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MICROSPONGES AS THE VERSATILE TOOL FOR TOPICAL ROUTE: A REVIEW

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ABSTRACT

The drug delivery technology landscape has become highly competitive and rapidly evolving. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. Conventional topical formulations are intended to work on the surface of the skin. Normally, upon application such formulations release their active ingredients and producing a highly concentrated layer of active ingredient that is quickly absorbed. Therefore, need exists for a system to increase the amount of time that an active ingredient is present either on skin surface as well as within the epidermis, at the same time, minimizing its transdermal penetration in the body. In recent times, microsponge delivery system (MDS) has been successively addressed for the controlled release of drugs onto the epidermis with assurance that the drug remains chiefly localized and does not enter the systemic circulation in major amounts. Drug loaded microsponge consist of microporous beads, typically 10-25 µm in diameter that possess a versatility to entrap wide range of active agents. Microsponge Systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as a gel, cream, liquid or powder. Microsponge technology offers entrapment of ingredients and is believed to contribute towards reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. In addition, numerous studies have confirmed that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic. This review article covers methods of preparation, release mechanism, characterization and applications of microsponge delivery system with patent information and marketed formulations.

INTRODUCTION: The human skin is a large and complex organ that protects and fosters the biological functions it encloses. As the interface between the organism and the external world, the skin is susceptible to injuries from the environment or from other organisms [1]. Topical drug delivery systems are formulated either to give local effect or to enter in to the systemic circulation, where skin serves as the portal of entry to the drug and various formulations made available in the market are creams, gels, lotions, ointments, TDS etc. Main drawbacks of topical preparations for local action are they may readily absorbed and hence, less duration of action and decreased activity. The effective therapy of the disease often seek high concentration of active medicament and produces the skin irritation problems reported in some research studies and also uncontrolled evaporation of active agents, potential incompatibility of drug with vehicles [2].

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Similarly topical preparations for systemic action have drawback like drug doesn't reaches the systemic circulation in sufficient amounts.

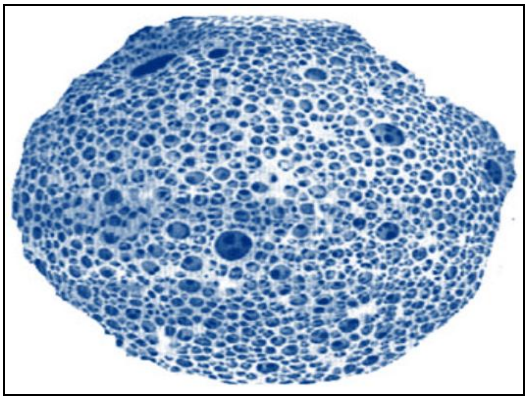

FIG. 1: PICTURE SHOWING THE HIGHLY POROUS NATURE OF A MICROSPONGE

A Microsponge Delivery System (MDS) is patented, highly cross-linked, porous, polymeric microspheres (**fig. 1 and 2**) that can entrap wide range of actives and then release them with desired rate [3]. This system is applicable for the improvement of performance of topically applied drugs. It is a unique technology for the controlled release of topical agents and consists of microporous beads, typically 10-25 microns in diameter, loaded with active agent.

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. Thus the microsponge should remain maximum time at the skin and below the epidermis and release the medicament slowly. For these reasons microsponge should meet the following characteristics [4]:

- Microsponge formulations are stable over range of pH 1 to 11;
- Microsponge formulations are stable at the temperature up to 130^{o}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 are non irritant, non mutagenic, non toxic, non greasy.
- Microsponge formulations have higher payload (50 to 60%), still free flowing and can be cost effective.

