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## **A REVIEW: MICROSPONGE A INNOVATIVE STRATEGY FOR DRUG DELIVERY SYSTEM, CURRENT STATUS AND FUTURE PROSPECTS**

Nikhil B Sinkar\*, Sheetal B Gondkar, Ravindranath B Saudagar

KCT'S R.G. Sapkal College of Pharmacy, Anjaneri, Nasik-422 213, Maharashtra, India.

### **Keywords:**

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development methods

### **For Correspondence:**

**Nikhil B Sinkar**

KCT'S R.G. Sapkal College  
of Pharmacy, Anjaneri,  
Nasik-422 213, Maharashtra,  
India.

### **E-mail:**

[nikhilsinkar3@gmail.com](mailto:nikhilsinkar3@gmail.com)

### **ABSTRACT**

Microsponge is recent novel technique for control release and target specific drug delivery system. Microsponges are polymeric delivery system composed of porous microspheres. They are tiny sponge-like spherical particle with a large porous surface. Microsponge system offers entrapment of ingredient and is believed to contribute towards reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. Microsponge systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as gel, cream, liquid or powder and have recently been used for oral administration. Microsponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects and modify drug release.

## INTRODUCTION

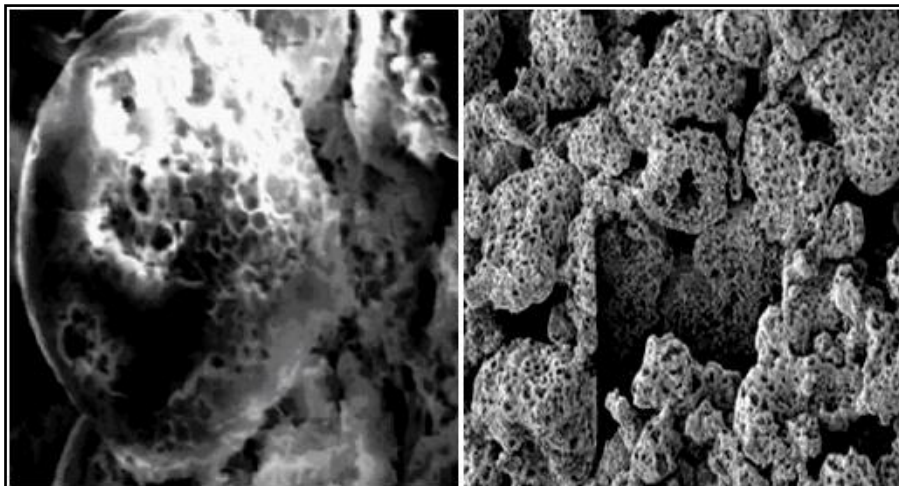
The drug delivery technology has become highly competitive and rapidly evolving. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. New classes of pharmaceuticals, biopharmaceuticals are the rapid evolution of drug delivery technology. These new drugs typically cannot be effectively delivered by conventional means.

In the contemporary years the development of new drugs is not sufficient for the drug treatment. But it also involves the development of suitable drug delivery system at site of action. The in-vivo fate of the drug is not only determined by the properties of the drug, but it is also determined by the carrier system, which permits a controlled and localized release of the active drug according to the specific need of the therapy. The most challenge up to date is to control the delivery rate of the medicaments by various modern technologies met by extensive research [1, 2].

Microsponges are polymeric delivery systems composed of porous microspheres. They are tiny sponge-like spherical particles with a large porous surface. Moreover, they may enhance stability, reduce side effects and modify drug release favorably. Microsponge technology has many favourable characteristics, which make it a versatile drug delivery vehicle. Microsponge systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide range of drugs and can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved aesthetic properties in an efficient manner [3, 4, 5]. To control the delivery rate of drug to a predetermined site in the human body has been one of the biggest challenges followed by Pharmaceutical researchers. Controlled release of active ingredient onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant quantity is a challenging area of research [6].

**Elucidate Microsponge:** Microsponge is a patented polymeric system consisting of porous microspheres. They are tiny sponge like spherical particles that consist of myriad of interconnecting voids within a non-collapsible structure with a large porous surface through which active ingredients are released in a controlled manner. The size of the microsponges range from 5-300 $\mu$ m in diameter and a typical 25 $\mu$ m sphere can have up to 250000 pores and an internal pore structure equivalent to 10 feet in length, providing a total pore volume of about 1ml/g for extensive drug retention. The surface can be varied from 20 to 500 m<sup>2</sup> / g

and pore volume range from 0.1 to 0.3 cm<sup>3</sup> / g [7, 8]. The microsp sponge technology was developed by Won in 1987, and the original patents were assigned to Advanced Polymer System, Inc. At the current time, this interesting technology has been licensed to Cardinal Health, Inc; for use in topical products [9].



