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A Review on Microsponge as Emerging Drug Delivery System

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ABSTRACT

A microsponge delivery system will entrap a wide variety of active pharmaceutical ingredients and then release them onto the skin over a time and additionally in response to different stimuli including rubbing, moisture, pH, friction, or ambient skin temperature. It can also be used for controlled oral delivery of drugs using water-soluble, water-insoluble and bio-erodible polymers. The primary aim of any drug delivery system is to provide a therapeutic quantity of drug to the suitable site in the body, to punctually achieve and retain the desired drug concentration. The elemental application of the microsponge technology arises as of the difficulty experienced with predictable formulations in release active ingredients over an extended period of time. Microsponges also enhanced bioavailability of active ingredient and increase the solubility of the poorly water-soluble drug. Microsponge is providing some advantages like controlled release and extended release of active agents by using different polymers. They become a reduced irritation and improved thermal, physical, and chemical stability of the product. The present review describes microsponge technology including its method of preparation, characterization, programmable parameters and release mechanism of microsponge drug delivery system. Microsponges can be designed to programmable release of drug by using different triggers like solubility triggered systems, pressure triggered systems, temperature triggered systems and pH triggered systems.

Keywords: Microsponge delivery system (MDS), programmable release, controlled release, porous microspheres, improves bioavailability.

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INTRODUCTION

To control the delivery rate of active agents to a predetermined site in the human body has been one of the greatest challenges faced by the pharmaceutical industry. To the controlled release of drug from the formulation into the epidermis such that the drug remains primarily localized with only a limited amount entering the systemic circulation is a means of controlling side-effects. Another prospective difficulty in the topical delivery of drugs relates to the use of unaesthetic vehicles which may be greasy, sticky and may cause discolorations since this can result reduce patient compliance. The vehicles of topical formulations need to hold high concentrations of active agents for useful therapy because of the low efficiency of the delivery system, consequential into irritation and allergic reactions in significant users. Other disadvantages of topical formulations are uncontrolled evaporation of active ingredient, potential incompatibility and obnoxious odour of drugs with the vehicles. Thus there is a requirement to maximize the amount of time that an active ingredient is present either on the skin surface or within the epidermis while minimizing its transdermal penetration into the body. Several predictable and reliable systems were developed for systemic drugs under the heading of the transdermal delivery system (TDS) using the skin as a portal of entry. It has improved the efficacy and safety of many drugs that may be better administered through the skin. But TDS is not practical for delivery of materials whose final target is skin itself. Further, these porous microspheres with active ingredients can be incorporated into formulations such as creams, lotions, and powders. The release of the drug into the skin is initiated by a variety of triggers, including rubbing and higher than ambient skin temperature.[1]

The microsponge technology was developed by Won in 1987 and the original patents were assigned to advanced polymer system, Inc. At current, this technology has been licensed to Cardinal Health, Inc., for use in topical products.[2] Microsponges are tiny, sponge-like spherical particles that consist of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface through

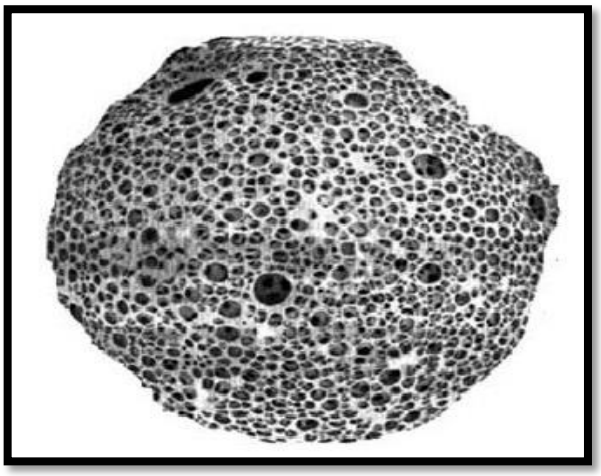
which active ingredients are released in a controlled manner. These microsponges have the capacity to entrap a wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens and anti-infective and used as a carrier for topical drug delivery.[3,4] To control the delivery rate of the drug to a predetermined site in the human body has been one of the greatest challenges followed by pharmaceutical researchers. Controlled release of active ingredient onto the epidermis with an assurance that the drug remains primarily localized and does not enter the systemic circulation in significant quality is a challenging area of research.[5]

