IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

MICROSPONGES as novel DRUG DELIVERY SYSTEM

Author: Omkar Dnyaneshwar Phopse.
Co-Author: Rutuja Suryakant Ingle.

Abstract:

Microsponges are polymeric, porous microspheres that are typically used for long-term topical application. Microsponges are used to deliver a pharmaceutically active substance at a low dose while also altering drug release patterns, enhancing stability, and reducing adverse effects. In addition, they might improve drug release, reduce adverse effects, and improve stability. The versatility of the Microsponges technology makes it a useful drug delivery vehicle. Based on microscopic polymer-based microspheres, Microsponges Systems can be incorporated into gel, cream, liquid, or powder formulations to suspend or entrap a wide range of substances. The external surface is commonly permeable, permitting a supported progression of substances out of the circle. Microsponges are polymeric, porous microspheres that are typically applied topically.

Keywords: Microsponges, Transdermal Drug Delivery, Programmable Release, Applications.

Introduction:

The micro-sponges technology was first developed by Won in 1987, and the initial patent was assigned to advance polymer systems. Micro-sponge drug delivery systems (MDS) are spherical, porous, polymeric, and used for prolonged topical administration. They are so small that they feel like spherical 5.300 m objects. The pore and surface volumes can be adjusted anywhere from 0.1 to 0.3 cm3/g and 20 to 500 m2/g, respectively. They can be used to make powders, lotions, and creams because of their inert and strong resistance to shear due to their non-collapsible structure of interconnected voids. Micro sponges are made to improve stability, reduce side effects, and alter drug release profiles while also efficiently delivering a pharmaceutically active ingredient at a low dose. Pressurizing or rubbing, as well as changes in skin temperature, pH, and solubility, facilitate drug release into the skin. In today's pharmaceutical industry, the development of formulations with controlled or sustained release

drug delivery systems is the primary focus. The active ingredients in this system are contained in a carrier system that enables the drug's duration and therapeutic index to be altered.

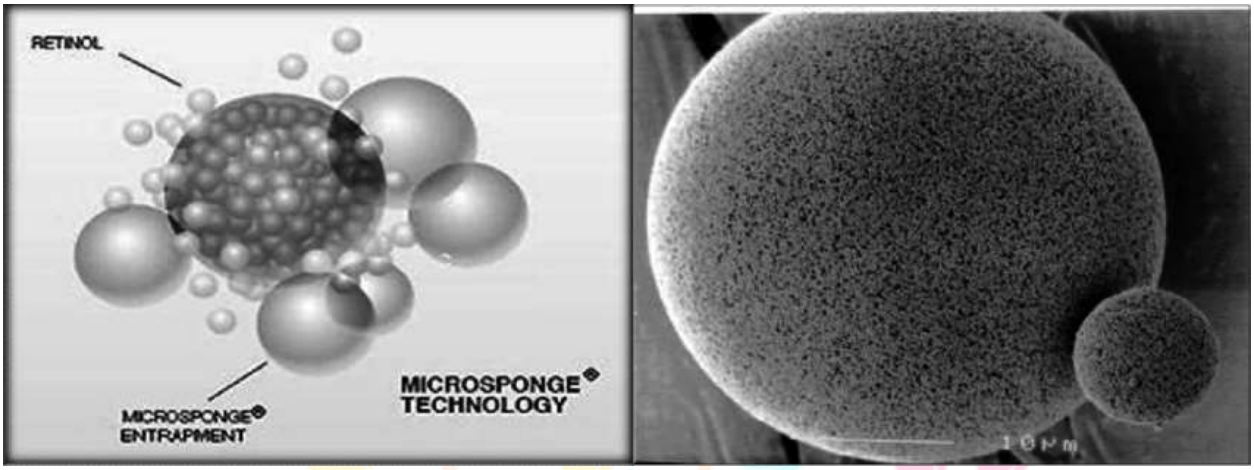

FIGURE 1: IMAGE OF MICROSPONGE

Characteristics of Microsponges:

1. The pH range of 1 to 11 and the temperature range of 130 °C are stable for the MDS system.
2. The majority of materials and vehicles are compatible with them.
3. Micro sponge formulations are self-sterilizing because of their tiny 0.25 µm pores, which prevent germs from entering.
4. Micro sponge compositions can be more economical 12 and have a greater payload (50 to 60%) while being free-flowing.
5. Microsponges are non-allergenic, non-aggravating, non-mutagenic and non-poisonous.
6. Microsponges can absorb oil up to six times their weight with out drying.
7. Microsponges can decreased infection and consequently improve affected person compliance.
8. Microsponges can enhance product overall performance.
9. Microsponges can enhance product elegancy.

