

Asian Journal of Pharmaceutical Education and Research

Vol -1, Issue-2, October-December 2012

ISSN: 2278 – 7496

REVIEW ARTICLE

Microsponge drug delivery system as an innovation in Cosmetic world: A Review

Ajay Saraf¹, Amit Dasani², H. K.Pathan^{3*}

- 1. Department of Pharmaceutical Sciences, Dr. Hari Singh Gour University, Sagar (M.P.), India
- 2. Rajiv Gandhi institute of Pharmacy, Satana (M.P.), India
- 3. Radharaman College of Pharmacy, Ratibad, Bhopal (M.P.), India

Article Received on 12 September 2012.

Revised on 15 September 2012,

Accepted on 18 September

*Correspondence for Author:

Mr. H. K. Pathan

RadharamanCollegeofPharmacy,Ratibad-462044,Bhopal (M.P.), India

Email: hkppharma@yahoo.com

Contact No: 09981014016

Abstract:

The purpose of writing this review to compile the present information's, current technologies and recent literatures and other contributing factors used to get controlled release of active drug and minimize the drawbacks of topical drug delivery systems like local cutaneous reactions i.e. unpleasant odour, greasiness and skin irritations and fail to reach the systemic circulation in sufficient amount which could be overcome by using a unique, versatile and novel approach Microsponge drug delivery system. Microsponges are highly porous, micro-sized particles with a unique ability for entrapping actives and offers a unique advantage of programmable release and they are biologically safe, yet are simple to produce, making them attractive in the field of topical drug delivery system. Microsponge technology has been explored for various applications like sunscreens, antiacne, antidandruff, OTC (over-the-counter) skin care preparations and skin-depigmentation. Its recently used in oral drugs as well as biopharmaceuticals (peptides, proteins and DNA-based therapeutics) drug delivery and tissue engineering. This article provides an introduction to the various aspects of the structure, development, applications and future of microsponges.

Keywords: Microsponge, Controlled release, Topical drug delivery, Oral drug delivery

Introduction

Today more and more developments in delivery systems are being integrated to optimize the efficacy and cost effectiveness of the therapy. With increasing competition and increased need for customer friendliness, innovations in cosmetic delivery systems have gained a lot of importance. Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Typically, such products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed.¹ Moreover, the application of topical drugs has many problems like greasiness, stickiness associated with the ointments and so on, that often result in lack of patient compliance. Conventional dermatological products typically provide active ingredients in relatively high concentrations but with a short duration of action. This may lead to a cycle of short term overmedication followed by long-term under medication. Rashes or more serious side effects can occur when active ingredients penetrate the skin. It could be overcome by using a unique, versatile and novel approach Microsponge drug delivery system. Microsponge technology allows an even and sustained rate of release, reducing irritation while maintaining efficacy.

The microsponge technology was developed by Won in 1987, and the original patents were assigned to Advanced Polymer Systems, Inc. This company developed a large number of variations of the technique and applied to the cosmetic as well as over the counter (OTC) and prescription pharmaceutical products. At present, this technology has been licensed to Cardinal Health, Inc., for use in topical products.

Structure:

Microsponge are uniform, spherical, porous polymeric microspheres having myriad of interconnected voids of particle size range 5-300µm (Fig.1). These microsponges have the capacity to entrap a wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens and anti-infective, etc. are used as a topical carrier system.³ Microspheres, averaging 25 µm in diameter⁴ and embedded in the vehicle, act like microscopic sponges, 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 10ft for extensive drug retention. Further these porous microspheres with active ingredients can be incorporated in to formulations such as creams, lotions and powders. Microsponges consisting of non-collapsible structures with porous surface through active ingredients are released in a controlled manner.¹

Release of drug into the skin is initiated by a variety of triggers, including rubbing and higher than ambient skin temperature. Their high degree of cross-linking results in particles 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 characteristic feature is the capacity to adsorb 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 its weight, differentiates microsponge products from other types of dermatological delivery systems. The active payload is protected in the formulation by the microsponge particle; it is delivered to 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 agents like α - hydroxy acids which may produce burning, stinging or redness in individuals with sensitive skin. Microsponge polymers possess the versatility to load a wide range of actives providing the benefits of enhanced product efficacy, mildness, tolerability, and extended wear to a wide range of skin therapies.⁵ When microsponge delivery system applied to the skin, the release of drug can be controlled through diffusion or other variety of triggers, including rubbing, moisture, pH, friction, or ambient skin temperature.