Defining microsponge:

The microsponge delivery system is a patented polymeric system consisting of porous microspheres. They are tiny sponge like spherical particles that consist of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface through which active ingredient are release in a controlled manner. The size of microsponge ranges from 5-300µm in diameter and a typical 25µm 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 1 ml/g for extensive drug retention. The surface can be varied from 20-500 m^2/g and pore volume range from 0.1-0.3cm^3/g. This is results in large reservoir within each microsponge, which can be loaded with up to its own weight of active agent. [6]

***Structure*:**

Microsponges are uniform, spherical, porous polymeric microspheres having myriad of interconnecting voids of particle size range 5-300µm(fig 1). These microspheres having the capacity to entrap a wide range of active ingredients such as emollients, fragrance, essential oils, sunscreens and anti-infective, etc. are as a topical carrier system. Microspheres, averaging 25µm in diameter and embedded in a vehicle, act like microscopic sponge, storing the active drug until its release is triggered by application to the skin surface. Micropores within the spheres comprise a total pore density of approximately 1ml/g, and pore length 10 ft for extensive drug retention. Further this porous microsphere with active ingredient can be incorporated in to formulation such as creams, lotions, and powders. Microsponge consist of non-collapsible structure with porous surface through active ingredient are release in controlled manner. Release of the drug into the skin is initiated by a variety of triggers, including rubbing and higher than ambient skin temperature. There is high degree of cross-linking result in particle that are insoluble, inert and of sufficient strength to stand up to the high shear commonly used in manufacturing of creams, lotions and powders. Their characteristics feature is the capacity to absorb or load a high degree of active materials into the particle and on to its surface. Its large capacity for entrapment of actives, up to three times of its weight, differentiates microsponge product from other types of dermatological delivery system. The active payload is protected in the formulation by the microsponge particles. It's delivered to the skin via controlled diffusion. This sustained release of actives to skin over time is an extremely valuable tool to extend the efficacy and lessen the irritation commonly associated with powerful therapeutic agent like α-hyroxy acid which may produce burning, stinging or redness in individual with sensitive skin. Microsponge polymers possess the versatility to load a wide range of actives providing the benefits enhanced product efficacy, mildness, tolerability, and extended wear to a wide range of skin therapies. When microsponge delivery system applied to the skin, the release of drug can be controlled through diffusion or other variety of triggers, include rubbing, moisture, pH, friction, or ambient skin temperature. [7]



[Source: IJPRA 2012; 2(2): 82**]**

Fig 1: Highly porous nature of Microsponge.[1]

Advantages:

- Advanced oil control, absorb up to 6th times its weight without drying.
- Reduce irritation formula.
- Allows novel product form.
- Extended release, continuous action up to 12 hours.
- Reduce irritation, better tolerance means broader consumer acceptance.
- Improves product aesthetics, gives product and elegant feel.
- Improves stability, thermal, physical and chemical stability.
- Allowed incorporation of immiscible products.
- Improves material processing e.g. Liquid can be converted to the powders.
- Allows for novel product forms.
- Improves efficacy in treatment.
- Cure or control confirm more promptly.
- Improve control of condition.
- Improve bioavailability of same drugs.[8]

Characteristics of microsponge:

- These formulations are stable over range of pH 1 to 11
- These formulations are stable at the temperature up to 130°C.
- These formulations are compatible with most vehicles and ingredients
- These are self-sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate
- These formulations are free flowing and can be cost effective.[9]
- Microsponge formulation have higher payload (50-60%), still free flowing and can be cost effective.[10]

Characteristics of the active moieties that is entrapped into microsponge:

- Active ingredients that are entrapped in microsponge can then be incorporated in to the many products such as creams, gels, powders, lotions and soaps.
- Certain considerations are taken into account while, formulating the vehicle in order to achieve desired product characteristics.
- It should be either fully miscible in monomer as well as capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be inert to monomers and should not increase the viscosity of the mixture during formulation.
- It should be water immiscible or nearly only slightly soluble.
- It should not collapsed spherical structure of the microsponges.
- It should be stable in contact with polymerization catalyst and also in conditions of polymerization.
- The solubility of actives in the vehicles must be limited.
- If not, the vehicle will deplete the microsponges before the application.
- Not more then 10-12% w/w microsponges must be incorporated into the vehicle in order to avoid cosmetic problems.
- Payload and polymer design of the microsponges for the active must be optimized for required release rate for given period of time.[11]