Advantages over ointments:

Ointments are typically unsightly due to their greasiness, stickiness, etc., which frequently causes patients to refuse to take them. Due to their poor delivery system efficiency, these vehicles necessitate high concentrations of active drugs for effective therapy, which might produce allergic responses and irritation in substantial users. Uncontrolled evaporation of the active ingredient, an unpleasant odor, and possible drug incompatibility with the vehicles are further disadvantages of topical formulations. Microsponges systems maximize the duration

that an active ingredient is present on the skin's surface or in the epidermis, while minimizing its transdermal penetration into the body.

Advantages over conventional Formulations:

Topical medication formulations that follow conventional methods are designed to target the skin's outer layers. When these products are applied, their active ingredients come out and form a highly concentrated layer that is quickly absorbed. Comparatively speaking, the Microsponges system can stop an excessive buildup of components in the dermis and epidermis. It is possible that the Microsponges system will considerably lessen the irritation caused by medications that work well without compromising their effectiveness. For instance, MDS-Benzoyl peroxide formulations, which distribute the active component to the skin gradually, exhibit high performance while causing minimum discomfort.

Advantages over microencapsulation and liposomes:

Compared to liposomes and microencapsulation, the MDS offers advantages. Actives are typically released at a rate that microcapsules cannot regulate. The active substances inside the microcapsules will leak out once the wall breaks. Liposomes have poorer payload, challenging formulation, poor chemical stability, and unstable microbiology. Unlike the systems mentioned above, the Microsponges system is stable in a pH range of 1 to 11 and can withstand temperatures of up to 130°C. It is also compatible with a wide range of vehicles and ingredients, and because its average pore size is 0.25µm, which prevents bacteria from penetrating, it is self-sterilizing. Additionally, it has a higher payload (50 to 60%) and is still free-flowing.

Method of Preparation of Microsponges:

Initially, there are two basic methods for loading drugs into Microsponges, which vary as a pyrogen if it is genera based on the physicochemical characteristics of the medication to be loaded. A drug is referred to as a pyrogen if it is generally an inert, non-polar substance that creates a porous structure. A pyrogen medication entraps free radicals in a single stage (liquid-liquid suspension) and neither impedes nor activates the polymerization process. Initially, there are two basic methods for loading drugs into Microsponges, which vary based on the physicochemical characteristics of the medication to be loaded. A drug is referred tolly an inert, non-polar substance that creates a porous structure. A pyrogen medication is entrapped in a one-step process (liquid-liquid suspension polymerization) and is stable to free radicals. It neither impedes nor activates the polymerization process.

Preparation strategies are described as follows;

1) Liquid-liquid suspension polymerization method.

2) Quasi-emulsion solvent diffusion method.

1)Liquid-liquid suspension polymerization:

Suspension polymerization is a one-step method used in liquid-liquid systems to create Microsponges. The active components (non-polar medication) and monomers are first dissolved in a suitable solvent solution of monomer before being agitatedly distributed throughout the aqueous phase. Surfactants, dispersants, and other additives (suspending agents) are commonly included in the aqueous phase to aid in the development of suspension.

Polymerization is initiated by introducing a catalyst, increasing the temperature, or applying radiation once the suspension has formed with distinct droplets of the appropriate size. The polymerization process results in the development of a structure that resembles a reservoir and has pores that open at the surface.

In certain instances, an inert liquid that is entirely miscible with monomer but immiscible with water is utilized to build the pore network during the polymerization process. Following the completion of the polymerization process, the liquid is withdrawn, leaving the Microsponges penetrate within the manufactured Microsponges. These Microsponges subsequently contain a number of active compounds, such as antifungal, anti-inflammatory, anti-acne, and rubefacients, and function as topical carriers. Solvents can occasionally be utilized to include useful chemicals more quickly and efficiently. In the event that the medication is polymerization susceptible, a two-step procedure is employed. Under mild circumstances, the functional material replaces the pyrogen utilized to produce the polymerization.

