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MICROSPONGE AS A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

Microsponges are porous microspheres, biologically inert particles that are made of synthetic polymers and the particles serve to protect the entrapped drug compound from physical and environmental degradation. It is a unique technology for controlled release of topical agents, oral as well as pharmaceutical products which consisting of microporous beads having the size range of 10-25µ in diameter. It has a self sterilizing capacity due to its small pore size where bacteria cannot penetrate into it. These can be prepared by liquid – liquid suspension polymerization and quasi emulsion solvent diffusion method .The prepared microsponges can be characterized for particle size analysis, entrapment efficiency, true density, dissolution studies, and compatibility studies.

Key words: Microsponges, Liquid-Liquid Suspension Polymerization, Quasi Emulsion Solvent Diffusion Method.

INTRODUCTION

A microsponge delivery system is highly cross linked, patented, porous, polymeric microspheres that acquire the flexibility to entrap a wide variety of active ingredients such as emollients, perfumes, sunscreens, volatile oils, anti-fungal and anti-inflammatory agents etc and are used as a topical carrier system [1-2]. These are non-irritating, non-mutagenic, nonallergenic and non-toxic. Application of drug topically causes decrease in absorption and irritation due to excess accumulation of active ingredients over the epidermis. So avoid this microsponge technology has came into existence over the conventional dosage forms. These microsponges will accumulate in the tiny nooks and crannies of skin and slowly release the trapped drug, as the skin wants it and also avoid the accumulation of ingredients within the epidermis and dermis. Potentially reduce the irritation of effective drugs without reducing their efficacy. In order to modify the control release pattern the drug should be incorporated into carrier system, so that it may alter the therapeutic index and duration of activity of drugs [3]. The rate of release associated with microsponge delivery system provides more control, which potentially has an impact on the intensity of skin irritancy provoked by the topical agent [4-5]. However, it can entrap active ingredients with certain characteristics. Widely regarded as a leading technology for addressing skin conditions such as acne, hyper pigmentation, keratosis, aging and photo damage, HBS reserved microsponge delivery system provides:

- Sustained release technology for quashing irritation of a wide range of APIs and other skin care actives thereby increasing patient/client compliance and results
- Increased formulation constancy assuring retentive term product efficacy and extended shelf life.
- Superior skin sense and exceptional product aesthetics.

Microsponge polymers possess the versatility to load a wide range of actives providing the benefits of enhanced product efficacy, softness, passable and extensive wear to a wide range of skin therapies.

Nature of actives entrapped into microsponges

Active ingredients that are trapped in microsponges can then be incorporated into 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 [6]

- Should be fully miscible in monomer or by making miscible by adding small amount of a water immiscible solvent.
- Inert to monomers and polymers without increasing the viscosity of the mixture during formulation.
- Water immiscible or nearly slightly soluble.

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- Microsponge spherical structure cannot be collapsed.
- It should be static in contact with polymerization catalyst and polymerization conditions.
- The solubility of active ingredient in the vehicle must be limited, so that the vehicle will not deplete microsponges before application.
- Incorporating not more than 10 – 12% w/w microsponges in to vehicle will avoid the cosmetic problems.
- Loading and polymer designing of the microsponges for the active must be optimized for required release rate for given period of time.
- Rate of release can be controlled through diffusion or other triggers such as moisture, pH, friction and temperature.

Important features of microsponges

- Stable over range of pH 1 to 11.
- Stable at the temperature up to 130˚C.
- Compatible with the most of vehicles and ingredients.
- It has self sterilizing capacity as their average pore size is 0.25µm where bacteria cannot permeate.
- Having higher loading capacity up to 50 to 60%.
- Free flowing and can be cost efficient [7].

Advantages of microsponge delivery system

- Microsponges can imbibe oil up to 6 times its weight without drying.
- Provides continuous action up to 12 hrs i.e. extended release.
- Improved product elegancy.
- Lesser the irritation and better tolerance leads to improved patient compliance.
- Possess better thermal, physical and chemical stability.
- Non-irritating, non-mutagenic, nonallergenic and non-toxic.
- It allows the incorporation of immiscible products.
- Improved formulation flexibility.
- In contrast to other techniques like microencapsulation and liposomes, it has wide range of chemical stability, higher payload and is easy to formulate.
- Liquids can be changed in to powders amending material processing.
- Flexibility to formulate new product forms.
- It can amend bioavailability of same drugs.
- It can also amend efficacy in treatment [8].