Formulations: [12-20] The MDS contain drug, polymer, vehicle and other additives like plasticizers that helps stabilize the structure. Various drugs used in microsponge drug delivery system are as follows:

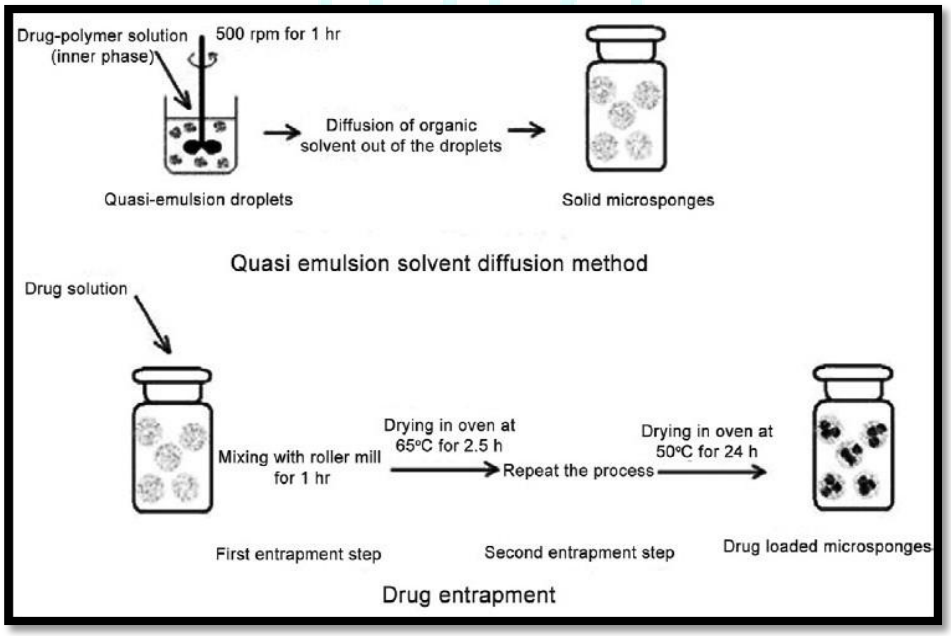
- Domperidone
- Chlorpheniramine Maleate,
- Fluconazole,
- Benzoyl Peroxide,
- Indomethacin,
- Dicyclomine,
- Diclofenac Sodium,
- Lornoxicam Microsponge,
- Pantoprazole.

Preparation of microsponges:

Drug entrapped in microsponges can take place in two ways, based on physicochemical properties of drug. One step process and two-step process with respective liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques. If the drug is typically and inert non polar material will create porous structure it is called porogen. Porogen drug, which neither hinders the polymerization nor become activated by it and stable to free radical entrapped with one step process.

A. Quasi emulsion solvent diffusion evaporation method:

The microsponges also prepared by a quasi solvent diffusion method by two step process(top-down approach: starting with performed polymer) using and external phase of containing 200ml of distilled water and 40mg polyvinyl alcohol (PVA) 72000. The internal phase consisted of drug, ethyl alcohol, polymer and tri-ethylcitrate (TEC), which was added at an amount of 20% of the polymer in order to facilitate the plasticity. At first, the internal phase was prepared at 60°C and added to the external phase at room temperature. After emulsification, the mixture was continuously stirred for two hours. Then the mixture was filtered to separate the microsponges. The product was washed and dried by vacuum oven at 40°C for 24hrs. (Shown in fig. 2)[7]