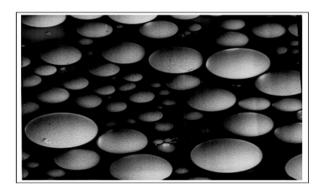


Fig. 1: Picture showing the highly porous nature of a microsponge

Advantages of Microsponge Delivery System over other technologies:

Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Typically, such products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. When compare to the Microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis. Potentially, the Microsponge system can reduce significantly the irritation of effective drugs

without reducing their efficacy. Application of topical drugs suffers many problems such as ointments, which are often aesthetically unappealing, greasiness, stickiness etc. that often results into lack of patient compliance. These vehicles require high concentrations of active agents for effective therapy because of their low efficiency of delivery system, resulting into irritation and allergic reactions in significant users. Other drawbacks of topical formulations are uncontrolled evaporation of active ingredient, unpleasant odour and potential incompatibility of drugs with the vehicles._ when microsponge system maximize amount of time that an active ingredient is present either on skin surface or within the epidermis, while minimizing its transdermal penetration into the body. Microcapsules cannot usually control the release rate of actives. Once the wall is ruptured the actives contained with in microcapsules will be released. Liposome's suffered from lower payload, difficult formulation, limited chemical stability and microbial instability. While microsponge system in contrast to the above systems are stable over range of pH 1 to 11, temperature up to 130 °C, compatible with most vehicles and ingredients, self sterilizing as average pore size is 0.25_m where bacteria cannot penetrate, higher payload (50 to 60%), still free flowing and can be cost effective.⁶

Advantages of Microsponge Delivery System:^{3,4}

- Microsponges can absorb oil up to 6 times its weight without drying.
- It provides continuous action up to 12 hours i.e. extended release.
- Improved product elegancy.
- Lessen the irritation and better tolerance leads to improved patient compliance.
- It can also improve efficacy in treatment.
- They have better thermal, physical and chemical stability.
- These are non-irritating, non-mutagenic, non-allergenic and non-toxic.
- MDS allows the incorporation of immiscible products.
- They have superior formulation flexibility.
- In contrast to other technologies like microencapsulation and liposomes, MDS has wide range of chemical stability, higher payload and are easy to formulate.
- Liquids can be converted in to powders improving material processing.
- It has flexibility to develop novel product forms.
- MDS can improve bioavailability of the drugs.

•

Characteristics of Microsponges:⁷

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

Characteristics of materials that are entrapped in Microsponges:⁸

Most liquid or soluble ingredients can be entrapped in the particles . Actives that can be entrapped in microsponges must meet following requirements,

- It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers.
- It should be stable in contact with polymerization catalyst and conditions of polymerization.

Formulation:⁸⁻¹⁶

The MDS contain drug, polymer, vehicle and other additives like plasticizers that help stabilize the structure. Various drugs used in MDS are :-

- Benzoyl peroxide,
- Dicyclomine,
- Fluconazole,
- Paracetamol,
- Retinol,
- Tretinoin,

- Flucinolone acetonide,
- Ketoprofen,
- Ibuprofen,
- Flurbiprofen

Various polymers can form a microsponge cage. These include Ethyl cellulose, Eudragit RS 100, Polystyrene, acrylic polymers and PHEMA etc In addition to actives; some microsponges contain plasticizers like Triethylcitrate (TEC) that help to stabilize their structure.¹⁷⁻²⁰

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 an inert non-polar material, will create the porous structure it is called porogen. Porogen drug, which neither hinders the polymerization nor become activated by it and stable to free radicals is entrapped with one step process.