**Figure 1: A typical diagram of Microsp sponge**

The scanning electron microscopy of the microsp sponge particle reveals that its internal structure as the “bag of marbles”. The porosity is due to the interstitial spaces between the marbles. The interstitial pores can entrap many wide ranges of active ingredients such as emollients, fragrances, essential oils, sunscreens, anti-infective and anti-inflammatory agents. These entrapped microsponges may then integrated or formulation into product forms, such as cream, lotion, powders, soaps, capsules and tablets. Microsp sponge after it has been applied to the skin elevates skin surface temperature introducing solvents for the entrapped material such as water, alcohol or even perspiration and controlling the rate of evaporation. Active ingredients entrapped in the porous polymeric structure display altered behavior, with respect to their release, which is restricted and prolonged [5].

#### **Characteristics of microsp sponge**

Characteristics of microsponges are as follows [9, 10-12]:

1. Microsp sponge formulations are compatible with most vehicles and ingredients.
2. Microsponges are non-allergenic, non-irritating, non-mutagenic and non-toxic.
3. Microsp sponge formulations are stable over range of (pH-1 to 11).
4. Microsp sponge formulations are stable at the temperature upto to (130<sup>0</sup>C).
5. Microsp sponge formulations have high entrapment upto 50 to 60%.
6. Microsp sponge formulations are free flowing and can be cost effective.

7. Microsponge formulations are self-sterilizing as their average pore size is about (0.25 $\mu$ m) where the bacteria cannot penetrate the pores.
8. Microsponges can absorb oil up to (6 times) its weight without drying.
9. It provides continuous action upto (12 hours) i.e. extended release.
10. They have superior formulation flexibility.
11. Microsponge formulations can be cost effective even for the cosmetic mass market use where the cost of the materials is important.

#### **Benefit of microsponge drug delivery system [6, 11]**

1. Improved product elegance.
2. Improved formulation flexibility.
3. Enhanced product performance.
4. Extended release.
5. Reduced irritation and hence improved patient Compliance.
6. Improved thermal, physical and chemical stability.
7. Flexibility to develop novel product forms.
8. Microsponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.

#### **Drug enclosed in microsponge drug delivery system [13, 14, 15]**

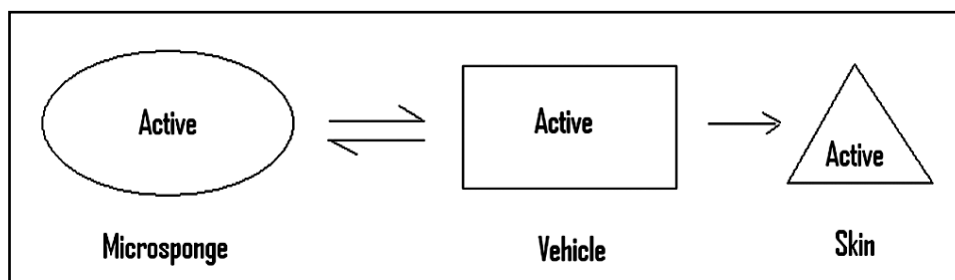
- Ketoprofen (Non-steroidal anti-inflammatory drugs)
- Retinol (Vitamin-A)
- Ibuprofen (Non-steroidal anti-inflammatory drugs)
- Paracetamol (Non-steroidal anti-inflammatory drugs)
- Fluconazole (Anti-fungal)
- Benzyl peroxide (Anti-acne)

#### **Methods of preparation of Microsponges**

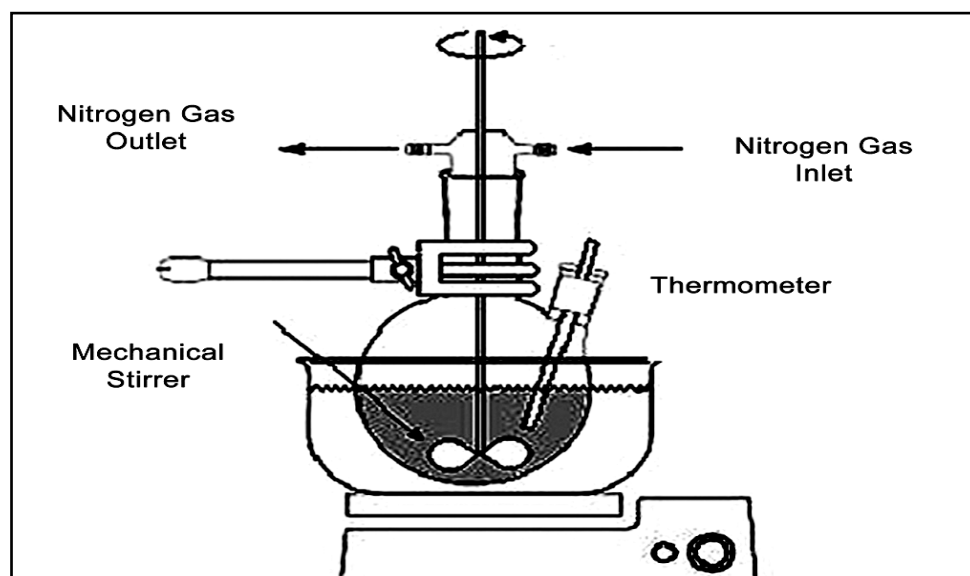
##### **Liquid-liquid suspension polymerization**