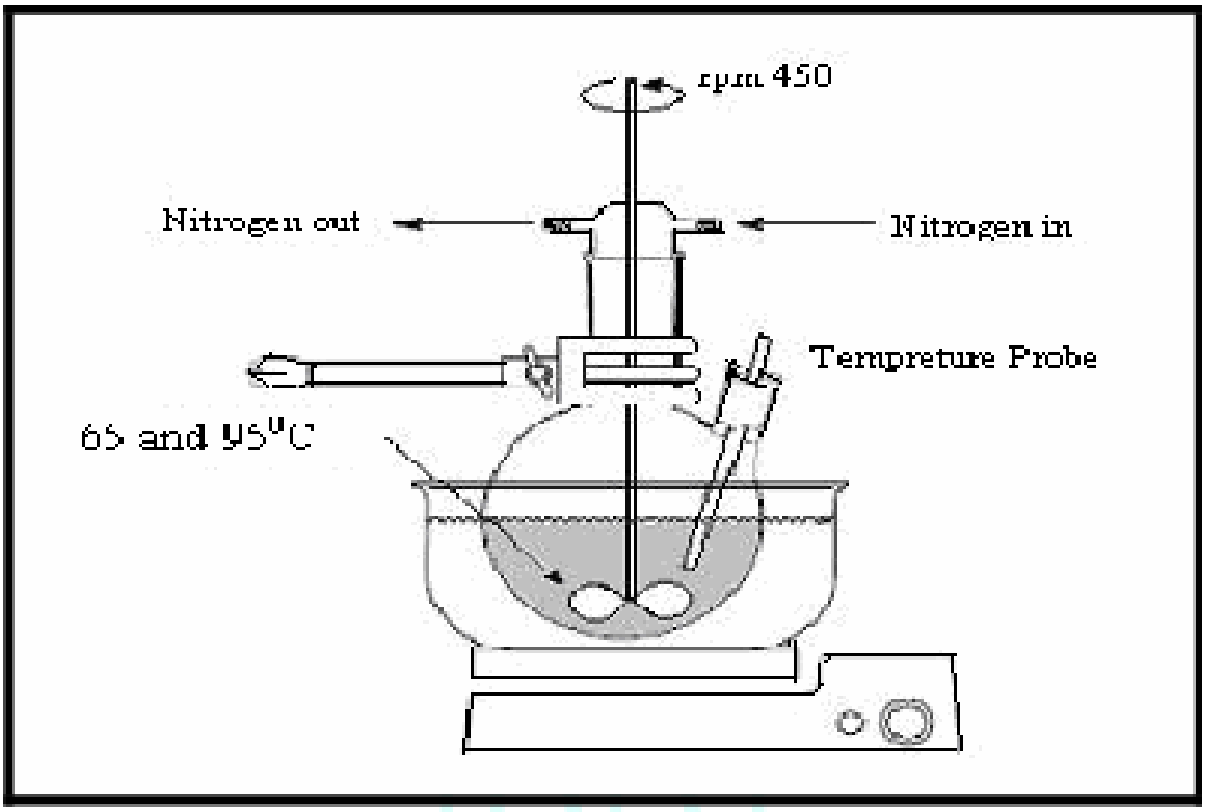


[Source: IJPSRR 2011; 8(2): 14-15**]**

Fig. 2: Quasi emulsion solvent diffusion evaporation method.[11]

B. Liquid-liquid suspension polymerization:

The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems. In their preparation, the monomers are first dissolved along with active ingredients in a suitable solvent solution of monomer and are then dispersed in the aqueous phase, which consist of additives (surfactant, suspending agents etc.). The polymerization is then initiated by adding catalyst or by increasing temperature or irradiation rate for given time period. Monomer or combinations of monomers are selected and polymerization begins to form chain monomers as a result of cross linking ladders are formed between chains of monomer. Monomer ladder are folded to form spherical particles i.e. agglomeration of microspheres, which give rise to formation of bunches of microspheres. Binding of bunches to form microsponges, a reservoir type of system, which opens at the surface through pores. Some time inert liquid immiscible with water but completely miscible with monomer is used during the polymerization to form the pore network. After the polymerization the liquid is removed leaving the porous microspheres, i.e. Microsponges, solvent may be used for faster and efficient incorporation of the drug substances. Reaction vessel of microsponges preparation by liquid-liquid suspension Polymerization (shown in fig.3). [21]



[Source: IJPSRR 2011; 8(2): 14-15.]

Fig. 3**:** Liquid-liquid suspension polymerization method

Table 1: The various steps summarized: [7]

Step 1: Selection of monomer or combination of monomers.
Step 2: Formation of chain monomers as polymerization begins.
Step 3: Formation of ladders as a result of cross linking between chain monomers.
Step 4: Folding of monomer ladder to form spherical particles.
Step 5: Agglomeration of microspheres, which give rise to formation, bunches of microspheres.
Step 6: Binding of bunches to form microsponges.