Quasi-Emulsion Solvent Diffusion:

The microsponges can also prepared by a quasi-emulsion solvent diffusion method by two step process (Top-down approach: starting with preformed polymer) using an external phase of containing 200 ml distilled water and 40 mg polyvinyl alcohol (PVA) 72 000. 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 2 hours. Then the mixture was filtered to separate the microsponges. The product was washed and dried by vacuum oven at 40°C for 24 hours ²⁰ (Shown in **fig. 2**).

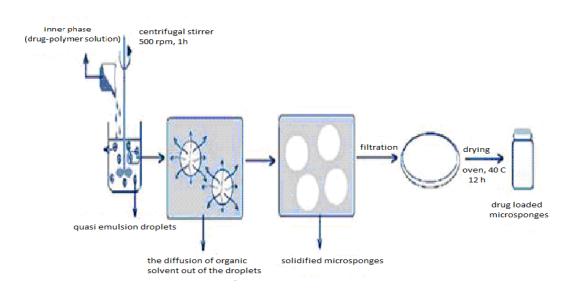


Fig. 2: Preparation of Microsponges By Quasi-Emulsion Solvent Diffusion Method

Liquid-Liquid Suspension Polymerization:

The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems.²¹ In their preparation, the monomers are first dissolved along with active ingredients in a suitable solvent solution of monomer and 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.

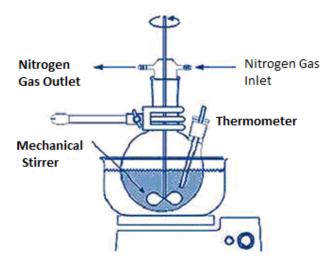


Fig.3: Reaction Vessel For Microsponge Preparation By Liquid-Liquid Suspension method

The polymerization process continues the formation of a reservoir type of system with spherical structure. After the polymerization process the solvent is removed leaving the spherical structured porous microspheres, i.e., microsponges. The various steps involved in the preparation of microsponges

The various steps summarized.²²

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

microspheres

6. Binding of bunches to form microsponges.

Limitations:

Both the methods usually use organic solvents as porogens, which pose an environmental hazard, as some may be highly inflammable, posing a safety hazard. Moreover, in case of the Bottom-Up approach traces of residual monomers have been observed, which may be toxic and hazardous to health. While the limitations seem to be serious, they can be easily overcome, by using proper quality control measures and proper washing post manufacture coupled with good standardization of the various processes.²⁷

Mechanism of Drug Release: (programmable release)

By proper manipulation of the aforementioned programmable parameters, microsponge can be designed to release given amount of active ingredients over time in response to one or more external triggers.

Temperature Change Triggered Systems:²³ 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.

Pressure Triggered Systems:²⁴ Rubbing or pressure applied can release the active ingredient from microsponges onto skin.

Solubility Triggered Systems:²⁵ 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.

 $\mathbf{P}^{\mathbf{H}}$ **Triggered Systems:**²⁶ Triggering the P^H-based release of the active can be achieved by modifying the coating on the microsponge. This has many applications in drug delivery.

Characterization: Ensuring A Good Formulation

(i) 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 stability²⁶

(ii) Morphology:

The presence of pores is an essential characteristic of microsponges, and therefore it requires characterisation. This is usually performed using scanning electron microscopy.²⁷

(iii) Porosity:

Most characteristics of a microsponge are attributable to its porous nature. Thus, it is very important to determine the porosity of the microsponge. This can be effectively accomplished by mercury intrusion porosimetry.^{29,30}

(iv) Determination of Loading Efficiency and Production Yield:

The loading efficiency (%) of the microsponges can be calculated according to the following equation. 31

Loading Efficiency = $\frac{\text{Actual drug control in}}{\text{Microsponges}} \times 100$ Theoritical drug content

The production yield of the microsponges can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microsponge obtained.

(v) **Determination of True Density:**³² The true density of microparticles is measured using an ultra-pycnometer under helium gas and is calculated from a mean of repeated determinations.

(vi) Compatibility studies:³³⁻³⁵

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 aluminum 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.

(vii) Polymer/monomer composition:³⁶

Factors such as microsphere size, drug loading, and polymer composition govern the drug release from microspheres. Polymer composition of the MDS can affect partition coefficient of the entrapped drug between the vehicle and the microsponge 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.