The various steps Involved in the preparation of Microsponges are summarized as follows:

- Choose the monomer and the monomer mixture.
- As polymerization begins, chain monomers are formed.
- Chain monomer cross-linking results in the formation of ladders.
- The monomer ladder is folded to create spherical particles
- Bunches of microspheres are produced when the microspheres agglomerate.
- Bunches bind together to form Microsponges.

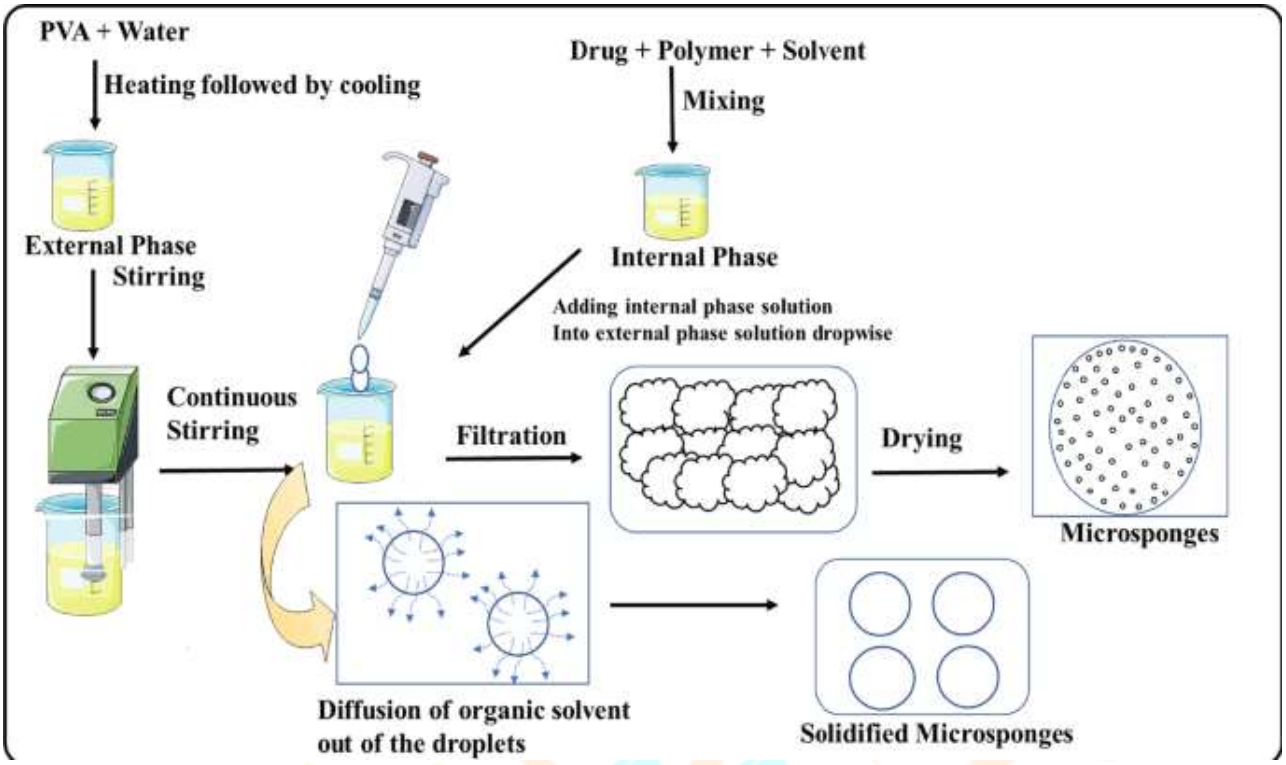

Figure 2 : Microsponges preparation by liquid-liquid Suspension polymerization.

2)Quasi-emulsion solvent diffusion:

Another method used to create porous microspheres, or Microsponges, was the quasi-emulsion solvent diffusion method, which involves two steps and an interior phase containing a polymer such as eudragit RS 100 dissolved in ethyl alcohol. After that, a plasticizer like triethyl citrate (TEC) is added to the polymer solution to help with its plasticity, and the medication is gradually added to it and dissolved under ultrasonication at 35°C. After that, the inner phase is added to the exterior phase, which is made up of distilled water and polyvinyl alcohol, and it is continuously stirred for two hours. The mixture was then filtered in order to extract the Microsponges. The product, Microsponges, was cleaned and allowed to dry for 12 hours at 40°C in an air-cooled oven.