RELEASE MECHANISM

Programmable drug release: Microsponges can be designed to release given amount of active ingredients over time in response to one or more external triggers.

- **Pressure triggered systems**:

Microsponges system releases the entrapped material when pressurized/rubbed; the amount released depends upon various characteristics of the sponge. By varying the type of material and different process variables, the microsponge best suited for a given application may be optimized. When compared with mineral oil-containing microcapsules, mineral oil containing microsponge showed much more softening effect. The duration of emolliency was also much more for the microsponge systems.

- **Temperature-triggered systems:**

Some entrapped active ingredients can be too viscous at room temperature to flow spontaneously from microsponge onto the skin. Increased in skin temperature can result in an increased flow rate and hence release. So it is possible to modulate the release of substances from the microsponge by modulation of temperature. For example, viscous sunscreens were found to show a higher release from microsponge when exposed to higher temperatures; thus a sunscreen

would be released from a microsponge only upon exposure to the heat from the sun.

- **pH triggered systems:**

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.

- **Solubility triggered systems:**

Presence of an aqueous medium such as perspiration can trigger the release rate of active ingredients. Ingredients such as antiseptics, deodorants and antiperspirants may be formulated in such types of systems. Release may be achieved based on the ability of the external medium to dissolve the active, the concentration gradient or the ability to swell the microsponge network. [22]

EVALUATION PARAMETERS OF MICROSPONGES

- Particle size (Microscopy).
- Morphology and Surface topography.
- Loading efficiency and production yield.
- Compatibility studies.
- Resiliency.
- Dissolution Studies.
- Kinetics of release.
- Determination of true density.
- Characterization of pore structure.
- **Particle Size Determination**: Particle size analysis of loaded and unloaded microsponges can be performed by laser light diffractometry or any other suitable method. The values can be expressed for all formulations as mean particle 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.
- **Morphology and Surface Topography of Microsponges**: For morphology and surface topography, prepared microsponges can be coated with gold-palladium under an argon atmosphere at room temperature and then the surface morphology of the microsponges can be studied by scanning electron microscopy (SEM). SEM of a fractured microsponge particle can also be taken to illustrate its ultra structure.
- **Determination of Loading Efficiency and production yield:** The loading efficiency (%) of the microsponges can be calculated according to the following equation:

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

- **Production Yield**: The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microsponge obtained.

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

- **Compatibility Studies:** Compatibility of drug with reaction adjuncts can be studied by thin layer chromatography (TLC) and Fourier Transform Infra-red spectroscopy (FT-IR). Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC). For DSC approximately 5mg samples can be accurately weighed into aluminium pans and sealed and can be run at a heating rate of 15°C/min over a temperature range 25–430°C in atmosphere of nitrogen.
- **Resiliency (viscoelastic propertie)**: 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 will be studied and optimized as per the requirement by considering release as a function of cross-linking with time.
- **Dissolution Studies:** Dissolution profile of microsponges can be studied by use of dissolution apparatus (USP XXIII) with a modified basket consisted of 5µm stainless steel mesh. 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.
- **Dissolution kinetics release:** In order to investigate the mode of release from the microsponges, the release data of optimized formulation was analyzed with the following mathematical models:
  - **Zero order kinetics:**

The equation for zero order kinetic is represented as;

$$K_0t = W_0 - W_t \quad \text{---------- (4)}$$

Where,

W_0 = initial amount of drug

W_t= amount of drug at time t

K_0=zero order release constant

  - **First order kinetics:**

The equation for zero order kinetic is represented as;

$$logQ_t = logQ_o + \frac{K1t}{2.303} \quad \text{---------- (5)}$$

Where,

Q_t= amount of drug released in time t

Q_0= initial amount of drug

K_1= first order release constant

  - **Higuchi model:**

The simplified Higuchi equation is represented as;

$$Q_t = K_H t^{1/2} \quad \text{---------- (6)}$$

Where,

Q_t= amount of drug released in time t

K_H = Higuchi's constant

A linear relationship between amount of drug released (Q) versus square root of time ($t^{1/2}$) is observed if the drug release from the matrix is diffusion controlled.

  - **Hixson-Crowell model:**

The simplified equation is represented as;

$$W_0^{1/3} - W_t^{1/3} = K_t \quad \text{---------- (7)}$$

Where,

W_0=initial amount of drug

W_t= remaining amount of drug at time t

K= cube root constant.