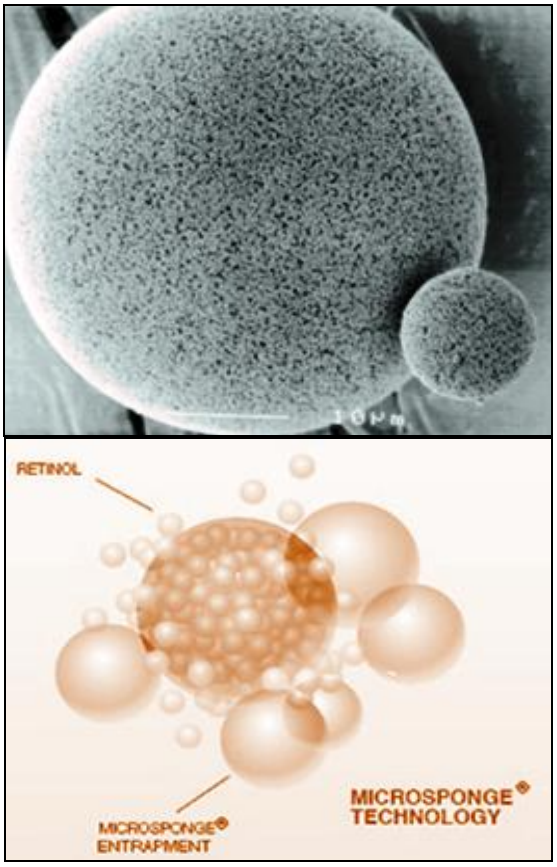

FIG. 2: VIEW OF A MICROSPONGE

Advantages of Microsponge Delivery System [5, 6]:

- 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]:

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Characteristics of materials that are entrapped in Microsponges: Most liquid or soluble ingredients can be entrapped in the particles [8]. 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.

Drugs explored in Microsponge Delivery System [9-17]:

- Ibuprofen
- Fluconazole
- Benzyl peroxide
- Ketoprofen
- Paracetamol
- Dicyclomine
- Flurbiprofen
- Ketoconazole
- Tretinoin
- Trolamine
- Retinol

Formulation Aids: Various polymers like Eudragit RS100, Dimethacrylate, Ethyl Cellulose, Polystyrene and PHEMA can form a microsponge 'cage'. In addition to actives; some microsponges contain plasticizers like Tri-ethyl citrate (TEC) that help to stabilize their structure [18-21].

Preparation of Microsponges: Drug loading in microsponges drug delivery system done in two ways, one step process or by two step process as discussed in liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques which are based on physicochemical properties of drug to be loaded. 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.

Liquid-Liquid Suspension Polymerization: The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems [22]. 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**)

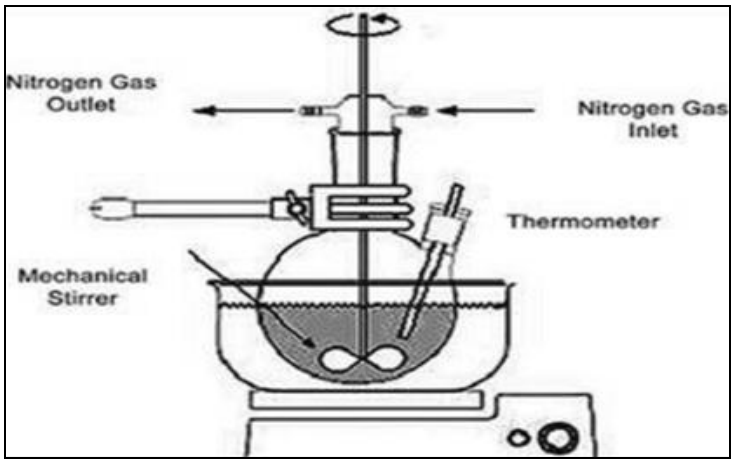
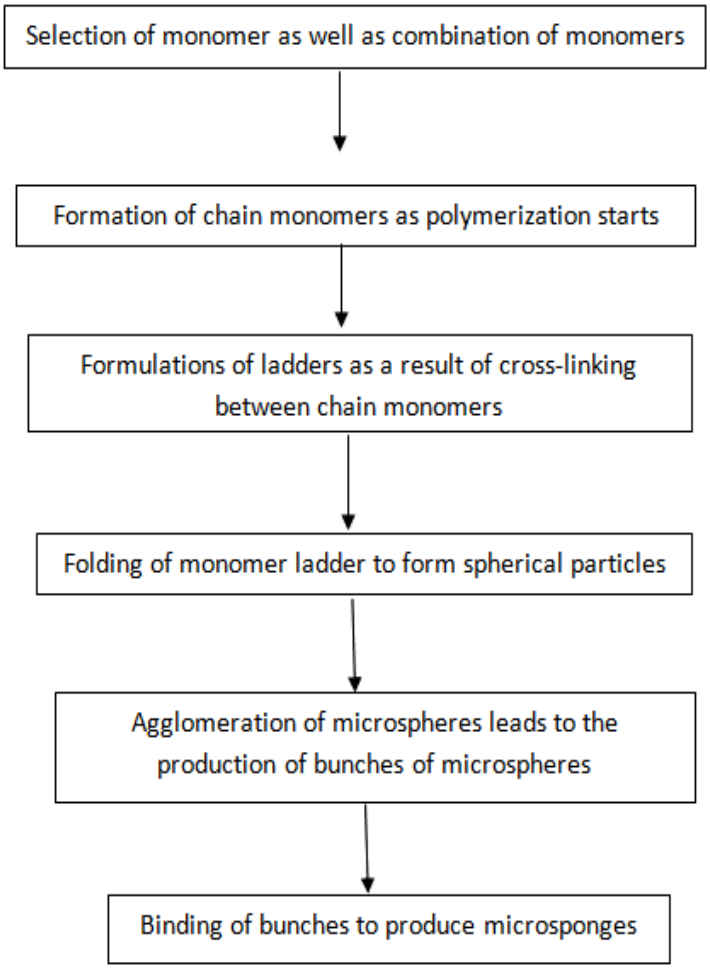