Preparation of Microsponges

Entrapment of drug in microsponges can takes place in two process, based upon physicochemical properties of drug. One-step and two-step process with respective liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques. If the drug is generally neutral non-polar material, will make the porous structure known as porogen.

Liquid-Liquid Suspension Polymerization

It is also referred to as Bottom-up approach (starting with monomer). In general, a solution is made comprising of monomers and the active ingredients (non polar). This phase is then suspended with agitation in an aqueous phase containing additives such as surfactants and dispersing agents. Once the suspension is established with discrete droplets of hoped size, polymerization is accomplished by triggering the monomers either by catalysis, enhanced temperature

The various steps summarized

- Choosing of monomer or combination of monomers
- Forming of chain monomers as polymerization begins
- Cross linking between chain monomers leads to formation of ladders
- Folding of monomer ladder to form sphere shape particles
- Agglomeration of microspheres, which give rise to formation, clusters of microspheres
- Binding of clusters to form microsponges.

The polymerization process leads to the formation of a reservoir system, which opens at the surface through small pores. Impregnating them within preformed microsponges then incorporates the functional substances. Sometimes solvent perhaps used for faster and efficient incorporation of the active substances. Once the polymerization is complete the solid that result from the process are recovered from the suspension. The particles are then rinsed and processed until they are substantially ready for use. The microsponge product can be made using styrene and divinyl benzene or methyl methacrylate and ethylene glycol dimethacrylate as starting materials (Reaction vessel is shown in fig 2).

Quasi -Emulsion Solvent Diffusion

When the drug is sensitive to the polymerization conditions, the microsponges can be prepared by using 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) . The internal phase consisted of drug, ethyl alcohol, polymer and tri-ethyl citrate (TEC), which was added at an amount of 20% of the polymer in order to facilitate the malleability. At first, the internal phase was developed at 60°C and added to the external phase at room temperature. Afterwards emulsification, the mixture was unceasingly stirred for 2 hr. Then the mixture was filtrated to separate the microsponges. The product was rinsed and dehydrated by vacuum oven at 40°C for 24 hr (Shown in fig 3).

Release Mechanism

In general, microsponges retard drug release. 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 up of studies. Thus, there appear to be lots of other factors affecting the release of the drug from the microsponges. Another significant parameter that regulates 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 [15].

The microsponge particles have an open structure and the active is free to move in and out from the particles and into the vehicle until equilibrium is reached. Once the finished product is put on to the skin, the active that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will turn unsaturated, therefore troubling the equilibrium. Such that it 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 absorbed. Even after that the microsponge particles retained on the surface of stratum corneum will continue to gradually release the active to the skin, providing prolonged release all over time. This suggested mechanism of action highlights the importance of formulating vehicles for use with microsponge entrapments [16]. If the active is too soluble in the desired vehicle during compounding of finished products, it will not provide the hoped benefits of gradual release. Therefore, while formulating microsponge system, it is important to plan a vehicle that has minimal solubilizing power for the actives and some solubility of the active in the vehicle is acceptable because the vehicle can provide the initial loading dose of the active until release from the microsponge.

Another way to avoid undesirable premature leaching of the active from the microsponge polymer is to formulate the product with some free and some trapped active, so the vehicle is pre saturated. In this case there is no leaching of the active form of polymer during compounding takes place. The rate of release of active will finally depend not only on the partition coefficient of the active ingredient between the polymer and the vehicle (or skin), and also on some of the parameters that characterize the beads which includes surface area and mean pore diameter. Release can also be controlled through diffusion or other triggers such as moisture, pH, pressure or temperature.

Pressure

Pressure/ Rubbing applied can release active ingredient from microsponge onto skin. 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.