The porous microspheres are prepared by suspension polymerization method in liquid-liquid system. In this method the monomers which are immiscible are first dissolved along with active ingredients in a suitable solvent monomer and are then dispersed in the aqueous phases which consist of additives like surfactant, suspending agent to facilitate formation of suspension. The polymerization is then activated by increasing temperature or irradiation or by addition of catalyst. The polymerization process the solvent is removed leaving the

spherical structure porous. After the polymerization process the solvent is removed leaving the spherical structure porous microspheres, i.e. microsponges [3, 16-18].



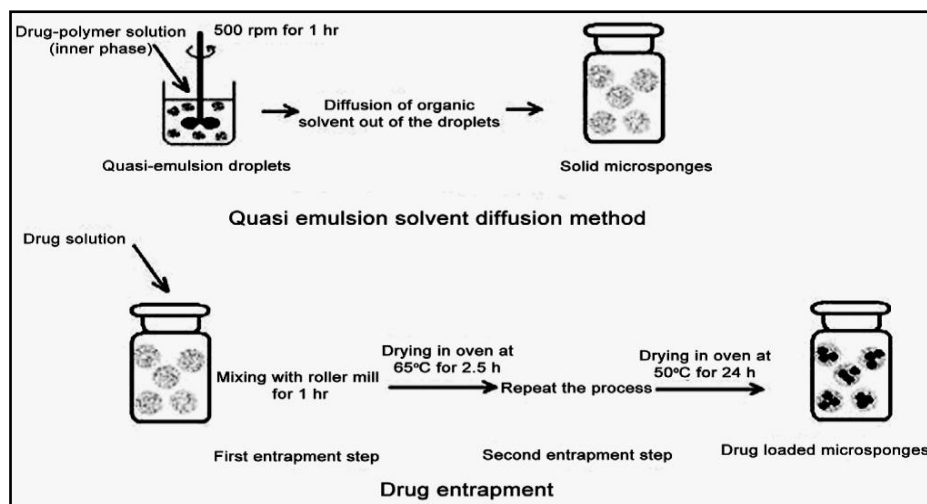
**Figure 2: Schematic representation of the distribution of the loaded material (active) on skin**



**Figure 3: Reaction vessel for microsphere preparation by liquid-liquid suspension polymerization**

### Quasi-emulsion solvent diffusion

Porous microsponges were also prepared by a quasi-emulsion solvent diffusion method [Two-step process] using an internal phase containing polymer which is dissolved in solvent. Then, the drug is slowly added to the polymer solution and dissolved under ultra-sonication at 35<sup>0</sup>C and plasticizer such as triethylcitrate (TEC) was added in order to aid the plasticity. The inner phase is then poured into external phase containing polyvinyl alcohol and distilled water continuous stirring for 2 hours. Then, the mixture was filtered to separate the microsponges. Then microsponges were washed and dried in air-heated oven at 40<sup>0</sup>C for 12 hours [14, 19].



**Figure 4: Preparation of microsponge by the quasi-emulsion solvent diffusion method**  
**Hypothetical mechanism of action of microsponge**

The active ingredient is added to the vehicle in an entrapped form. As the microsponge particles have an open structure (i.e. they do not have a continuous membrane surrounding) the active is free to move in and out from the particles and into the vehicle until equilibrium is reached, when the vehicle becomes saturated. Once the finished product is applied to the skin, the active that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore, disturbing the equilibrium. This will start a flow of the active from the microsponge particle into the vehicle, and from it to the skin, until the vehicle is either dried or absorbed. Even after that the microsponge particles retained on the surface of the stratum corneum will continue to gradually release the active to the skin, providing prolonged release over time. This proposed mechanism of action highlights the importance of formulating vehicles for use with microsponge entrapments. If the active is too soluble in the desired vehicle during compounding of the finished products, the products will not provide the desired benefits of gradual release. Instead they will behave as if the active was added to the vehicle in a free form. Therefore, while formulating microsponge entrapments, it is important to design a vehicle that has minimal solubilizing power for the actives. This principle is contrary to the conventional formulation principles usually applied to topical products. For these conventional systems it is normally recommended to maximize the solubility of the active in the vehicle [4, 20].