FIG. 3: REACTION VESSEL FOR MICROSPONGE PREPARATION BY LIQUID-LIQUID SUSPENSION METHOD

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 are summarized in **scheme 1** as follows:

Quasi-emulsion Solvent Diffusion: Microsponges prepared by a quasi-emulsion solvent diffusion method (**fig. 3**) using an external phase of containing distilled water and polyvinyl alcohol (PVA) 72 000. The internal phase consisted of Drug, ethyl alcohol, polymer and 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 [19].



SCHEME 1: STEPS IN THE PREPARATION OF MICROSPONGES

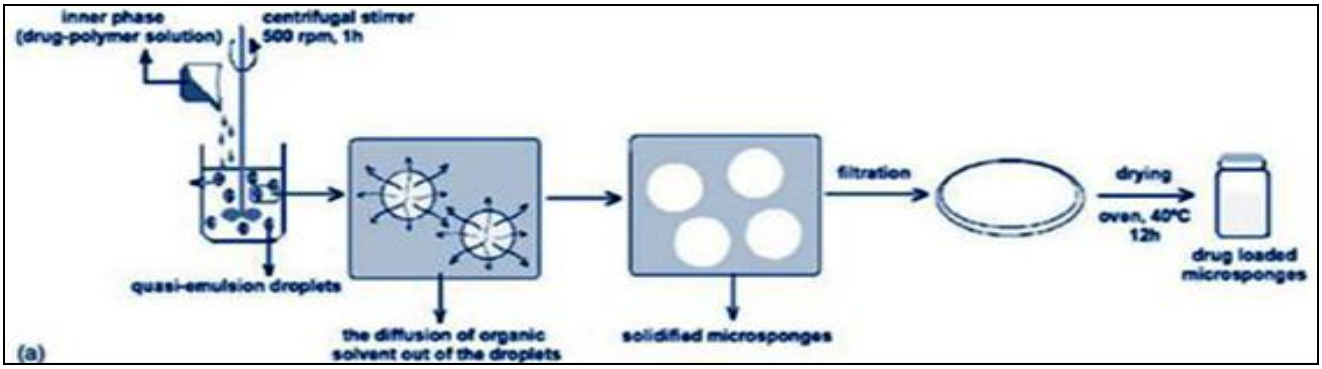


FIG. 3: PREPARATION OF MICROSPONGES BY QUASI-EMULSION SOLVENT DIFFUSION METHOD

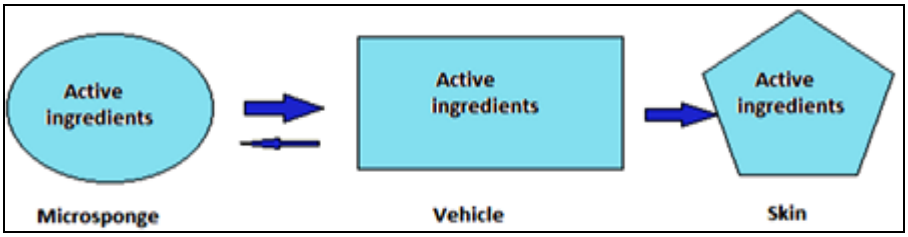


FIG. 4: MECHANISM OF ACTION OF THE MICROSPONGE DELIVERY SYSTEM

Fig. 4 shows the mechanism of action of a Microsponge Delivery System (MDS) dispersed 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.