(viii) Resiliency (viscoelastic properties):³⁷

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.

(ix) Dissolution studies:³⁸

Dissolution profile 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 analyzed by suitable analytical method at various intervals.

(x) 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 $\log Q = \log k_1 + n \log t \dots (3)$

Where Q is the amount of the released at time (h), n is a diffusion exponent which indicates the release mechanism, and k_1 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 k_1 were calculated.

For comparison purposes, the data was also subjected to Eq.(4), which may be considered a simple, Higuchi type equation.

$$Q = k_2 t^{0.5} + C \dots (4)$$

Eq.(4), for release data dependent on the square root of time, would give a straight line release profile, with k_2 presented as a root time dissolution rate constant and C as a constant.

Release Modulation:

In general, microsponges retard the release of the drug. Various groups have studied the release of actives from such systems.^{39, 41, 42, 43} 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.⁴⁴

Safety Considerations:^{40, 45, 46} 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 used mostly 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.

Microsponge for Topical Delivery:

Di Sapio Aj,*et al*⁴⁷ reported that microporous polymeric particles fill up the skin's creases and valleys. This means that an even and effective spread is achieved. It also states that another important advantage of the microporous system is that it can prevent the degradation of actives such as retinol. Retinol, in high concentrations is used to reduce the appearance of lines and wrinkles on the skin. But, the formulation of high concentrations becomes difficult due to the instability of the molecule to oxygen. Interestingly, some emulsions facilitate decomposition by diffusion of oxygen. In such a case, the microsponge system not only helps to shield retinol but also helps to improve the effectiveness of the antioxidant system of the formulation.

Sunscreens:

Melanosponge- α which contains genetically engineered melanin, is designed to spread this melanin evenly and hence give a superior sun protective effect against UV-A as well as UV-B⁴⁸

Anti-acne:

Many anti-acne actives cause severe skin irritation and therefore a controlled release would help overcome the toxic effect caused by such actives. A reduction in the irritation caused by benzoyl

peroxide when entrapped in the microsponges has been reported and it is available commercially in form of a cream.⁴⁹

Antidandruff:

Microsponges may be very useful in the odour masking of malodorous actives. The unpleasant odour and irritation associated with antidandruff actives, namely zinc pyrithione and selenium sulphide, were masked and an increase in the efficacy was reported.⁴⁸

Skin de-pigmentation products:

Typical Skin de-pigmentation products like hydroquinone are known to be highly susceptible to oxidation. Entrapment of hydroquinone into microsponges was shown to improve the stability of hydroquinone, besides improving efficacy.⁵⁰

D'souza *et al.*³⁰ developed topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. Fluocinolone acetonide (FA) is a corticosteroid chiefly used in dermatology to lessen skin inflammation and relieve itching. The entrapped dimethicone of microsponge 5700. Dimethicone is a blend of 78% 350 cst(centistokes) polydimethylsiloxane and 22% 1000 cst polydimethylsiloxane.⁵¹

Fluconazole is an active agent against yeasts, yeasts like fungi and dimorphic fungi, with possible drawback of itching in topical therapy. Microsponges were prepared by liquid-liquid suspension polymerization of styrene and methyl methacrylate.⁵²

Aceclofenac is a NSAIDs having excellent anti-inflammatory and analgesic activity but NSAID produces GIT ulceration, liver and kidney trouble especially in case of oral administration. In view, of adverse drug reaction associated with oral formulations, aceclofenac is increasingly administered by topical route. Aceclofenac loaded microsponge are prepared by using quasi-emulsion solvent diffusion method. It is incorporated in gel base and various parameters are studied.⁵³ Gel formulation is subjected to rats and studied anti-inflammatory activity by Carrageen an induced paw edema method.