Temperature change

At room temperature, few entrapped active ingredients can be too viscous. With increase in skin temperature, flow rate also increases such that release rate is also enhanced. 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 microsponges when exposed to higher temperatures; thus a sunscreen would be released from a microsponge only upon exposure to the heat from the sun.

Solubility

The microsponge loaded with water- soluble ingredients like anti-perspirants and antiseptics will release the ingredient in the presence of water. Thus release may be achieved based on the ability of external medium to dissolve the active ingredient, the concentration gradient varies or the ability to swell the microsponge network.

pH

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

Microsponge Delivery System (MDS) - Mechanism of action

This system consists of a multitude of nanometer sized porous microspheres that contain a complex network of interconnecting voids with a non-collapsible structure. These microspheres can absorb a wide range of active ingredients such as emollients, volatile oils, sunscreens, perfumes, and anti-infective and antifungal agents. Depending on several modifiable factors, such as pore diameter, extent of cross-linking of the polymers, concentration difference of the active ingredient between the microspheres and the vehicle in which these spheres reside[17] based on this the release rate of the active ingredients can be determined before they are entrapped in the microspheres.

The topical agent formulation with this system can be prepared in many different forms such as a gel, cream, or lotion. Apply the formulation topically to the desired area of the skin, the active ingredients diffuse out of the spheres into the vehicle and then onto the skin (see fig.4). While the rate of release of the active ingredient from the formulation can be predetermined, the release can be initiated by many release triggers, including pressure and temperature changes and moisture. The microsponges cannot pass through to the stratus corneum because of their size, so they retained on the skin surface, releasing slowly the active ingredients over a period of time. The rate of release associated with MDS provides more control, which potentially has an impact on the intensity of skin irritancy provoked by the topical agent. However, the MDS technology is limited in that it can only entrap active ingredients with certain characteristics.

CHARACTERIZATION OF MICROSPONGES

Particle size determination

Particle size analysis of loaded and unloaded microsponges can be performed by laser light diffractometry. The values (d50) can be expressed for all formulations as mean size range. Percentage cumulative drug release from microsponges of different particle size will be plotted against time to study effect of particle size on drug release. Particles greater than 30 μm can give gritty feeling and hence particles of same size between 10 to 25 μm are preferred to use [18-26].

Scanning Electron Microscope (SEM) study

The microsponges MDS were subject to Scanning Electron Microscopy (SEM) studies. The morphology of microsponges (size and shape) was examined with SEM. The samples were mounted on a metal stub with double adhesive tape and coated with Platinum alloy or gold-palladium under an argon atmosphere at room temperature to a thickness of 100 A using a spotter coater under vacuum.

Entrapment efficiency and production yield

Accurately weighed quantities of microsponges were kept in a suitable buffer solution for sufficient time that breaks cross linked structure and/or liberates entrapped drug. Theoretical quantity of drug was calculated as a ratio of added drug amount to total amount of drug and additives. The entrapment efficiency can be calculated by following formula: The entrapment efficiency was calculated by using following formula.

$$\text{Entrapment Efficiency} = \left(\frac{\text{actual drug in microsponges}}{\text{theoretical drug concentration}}\right)100$$

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.

$$\text{Production yield} = \left(\frac{\text{practicalmass}}{\text{theoriticalmass}}\right)10$$

Here, theoretical mass = polymer + drug

Determination of true density

The true density of microsponges was measured using an ultra-pycnometer under helium gas and was calculated from a mean of repeated determinations.

Polymer/ Monomer composition

Factors such as microsphere size, drug loading, and polymer composition regulate the drug release from microspheres. Polymer composition of the MDS can affect partition coefficient of the trapped drug between the vehicle and the microsponge system and hence have direct influence on the release of entrapped drug. Drug release from microsponge systems of different polymer compositions can be studied by plotting cumulative % drug release against time.

Resiliency

Resiliency of microsponges can be modified to produce beadlets that is softer or firmer according to the needs of the final formulation. Enhanced cross-linking tends to slow down the rate of release. Hence resiliency of microsponges will be dried and optimized as per the requirement by considering release as a function of cross-linking with time.