Parameters of Microsponges:

- Particle size (Microscopy)
- Morphology and Surface topography
- Characterization of pore structure
- Loading efficiency and production yield
- Characterization of pore structure
- Compatibility studies
- Resiliency
- Drug release study

Physical Characterization of Microsponges:

Particle Size Determination [22]: 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. Particles larger than 30µm can impart gritty feeling and hence particles of sizes between 10 and 25µm are preferred to use in final topical formulation.

Morphology and Surface Topography of Microsponges [23]: 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 [24]: The loading efficiency (%) of the microsponges can be calculated according to the following equation:

$$\text{Loading efficiency} = \frac{\text{Actual Drug Contentin Microsponge}}{\text{Theoritical Drug Content}} \times 100$$

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.

$$\text{Production Yeild(PY)} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoritical Mass(polymer + Drug)}} \times 100$$

Determination of True Density [25]: The true density of Microparticles is measured using an ultra - pycnometer under helium gas and is calculated from a mean of repeated determinations.

Characterization of Pore Structure [26]: Porosity parameters of microsponges such as intrusion extrusion isotherms, pore size distribution, total pore surface area, average pore diameters, shape and morphology of the pores, bulk and apparent density can be determined by using mercury intrusion porosimetry. Incremental intrusion volumes can be plotted against pore diameters that represented pore size distributions. The pore diameter of microsponges can be calculated by using Washburn equation:

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

Here; D is the pore diameter (µm), is the surface tension of mercury (485 dyn cm^{-1}), θ is the contact angle (130°), and P is the pressure (psia). Total pore area (Atot) was calculated by using equation,

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

Here, P is the pressure (psia), V is the intrusion volume (ml g−1), Vtot is the total specific intrusion volume (ml g−1). The average pore diameter (Dm) was calculated by using equation:

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

Envelope (bulk) density (ρse) of the microsponges was calculated by using equation:

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

Here, Ws is the weight of the microsponge sample (g), Vp is the empty penetrometer (ml), VHgis the volume of mercury (ml). Absolute (skeletal) density (ρsa) of microsponges was calculated by using equation:

$$\rho_{sa} = \frac{\mathrm{Ws}}{\mathrm{Vse} - V_{tot}}$$

Here, Vse is the volume of the penetrometer minus the volume of the mercury (ml). Finally, the percent porosity of the sample was found from equation,

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

Pore morphology can be characterized from the intrusion–extrusion profiles of mercury in the microsponges as described by Orr.

Compatibility Studies: Compatibility of drug with reaction adjuncts can be studied by thin layer chromatography (TLC) and Fourier Transform Infra-red spectroscopy (FT-IR) [27]. Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC) [28]. 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 [29,30].

Polymer/Monomer Composition: Factors such as microsponge size, drug loading, and polymer composition govern the drug release from microsponges. 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. Release rate and total amount of drug released from the system composed of methyl methacrylate/ ethylene glycol dimethacrylate is slower than styrene/divinyl benzene system [31].

Resiliency: Resiliency (viscoelastic properties) of microsponges can be modified to produce beadlets that is softer or firmer according to the needs of the final formulation. Increased cross-linking tends to slow down the rate of release. Hence resiliency of microsponges will be studied and optimized as per the requirement by considering release as a function of cross-linking with time [32].

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 [33].

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:

$$Q = k_1 t^n \; OR \log \mathrm{Q} = \log \mathrm{k_1} + \mathrm{n} \log \mathrm{t}$$

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 k1 were calculated. For comparison purposes, the data was also subjected to Eq., which may be considered a simple, Higuchi type equation;

$$Q = k_{2\ t^{0.5}} + C$$

Above Eq. 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.

Mechanism of Drug 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 [34]: 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 [35]: Rubbing or pressure applied can release the active ingredient from microsponges onto skin.

Solubility [36]: 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.

pH Triggered Systems [37]: 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.

Safety Considerations [36, 38, 39:] 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

Formulation Consideration

- Actives entrapped in MDS can then be incorporated into many products such as creams, lotions, powders and soaps. When formulating the vehicle, certain considerations are taken into account in order to achieve desired product characteristics.
- The solubility of actives in the vehicle must be limited. Otherwise the vehicle will deplete the microsponges before the application.
- To avoid cosmetic problems; not more than 10 to 12% w/w microsponges must be incorporated into the vehicle.
- Polymer design and payload of the microsponges for the active must be optimized for required release rate for given time period.

