were able to release the drug up to 8 hours.
Karthika.R et.al., (2013)	Lornoxicam	Eudragit RS 100	Quasi-emulsion solvent diffusion	Prolonged release of drug
Ramani Gade et.al., (2013)	Hydroxyzine Hydrochloride	Methocel 10000cps, Eudragit –S100, Eudragit-L100, Eudragit-RL100 and Eudragit-RS100	Oil in oil emulsion solvent diffusion method.	The Microsponges tablet formulation, F11 showed controlled release of hydroxyzine hydrochloride for 12hrs.

Roaa A. Nief et.al., (2014)	Meloxicam	Eudragit RS-100, Eudragit S 100, Eudragit-E 100,	Quasi-emulsion solvent diffusion	Meloxicam Microsponges markedly enhanced dissolution rate.
Hamid Hussain et.al., (2014)	diclofenac sodium	Ethyl cellulose	Quasi emulsion technique	they observed that cummulative drug Release of 49.89 % in 24 hour,
Makwana Rajeshree et.al., (2014)	Miconazole	Ethyl Cellulose	Quasi-emulsion solvent diffusion	The Microsponges showed higher photo stability as compared to plain drug and other physical mixture.
Sonali et.al., (2014)	Prednisolone	Eudragit RS 100	Quasi-emulsion solvent diffusion	That drug release in colon could be controlled by Eudragit RS 100 and Cumulative release for the Microsponges over 8 h ranged from 48 - 87 %.
Riyaj ali M. osmani et.al., (2015)	Diclofenac Diethylamine	Eudragit RS 100	Quasi-emulsion solvent diffusion	The drug- polymer ratio (1:2) were more efficient to give extended release of 75.8 % at end of 8 hrs.
Riyaz Ali M. Osmani et.al., (2015)	Domperidone	Eudragit RS100	Quasi-emulsion solvent diffusion	Extended drug release of 76.38 % at the end of 8 h, superior in contrast to conventional marketed formulation Domstal®;
Rajurkar VG et.al., (2015)	Naproxen	Eudragit RS100	Quasi-emulsion solvent diffusion	The results showed that, generally an increase in the ratio of the drug: polymer resulted control release rate of naproxen from micro sponges.

Table-4: Examples of prepared drug loaded Microsponges incorporated in final product [25,26]

Microsponges Delivery Systems	Drug
Gels	Erythromycin, Benzoyl peroxide, Mupirocin, Fluconazole Naproxen, Acyclovir, Meloxicam, Diclofenac sodium Hydroxyzine HCl, ketotifen, Terbinafine HCl
Tablets	Indomethacin, Paracetamol, Chlorpheniramine, maleate Ketoprofen, Fenofibrate, Meloxicam,, metoprolol
Creams	Hydroquinone and Retinol
Implants	Poly(DL-lactic-co-glycolic acid)
Lotions	Benzoyl peroxide
Injection	Poly (lactic-co glycolic acid)
Grafts	Poly (lactic-co glycolic acid)
Capsules	5 Florouracil

Table-5: Processing parameters [27,28]

Parameter	observation					
Concentration of drug and retardant material in the internal phase	Concentration of retardant material affect the Particle size, Production yield (%),Physical appearance, encapsulation efficiency, drug release, Ravi R et al (2013) developed the process parameters for erythromycin loaded Microsponges by quassi emulsion solvent diffusion method using ethyl cellulose and they observed that increasing the concentration of retardant material of internal phase (1-6% of internal phase), the particle size and Production yield were increased and Spherical rigid Microsponges was formed Riyaz Ali M. Osmani el al (2015) observed that increasing the drug: polymer ratio (1:1-1:6) with increasing the particle size and production yield but decrease encapsulation efficiency and % CDR					
Concentration of surfactant	Ravi R et al (2013) observed that increasing the contraction of surfactant with increase the particle size and Irregular Physical appearance, Foaming Characteristics of emulsion produce. Riyaz Ali M. Osmani el al (2015) observed that increasing the contraction of surfactant (sodium algenate30-70mg) ,the particle size, production yield and encapsulation efficiency were increased while drug release were slightly decreased.					
volume external phase	Ravi R et al (2013)	External phase volume (ml)	Observation Particle size in µm	Entrapment (%)	Drug content (%)	Physical appearance
		60	170-260±4.56µm	67.33	76.8	Irregular, non-uniform
		90	280-360±3.82µm	84.77	89.3	Spherical, uniform
		120	380-460±4.39µm	82.55	89.2	Spherical, uniform
		150	490-580±5.67µm	72.63	78.2	Spherical, uniform
stirring speed	Increasing the stirring rate .with decrease the particle size.					