Compatibility studies

Compatibility of drug with excipients 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 Calorimetry (DSC).

Stability studies

Technically stability and durability may be defined as the capacity of particular formulation in a specific container, to stay between its physical, chemical, microbiological, therapeutic and toxicological specification in pharmaceutical sense. Stability of Microsponge gel formulation on storage is of a great concern as it is the major resistance in the development of marketed preparations. The prepared formulation was tested for stability on storing them at 4 ± 1ºC, 25 ± 2ºC and 37 ± 5ºC & RH (Relative Humidity) 75 %. After one month and the three months they were evaluated for the following parameters: Appearance, pH, Drug content analysis, Drug release profiles, Rheological properties etc.

Statistical analysis

The data obtained from each experiment were subjected to statistical analysis by student t-test and one-way analysis of variance (ANOVA) using Graph Pad Instat software. $P < 0.05$ was considered to be indicative of significance.

Dissolution studies

Dissolution profile of microsponges can be studied by using USP dissolution apparatus XXIII with a modified basket consisted of 5µm stainless steel mesh and the rotation speed 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.

SAFETY CONSIDERATIONS

Skin irritation studies in rabbits

The scores for erythema totalled for intact and abraded skin for all rabbits at 24 and 72 hr. The primary irritation index was calculated based on the sum of the scored reactions divided by 24 (two scoring intervals multiplied by two test parameters multiplied by six rabbits [27-30]

Anti-inflammatory activity by ear edema measurement

Experiments reported in this study were performed after approval by the Animal Ethics Committee of our College and were carried out in accordance with the CPCSA guidelines Anti inflammatory activity was done by Male Swiss mice (25–35 g) housed at 22±2 ºC under a 12- hr light/12-hr dark cycle and with access to food and water, which were performed during the light phase of the cycle. The animals were allowed to acclimate to the laboratory for at least 2hr before testing and were used only once. Edema was induced in the right ear by topical application of 0.1mg/ear of croton oil dissolved in 20µl of acetone. In house gels of FA containing free, entrapped drug and marketed gel were applied topically simultaneously with the croton oil. Ear thickness was

measured before and 6 hr after the induction of inflammation using a digital vernier calliper and reported.

Primary eye irritation study (Unwashed Eyes)

Test substance is instilled into one eye of each of 6 rabbits (unwashed eyes), the cornea, iris and cojunctival tissue of the treated eyes is graded for irritation effects at 1, 24, 48 and 72 hours after instillation. Observation period may be extended for up to 21 days to evaluate the reversibility of the effects observed.

Other evaluation studies

Oral toxicity examines in rats, mutagenicity in bacteria, allergenicity in guinea pigs, Compatibility studies by (TLC) thin layer chromatography.

Applications of Microsponge drug delivery system

Microsponges are used mostly for topical delivery and recently for oral as well as biopharmaceutical delivery. It provides the formulator a range of alternatives to develop drug and cosmetic products. Microsponges are planned to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to increase stability, decrease side effects and alter drug release.

(i)Topical drug delivery employing microsponge technology

Benzoyl peroxide (BPO) is commonly used in topical formulations for the treatment of acne and athletes foot. Skin eruption is a common side effect, and 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. Benzoyl peroxide micro particles were prepared 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 [31-33].

Mupirocin microsponges were prepared by an emulsion solvent diffusion method. The optimized microsponges were incorporated into an emulgel base. Drug release through cellulose dialysis membrane showed diffusion controlled release pattern and drug deposition studies using rat abdominal skin exhibited significant retention of active in skin from microsponge based formulations by 24 hr. The optimized formulations were static and nonirritant to skin as demonstrated by Draize patch test. Microsponges emulgel formulations showed prolonged efficacy in mouse surgical wound model infected with S. aureus. Mupirocin was static in topical emulgel formulations and showed enhanced retention in the skin indicating better potential of the delivery system for treatment of primary and secondary skin infections, such as impetigo, eczema, and atopic dermatitis.