There remains equilibrium between microsponge and vehicle and microsponge releases drug in response to the depletion of drug concentration in the vehicle. Drug concentration in the vehicle is depleted by absorption of the drug into skin. Hence continuous and steady release of actives onto the skin is accomplished with this system. Drug release from the topical semisolid formulation can be studied by using Franz-type static diffusion cells [40].

Applications of Microsponge Systems[35]: Microsponges are designed to deliver the pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects and modify drug release. Microsponges are porous, polymeric microspheres that are used mostly for topical but recently used for oral administration **(Table 1).**

TABLE 1: APPLICATIONS OF MICROSPONGE SYSTEMS

Sr. No.	Active agents	Applications
1.	Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even atelevated concentration and with reduced irritancy and sensitization.
2.	Anti-acne e.g. Benzoyl peroxide	Maintained efficacy with decreased skin irritation and sensitization.
3.	Anti-fungals	Sustained release of actives.
4.	Anti-inflammatory e.g. hydrocortisone	Long lasting activity with reduction of skin allergic response and dermatoses.
5.	Anti-dandruffs e.g. zinc pyri-thione, sele-nium sulfide	Reduced unpleasant odour with lowered irritation with extended safety and efficacy.
6.	Antipruritics	Extended and improved activity.
7.	Rubefacients	Prolonged activity with reduced irritancy greasiness and odour.
8.	Skin depig-menting agents e.g. hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.

Microsponge for Topical Delivery: Benzoyl peroxide is mainly used in the treatment of mild to moderate acne and athlete's foot and the most common side effect associated with Benzoyl peroxide is skin irritation and it has been shown that controlled release of Benzoyl peroxide from a delivery system to the skin could lessen the side effect while reducing percutaneous absorption. Topical delivery system with reduced irritancy was successfully developed [41].

Jelvehgari *et al.*, developed Benzoyl peroxide microsponges by using emulsion solvent diffusion method and investigate the parameters affecting the morphology and other characteristics by using scanning electron microscopy (SEM). The morphology and particle size of microsponges were affected by drug: polymer ratio, amount of emulsifier used and stirring rate. The results showed that with increase in the ratio of drug: polymer resulted in a reduction in the rate of release of Benzoyl peroxide from the microsponges. The release data showed that the highest and the lowest release rates were obtained from lotions containing plain Benzoyl peroxide particles and Benzoyl peroxide microsponges with the drug: polymer ratio (13:1) respectively 19 [42].

Amrutiya *et al.*, developed microsponge based topical delivery system of mupirocin by using emulsion solvent diffusion method for sustained release and enhanced drug deposition in the skin. In-vitro drug release, ex-vivo drug deposition, and in-vivo antibacterial activity of mupirocin loaded formulations were studied. Microsponges were spherical and porous, and there was no interaction between drug and polymer molecules. Emulgels containing microsponges showed desired physical properties. 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 h 40 [43].

D'souza *et al.*, developed topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. FA is a corticosteroid chiefly used in dermatology to lessen skin inflammation and relieve itching. The percutaneous absorption increases risk related with systemic absorption of topically applied formulation. Thus, the goal of the study was to produce FA entrapped microsponges which were prepared by quasi-emulsion solvent diffusion method in order to control release of drug to the skin which in turn lessens the side effect whereas also reducing percutaneous absorption. FTIR and DSC studies showed that there is no incompatibility between formulation adjuvant and process parameters. Surface morphology can be done by SEM which showed microporous nature of microsponges. Drug release was also observed controlled with comparative anti-inflammatory activity with the gels that contains free drug [44].

Grimes *et al.*, developed microsponge based delivery of hydroquinone 4% and retinol 0.15% for the treatment of melasma and post-inflammatory hyper-pigmentation and also to minimize skin irritation. Hydroquinone (HQ) bleaching creams are generally considered as the gold standard for treating hyper-pigmentation. The formulation was evaluated in a 12 week open label study for safety and efficacy. The study included pigmentation intensity, disease severity, lesion area and Colorimetry assessments. Adverse events were also recorded.

