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## MICROSPONGE FOR TOPICAL DRUG DELIVERY SYSTEM

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### Abstract

Microsponge get controlled release of active drug and minimize the drawbacks of topical drug delivery systems. Local cutaneous reactions. Microsponge reduce unpleasant odour, greasiness and skin irritations and fail to reach the systemic circulation in sufficient amount. Overcome side effect and disadvantage of conventional drug delivery system unique, versatile and novel approach Microsponge drug delivery system (MDS) use. The novel drug delivery technology has become highly competitive and rapidly evolving. To optimize the efficacy and cost-effectiveness of topical therapy. A MDS is porous and polymeric microspheres polymeric system consisting of porous microspheres that can entrap wide range of actives. Active ingredient release them onto the skin over a time. It is a unique technology for the controlled release of topical drug delivery system. MDS consists of Microporous beads, typically 10-25 microns in diameter, loaded with active agent. MDS releases its active ingredient on a time mode and also in response to other stimuli (rubbing, temperature, pH, etc). MDS has been explored for various applications like sunscreens, antiacne, antidandruff, over-the-counter (OTC) skin care preparations and skin-depigmentation. MDS 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. Microsponge provide sustain release upto particular required time period.

**Key words:** Microsponge drug delivery system (MDS), Controlled release and Topical drug delivery, over-the-counter (OTC).

## **Introduction**

The objective of any drug therapy is to achieve desired concentration of active ingredient in blood or tissue which is therapeutically effective and nontoxic for extended period of time. This goal can be achieved by formulation of sustained release formulation. Microsponge is a common technique used in the production of sustained release dosage forms. Microsponge based drug delivery system has received considerable attention in recent years. Numbers of methods have been devised to prepare microsponge of desired size, shape and surface properties. Ethyl cellulose microsponge have been extensively studied for controlled release. Ethyl cellulose being insoluble in water serves as good candidate for sustained release of active ingredient. The aim of this study was to prepare ethyl cellulose microsponge containing drug to achieve a controlled drug release profile suitable for topical delivery. These vehicles necessitate a high concentration 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.<sup>2</sup>

The fundamental appeal of the microsponge technology stems used instead of conventional formulations for releasing active ingredients for particular period of time. Microsponges release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. The significance of topical drugs suffers from various problems like greasiness, stickiness associated with the ointments and so on, that often result in lack of patient compliance. So overcome drawback of ointment microsponge delivery system use.<sup>3</sup>

Several systems were developed for systemic drug delivery under for topical delivery system (TDS) using for skin. It has improved the efficacy and safety of many drugs. Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Conventional products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. Such product has many problems like greasiness, stickiness. Other drawbacks of topical formulations are uncontrolled evaporation of active ingredient, unpleasant odor. These vehicles require a high concentration of active agents for effective therapy because of their low efficiency of delivery system, resulting in irritation and allergic reactions in significant users. That often result in lack of patient compliance.

Conventional topical products typically provide concentrations but with a short duration of action. Various serious side effects can occur when active ingredients penetrate the skin. Microsponge technology allows sustained rate of release, reducing irritation while maintaining efficacy. Microsponge delivery systems are uniform, spherical and porous polymeric microspheres having myriad of interconnected voids of particle size less than 300µm.<sup>1</sup>

A Microsponge delivery system (MDS) is a patented and polymeric microspheres polymeric system consisting of porous microspheres particles. A typical 25µm sphere can have up to 250000 pores and an internal pore structure equivalent to 10ft in length providing a total pore volume of about 1ml/g. Microsponge do not pass through the skin (capable of holding four times their weight in skin secretions).<sup>2</sup>

MDS is comprised of a polymeric bead having network of pores with an active ingredient held within was developed to provide controlled release of the active ingredients whose final target is skin itself. MDS was employed for the improvement of performance of topically applied drugs. The common methods of formulation remains same; the incorporation of the active substance at its maximum thermodynamic activity in an optimized vehicle and the reduction of the resistance to the diffusion of the stratum corneum. Application Solubility enhancement Site specific action produced on the target organ. Increase stability of drug Targeted drug delivery Controlled release drug delivery.<sup>3</sup>

#### **Advantages of Microsponge Delivery System over other technologies<sup>7</sup>:**

Microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis.