(ii) Oral drug delivery employing microsponge technology

In oral drug delivery the microsponge system increase the rate of solubilization of poorly water soluble drugs by entrapping them in the small pores. As the pores are very small the drug is in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increase the rate of solubilisation [34-38].

Dicyclomine loaded, Eudragit based microsponges were prepared using a quasiemulsion solvent diffusion method. Kinetic analysis showed that the main mechanism of drug release was by Higuchi matrix controlled diffusion. Drug release was biphasic with an initial burst effect with 16 – 30 % in the first hour and the cumulative release for the microsponges over 8 hours i.e. 59 - 86 %.

(iii) Bone tissue engineering employing microsponge technology

A novel three-dimensional porous scaffold has been developed for bone tissue engineering by hybridizing synthetic poly (DL-lactic-co-glycolic acid) (PLGA), naturally derived collagen, and inorganic apatite. First, a porous PLGA sponge was prepared and collagen microsponges were formed in the pores of the PLGA sponge. Finally, apatite particulates were deposited on the surfaces of the collagen microsponges in the pores of PLGA sponge. The PLGA-collagen sponge served as a template for apatite deposition, and the deposition was accomplished by alternate immersion of PLGA–collagen sponge in $CaCl_2$ and Na_2HPO_4 aqueous solutions and centrifugation. The deposited particulates were small and scarce after one cycle of alternate immersion. Their number and size increased with the number of alternate immersion cycles [39].

The surfaces of collagen microsponges were completely covered with apatite after three cycles of alternate immersion. The porosity of the hybrid sponge decreases with increase in number of alternate immersion. Use of the PLGA sponge as a mechanical skeleton facilitated formation of the PLGA–collagen– apatite hybrid sponge into desired shapes serve as a useful three-dimensional porous scaffold for bone tissue engineering and collagen microsponges facilitated the uniform deposition of apatite particulates throughout the sponge.

(iv) Cardiovascular engineering employing microsponge technology

A biodegradable material with autologous cell seeding requires a complicated and invasive procedure that carries the risk of transmission. To overcome these problems, a biodegradable graft material containing collagen microsponge that would permit the regeneration of autologous vessel tissue has developed. The power of this material to induce in situ cellularization with autologous endothelial and smooth muscle cells was tested with and without pre cellularization. Poly (lactic-co-glycolic acid) as a biodegradable scaffold was compounded with collagen microsponge to form a vascular patch material. These poly (lacticco- glycolic acid)-collagen patches with (n = 10) or without (n = 10) autologous vessel cellularization were used to patch the canine pulmonary artery trunk. Histologic and biochemical appraisals were performed 2 and 6 months after the implantation. Formation of thrombus was not there in either group, and the poly (lactic-co-glycolic acid) scaffold

was almost completely absorbed in both groups. Histologic results reveal the formation of an endothelial cell monolayer, a parallel alliance of smooth muscle cells, and reconstructed vessel wall with elastic and collagen fibers. The cellular and extracellular elements in the patch had increased to levels similar to those innative tissues at 6 months. This patch shows promise as a bioengineered material for promoting in situ cellularization and the regeneration of autologous tissue in cardiovascular surgery [40].

(v) Reconstruction of vascular wall employing microsponge technology

The tissue-engineered patch was fabricated by compounding a collagen-microsponge with a biodegradable polymeric scaffold composed of polyglycolic acid crumpled mesh, built with woven polylactic acid on outside. Tissue-engineered patches in absence of precellularization were transplanted into the porcine descending aorta (n = 5), the porcine pulmonary arterial trunk (n = 8), or the canine right ventricular outflow tract (as the large graft model; n = 4). Histologic and biochemical assessments were performed 1, 2, and 6 months later on implantation and was no thrombus formation in any animal. Two months after grafting, all the transplants showed good in situ cellularization by hematoxylin/eosin and immunostaining. The limitation of the cell population by polymerase chain reaction showed a large number of endothelial and smooth muscle cells 2 months after implantation. In the large transplant model, i.e. 6 months after implantation the architecture of the patch was similar to that of native tissue and can be used as a novel surgical material for the repair of the cardiovascular system [41].