Hydroxyzine HCl loaded with microsponges was prepared solvent diffusion method using Eudragit RS-100 polymer. In this preparation, acetone as dispersing solvent and liquid paraffin as the continuous medium. Magnesium stearate was added to the dispersed phase to prevent flocculation of Eudragit RS-100 microsponges. Pore inducers such as sucrose and pre-gelatinized

starch were used to enhance the rate of drug release. Microsponges of nearly 98% encapsulation efficiency and 60-70% porosity were produced. The pharmacodynamic effect of the chosen preparation was tested on the shaved back of histamine-sensitized rabbits.⁵⁴Itraconazole loaded microsponges were prepared using Quasi-emulsion solvent diffusion technique. Itraconazole is a triazole antifungal agent used to treat both superficial and systemic fungal infections.⁵⁵ 5-Fluorouracil (5-FU) is an effective chemotherapeutic agent for treating actinic keratosis, a pre-cancerous, hardened-skin condition caused by excessive exposure to sunlight.⁵⁶ Mupirocine containing microsponges were prepared by emulsion solvent diffusion method. It is used for the treatment of primary and secondary skin infections such as impetigo, eczema and atopic dermatitis.⁵⁷

Marketed Formulations:^{33, 58}

Product name	Manufacturer	Advantages
Retin-A-Micro		For topical treatment of <i>acne vulgaris</i> tretinoin (0.1% & 0.04 %) entrapped in MDS.This formulation uses patented methyl metha-crylate/glycol dimethacry-late cross-polymer porous microspheres (MICROSPONGE [®] System) to enable inclusion of the active ingredient, tretinoin, in an aqueous gel.
Carac Cream, 0.5%	Dermik Laboratories, Inc. Berwyn, PA 19312 USA	Carac is a once-a-day topical prescription product for the treatment of actinic keratoses (AK). It contains 0.5% fluorouracil, with 0.35% being incorporated into a patented porous microsphere composed of methyl methacrylate/ glycol dimethacrylate cross-polymer and dimethicone. The product has a number of advantages over existing topical therapies, including reduced dosage frequency and less irritation with shorter duration of therapy.
Retinol cream	Biomedic	Retinol is a topical vitamin-A derivative which helps maintain healthy skin, hair and mucous membranes. For protect the potency of the vitamin A, retinol molecule is entrapped in the MDS. This helps to maximize retinol dosage while reducing the possibility of irritation.

Line Eliminator Dual Retinol Facial Treatment	Avon	Lightweight cream with a retinol (pure Vitamin A) in MDS, delivers both immediate and time released wrinkle-fighting action.
EpiQuin Micro	SkinMedica Inc	The Microsponge® system uses microscopic reservoirs that entrap hydro-quinone and retinol. The MDS release these ingredients into the skin gradually throughout the day. This provides the skin with continuous exposure to hydroquinone and retinol over time, which may minimize skin irritation. ⁴⁹
Sportscream RS and XS	Embil Pharmaceutical Co. Ltd.	Topical analgesic, anti-inflammatory and counterirritant actives in a MDS for the management of musculoskeletal conditions. ⁴⁸
Oil free matte block spf20	Dermalogica	Protect the skin from damaging UV - rays and control oil production with this invisible sunscreen. Microsponge technology absorbs oil, maintaining an all day matte finish and preventing shine without any powdery residue. Cornstarch and Vinyl Dimethicone/Methicone Silsesquiox- ane Cross-polymer act as microsponges to absorb excess surface oils on skin.
Oil Control Lotion	Fountain Cosmetics	A feature-light lotion with technically advanced microsponges that absorb oil on the skin's surface during the day, for a matte finish. Eliminate shine for hours with this feature - weight lotion, formulated with oil-absorbing Microsponge technology

The naturally antibiotic Skin Response Complexes soothes inflammation and tightness to promote healing. Acne-Prone, oily skin conditions.

and hydrating botanicals.

Lactrex TM 12%	« SDR	It contains 12% lactic acid as the neutral ammonium salt,
Moisturizing	Pharmaceuticals	ammonium lactate. Microsponge® technology has been
Cream	, Inc., Andover,	included for comfortable application and long lasting
	NJ , U.S.A. 07821	moisturization. Lactrex [™] also contains water and glycerin, a natural humectant, to soften and help moisturize dry, flaky, cracked skin.
Aramis fragrances	Aramis Inc.	24 Hour High Performance Antiperspirant Spray Sustained release of fragrance in the microsponge. The microsponge comes in the form of an ultra light powder, and because it is micro in size, it can absorb fragrance oil easily while maintaining a free-flowing powder characteristic where release is controlled due to moisture and temperature.
Ultra Guard	Scott Paper	Microsponge system that contains dimethicone to help protect

Ultra Guard	Scott Paper	Microsponge system that contains dimethicone to help protect
	Company	a baby's skin from diaper rash.