Note-The other parameter like starring time affect the righty of particle and volume of internal phase affect the viscosity of polymer and particle size, the temperature of internal phase and external phase is affect the formation of Microsponges and rate of volatility of internal organic phase.

Characterization parameters of Microsponges:

- Micromeritics and rheological characterization of Microsponges
  - Particle size determination
  - Morphology and surface topography of Microsponges
  - Characteristic of pore structure & porosity
  - Bulk and tapped density
  - Hausner's ratio
  - Carr's index
  - Angle of repose
- Determination of loading efficiency and production yield,
- In-vitro dissolution studies
- Kinetics of release
- Resiliency

Micromeritics and rheological characterization of Microsponges[27,28]

Particle size determination

Particle size is measured by optical microscope using optical micrometer and means particle size is used as distribution of Microsponges particles. Laser light diffractometry is used also as particle size determination. For topical use the particle size should be below 25µm, hence particles having sizes range between 10 and 25µm are preferred to use in final topical formulation.

Morphology and surface topography of Microsponges[27,28]

Scanning electron microscopy is used as surface morphology of Microsponges, in this method prepared Microsponges can be coated with gold platinum under an argon atmosphere at room temperature and then the surface morphology of the Microsponges can be studied by scanning electron microscopy (SEM).

Characteristic of pore diameter & porosity [27,28]

Pore volume and diameter are vital in controlling the intensity and duration of effectiveness of the active ingredient, pore size distribution, average pore diameters, total pore surface area, shape and morphology of the pores, bulk and apparent density can be determined by using mercury intrusion

porosimetry and true density of micro sponges is measured using an ultra-pycnometer under helium gas.

Bulk and tapped density, Hausner's ratio, Carr's index, Angle of repose[29]

The tapped density and percent compressibility index of the micro sponges were measured by a tapping method. Angle of repose (θ) of the micro microsponges, which measures the resistance to particle flow, was determined by a fixed funnel method and all parameters are calculated using following equation.

Bulk density = Mass of Microsponges/Volume of microsponges before tapping (1)

Tapped density = Mass of Microsponges/ Volume of microsponges after tapping(2)

Hausner's ratio = Tapped density/ Bulk density (3)

Carr's index = (Tapped density- Bulk density)/ Tapped density X100 (4)

Angle of repose (θ) = $\tan^{-1}$ (h/r) (5)

Where, h = Height of the powder cone and r = Radius of powder cone.

Determination of loading efficiency and production yield[30,31]

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

Loading Efficiency =Actual Drug Content in Microsponges/ Theoretical drug content X 100 (6)

The production yield of the Microsponges can be calculated by accurately weighing the initial weight of the raw materials and the final weight of the Microsponges obtained.

Production yield =Practical mass of Microsponges/ Theoretical mass (polymer + drug) X 100 (7)

In vitro drug release study[32]

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

Kinetics of Release [33,34]

The dissolution profile of each formulation have been subjected to various models such as Zero order kinetics (percentage drug release against time), First order kinetics (log percentage drug unreleased against time), Higuchi (percentage drug released against square root of time) and Korsemeyer-Peppas (log percent drug released against log of time) were applied to access the kinetics of drug release from prepared Microsponges.

Resiliency [34,35]

Resiliency (visco-elastic properties) of Microsponges can be modified to reduce beadlets that are softer or firmer according to the need of the final formulation. Increased cross-linking tends to slow down the rate of release. Hence resiliency of Microsponges will be studied and optimized as per the requirement by considering release as a function of cross-linking with time.

Table-6: List of patent Patents Filed Related to Microsponges drug delivery[36]

Inventors	Publish year	Patent no
Wright, Steven G et al	2005	US20050271702
Shefer et al	2005	US20030232091
Cattaneo, Maurizio	2004	US20040247632
Tomlinson et al	2001	US6211250
Straub et al.	1999	US6395300
Lo; Ray J. R	1996	US5725869
Eury, Robert P et al.	1994	US5316774
Fanchon; Chantal et al	1994	US5679374
Katz et al	1992	US5135740
Schaefer et al	1989	US5292512
Dean RC Jr et al.	1989	US4863856
Won, Richard	1987	US4690825

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