Microsponge system can reduce significantly the irritation of effective drugs without reducing their efficacy.

Microsponge system has patient compliance..

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.

Microsponge system stable over range of pH 1 to 11, temperature up to 130 oC,

Microsponge system compatible with most vehicles and ingredients, self sterilizing as average pore size is 0.25µm where bacteria cannot penetrate, higher payload (50 to 60%), still free flowing and can be cost effective.

#### **Advantages of Microsponge Delivery System<sup>13,14</sup>:**

- Improved product elegancey.

- Lessen the irritation and better tolerance leads to improved patient compliance.
- It can also improve efficacy in treatment.
- MDS can improve bioavailability of the drugs.
- They have better thermal, physical and chemical stability.
- These are non-irritating, non-mutagenic, non-allergenic and non-toxic.
- Microsponge 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.

#### **Characteristics of Microsponges<sup>11</sup>:**

- Microsponge formulations are stable at the temperature up to 130oC;
- 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<sup>12</sup>:**

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

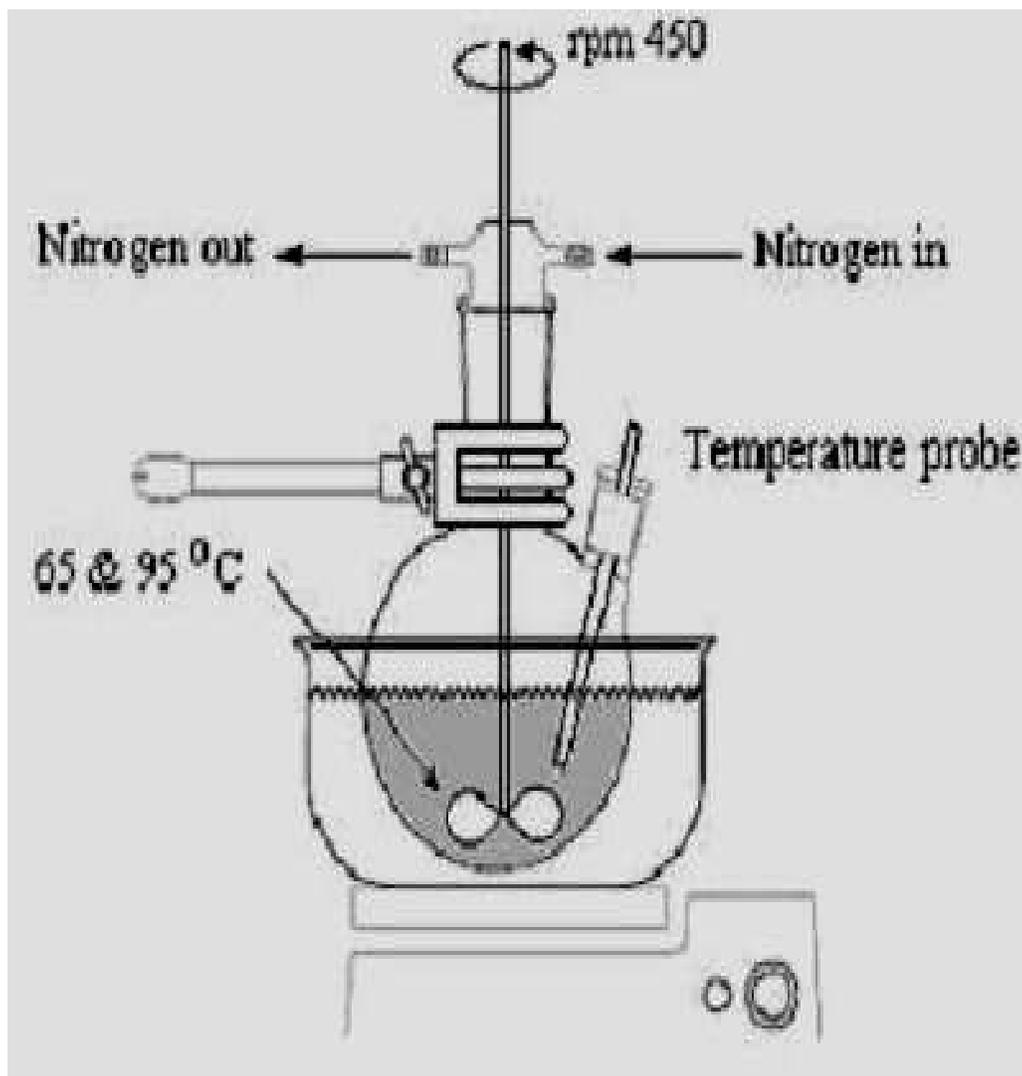
- It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers.
- It should be stable in contact with polymerization catalyst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