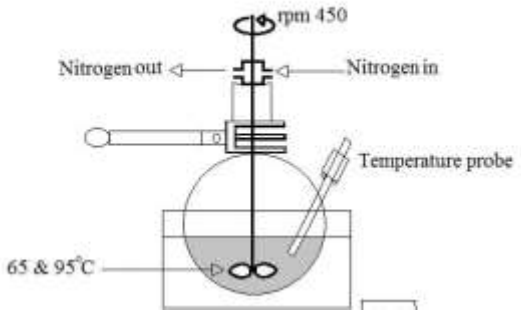

Figure3: Preparation of Microsponges by quasi-Emulsion solvent diffusion method

Release mechanism:

The previously mentioned programmable parameters can be effectively adjusted to create a Microsponges transport mechanism that releases a valuable substance gradually in response to one or more external inputs. The launch mechanism of this system is specially as observe;

A. Sustained or time release:

While pore diameter, quantity, and resilience of the polymeric Microsponges are evaluated to present significant sustained launch results, specific physiological and chemical parameters of the entrapped energetic substance along with volatility, viscosity, and solubility will be studied in the development of a sustained release Microsponges.

B. Release on command:

A Microsponges may be engineered to respond to one or more external triggers by gradually releasing the specified quantity of alive components.

1. Pressure launch:

Microsponges gadget unleash fluid or active factor when it is pressed or squeezed, there by means of replenishing the level of entrapped energetic aspect onto the skin. The quantity released may depend on the release of the sponge and the resilience of the Microsponges.

2. Temperature release:

Temperature can be used to activate the release of active substances from the Microsponges. A small number of the entrapped active substances may be too viscous at room temperature to fall off the Microsponges and onto the skin by accident. A rise in skin temperature also multiplies the drift fee, leading to an increase in release.

3. PH based totally release:

You can modify the coating at the Microsponges to initiate the pH-primarily based release of the living. pH is particularly useful in the delivery of drugs.

4. Solubility based release:

When there is water present, Microsponges containing water-miscible substances such as antiperspirants and antiseptics will become active. Diffusion, but carefully considering the factor's partition coefficient between the Microsponges and the external machine, can initiate the launch.

Physical characterization of Microsponges:

1. Particle size determination:

It is possible to analyze the particle sizes of loaded and unloaded Microsponges using laser light diffractometry or any other appropriate technique. For any formulation, the values may be stated as the mean size range. Plotting the cumulative percentage of drug release from Microsponges with varying particle sizes versus time will allow researchers to examine how particle size affects drug release. Particles bigger than 30μm

have the potential to produce a grainy texture, thus in the final topical formulation, particles between 10 and 25µm are ideal.

2. Morphology and surface topography of Microsponges:

Prepared Microsponges can be coated with gold–palladium for surface topography and morphology at room temperature in an argon environment. Scanning electron microscopy (SEM) can then be used to examine the Microsponges' surface morphology. An image of a broken Microsponges particle's ultra structure may also be obtained using SEM.

3. Determination of loading efficiency and production yield:

The loading efficiency (%) of the Microsponges can be calculated according to the following equation:

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

Precisely calculating the beginning weight of the raw materials and the final weight of the Microsponges generated will provide the production yield of the microparticles.

$$\text{Production Yield (PY)} = \frac{\text{Practical mass of microsponges}}{\text{Theoritical mass (Polymer + drug)}} \times 100$$

4. Determination of true Density:

With an ultra-pycnometer operating in helium gas, the real density of microparticles is determined by taking the mean of several measurements.

5. Characterization of pore structure:

The width and volume of the pores play a crucial role in regulating the duration and potency of the active component. The migration of the active components from Microsponges into the vehicle in which the substance is disseminated is also influenced by the diameter of the pores. To investigate the relationship between the pore width and volume and the rate of drug release from Microsponges, mercury intrusion porosimetry can be utilized. Mercury intrusion porosimetry may be used to evaluate the porosity characteristics of Microsponges, such as bulk and apparent density, average pore diameters, total pore surface area, pore size distribution, shape and morphology of the pores, and bulk and pore shape.