## **Release mechanism**

The mentioned programmable parameters can be effectively manipulated to design Microsponge delivery system for the release of functional substance over a period of time in response to one or more external stimuli. The release mechanism of this system is mainly:-

### **A. Time release or Sustained release**

In the development of a sustained release Microsponge, different physical and chemical parameters of the entrapped active substance such as volatility, viscosity and solubility will be studied while in case of polymeric microsponge pore diameter, volume, and resiliency of the polymeric microsponge are evaluated to give necessary sustained release effects [4].

### **B. Released on Command**

Microsponges can be designed to release the given amounts of active ingredients over time in response to one or more external triggers.

#### **1. Pressure Release**

Microsponge system releases fluid or active ingredient when it is pressed or squeezed, thereby replenishing the level of entrapped active ingredient onto the skin. The amount released may also depend upon the release of the sponge and the resiliency of the Microsponges [21].

#### **2. Temperature Release**

The release of active ingredients from microsponges can be activated by temperature. At room temperature, few entrapped active ingredients can be too viscous to flow suddenly from microsponges onto the skin. With increase in skin temperature, flow rate is also increased and therefore release is also enhanced [22].

#### **3. pH**

Triggering the pH-based release of the active can be achieved by modifying the coating on the microsponge. This has many applications in drug delivery [21].

#### **4. 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 activated by diffusion but taking into consideration, the partition coefficient of the ingredient between the microsponges and the external system [23].

## **Microsponge-based delivery system for drug triggering**

### **Topical drug delivery using microsponge technology**

Microsponging delivery of Benzoyl peroxide was developed using an emulsion solvent diffusion method, by adding an organic internal phase containing benzoyl peroxide, ethyl cellulose, and dichloromethane into a stirred aqueous phase containing polyvinyl alcohol, and by suspension polymerization of styrene and divinyl benzene [24-26]. The prepared microsponges were dispersed in a gel base and the microsponging gels were evaluated for anti-bacterial and skin irritancy. The entrapped system released the drug at a slower rate than the system containing free BPO.

New formulation of Hydroquinone (HQ) 4%, with retinol 0.15%, entrapped in microsponge reservoirs, was developed to release HQ gradually, to prolong exposure to treatment and to minimize skin irritation. The safety and efficacy of this product were evaluated in a 12-week, open label study. In this open-label study, HQ 4% with retinol 0.15% was safe as well as effective [27]. An MDS system for retinoic acid was developed and tested for drug release and anti-acne efficacy. Statistically significant, greater reductions in inflammatory and non-inflammatory lesions were obtained with retinoin entrapped in the microsponge.

Topical analgesic, anti-inflammatory, and counter-irritant drugs in a microsponge® are used for the management of the musculoskeletal system [28].

### **Oral drug delivery using microsponge technology**

In oral applications, the microsponge system has been shown to increase the rate of solubilization of poorly water-soluble drugs by entrapping such drugs in the microsponge system's pores. As these pores are very small, the drug is in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increases the rate of solubilization. Controlled oral delivery of ibuprofen microsponges is achieved with an acrylic polymer, eudragit RS, by changing their intraparticle density [15]. Sustained release formulation of chlorpheniramine maleate, using powder-coated microsponges, is prepared by the dry impact blending method, for oral drug delivery [10]. Controlled oral delivery of Ketoprofen prepared by quasi-emulsion solvent diffusion method with Eudragit RS 100 and afterwards tablets of microsponges were prepared by the direct compression method. Results indicated that compressibility was much improved in the physical mixture of the drug and polymer; due to the plastic deformation of the sponge-like microsponge structure, producing mechanically strong tablets [29].



Colon-specific, controlled delivery of flurbiprofen was conducted by using a commercial Microsponge® 5640 system. *In vitro* studies exhibited that compression-coated colon-specific tablet formulations started to release the drug at the eighth hour, corresponding to the proximal colon arrival time, due to addition of the enzyme, following a modified release pattern, while the drug release from the colon-specific formulations prepared by pore plugging the microsponges showed an increase at the eighth hour, which was the point of time when the enzyme addition was made [30].

### **Characterization of microsponges**

#### **1. Particle size and size distribution**

Particle size and size distribution are evaluated using either an optical microscope or an electron microscope. This is an extremely crucial step, as the size of the particles greatly affects the texture of the formulation and its stability. Free-flowing powders with fine aesthetic attributes are possible to obtain by controlling the size of particles during polymerization. Particle size analysis of loaded and unloaded Microsponges can be performed by laser light diffractometry or any other suitable method. The values (d50) can be expressed for all formulations as mean size range. Cumulative percentage drug release from Microsponges of different particle size will be plotted against time to study effect of particle size on drug release [31].

#### **2. Morphology and Surface topography of microsp sponge**

For morphology and surface topography, various techniques have been used like photon correlation spectroscopy (PCS), Scanning electron microscopy (SEM), transmission electron microscopy (TEM) etc. SEM is used widely for which prepared Microsponges are coated with gold–palladium under an argon atmosphere at room temperature and then the surface morphology of the Microsponges is studied [32].