Patients were applied the microsponge formulation entrapped HQ 4% to the full face in morning and evening (twice) daily. After 15 minutes of application of the test product, a broad-spectrum sunscreen was applied once in the morning. Then, patients were evaluated at baseline and at 4, 8, and 12 weeks. The study showed that micro-entrapped HQ 4% with retinol 0.15% formulation produced improvement at all study end points. The open-label study concluded that micro-entrapped HQ 4% with retinol 0.15% was safe and effective [45].

Future impact of Microsponge Drug Delivery System: Microsponge is one of the novel drug delivery systems, for the topical preparations for drug delivery through skin. Not only it is limited to the topical preparations it shown its activity in oral delivery, also shown its activity in biopharmaceuticals i.e. it is useful in drug delivery systems in various forms. Main advantage is that liquids can be transformed into free flowing powders. Its produce less toxic, non greasiness, non irritant, it requires less amount of drug due to delayed release.

Normal topical preparations shows toxic reactions, incompatibilities, unpleasant odour, etc. by this microsponge products are advantageous some products are already approved and available in market; several products under development.

Marketed Formulations: MDS is ideal for skin and personal care products. They can absorb large amounts of excess of skin oil, while retaining an elegant feel on the skin's surface. The technology is currently employed in almost number of products sold by major cosmetic and toiletry companies worldwide. Among these products are skin cleansers, conditioners, oil control lotions, moisturizers, deodorants, razors, lipstick, makeup, powders, and eye shadows; which offers several advantages, including improved physical and chemical stability, greater available concentrations, controlled release of the active ingredients, reduced skin irritation and sensitization, and unique tactile qualities.

Marketed formulation using the MDS includes Ethical Dermatological products **(**APS defined ethical dermatology products as prescription and non-prescription drugs that are promoted primarily through the medical profession for the prevention and treatment of skin problems or diseases). Several ethical dermatology products approved by USFDA, OTC and personal care products are sold in the United States. Results from various human clinical studies proved that the technology offers the potential to reduce the drug side effects, maintain the therapeutic efficacy and potentially increase patient compliance with the treatment regimen (Shown in **Table 2**).

TABLE 2: LIST OF MARKETED PRODUCTS USING MICROSPONGE DRUG DELIVERY SYSTEM PRODUCT

Name	Advantages	Manufacturer
Retin-A-Micro	0.1% and 0.04% tretinoin entrapped in MDS for topical treatment of acne vulgaris. This formulation uses patented methyl methacrylate/ glycol dimethacrylate cross-polymer porous microspheres to enable inclusion of the active ingredient, tretinoin, in an aqueous gel.	Ortho-McNeil Pharmaceutical, Inc.
Line Eliminator Dual Retinol Facial Treatment	Lightweight cream with a retinol (Vitamin A) in MDS, dual-system delivers both immediate and time released wrinkle-fighting action. Visibly diminishes appearance of fine lines, wrinkles & skin discolorations associated with aging.	Avon
Retinol cream, Retinol 15 Night cream	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.	Biomedic, Sothys
EpiQuin Micro	The Microsponge® system uses microscopic reservoirs that entrap hydroquinone and retinol. The microsponges 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. EpiQuin Micro is a prescription moisturizing fading cream that reduces the impact of these conditions known as melasma, post inflammatory hyper pigmentation or solar lentigines. Also help in Age spots, Sun spots, and Facial discoloration.	Skin Medica Inc
Salicylic Peel 20 & 30	Deep BHA peeling agent for (professional use only): Salicylic acid 20%, Microsponge Technology, Excellent exfoliation and stimulation of the skin for more resistant skin types or for faster results. Will dramatically improve fine lines, pigmentation, and acne concerns. Salicylic Acid moves easily through the pores, clearing them out while reducing inflammation. This treatment effectively combats acne, leaving a wonderfully smooth and clear complexion.	Biophora.
Sportscream RS and XS	Topical analgesic-anti-inflammatory and counterirritant actives in a Microsponge® Delivery System (MDS) for the management of musculoskeletal conditions.	Embil Pharmaceutical Co. Ltd.
Carac Cream	Carac Cream contains 0.5% fluorouracil, with 0.35% being incorporated into a patented porous microsphere (Microsponge) composed of methyl methacrylate / glycol dimethacrylate cross-polymer and dimethicone. Carac is a once-a-day topical prescription product for the treatment of actinic keratosis (AK), a common pre-cancerous skin condition caused by over-exposure to the sun.	Dermik Laboratories, Inc. Berwyn , PA 19312 USA