## Preparatio of Microspoges<sup>4</sup>

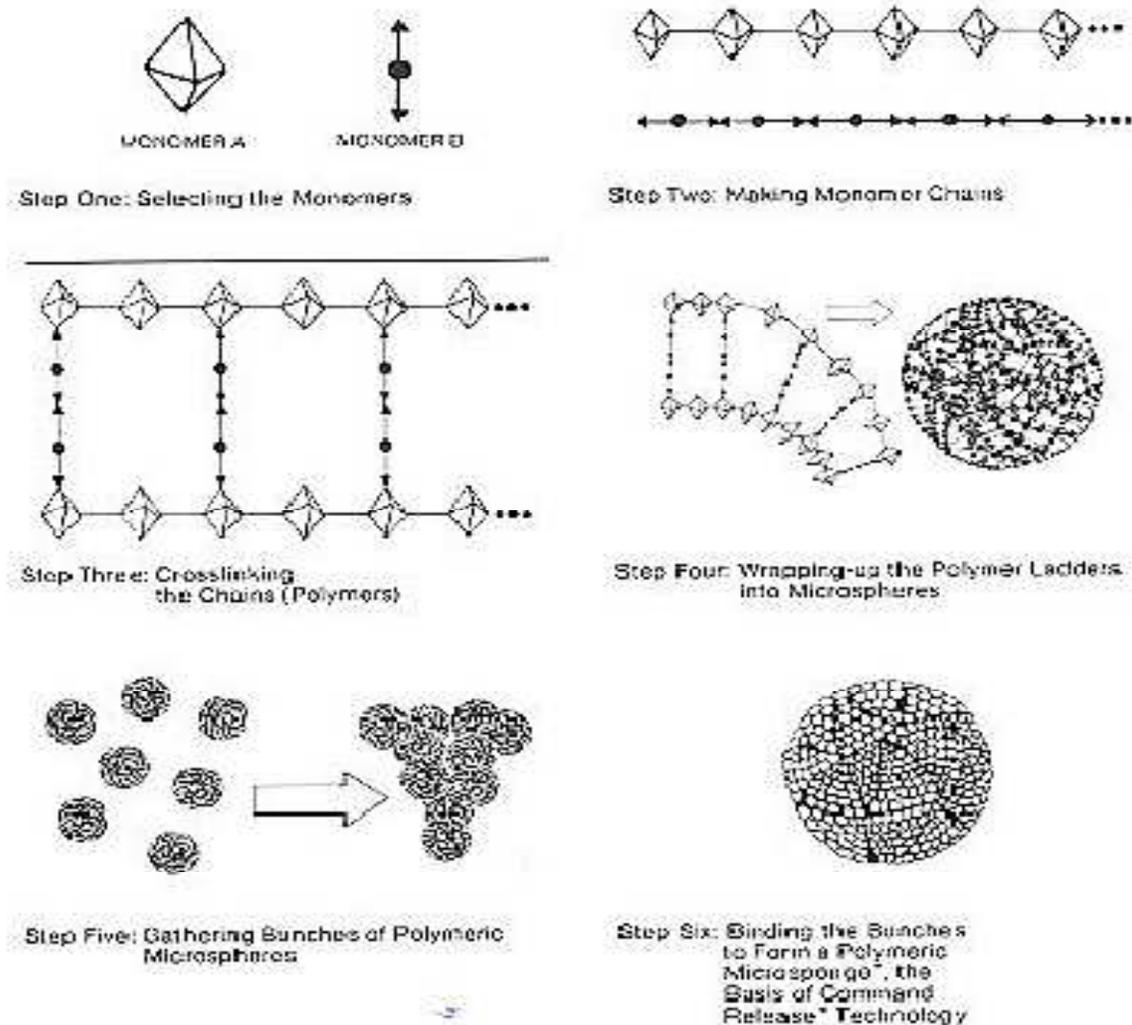
Drug loading in microsponges can take place in two ways, one-step process or by two-step process; based on physico-chemical properties of drug to be loaded. If the drug is typically an inert non-polar material, will create the porous structure it is called porogen. Porogen drug, which neither hinders the polymerization nor become activated by it and stable to free radicals is entrapped with one-step process.