#### **3. Determination of loading efficiency and production yield**

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

$$\% \text{Loading efficiency} = \frac{\text{actual drug content in microsponges}}{\text{theoretical drug content}} \times 100$$

The production yield of the micro-particles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the SPM obtained [33].

$$\% \text{Production yeild} = \frac{\text{Production yeild}}{\text{therotical mass (polymer + drug)}} \times 100$$

#### 4. Determination of true density

The true density of Microsponges can be measured using an ultra-pycnometer under helium gas and is calculated from a mean of repeated determinations [32].

#### 5. Characterization of pore structure

Pore volume and diameter are vital in controlling the intensity and duration of 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 effect of pore diameter and volume with rate of drug release from Microsponges.

Porosity parameters of Microsponges include 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. Incremental intrusion volume scan be plotted against pore diameters that represented pore size distributions. The pore diameter of Microsponges can be calculated by using Washburn equation:

$$D = \frac{-4\gamma\cos\theta}{P}$$

Where D is the pore diameter ( $\mu\text{m}$ );  $\gamma$  the surface tension of mercury ( $485 \text{ dyn cm}^{-1}$ );  $\theta$  he contact angle ( $130^\circ$ ); and P is the pressure (psia).

Total pore area ( $A_{tot}$ ) was calculated by using equation,

$$A_{tot} = \frac{1}{\gamma\cos\theta} \int_0^{V_{tot}} P \cdot dV$$

Where P is the pressure (psia); V volume ( $\text{mL g}^{-1}$ );  $V_{tot}$  is the total specific intrusion volume ( $\text{mL g}^{-1}$ ). The average pore diameter ( $D_m$ ) was calculated by using equation,

$$D_m = \frac{4V_{tot}}{A_{tot}}$$

Envelope (bulk) density ( $\rho_{se}$ ) of the Microsponges was calculated by using equation,

$$\rho_{se} = \frac{W_s}{V_p - V_{Hg}}$$

Where  $W_s$  is the weight of the SPM sample (g);  $V_p$  the empty penetrometer (mL);  $V_{Hg}$  is the volume of mercury (mL).

Absolute (skeletal) density ( $\rho_{sa}$ ) of Microsponges was calculated by using equation,

$$\rho_{sa} = \frac{W_s}{V_{se} - V_{tot}}$$

Where  $V_{se}$  is the volume of the penetrometer minus the volume of the mercury (mL).

Finally, the % porosity of the sample was found from equation,

$$\text{Porosity (\%)} = \left(1 - \frac{\rho_{se}}{\rho_{sa}}\right) \times 100$$

Pore morphology can be characterized from the intrusion–extrusion profiles of mercury in the Microsponges [34, 35].

## 6. Compatibility studies

The drug-excipients compatibility studies are carried out in order to ensure that there is no inadvertent reaction between the two when formulated into a dosage form. These studies are commonly carried out by recording the differential scanning Calorimetry (DSC) of the chemicals viz., API and excipients individually and also together and checking for any addition or deletion of any peaks or troughs. For DSC approximately 5 mg samples can be accurately weighed into aluminium pans and sealed and can be run at a heating rate of 15oC/min over a temperature range 25–430oC in atmosphere of nitrogen [15]. Infrared (IR) spectroscopy can also reveal the incompatibilities between the chemical moieties. Compatibility of drug with reaction adjuncts can also be studied by thin layer chromatography (TLC) and FT-IR [36]. Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC) [37].

## 7. Polymer/Monomer composition

Factors such as particle size, drug loading, and polymer composition govern the drug release from Microsponges. Polymer composition of the Microsponges Drug Delivery system can affect partition coefficient of the entrapped drug between the vehicle and the Microsponges system and hence have direct influence on the release rate of entrapped drug. Release of drug from Microsponge systems of different polymer compositions can be studied by plotting cumulative % drug release against time. Release rate and total amount of drug released from the system composed of methyl methacrylate/ ethylene glycol di-methacrylate is slower than styrene/divinyl benzene system. 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 combinations will be screened for their suitability with the drugs by studying their drug release profile [38].

## 8. Resiliency

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. Hence resiliency of Microsponges is studied and optimized as per the requirement by considering release as a function of cross linking with time [39].

## 9. Drug Release

Dissolution profile of Microsponges can be studied by use of dissolution apparatus USP XXIII with a modified basket consisted of 5 $\mu$ m 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 analyzed by suitable analytical method at various intervals [40].

### Kinetics of release

To determine the drug release mechanism and to compare the release profile differences among microsponges, the drug released amount versus time was used. The release data were analyzed with the following mathematical models:

$$Q = k_1 t^n$$

Or ..... Equation [1]

$$Q = \log k_1 + n \log t$$

Where Q is the amount of the released at time (h), n is a diffusion exponent which indicates the release mechanism, and k1 is a constant characteristic of the drug–polymer interaction. From the slope and intercept of the plot of log Q versus log t, kinetic parameters n and k1 were calculated.