Table 1. Applications of microsponge system [42]

Active agents	Applications
Anti-inflammatory e.g. Hydrocortisone	Long lasting activity with lessening of skin allergic response and dermatoses.
Anti-dandruffs e.g. zinc pyrithione, selenium sulfide	Reduced unpleasant odor with reduced irritation with extended efficacy and safety.
Skin depigmenting agents e.g.hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.
Anti-fungal	Sustained release of actives.
Anti-acne e.g. Benzoyl peroxide	Maintained efficacy with reduced skin irritation and sensitization.
Antipruritics	Extended and improved activity.
Sunscreens	Long lasting product efficacy with amended protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization.
Rubefacients	Sustained activity with reduced irritancy, greasiness and odor.

Table 2. Marketed formulations of microsponges [43-44]

Product name	Manufacturer	Advantages
Carac Cream	Dermik Laboratories, Inc.Berwyn, PA 19312 USA	Carac cream contains 0.5% fluorouracil; with 0.35% being incorporated into a patented porous microsphere consisted of methyl methacrylate/ glycol dimethacrylate cross-polymer and dimethicone. Once-a-day topical prescription product for the treatment of actinic keratosis (AK) caused by over exposure to the sun.
Retin-A-Micro	Ortho-McNeil Pharmaceutical, Inc.	Retin-A-Micro contains 0.1% and 0.04% tretinoin entrapped into a patented porous microsphere consisted of methyl methacrylate/ glycol dimethacrylate cross-polymer to enable inclusion of the active ingredient, tretinoin, in an aqueous gel used for the topical treatment of acne vulgaris.
Salicylic Peel 20 & 30	Biophora	Salicylic acid 20%, microsponge technology has excellent exfoliation and used for stimulation of the skin for more resistant skin types or for faster results. It will considerably improve pigmentation, fine lines and acne concerns. Salicylic acid moves easily through the pores, clearing them out while reducing inflammation. This treatment effectively combats acne leaving an amazingly smooth and clear complexion.
Line Eliminator Dual RetinolFacialTreatment.	Avon	Lightweight cream with a retinol (Vitamin A) in MDS, dual-system delivers both immediate and time released wrinkle-fighting action. Clearly diminishes appearance of fine lines, wrinkles & skin discolorations associated with aging.
Micro Peel Plus /Acne Peel	Biomedic	The MicroPeel ® Plus procedure stimulates cell turnover through the application of salicylic acid in the form of microcrystals using microsponge® technology. These microcrystals target the exact areas on

		the skin that need improvement.
Retinol cream, Retinol 15 Night cream	Biomedic, Sothys	A night time treatment cream with microsponge technology using a stabilized formula of pure retinol, Vitamin A. Continued use of Retinol 15 will result in the visible diminishment of fine lines and wrinkles, a noticeable improvement in the skin discolorations due to aging, and enhanced skin smoothness.
Lactrex™ 12% Moisturizing Cream	SDRPharmaceuticals, Inc., Andover , NJ , U.S.A. 07821	Lactrex™ 12% moisturizing cream contains 12% lactic acid as the neutral ammonium salt, ammonium lactate. Microsponge® technology has been included for easy application and long lasting moisturization. Lactrex™ also contains water and glycerin, a natural humectant to soften and help moisturize dry, flaky, cracked skin.
EpiQuin Micro	SkinMedica Inc	EpiQuin Micro is a prescription moisturizing fading cream that reduces the melasma, post inflammatory hyper pigmentation or solar lentigines. Also help in age spots, sun spots and facial discoloration.
Oil free matte block spf20	Dermalogica	Oil free matte formulated with microsponge technology, block absorbs oil and preventing shine without any powdery residue.
Sports cream RS and XS	EmbilPharmaceutical Co. Ltd.	Topical analgesic-anti-inflammatory and counter irritant actives in a microsponge® delivery system (MDS) for the management of musculoskeletal conditions.
Oil Control Lotion	FountainCosmetics	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 complex soothes inflammation and tightness to promote healing. acne-prone, oily skin conditions.
Ultra Guard	Scott Paper Company	Microsponge system that contains dimethicone to help protect a baby's skin from diaper rash. The new wipe contains a skin protectant that helps keep wetness and irritants from the baby's skin. The solution is alcohol-free, hypoallergenic and contains dimethicone, an element found in baby creams, lotions and skin protectants.
Aramis fragrances	Aramis Inc.	24 hour high performance antiperspirant spray sustained release of fragrance in the microsponge comes in the form of an ultra light powder, it can imbibe fragrance oil well controlled the release due to moisture and temperature.