- **Liquid-liquid suspension polymerization:** Microsponges are conveniently prepared by *liquid-liquid suspension polymerization*. Polymerization of styrene or methyl methacrylate is carried out in round bottom flask.

A solution of drug is made in the monomer, to which aqueous phase, usually containing surfactant and dispersant to promote suspension is added. Polymerization is effected, once suspension with the discrete droplets of the desired size is established; by activating the monomers either by catalysis or increased temperature.



**Figure 1: Reaction Vessel for Microsponge formulation by liquid-liquid suspension polymerization.**



**Figure-2: Microsponges formulate by Suspension Polymerization**

When the drug is sensitive to the polymerization conditions, two-step process is used. The polymerization is performed using substitute porogen and is replaced by the functional substance under mild experimental conditions .

- **Quasi-emulsion solvent diffusion**

As explained in *Figure 3* the microsponges can also be prepared by *quasi-emulsion*

*solvent diffusion* method using the different polymer amounts. The processing flow chart is presented in Fig. 1a. To prepare the inner phase, Eudragit RS 100 was dissolved in ethyl alcohol. Then, drug can be then added to solution and dissolved under ultrasonication at 35 oC. The inner phase was poured into the PVA solution in water (outer phase). Following 60 min of stirring, the mixture is filtered to separate the microsponges. The microsponges are dried in an air-heated oven at 40 oC for 12 h and weighed to determine production yield (PY).