The Future Perspective:

• Nanosponges:

Today, as we realize the immense advantages offered by the nano-size, the micro sized products are likely to be outdated. The nanosized particles have a very high surface area to size ratio and a greater potential to modulate the release of actives compared to micro-sized particles. While inorganic nanosponges have many applications in electronics, the first pharmaceutical nanosponges based on cross linked cyclodextrins have been reported by Roberta Cavalli et al. (21) and Swaminathan et al. (22). These are nanosized, highly porous materials composed of beta-cyclodextrins cross linked with carbonate bonds.

• Role in Natural active delivery considerations

Although natural actives are important consumer attractants, now the focus has shifted on using multifunctional natural ingredients. For example, Marinosomes®, liposomes made from natural antiinflammatory lipid extracts, have set a new paradigm in using such functional 'active

excipients'. The possibility of using such substances for constructing a microsponge structure appears to be cost effective and innovative.

• Application in oral care cosmetics: a new heights in cosmetic world

An interesting application of the microsponge technology could be in oral cosmetics, such as to sustain the release of volatile ingredients, thus increasing the duration of the 'fresh feel'. Microsponges of such volatile ingredients may be easily incorporated in tooth pastes or mouth washes.

• Long lasting coloured cosmetics: a new application for microsponges

Colours entrapped in microsponges may be used in a variety of coloured cosmetic products such as rouge or lipsticks to make them long lasting. As stated above, microsponges help in uniform spreading and improving covering power. Thus, coloured cosmetics formulated with microsponges would be highly elegant.

Conclusion:

Microsponges: An innovative ,unique & Versatile approach in cosmetic world

Based on the literature surveyed, it may be concluded that simple production, various innovative applications with a programmable release makes Microsponge drug delivery system unique, novel and versatile and extremely attractive in cosmetic world for delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, antipruritics, antifungal ,rubefacients etc. and also expands its application in oral ,biopharmaceutical drug delivery & tissue engineering. Thus Microsponge technology has got a lot of potential and is a very emerging field which is needed to be explored for patient compliance provides the improved efficiencies of various types of pharmacotherapies with novel product development therefore it is easy to say that it has potential to create new era in cosmetic world.

References:

- Nacht S and Katz M: The microsponge a novel topical programmable delivery system, In: Osborne DW and Amman AH (Eds.), Topical Drug Delivery Formulations, Marcel Dekker, New York, Basel, 1990: 299-325.
- 2. 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. Patent No. 4690825.US: 1987.

- 3. Vyas SP and Khar RK: Targeted and Controlled Drug Delivery-Novel Carrier System. CBS Publication, New Delhi, First edition 2002: 453.
- Embil K and Nacht S. The Microsponge Delivery System (MDS)- a topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. J Microencapsul 1996; 13(5): 575-88.
- 5. Delattre L and Delneuville I. Biopharmaceutical aspects of the formulation of dermatological vehicles. Journal of the European Academy of Dermatology and Venereology 1995; 5: 70.
- Aritomi H, Yamasaki Y, Yamada K, Honda H and Koshi M. Development of sustained release formulation of chlorpheniramine maleate using powder coated microsponges prepared by dry impact blending method. J. Pharm. Sci. Tech., 1996; 56(1): 49-56.
- D'souza JI, Masvekar RR, Pattekari PP, Pudi SR and More HN. Microspongic delivery of fluconazole for topical application. Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech., 2004: 76.
- Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y.Control of Prolonged Drug Release and Compression Properties of Ibuprofen microsponges with acrylic Polymer, Chemical & pharmaceutical bulletin, 1992; 40(1): 196-201.
- D'souza JI, Masvekar RR, Pattekari PP, Pudi SR and More HN. Microspongic Delivery Of Fluconazole For Topical Application, 1st Indo- Japanese International Conference On Advances In Pharmaceutical Research And Technology, Mumbai, 2005: 25-29.
- 10. Grimes PE. A microsponge formulation of hydroquinone 4% and retinol 0.15% in the treatment of melasma and post-inflammatory hyper-pigmentation. Cutis, Vitiligo and Pigmentation Institute of Southern California, Los Angeles, Vol. 74(6), 2004: 362-368.
- Wester RC, Patel R, Nacht S, Leydan J, Malendres J and Maibch H. Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy. J. Am. Acad. Dermatol, 1991; 24: 720-726.
- Tansel C. Preparation and *in vitro* evaluation of modified release ketoprofen microsponge. II Farmaco, 2003; 58: 101-106.
- Jain V and Singh R. Development and characterization of eudragit RS 100 loaded microsponges and its colonic delivery using natural polysaccharides. Acta Poloniae Pharmaceutical-Drug Research, 2010; 67: 407-415.
- 14. Jain V and Singh R. Dicyclomine loaded eudragit based microsponge with potential for colonic delivery, Preparation and characterization. Trop J. Pharm Res., 2010; 9(1): 67-72.