For comparison purposes, the data was also subjected to Equation (2), which may be considered a simple, Higuchi type equation.

$$Q = k_2 t^{0.5} + C \dots\dots\dots \text{Equation [2]}$$

Equation (2), for release data dependent on the square root of time, would give a straight line release profile, with k2 presented as a root time dissolution rate constant and C as a constant [41].

### Application of microsponges

Microsponge delivery systems are used to enhance the safety, effectiveness and aesthetic quality of topical prescription, over-the-counter and personal care products.

Microsponges can be used in variety of applications. It is used mostly for topical and recently for oral administration. Several patents have reported that it can be used as excipients due to its high loading capacity and sustained release ability. It offers the formulator a range of alternatives to develop drug and cosmetic products. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects and modify drug release. Over-the-counter products that incorporate microsponge drug delivery system include numerous moisturizers, specialized rejuvenative products, and sunscreens.

### Application of microsponges with respect to their advantages

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

**Examples of microsp sponge drug delivery with their formulations [41]**

Microsp sponge Delivery System	Drug	Disease
Gels	<b>Benzoyl peroxide</b>	<b>Anti-Acne Treatment</b>
	<b>Fluconazole</b>	<b>Inflammation</b>
	<b>Diclofenac Sodium</b>	<b>Inflammation</b>
	<b>Acyclovir</b>	<b>Viral infection</b>
	<b>Terbinafine HCl</b>	<b>Anti-Fungal</b>
Lotions	<b>Benzoyl peroxide</b>	<b>Anti-Acne Treatment</b>
Creams	<b>Hydroquinone and Retinol</b>	<b>Melanoma</b>
Implants	<b>Poly(DL-lactic-co-glycolic acid)</b>	<b>Skin tissue engineering</b>
Grafts	<b>Poly(lactic-co-glycolic acid)</b>	<b>Cardiovascular surgery</b>
Injection	<b>Basic fibroblast growth facto</b>	<b>Growth factor</b>
Tablets	<b>Indomethacin</b>	<b>Inflammation</b>
	<b>Paracetamol</b>	<b>Anti-pyretic</b>
	<b>Ketoprofen</b>	<b>Musculoskeletal pain</b>
	<b>Fenofibrate</b>	<b>Gout</b>
	<b>Meloxicam</b>	<b>Arthritis</b>
	<b>Dicyclomine</b>	<b>Anticholinergic</b>
	<b>Flurbiprofen</b>	<b>Metabolic ratio</b>
Other	<b>Ibuprofen</b>	<b>NSAID</b>
	<b>Mefenamic acid</b>	<b>Rheumatoid arthritis</b>
	<b>Benzoyl peroxide</b>	<b>Anti-Acne Treatment</b>

**Recent advance in microsp sponge drug delivery system**

Various advances were made by modifying the methods to form nanosp sponges, nanoferrosp sponges and porous microbeads.

$\beta$ -CD nanosp sponges were also developed that can be used for hydrophobic as well as hydrophilic drugs, in contrast to polymeric micro or nanosp sponges. These advanced systems were studied for oral administration of dexamethasone, flurbiprofen, doxorubicin hydrochloride, itraconazole and serum albumin as model drug. These nanosp sponges were developed by cross-linking the  $\beta$ -CD molecule by re-acting the  $\beta$ -CD with diphenyl carbonate.

Some researchers also observed the nanosponges as good carrier for the delivery of gases. Researchers also observed that incorporating a cytotoxic in a nanosponge carrier system can increase the potency of the drug suggesting that these carriers can be potentially used for targeting the cancerous cells [42].

Nanoferrosponges, a novel approach constituted the self-performing carriers having better penetration to the targeted site due to the external magnetic trigger which enforces the carriers to penetrate to the deeper tissue and then causing the removal of magnetic material from the particle leaving a porous system [43].

Due to the improved characteristics of porous microspheres, process was developed to produce the porous micro beads. This method (High internal phase emulsion, HIPE) consisted of the monomer containing continuous oil phase, cross linking agent and aqueous internal phase [44]. They also observed an improved stability of RNA and the relatively effective encapsulation process of siRNA. The approach could lead to novel therapeutic routes for siRNA delivery [45].

#### **Future prospects**

Microsponge drug delivery system holds a promising option in various pharmaceutical applications in the upcoming future as it has unique properties like enhanced product performance and elegance, extended release, improved drug release profile, reduced irritation, improved physical, chemical and thermal stability which makes it flexible to develop novel product forms. The real challenge in future is the development of the delivery system for the oral peptide delivery by varying ratio of polymers. The use of bioerodible and biodegradable polymers for the drug delivery is validating it for the safe delivery of the active material. As these porous systems have also been studied for the drug delivery through pulmonary route which shows that these system can show effective drug release even in the scarce of the dissolution fluid thus colon is an effective site for targeting for drug release. These carriers also require to be developed for alternative drug administration routes like parenteral and pulmonary route. These particles can also be used as the cell culture media and thus can also be engaged for stem cell culture and cellular regeneration in the body. Due to their distinction, these carrier systems have also found their application in cosmetics. These developments enabled researchers to utilize them variably. These novelties in formulation also open new ways for drug deliver [46].