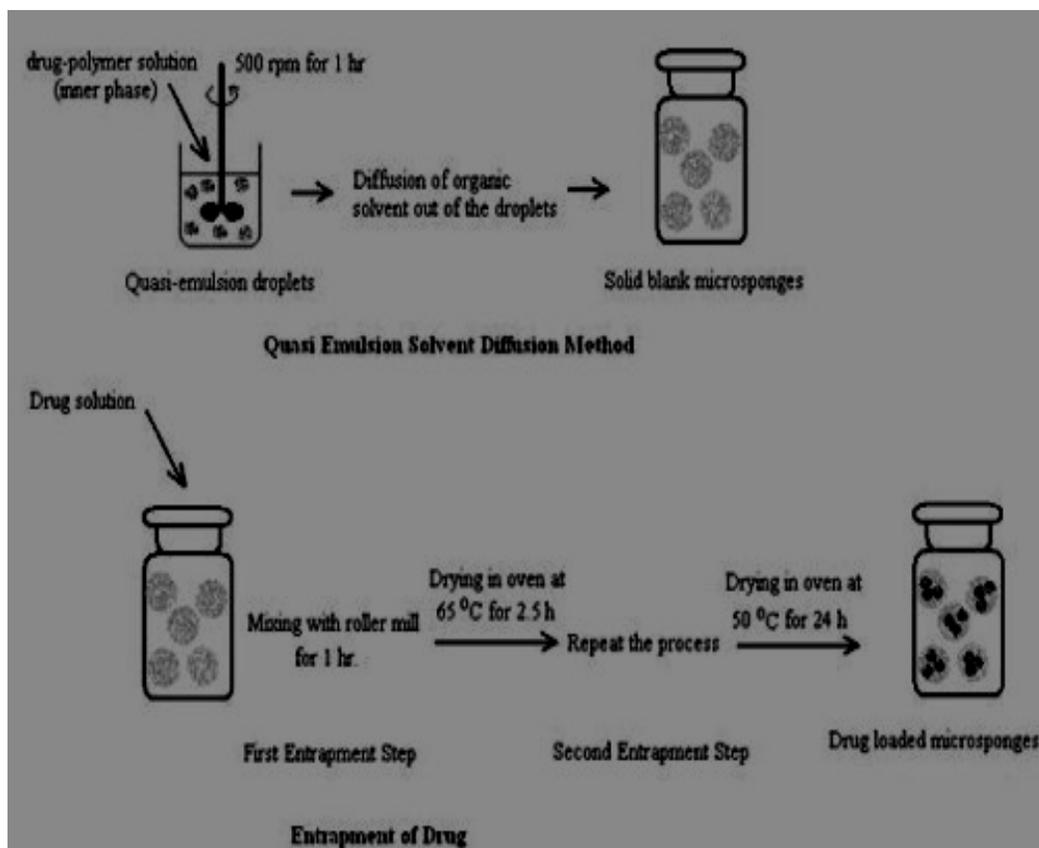


Figure 3: Preparation of microsponges by quasi emulsion solvent diffusion method.

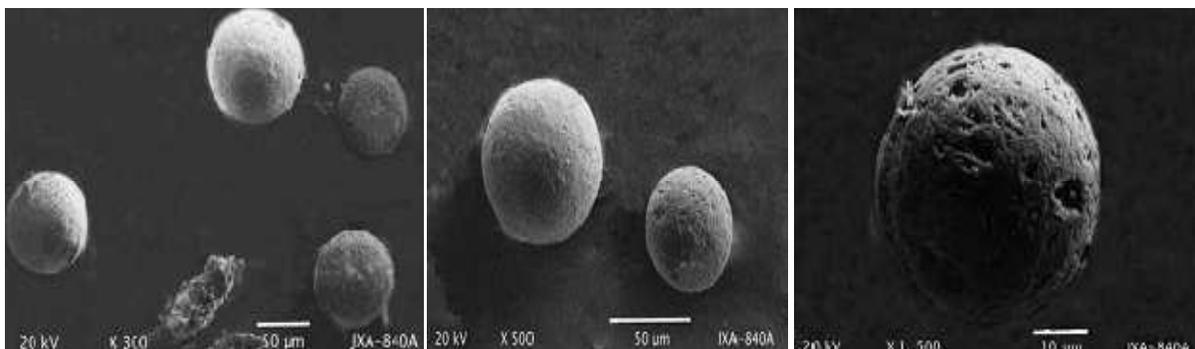
### Evaluation of Microsponges :

#### (1) Particle size determination<sup>15</sup>

Particle size analysis of loaded and unloaded Microsponge can be performed by laser light diffractometry or any other suitable method. The values ( $d_{50}$ ) can be expressed for all formulations as mean size range. Cumulative percentage drug release from microsponges of different particle size will be plotted against time. Particles larger than 30  $\mu$ m can impart gritty feeling and hence particles of sizes between 10 and 25  $\mu$ m are preferred to use in final topical formulation.

#### (2) Morphology and surface topography of Microsponges<sup>8</sup> :

For morphology and surface morphology and size of prepared microsponge known by particle coated with gold-palladium under an argon atmosphere at room temperature. Then the surface morphology of the microsponges can be studied by scanning electron microscopy (SEM). SEM of a microsponge particle can be taken to illustrate its ultrastructure .



**Figure 4: SEM photographs of microsphere formulations at different magnification.**

### **(3) Determination of loading efficiency and production yield<sup>17</sup>:**

The production yield of the microsphere can be determined by calculating initial weight of the raw materials and the last weight of the microsphere obtained. The loading efficiency (%) of the microspheres can be calculated by following equation:

$$\text{Loading Efficiency} = \frac{\text{Actual Drug Content in microspheres}}{\text{Theoretical Drug Content}} \times 100$$

### **(4) Determination of true density<sup>18</sup>:**

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

### **(5) Polymer/ monomer composition<sup>19</sup>:**

Selection of monomer is dictated both by characteristics of active ingredient ultimately to be entrapped and by the vehicle into which it will be dispersed. Polymers with varying electrical charges or degrees of hydrophobicity or lipophilicity may be prepared to provide flexibility in the release of active ingredients. Various monomer combinations will be screened for their suitability with the drugs by studying their drug release profile .