6. Compatibility studies:

Fourier Transform Infrared Spectroscopy (FT-IR) and thin layer chromatography (TLC) can be used to examine a drug's compatibility with reaction adjuncts. Drug crystallinity can be examined using powder X-ray diffraction (XRD) and differential scanning calorimetry (DSC) to determine the impact of polymerization. About 5 mg of

samples may be precisely weighed into aluminum pans, sealed, and heated at a rate of 15 °C per minute throughout a temperature range of 25 to 430 °C in a nitrogen environment for DSC analysis.

7. Polymer/ monomer composition:

The drug release from microspheres is controlled by variables such polymer composition, drug loading, and microsphere size. The polymer composition of the MDS can directly impact the release rate of the entrapped drug by affecting the partition coefficient of the drug between the vehicle and the Microsponges system. A useful method for studying drug release from Microsponges systems with varying polymer compositions is to plot the cumulative percentage of drug release versus time.

8. Resiliency (viscoelastic properties):

In order to create beadlets that are either softer or harder depending on the requirements of the final formulation, the resilience of Microsponges can be changed. The rate of release is usually slowed down by increased cross-linking.

9. Dissolution studies:

A modified basket made of 5μm stainless steel mesh can be used with the dissolution equipment USP XXIII to study the dissolution profile of Microsponges. There has a 150-rpm rotational speed. In order to guarantee sink conditions, the dissolving medium is chosen while taking the solubility of the actives into account. At different times, samples from the dissolving media can be examined using an appropriate analytical technique.

10. Kinetics of release:

To determine the drug release mechanism and to compare the release profile differences among Microsponges, the drug released amount versus time was used. The release data were analyzed with the following

Mathematical models:

$Q = k_1 t^n$ or $\log Q = \log k_1 + n \log t$ …. (3)

Where Q is the amount of the released at time (h), N is a diffusion exponent which indicates the release mechanism, and K1 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. (4), which may be considered a simple, Higuchi type equation.

$Q = k2t^{0.5} + C$ ……. (4)

Eq. (4), for release data dependent on the square root of time, would give a straight-line release profile, with k2 presented as a root time dissolution rate constant and C as a constant.

Applications of Microsponges:

Microsponges delivery methods improve the safety, efficacy, and aesthetics of topical prescription, OTC, and personal care items. Topical Microsponges systems are used in three ways in products now in development or on the market:

1. As reservoirs gradually release active ingredients over time
2. Useful for absorbing unwanted substances, such as excess skin oils.
3. As closed packing containers preserving substances away from the skin for superficial movement

Traditional products often include high concentrations of active ingredients, which can be absorbed unexpectedly by the skin. Overmedication often leads to a period of undertreatment until the next software is used. Active chemicals may cause rashes and other negative effects as they quickly permeate the skin. Microsponges technology allows for longer release of active ingredients, potentially reducing adverse effects while maintaining therapeutic efficacy.

In topical drug delivery

A number of factors, including pressure or rubbing, temperature changes, pH, and solubility, can help a medication release into the skin.9. Melanosponge-α, a kind of Microsponges that act as sunscreens, contains genetically modified melanin that is equally distributed to offer protection against UV-A and UV-B rays 46. A corticosteroid called fluocinolone acetonide (FA) is mostly used in dermatology to lessen skin inflammation and irritation.

In oral drug transport

Medications that are not particularly soluble in water are made more soluble in the oral drug delivery system by trapping them in the pores of MDS. The medication is reduced to minute particles by the small holes in the Microsponges, which increases the surface area and, thus, the solubility. The medication in the Microsponges is housed in a protected environment that allows for regulated transport of the medication to the gastrointestinal tract (GI tract), where it is released when the colon's particular enzymes come into contact with it. Furthermore, the MDS system lengthens the drug's GI retention period, which improves absorption.

In bone tissue engineering

Pre-polymerized polymethyl-methacrylate and liquid methyl methacrylate monomer powders are combined with two aqueous dispersions of calcium-deficient hydroxyapatite (CDHA) powders and a-tri calcium phosphate (a-TCP) grains to create the Microsponges for the bone replacement product. A collagen sponge sheet containing fibroblast growth factor (bFGF) showed dose-dependent local angiogenic activity and sustained release in the mouse subcutis based on the sponge matrix's biodegradation 51. In order to facilitate the regeneration

of autologous artery tissue during cardiovascular tissue transplantation, a biodegradable graft material comprising collagen Microsponges was created.