## CONCLUSION

The microsp sponge delivery system is a distinctive technology for the controlled release of macroporous beads, loaded with active agent, offering an embryonic reduction in side effects, while maintaining their therapeutic efficacy. The microsp sponge drug delivery system extends entrapment of its ingredients and is believed to contribute toward reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. In addition, multitudinous studies have confirmed that microsp sponge systems are non-irritating, non-mutagenic, non-allergenic, and nontoxic. This technology is being used currently in cosmetics, over-the-counter skin care, sunscreens, and orally administered formulations. This kind of drug delivery technology may lead to a better appreciation of the healing of several diseases. Hence, the microsp sponge-based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future. So microsp sponge drug delivery system has got a lot of potential and is a very arising field which is needed to be explored in the future with most research study.

## REFERENCES

1. Shaha V; Jain H; Jethva K; Patel P; Microsp sponge drug delivery: A Review. *Int. J. Res. Pharm. Sci*; 2010; 1(2): 212-218.
2. Kydonieus A.F; Berner B. *Transdermal Delivery of Drugs*. CRC Press, Raton: 1987.
3. Nanda S; Kaur M; Sood N; Nagpal S; Microsp sponge drug delivery system: an overview; *World Journal of Pharmacy and Pharmaceutical Science*; 2013; 2(3): 1032-1043.
4. Kaity S; et.al, Microsp sponge: A novel strategy for drug delivery system; *J Adv Pharm Technol Res*; 2010; 1(3): 90-283.
5. Chadawar V; Shaji J; Microsp sponge delivery system; *Curr Drug Deliv*; 2007; 4(2): 9-123.
6. Aloorkar N H; Kulkarni A S; Ingale D J; Patil R A; Microsp sponge as Innovative Drug Delivery system; *International Journal of pharmaceutical Science and Nanotechnology*; 2012; 5(1): 1597-1606.
7. Embil K; Nacht S; The Microsp sponge Delivery System (MSD): A topical delivery system with reduced irritancy incorporating multiple triggering mechanism for the release of active; *J. Microencapsul*; 1996; 3(5): 574-588.
8. Nachit S; Kantz M; The microsp sponge: A novel topical programmable delivery system; *Top Drug Delivery System*; 1992; 42: 299-325.
9. Won R; Method for delivering an active ingredient by controlled time release utilizing a novel delivery vehicle which can be prepared by a process utilizing the active ingredients as a Porogen. 1987; US Patent No. 4690825.
10. Aritomi H; Yamasaki Y; Yamada K; Honda H; Koshi M; Development of sustained release formulation of chlorpheniramine maleate using powder coated microsp sponges prepared by dry impact blending method; *Journal of Pharmaceutical Sciences and Technology*; 1996; 56(1): 49-56.
11. D'souza J.I; Masvekar R.R; Pattekari P.P; Pudi S.R.; More H.N; Microsp spongy delivery of fluconazole for topical application. *Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech.*; 2004; 76.
12. Parthiban K.G; Manivannan R.; Krishnarajan D; Chandra S; Nidhin R; Microsp sponge role in novel drug delivery system; *Intl. J. Pharm. Res. Devel*; 2011; 3(4): 117-125.
13. Pradhan S K; Microsp sponges are as the versatile tool for drug delivery system; *International Journal of Research in Pharmacy and Chemistry*; 2011; 40(1): 196-201.