### **(6) Compatibility studies<sup>20</sup>:**

Compatibility of drug with excipient can be studied by following method:

- a) *Thin layer chromatography (TLC)*
- b) *Fourier Transform Infra-red spectroscopy(FT-IR)*
- c) *X-ray diffraction (XRD)* : Effect of polymerization on crystallinity of the drug can be studied by powder XRD

d) *Differential Scanning Colorimetry (DSC)* : For DSC approximately 5 mg samples can be accurately weighed into aluminum pans and sealed and can be run at a heating rate of 15oC/min over a temperature range 25–430 oC in atmosphere of nitrogen .

### (7) Dissolution tests<sup>9</sup>:

Dissolution profile of microsponges can be studied by use of dissolution apparatus USP XXIII with a modified basket. It consisted of 5m stainless steel mesh. The speed of the rotation is 100 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.

### (8) Skin irritation test:

Albino rabbits (2- 2.5 kg wt) number of six were used for testing. Animal maintained standard condition animal in fast condition free access to water. Hair of saved back of rabbits and mark by picric acid to identification of rabbits. One side control plane gel applied while other side test formulation applied rabbits. Formulation of microsp sponge applied twice a day for 7 days. Site observed for any sensitivity like edema , erythma or redness.

**Table 1. Applications of Microsp sponge.**

Active agents	Applications
Rubefaciants	Prolonged activity with reduced irritancy greasiness and odor.
Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization
Anti-inflammatory e.g. hydrocortisone	Long lasting activity with reduction of skin allergic response and dermatoses
Antifungals	Sustained release of actives
Antidandruffs e.g. zinc pyrithione, selenium sulfide	Reduced unpleasant odor with lowered irritation with extended safety and efficacy.
Antipruritics	Extended and improved activity.
Skin depigmenting agents e.g. hydroquinone	Improved stabilization against oxidation with improved efficacy and aesthetic appeal.

**Marketed products using Microsponge Delivery System<sup>5</sup>****Retin-A-Micro:**

This product is marketed by Ortho-McNeil pharmaceutical, Inc.

**Sportscream RS and XS:**

Embil Pharmaceutical Co. Ltd is the manufacturer of this product

**Carac cream:**

Dermik Laboratories, Inc., USA is the manufacturer of this product.

**Lactrex<sup>TM</sup> 12% Moisturizing Cream:**

SDR Pharmaceuticals, USA is the manufacturer of this product.

**EpiQuin Micro:**

This product is marketed by SkinMedica, Inc.

**Table-2. Marketed formulations of Microsponge.**

Product name	Manufacturer	Advantages
Retinol cream	Biomedic	Microspongesystem helps to maximize retinol dosage while reducing the possibility of irritation. Retinol is a topical vitamin A deriva-tive which helps maintain healthy skin, hair and mucous membranes.
Dermalogica Oil Control Lotion	John and Ginger Dermalogica Skin Care Products	Microsponge technology has exclusive skin response complex soothes and purifies, provides effective skin hydration, without adding excess oil.
Oil free matte block spf20	Dermalogica	Microsponge technology absorbs oil, maintaining an all-day matte finish and preventing shine without any powdery residue. Oil free formula contains soothing Green Tea to help calm inflammation caused by breakouts. Contains no artificial fragrance or color.

**Conclusion:**

The microsponge delivery system is unique, porous, polymeric and controlled delivery system useful for topical delivery. MDS was developed in 1980s to fill the void and use for disease condition. They are very simple and practical to use because they can be incorporated into conventional dosage form such as creams, gels, and lotions and more

patient compliance. Microsponge drug delivery reducing the possible side effects such as irritation, erythema and over drying and reducing drawback associate with conventional formulation. It facilitates the development of novel product forms.

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