Long-Lasting Colored Cosmetics:

The use of micro-sponges in the formulation of colored cosmetics, such as rouge or lipsticks, results in more even distribution and better coverage, making the items extremely elegant.

In cardiovascular engineering:

The process of utilizing autologous mobile seeding with a biodegradable cloth is intricate and intrusive, and it carries a risk of contamination. The development of a biodegradable graft material with collagen Microsponges that might enable the regeneration of autologous vascular tissue has been necessary to prevent these issues. This fabric's ability to speed up in situ cellularization using smooth muscle and autologous endothelial cells was evaluated both with and without precellularization. Poly (lactic-co-glycolic acid) as a biodegradable scaffold turned into compounded with collagen Microsponges to shape a vascular patch material. These polys (lactic-co-glycolic acid) collagen patches with (n=10) or without (n=10) autologous vessel cellularization were used to patch the dog pulmonary artery trunk. Histologic and biochemical assessments had been done 2 and 6 month after the implantation. There was no thrombus formation in either institution, and the poly (lactic-co-glycolic acid) scaffold changed into nearly completely absorbed in both corporations. Histologic outcomes confirmed the formation of an endothelial cellular monolayer, a parallel alignment of smooth muscle cells, and reconstructed vessel wall with elastin and collagen fibers. The cell and extracellular additives in the patch had multiplied to ranges similar to those in native tissue at 6 month. This patch shows promise as a bioengineered material for selling in situ cellularization and the regeneration of autologous tissue in cardiovascular surgery.

TABLE1: Application of different active ingredients in Microsponges formulation.

Sr. No.	Active ingredients	Application
1	Anti-inflammatory e.g. hydrocortisone	Prolonged activity with reduction of skin allergic response and dermatoses
2	Anti-acne e.g. Benzoyl peroxide	Maintained efficacy with reduced skin irritancy and sensitization
3	Skin depigmenting agents. g. hydroquinone	Enhanced stability against oxidation with improved efficacy and aesthetic appeal
4	Antipruritic	Extended and improved activity

5	Anti-dandruffs e.g. zinc pyritino, selenium Sulfide	lowered unpleasant odor with decreased irritation with enhanced safety and efficacy
6	Rubefacients	prolonged activity with reduced irritancy greasiness, and odor
7	Anti-fungal	Sustained release of actives
8	Sunscreens	Prolonged product efficacy, with improved protection against sunburns and sun-related injuries even at high concentration and with decreased irritations and sensitization

Table 2: Example of MDS with their formulation:

MDS	Drugs	Disease treatment
Gels	Benzoyl peroxide	Anti-acne Treatment
	Fluconazole	Anti-fungal
	Diclofenac sodium	Anti-inflammation
	Terbinafine HCL	Anti-fungal
Lotions	Benzoyl peroxide	Anti-acne Treatment
Creams	Hydroquinone and Retinol	Melanoma
Other	Ibuprofen	NSAID
	Mefenamic acid	Rheumatoid arthritis

Table 3: Marketed formulations of MDS

Product Name	Active Ingredient	Treatment	Manufacturer
Retin-A-Micro	0.1% and 0.4% tretinoin in an aq. gel.	Acne vulgaris	Ortho-McNeil Pharmaceutical, Inc.
Creak Cream, 0.5%	0.5% fluorouracil	Actinic Keratoses (AK).	Dermic Laboratories, Inc. Berwyn, PA 19312 USA.
Oil Control Lotion	Natural antibiotics	Acne-Prone, oily skin conditions.	Fountain Cosmetics.
Ultra Guard	Dimethicone	Protect a baby's skin from diaper rash.	Scott Paper Company.
Salicylic Peel 20	Salicylic acid 20%	Improve fine lines,	Biophora

		pigmentation and acne concerns.	
Salicylic Peel 30	Salicylic acid 30%	Improve fine lines, pigmentation and acne concerns.	Biophora
Lactrex™ 12% Moisturizing Cream	12% lactic acid as the neutral ammonium salt, ammonium lactate.	Long lasting moisturization.	SDR Pharmaceuticals, Inc., Andover, NJ U.S.A. 07821.
EpiQuin Micro	Retinol and Hydroquinone	Minimize skin irritation, Reduce age spot, sun spot etc.	Skin Medica Inc.
Line eliminator Dual Retinol Facial Treatment	Retinol (vitamin A)	Diminish wrinkle, appearance of fine lines etc.	Avon
Sport scream RS and XS	Topical analgesic, anti-inflammatory and counterirritant.	Management of Musculoskeletal conditions.	Embil Pharmaceutical Co. Ltd.
Micro peel plus / Acne peel	Salicylic acid in forms of Microcrystals.	Remove all dead cells doing no damage to skin.	Biomedic.