14. Tansel C et, al; Preparation and in-vitro evaluation of modified release ketoprofen microspoonge; II Farmaco; 2003; 58: 101-106.
15. Kawashima Y; Niwa T; Takeuchi H; Hino T; Ito Y; Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microspoonge with Acyclic Polymer, Eudragit RS, by changing their Intra particle porosity; Chemical & Pharmaceutical Bulletin; 1992; 40(1): 196-201.
16. Brunton LL; Lazo J S; Parker K L; Goodman and Gilman's "The Pharmacological Basis of Therapeutics". 2006; 11<sup>th</sup> Edition; 1021
17. Cooke CIET, Flora of Presidency of Bombay; Published under the authority of Secretary of State for Council (1903)
18. Vyas SP; Khar RK; Targeted and Controlled Drug Delivery-Novel Carrier System; New Delhi; CBS Publication: 453. 2002
19. Jain N; Sharma PK; Banik A; Recent advance on microspoonge delivery system; International Journal of Pharmaceutical Science Review and Research; 2011; 8(2): 13-23
20. Jadhav N; Patel V; Mungekar S; Karpe M; Kadam V; Microspoonge delivery system: an update review, current status and future prospects; world Journal of Pharmacy and Pharmaceutical Science; 2013; 2(6): 6463-6485.
21. Christensen M.S; Hargens C.W; Nacht S; Gans E.H; Viscoelastic properties of intact human skin instrumentations, hydration effects and contribution of the stratum corneum; J Invest Dermatol; 1977; 69: 282-286.
22. Sato T; Kanke M; Schroeder G; Deluca P; Porous biodegradable microspheres for controlled drug delivery. Assessment of processing conditions and solvent removal techniques; Pharm Res; 1988; 5:21- 30.
23. Guyot M. and Fawaz F; "Microspheres- Preparation and physical characteristics"; Int. J. Pharmaceutics; 1998; 175:61-74.
24. Yazici e; Kas HS; Hincal AA; Microspoonge, Farmasotik Bilimler Dergisi (Turkey); 1994; 19: 8-121.
25. Wester R; Patel R; Natch S; Leyden J; Melendres; Maibach H; Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy; J Am Acad Derm; 2004; 24: 6-720.
26. D'souza JI; Saboji JK; Killedar SG; More NH; Design and Evaluation of Benzoyl Peroxide Microsponges to Enhance Therapeutic Efficacy in Acne Treatment; 20<sup>th</sup> FAPA Congress, Bangkok; Thailand: FAPA Congress; 2004 Nov 30- Dec 3.
27. Fincham JE; Kamik KA; Patient Counseling and Derm therapy; US Pharm; 1994; 19:56-57, 61-2, 66, 71-2, 74, 77-8, 2-81.
28. Embil VP; OTC External analgesic cream/topical analgesic-anti-inflammation, counterirritant utilizing the Microspoonge Delivery System (MDS) for controlled release of actives. Patent Application No: 0101058; Uk-2000.
29. Comoglu T; Gonul N; Baykara T; Preparation and in-vitro evaluation of modified release Ketoprofen microspoonge; Farmaco; 2003 ;58: 6-101
30. Orlu M; Cevher E; Araman A; Design and evaluation of colon specific drug delivery system containing flurbiprofen microspoonge; Int J Pharm; 2006; 318:77-103.
31. Martin A; Swarbrick J; Cammarrata A; In: Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences. 3rd Ed.1991; 527.
32. Emanuele A.D; Dinarvand R; Preparation, characterization and drug release from thermo responsive microspheres; Int. Journal of Pharmaceutics; 1995; 237-242.
33. Kilicarlsan M; Baykara T; The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. Int. J. Pharm.; 2003; 252:99-109.
34. Washburn E.W; Note on a method of determining the distribution of pore sizes in a porous material. Proc Natl Acad Sci; 1921; 7(4):115-116.
35. Orr Jr. Application of mercury penetration to material analysis. Powder. Technol. (1969); 3:117-123.
36. Anderson D.L.; Cheng C.H; Nacht S; Flow characteristics of loosely compacted macroporous microspoonge polymeric systems. Powder technology; 1994; 78:15-18.
37. Ford J.L.; Timmins P; Pharmaceutical Thermal Analysis- Techniques and Applications. Ellis Horwood Ltd.: Chichester .1989.

38. Chowdary KPR; Rao Y.S; Mucoadhesives Microspheres for Controlled Drug Delivery. *Biol. Pharm. Bull*; 2004; 27(11):1717- 1724.
39. Barkai A; Pathak V; Benita S; Polyacrylate (Eudragit retard) microspheres for oral controlled release of nifedipine. I.Formulation design and process optimization. *Drug Dev. Ind. Pharm*; 1990; 16:2057-2075.
40. Jayaweera D.M; Medicinal Plants (Indigenous and exotic) used in Ceylon. Part-II. A Publication of the Natural Sciences Council of Sri Lanka: Colombo .1980.
41. Peppas N.A; Analysis of Fickian and non-Fickian drug release from polymers. *Pharm. Acta Helv.* 1985; 60: 110–111.
42. Trotta F; Cavalli R; Tumiatti W; Cyclodextrin-based nanosponges for drug delivery. *J Incl PhenomMacrocyclic Chem.*; 2006; 56:209-13.
43. Hu S.H; Liu T.Y; Liu D.M; Nano-ferrosponges for controlled drug release. *J Control Release*; 2007; 121(3):181-9.
44. Li NH; Benson JR; Kitagawa N; Polymeric microbeads and method of preparation. International publication number. WO1995033553; 2003.
45. Lee JB; Hong J; Bonner DK; Self-assembled RNA interference microsponges for efficient siRNA delivery; *Nat Mater*; 2012; 11(4): 316-22.
46. Srivastava R; Pathak K; Microsponges: a futuristic approach for oral drug delivery. *Expert Opin. Drug Deliv*; 2012; 9(7): 863-878.