- 15. Orlu M, Cevher E and Araman A. Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges. Int J. Pharm, 2006; 318: 103-117.
- 16. Saboji JK, Manvi FV, Gadad AP and Patel BD. Formulation and evaluation of ketoconazole microsponge gel by quassi emulsion solvent diffusion. Journal of Cell and Tissue Research, 2011; 11(1): 2691-2696
- Vyas LK, Tapar KK, Laddha BH, Lahoti AO and Nema RK. Formulation and development of anti-blemish preparation using microsponge technology. J. Chem. Pharm. Res., 2010; 2(5): 562 571.
- Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Gary P, Martin and Nokhodchi A. The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies. International Journal of Pharmaceutics, 2006, 308: 124-132.
- 19. Ruckenstein E and Hong L. Concentrated emulsion polymerization pathway to hydrophobic and hydrophilic microsponge molecular reservoirs. Chem. Mater, 1992; 4: 1032-1037.
- Chadawar V and Shaji J: Microsponge delivery system. Current Drug Delivery, 2007; 4: 123-129.
- 21. Hainey P, Huxham IM, Rowatt B and Sherrington DC. Synthesis and ultrastructural studies of styrene-divinylbenzene polyhipe polymers. Macromolecules 1991; 24: 117-121.
- 22. Anderson DL, Cheng CH and Nacht S. Flow Characteristics of Loosely Compacted Macroporous Microsponge(R) polymeric systems. Powder Technology, 1994; 78: 15-18.
- 23. Chadawar V and Shaji J. Current Drug Delivery, 2007; 4: 123-129
- 24. Khopade AJ, Jain S and Jain NK. The Microsponge. Eastern Pharmacist 1996; 39: 49-53.
- 25. Guyot M. and Fawaz F. Microspheres- Preparation and physical characteristics. Int. J. Pharmaceutics, 1998; 175: 61-74.
- 26. Christensen MS and Natch SJ. Invest. Dermato, 1983; 69: 282.
- Chadawar V and Shaji J. Microsponge delivery system. Current Drug Delivery, 2007; 4: 123-129.
- 28. Martin A, Swarbrick J and Cammarrata A. In: Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences. 1991; 3: 527.
- Barkai A, Pathak V and 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.
- D'souza JI. The Microsponge Drug Delivery System: For Delivering an Active Ingredient by Controlled Time Release. Pharma.info.net, 2008; 6(3): 62.