Reference:

I. Patel A, Upadhyay P. Microsponges As The Versatile Tool For Topical Route: A Review. Int J Pharm Sci. Res. 2012;3(9): 2926- 2937.

II. Shaha V, Jain H. Microsponge Drug Delivery: A Review. Int J Res Pharm Sci. 2010;1(2):212-218.

III. Yerram C, Shaik F, Rubia Y. Microsponges: A Novel Drug Delivery System For Controlled Delivery of Topical Drugs. Int J Pharm Res. 2012;2(2):79-86.

IV. Ravi R, Senthilkumar Sk. Microsponges Drug Delivery System: A Review. Int J Pharm Rev Res. 2013;3(1):6-11.

V. Nacht S, Kantz M. The Microsponge: A Novel Topical Programmable Delivery System. 1992;42:299-325.
Available at:
http://www.microsponge.com/Technology.aspx

VI. Amrutiya N, Bajaj A, Madan M. Development of Microsponges for Topical Delivery of Mupirocin. AAPS PharmSciTech 2009;10(2):402-408.

VII. Yazici E, Kas HS, Hincal AA. Microsponges. Farmasotik Bilimler Dergisi (Turkey) 1994;19(3):121-128.

VIII. Vyas SP, Khar RK. Targeted and Controlled Drug Delivery-Novel Carrier System: New Delhi: CBS Publication, First edition; 2002:453.

IX. Shah VP. Determination of In-vitro Release from Hydrocortisone Creams. International Journal of Pharmaceutics 1989;53:53-59.

X. shantanu Kaity, Sabyasachi Maiti, Ashoke Kumar Ghosh, Dilipkumar Pal, Animesh Ghosh and Subham Banerjee. Microsponges: A novel strategy for drug delivery system: A Review. J Adv Pharm Technol Res. 2010 Jul-Sep; 1(3): 283–290.
Available at:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255415/

XI. Lendave A. S., "Microsponge Technology for Innovative Drug Delivery System", International Journal of Scientific Research in Science and Technology (IJSRST), Online ISSN : 2395-602X, Print ISSN : 2395-6011, Volume 7 Issue 5, pp. 63-75, September-October 2020. Available at doi : https://doi.org/10.32628/IJSRST207521
Journal URL : http://ijsrst.com/IJSRST207521

XII. Cross S. E., Roberts M. S., Subcutaneous Absorption Kinetics of Interferon and Other Solutes, J Pharm Pharmacol., (1993); 45: 606-609.

XIII. Shaha V, Jain H, Jethva K. “Microsponge drug delivery”. Int. J. Res. Pharm. Sci. 2010; 1(2): 212-218.

XIV. Emanuele A. D., Dinarvand R., Preparation, Characterization and Drug Release from Thermo Responsive Microspheres, Int J Pharm., (1995): 237-242.

XV. Aritomi H, Yamasaki Y, Yamada K, Honda H, Koshi M. Development of sustained release formulation of chlorpheniramine maleate using powder coated microsponges prepared by dry impact blending method. Journal of Pharmaceutical Sciences and Technology 1996;56(1):49-56.

XVI. Vyas SP, Khar RK. Targeted and Controlled Drug Delivery-Novel Carrier System: New Delhi: CBS Publication, First edition; 2002:453.

XVII. Kilicarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres; International Journal of Pharmaceutics 2003;252:99-109.

XVIII. Amrutiya N, Bajaj A, Madan M. Development of Microsponges for Topical Delivery of Mupirocin. AAPS PharmSciTech 2009;10(2):402-408.

XIX. Monteiro-Riviere NA, Wiench K, Landsiedel R, Schulte S, Inman AO and Riviere JE: Safety evaluation of sunscreen formulations containing titanium dioxide and zinc oxide nanoparticles in uvb sunburned skin. An In-vitro and in-vivo Study. Toxicological Sciences 2011; 123: 264-80

XX. Paula T: Nucleic acid particles, methods and use there of 2015; US9737557B2.