- **Korsmeyer- Peppas model:**

The Korsmeyer-Peppas model relates drug release exponentially to time. It is described by the following equation;

$$\frac{M_t}{M_\infty} = at^n \text{ ---------- (8)}$$

Where,

Mt/M∞ = fractional release of drug

a = constant incorporating structural and geometric characteristics of the drug dosage form

n= release exponent

The value of n indicates the drug release mechanism. This model is used to analyze the release of drug from polymeric dosage forms, when the release mechanism is not well known or when there is a possibility of more than one type of release mechanisms are involved.

- **Determination of true density**:

The true density of microparticles is measured using an ultra-pycnometer under helium gas and is calculated from a means of repeated determinations.

- **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 such as intrusion–extrusion isotherms, pore size distribution, total pore surface area, average pore diameters, interstitial void volume, percent porosity, percent porosity filled, shape and morphology of the pores, bulk and apparent density can be determined by using mercury intrusion porosimetry. [22,23,24]

RELEASE MODULATION

In general, microsponges retard the release of the drug. Various groups have studied the release of actives from such systems. Some studies have shown an improved rate of release by increasing the active/polymer ratio and lowering the polymer wall thickness; however these results are not supported by another set of studies. Thus, there seem to be many other factors affecting the release of the drug from the microsponges. Another important parameter that governs the release seems to be the pore diameter. However, another study has shown that even the overall porosity (including the pore diameter and the number of pores) also affects the drug release.

SAFETY CONSIDERATIONS

Safety studies of microsponges can be confirmed by:

- Allergenicity in guinea pigs.
- Eye irritation studies in rabbits.
- Mutagenicity in bacteria.
- Oral toxicity studies in rats.
- Skin irritation studies in rabbits.

Microsponges are mainly used for topical and recently for oral administration as well as biopharmaceutical delivery. It offers the formulator a range of alternatives to develop drug and cosmetic products. These are developed to deliver an active ingredient efficiently at the low dose and also to enhance stability, reduce side effects and modify drug release. [7]

UTILIZATION OF MICROSPONGES IN PHARMACEUTICAL INDUSTRY

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 an excipient 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 reduce side effects, also enhance stability and modify drug release. Over-the-counter products that incorporate microsponge drug delivery system include numerous sunscreens, specialized rejuvenated products, and moisturizers.

1. Microsponge for topical delivery

The Microsponge systems are based on microscopic, polymer based microspheres that can bind, suspend or entrap a wide variety of substances and then be incorporated into a formulated product, such as a gel, cream, liquid or powder. A single Microsponge is as tiny as a particle of talcum powder, measuring less than one-thousandth of an inch in diameter. Like a true sponge, each microsphere consists of a myriad of interconnecting voids within a non-collapsible structure that can accept a wide variety of substances. The outer surface is typically porous, allowing the controlled flow of substances into and out of the sphere. Several primary characteristics, or parameters, of the Microsponge system can be defined during the production phase to obtain spheres that are tailored to specific product applications and vehicle compatibility. Microsponge systems are made of biologically inert polymers. Extensive safety studies have demonstrated that the polymers are non-irritating, non- mutagenic, non-allergenic, non-toxic and non-biodegradable. As a result, the human body cannot convert them into other substances or break them down. Although they are microscopic in size, these systems are too large to pass through the stratum corneum when incorporated into topical products. Benzoyl peroxide (BPO) is commonly used in topical formulations for the treatment of acne, with skin irritation as a common side effect. It has been shown that controlled release of BPO from a delivery system to the skin could reduce the side effect while reducing percutaneous absorption. Therefore, microsponge 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. The prepared microsponges were dispersed in gel base and microsponge gels are evaluated for anti-bacterial and skin irritancy. The entrapped system released the drug at slower rate than the system containing free BPO. Topical delivery system with reduced irritancy was successfully developed.

2. *Microsponge for oral delivery:*

In oral applications, the microsponge system has been shown to increase the rate of solubilisation 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 solubilisation. Controlled oral delivery of ibuprofen microsponges is achieved with an acrylic polymer, Eudragit RS, by changing their intraparticle density. Sustained release formulation of chlorpheniramine maleate, using powder-coated microsponges, is prepared by the dry impact blending method, for oral drug delivery. 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. 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.