- 31. Emanuele AD and Dinarvand R. Preparation, Characterization and Drug Release from Thermo responsive Microspheres. International Journal of Pharmaceutics, 1995: 237-42.
- 32. Kilicarslan M and Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. Int. J. Pharm, 2003; 252: 99–109.
- 33. Pradhan SK. Microsponges as the versatile tool for drug delivery system. IJRPC, 2011; 1(2); 243-246.
- 34. Jones DS and Pearce KJ. Investigation of the effects of some process variables on, microencapsulation of propranolol HCl by solvent evaporation method. Int J. Pharm, 1995; 118: 99-205.
- 35. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y and Furuyama S. Characterization of polymorphs of tranilast anhydrate and tranilast monohydrate when crystallized by two solvent change spherical crystallization techniques. J. Pharm. Sci., 1991; 81: 472-478.
- 36. Bodmeier R and Chen H. Preparation and characterization of microspheres containing the antiinflammatory agents, indomethacin, ibuprofen, and ketoprofen. J. Control Release, 1989; 10: 165-75.
- Barkai A, Pathak V and 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.
- 38. Jayaweera DM: Medicinal Plants (Indigenous and exotic) used in Ceylon. Part-II. A Publication of the Natural Sciences, Council of Sri Lanka, Colombo 1980.
- 39. Yeung D, Maibuch et al., J. Am. Acad. Dermatol, 1983; 9: 920-924.
- 40. Sato T, Kanke M, Schroeder G and Deluca. Porous biodegradable microspheres for controlled drug delivery.I. Assessment of processing conditions and solvent removal techniques. Pharm Res., 1988; 5: 21-30.
- 41. Pongpaibul Y and Whitworth C. Drug Dev. Ind. Pharm., 10: 1597-1616.
- 42. Comolu T and Baykara T. Il Farmaco.2003; 58: 101-106.
- 43. Kim C and Oh K. Int. J. Pharmaceutics, 1994; 106: 213-219.
- 44. Jelvehgari M and Nokhodchi A. Int. J. Pharmaceutics, 2006; 308: 124-132.
- 45. Kilicarslan M and Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. Int. J. Pharm, 2003; 18: 99-109.
- 46. Draize JH, Woodard G and Calvery HO. Methods for the study of irritation and toxicity of substances applied as topically to the Skin and Mucous Membranes. J. Pharm., acol Exp Ther. 1944; 82: 377-389.

- 47. Di Sapio AJ, Global Cosmetic Industry, 1999; 165: 28-34.
- 48. Patravale VB. Mandawgade SD, Int. J. Cosmetic Sci., 2008; 30: 19-33.
- 49. Drug Week, Atlanta, 2007; 302.
- 50. Chadawar V and Shaji J. Current Drug Delivery. 2007; 4: 123-129.
- 51. icis.advancedpolymers-new-entrapment-system. Articles, 1998; 04/27/87201.
- 52. James J, Leyden, Shalita A, Thiboutot D, Washenik K, and Webster G: Topical Retinoids in Inflammatory Acne: A Retrospective, Investigator-Blinded, Vehicle Controlled, Photographic Assessment, Clin. Therapeutics, 2005; 27: 216-224.
- 53. Dandagi PM, Upadhyay M R, Gadad A.P and Mastiholimath VS. Design and Evaluation of Aceclofenac Loaded Microsponge for Topical Delivery, Journal of Pharmaceutical Research & Clinical Practice, Apr-June 2011; 1(2): 90-101.
- 54. Zaki Rizkalla CM, Latif Aziz R and Soliman II. In Vitro and In Vivo Evaluation of Hydroxyzine Hydrochloride Microsponges for Topical Delivery, AAPS Pharm. Sci. Tech., DOI: 10.1208/s12249-011-9663-5.
- 55. Bhimavarapu R, Chitra KP, Karunkiran P, Raviteja G, Meharagavendra Y, Sundaramma S and Chaitanya D. Itraconazole Loaded Microsponges-A Novel Carrier System, The Pharma Professionals, May-August 2011; 1 (2): 21.
- 56. Talisuna AO, Bloland PD and Alessandro U. History, Dynamics, and public haelth importance of malaria parasite resistance. Clinical microbiology reviews, 2004; 17: 235-254.
- 57. Amrutiya N, Bajaj A and Madan M. Development of microsponges for topical delivery of mupirocin, AAPS Pharm Sci. Tech., 2009; 10: 402-408.
- 58. Embil VP. OTC external analgesic cream/topical analgesic anti-inflammatory, counter irritant utilizing the microsponge delivery system for controlled release of actives, UK Patent 01010586; 2000.