Micro Peel Plus /Acne Peel	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. The MicroPeel Plus aggressively outperforms other superficial chemical peels by freeing the skin of all dead cells while doing no damage to the skin.	Biomedic
Oil Control Lotion	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.	Fountain Cosmetics
Oil free matte block spf20	This invisible oil-free sunscreen shields the skin from damaging UV sun rays while controlling oil production, giving you a healthy matte finish. Formulated with microsponge technology, Oil Free Matte Block absorbs oil, preventing shine without any powdery residue.	Dermalogica
Lactrex™ 12% Moisturizing Cream	Lactrex™ 12% Moisturizing Cream contains 12% lactic acid as the neutral ammonium salt, ammonium lactate. Microsponge® technology has been included for comfortable application and long lasting moisturization. Lactrex™ also contains water and glycerin, a natural humectant, to soften and help moisturize dry, flaky, cracked skin.	SDR Pharmaceutical, Inc.,Andover , NJ,U.S.A. 07821
Dermalogica Oil Control Lotion	A feather-light lotion containing microsponges to absorb oil on the skin's surface, helping to combat shine and maintain an all-day matte finish. Niacinamide, Zinc Gluconate, Yeast Extract, Caffeine and Biotin purify and inhibit overactive sebaceous gland activity while soothing irritation. Salicylic Acid clears congested follicles to minimize future breakout activity, while Enantia Chlorantha Bark Extract controls over-active oil glands, helping to reduce oily shine on skin's surface.	John and Ginger Dermalogica Skin Care Products
Ultra Guard	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 ingredient found in baby creams, lotions and skin protectants.	Scott Paper Company
Aramis fragrances	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.	Aramis Inc.

CONCLUSION: Microsponges have a discrete advantage over the existing conventional topical dosage forms for the treatment of dermatological diseases. A Microsponge Delivery System can entrap wide range of actives and then release them onto the skin over a time and in response to trigger. It is a unique technology for the controlled release of topical agents and consists of microporous beads loaded with active agent for topical and also use for oral as well as biopharmaceutical drug delivery.

It provides a wide range of formulating advantages; Liquids can be transformed into free flowing powders. MDS is originally developed for topical delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, anti-pruritics, rubefacients etc. Formulations can be developed with incompatible ingredients with prolonged stability without use of preservatives. Safety of the irritating and sensitizing drugs can be increased and programmed release can control the amount of drug release to the targeted site.

Hence, the microsponge drug delivery system focus as an important tool for future inventions in controlled drug delivery system.

Thus, microsponge has got a lot of prospective and is a very up-and-coming field which is needed to be explored.

REFERENCES:

1. Freinkel R K and Woodley D T, "The biology of the skin", Parthenon, NewYork.2000.
2. Chowdary K P, and Rao Y S, "Mucoadhesive Microspheres for Controlled Drug Delivery", Biol. Pharm. Bull., 2004, 27(11), 1717-1724.
3. Nacht S, Kantz M. The Microsponge, "A Novel Topical Programmable Delivery System". 1992; 42:299-325.
4. D'souza J I, Masvekar RR, Pattekari PP, Pudi SR, More HN, "Microspongic delivery of fluconazole for topical application". Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech 2004:76.
5. Vyas S P, Khar R K, "Targeted and controlled drug delivery-Novel carrier system". CBS Publication, New Delhi, Edition 1, 2002:453.
6. 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. Microencapsulation 1996; 308:124-132.
7. D'souza JI, Masvekar RR, Pattekari PP, Pudi SR, More HN" Microspongic delivery of fluconazole for topical application". Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech 2004:76.
8. Aritomi H, Yamasaki Y, Yamada K, Honda H and Koshi M.,"Development of sustained release formulation of chlorpheniramine maleate using powder coated mi-crosponges prepared by dry impact blending method". Journal of Pharmaceutical Sciences and Tech-nology. 1996, 56(1): 49-56.
9. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y "Control of Prolonged Drug Release and Compression Properties of Ibuprofen microsponges with acrylic Polymer, Eudragit RS, by changing their intraparticle porosity". Chemical & pharmaceutical bulletin 1992; 40(1):196-201.
10. D' souza JI, Masvekar RR, Pattekari PP, Pudi SR, 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.
11. Wester RC, Patel R, Nacht S, Leydan J, Malendres J, 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.
12. Tansel C, "Preparation and *in vitro* evaluation of modified release ketoprofen microsponge", II Farmaco 2003; 58:101-106.
13. Jain V, Singh R, "Development and characterization of eudragit RS 100 loaded microsponges and its colonic delivery using natural polysaccharides", Acta Poloniae Pharmaceutica - Drug Research 2010; 67:407-415.
14. Jain V, 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, 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.
17. 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.
18. 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.
19. Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Gary P, Martin, Nokhodchi A, "The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies". International Journal of Pharmaceutics 2006, 308:124-132.
20. Ruckenstein E, Hong L., "Concentrated emulsion polymerization pathway to hydrophobic and hydrophilic microsponge molecular reservoirs" Chem. Mater. 1992; 4:1032-1037.
21. Chadawar V, Shaji J, "Microsponge delivery system" Current Drug Delivery 2007; 4:123-129.
22. Hainey P, Huxham IM, Rowatt B, Sherrington DC," Synthesis and ultrastructural studies of styrene -divinylbenzene polyhipe polymers". Macromolecules 1991; 24:117-121.
23. Nacht S, Katz M, "The microsponge: a novel topical programmable delivery system. In: Osborne, D.W., Amann, A.H. (Eds.), Topical Drug Delivery Formulations". Marcel Dekker, New York, 1990:299–325.
24. Kilicarslan M, Baykara T, "The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres". Int. J. Pharm. 2003; 252:99–109.
25. Emanuele AD, Dinarvand R, "Preparation, characterization and drug release from thermo responsive microspheres". Int. Journal of Pharmaceutics 1995; 237-242.
26. Washburn EW, "Note on a method of determining the distribution of pore sizes in a porous material". Proc Natl Acad Sci 1921; 7(4):115-116.
27. Anderson DL, Cheng CH and Nacht S, "Flow characteristics of loosely compacted macroporous microsponge polymeric systems",Powder technology 1994; 78:15-18.
28. Ford JL, Timmins, P, "Pharmaceutical Thermal Analysis-Techniques and Applications. Ellis Horwood Ltd., Chichester 1989.
29. Jones DS, 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.
30. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y, 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.
31. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y, 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.
32. Barkai A, Pathak V, Benita S, "Polyacrylate (Eudragit retard) microspheres for oral controlled release of nifedipine. I. Formulation design and process optimization". Drug Dev. Ind. Pharm. 1990; 16:2057-2075.
33. Jayaweera DM, "Medicinal Plants (Indigenous and exotic) used in Ceylon". Part-II. A Publication of the Natural Sciences Council of Sri Lanka, Colombo 1980.
34. Sato T, Kanke M, Schroeder G, Deluca P, "Porous biodegradable microspheres for controlled drug delivery. Assessment of processing conditions and solvent removal techniques". Pharm Res. 1988; 5:21-30.
35. Khopade AJ, Jain S, Jain NK, "The Microsponge". Eastern Pharmacist 1996; 39:49-53.

36. Guyot M. and Fawaz F, "Microspheres- Preparation and physical characteristics". Int. J. Pharmaceutics 1998; 175:61-74.
37. Christensen MS, Natch SJ: Invest. Dermato1983; 69:282.
38. 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.
39. Draize JH, Woodard G, Calvery HO, "Methods for the study of irritation and toxicity of substances applied topically to the Skin and Mucous Membranes". J Pharmacol Exp Their 1944; 82:377-389.
40. Franz T. J., "Percutaneous absorption. On the relevance of in vitro date. J. Invest. Dermatol", 1975; 45: 498-503.
41. D'souza JI, Jagdish K, Saboji, Suresh G, Killedar, Harinath N"Design and evaluation of benzoyl peroxide microsponges to enhance therapeutic efficacy in acne treatment", accepted for presentation in 20th FAPA congress, Bangkok, 2004.
42. Jelvehgari M, Siahi-Shadbad MR, Azarmi S, Gary P, Martin, Nokhodchi A, "The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies", International Journal of Pharmaceutics 2006, 308:124-132.
43. Amrutiya N, Bajaj A & Madan M, "Development of microsponges for topical delivery of mupirocin", AAPS PharmSciTech 2009; 10(2):402-409.
44. D'souza JI, Harinath N.M, "Topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system", Research J Pharm and Tech 2008; 1:502-506.
45. 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.

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