1

Figure 1. Microsponge

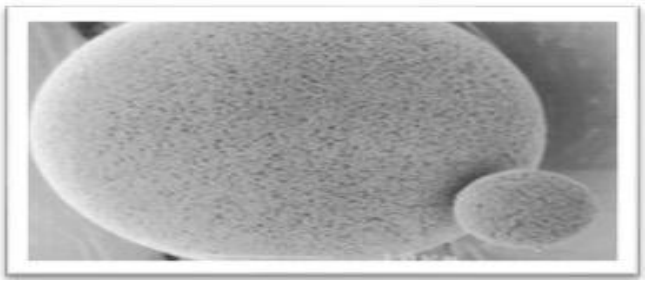


Figure 2. Liquid – liquid suspension polymerization

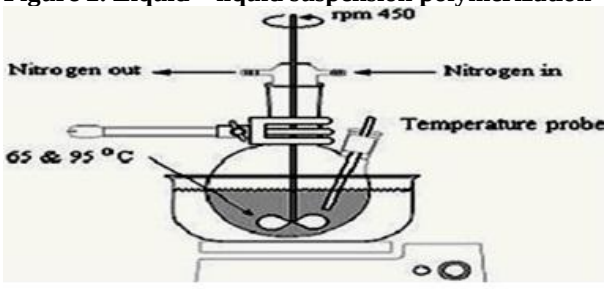


Figure 3. Method of quasi-emulsion solvent diffusion

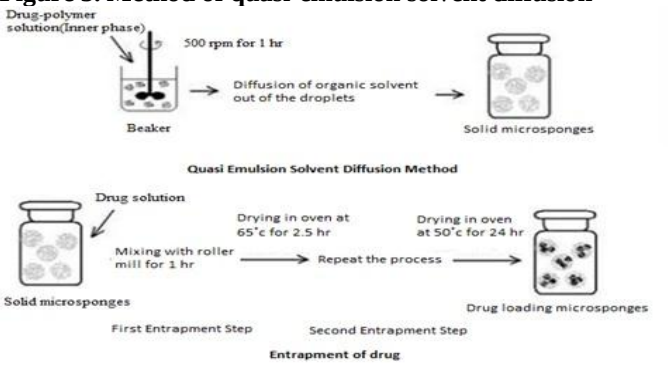
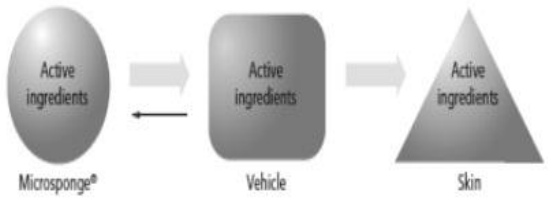


Figure 4. Mechanism of action of MDS



The schematic shows the mechanism of action of a Microsponge Delivery System (MDS) dispensed in a vehicle once it has been applied to the skin. The skin depletes the vehicle concentration, and the microsponge then releases active ingredients in response to the vehicle depletion.

CONCLUSION

MDS is a very emerging field in various pharmaceutical applications in the coming years as they have unique properties like extended release, reduced irritancy, self sterilizing capacity due to its small size and compatible with most of vehicles and ingredients and is flexible to develop novel product forms. It is a unique technology for the controlled release of topical agents and consists of microporous beads loaded with active agent and also use for oral as well as biopharmaceutical drug delivery. Main advantage is that liquids can be transformed into free flowing powders. Now days it can also be used for tissue engineering and controlled oral delivery of drugs using bio erodible polymers, specially for colon specific delivery.

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