3. *Microsponge for Bone and Tissue Engineering:*

Bone-substitute Compounds were obtained by mixing pre polymerized powders of polymethyl methacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium deficient hydroxyapatite powders. The final composites appeared to be porous and acted as microsponges. Basic fibroblast growth factor (bFGF) incorporated in a collagen sponge sheet was sustained released in the mouse sub-cutis according to the biodegradation of the sponge matrix, and exhibited local angiogenic activity in a dose-dependent manner. The injection of collagen microsponges incorporating bFGF induced a significant increase in the blood flow, in the murine ischemic hind limb, which could never have been attained by the bolus injection of bFGF. These results suggest the significance and therapeutic utility of the type I collagen as a reservoir of bFGF. [25]

RECENT IMPROVEMENT IN MICROSPONGE DRUG DELIVERY SYSTEM

Various advances were made by modifying the methods to form Nanosponges, nanoferrosponges and porous micro beads. β - CD nanosponges were also developed that can be used for hydrophobic as well as hydrophilic drugs, in contrast to polymeric micro or nanosponges. These advanced systems were studied for oral administration of dexamethasone, Flurbiprofen, doxorubicin hydrochloride, itraconazole and serum albumin as model drug. These nanosponges were developed by cross- linking the β CD molecule by reacting the β-CD with biphenyl 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.[6]

FUTURE PROSPECTS

Microsponge drug delivery system holds a promising opportunity in various pharmaceutical applications in the upcoming future as it has unique properties like enhanced product performance and elegancy, 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 facilitating 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 employed for stem cell culture and cellular regenaration in the body. Due to their elegance, 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 delivery. [26]

Table 2: Marketed products based on microsponge delivery system: [27]

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

RECENT RESEARCH ON MICROSPONGE DRUG DELIVERY SYSTEM: [28-32]

Several studies reported the formulation and evaluation of Microsponge loaded drugs for different purposes. Recent research on microsponge drug delivery system is summarized in (Table 3).

Table 3: Summary of Recent Research on Microsponge Drug Delivery System.

DRUG	METHOD USED	EXCIPIENT USED	RESULT
Prednisolone	Quasi-emulsion solvent diffusion method	Eudragit RS-100, Triethylcitrate, polyvinyl alcohol	The in-vitro dissolution studies of microsponges in the media with different ph (1.2, 7.4 and 6.8) showed that drug release in colon could be controlled by Eudragit RS 100
Oxybenzone	Quasi-emulsion solvent diffusion method	Ethyl cellulose-N10, Polyvinyl alcohol, Hydroxy propyl methyl cellulose.	In vitro and ex vivo study revealed enhanced topical dichloromethane, retention of drug and increased methanol
Valsartan	Quasi-emulsion solvent diffusion method	Ethyl cellulose, polyvinyl alcohol, Hydroxy propyl methyl cellulose.	Increase in the ratio of the drug: polymer and stirring rate resulted the cumulative percentage drug release up to 8 hrs
Naproxen	Quasi-emulsion solvent diffusion method	Eudragit RS-100, carbopol, polyvinyl alcohol	Increase in the ratio of the drug: polymer, Resulted control release rate
Diclofenac Diethylamine	Quasi-emulsion solvent diffusion method	Eudragit RS 100, sodium alginate, dibutyl phthalate,	Extended drug release (75.88% at 8 h)

CONCLUSION

From the above study, it is concluded that the microsponges have the ability to include hydrophobic drugs and release them in a controlled manner and predictable manner in the targeted site of the body. Microsponge delivery systems are considered as a promising carrier for the controlled release and targeted release of many topical and oral active agents as well as biopharmaceutical drug delivery. Microsponge drug delivery system is innovative and creative techniques to deliver active agents, they can realize the full capacities of these different materials providing improved safety, increased strength, reduce side effects of active pharmaceutical drug delivery system. It also enhanced flexibility and improved active pharmaceutical ingredient compatibility. Microsponge delivery system can be an acceptable approach for a new generation of Pharmaceutical and Cosmetic industry. Microsponge formulations are self-sterilizing as their average pore size is 0.25 µm where bacteria cannot penetrate, they can be developed with prolonged stability without the use of preservatives. The porous structure of microsponge their ability to release their active ingredients in a controlled manner.

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