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Review Article

## Microsponges: A Novel Strategy to Control the Delivery Rate of Active Agents with Reduced Skin Irritancy

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### ABSTRACT

Microsponges are particulate system which is composed by porous polymeric material. As compare to Conventional topical formulations, microspoonge provide controlled release of the drug in the epidermis, it is to ensure that the drug is mainly localized and does not unduly entering the systemic circulation, it is a new area of research. The active ingredient needs to maximize the time to stay on the skin, while reducing transdermal penetration. Apart from this, there is a problem of unethical vehicles that can be viscous sticky deformation and skin irritation. One of the biggest challenges of now a days is to control irritability for a predetermined site of active agents in the human body. Microsponges delivery system is a unique technique for controlled release with low irritant involving many triggers of Mechanism for the release of drugs. The Microspoonge Delivery system is a polymeric porous microspheres, which can trap a wide range of effective elements such as anti-fungus, anti-infected, anti-inflammatory agent, fragrance and essential agent. This review includes different techniques used to prepare microsponges, formulation consideration, safety consideration, drug release mechanism, and challenges with microspoonge drug delivery system along with their advantages, disadvantages and applications. In the current review, we summarize the updated application and capacity of Microspoonge as an effective drug-delivery system to reduce skin irritation.

**Keywords:** Microsponges; quasi-emulsion solvent diffusion; Porous microspheres; Controlled release.

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## 1. INTRODUCTION

All conventional topical formulations are work on the outer layers of the skin. When the active ingredients of these formulations are released after application, an extremely concentrated layer of active ingredient is fashioned, that is speedily absorbed. Thus, there is a rightful require for drug delivery systems to prolong the time so that active ingredients can be retained on the surface of the skin or abandoning transdermal penetration within epidermis. In addition, as a result of high concentration of active agents in traditional topical dosage forms, many side effects are recorded such as irritation and allergic reactions [1]. The additional potential limitation of topical conventional formulations is uncontrolled evaporation of the active ingredient, unethical vehicles that are sleek, sticky and discoloration, and drugs may be cause the discrepancy with vehicles. This reduces the compliance of patients' treatment [2]. One of the biggest challenges for pharmaceutical science is to control the distribution rate of active ingredients in a human body on a predetermined site, to control the release of the drug in epidermis, ensuring that the drug is mostly localized and does not enter unnecessarily in systemic circulation, [3]. The scenario of drug delivery technology has

become very enthusiastic and is developing rapidly. The greater development in the delivery system is being integrated to optimize the effectiveness and cost effectiveness of the medicine [4]. In the last few years, there has been a significant growth in the number of products based on the new drug delivery system, for improving safety, efficacy and patient compliance has been achieved by incorporating an existing drug into a new drug delivery system [5].

Carrier technologies are a possible solution to these challenges. Microparticles and nanoparticles have been researched rapidly for targeted and continuous release of drugs. It includes microspheres, liposomes, and nanoparticles, which modify the absorption and release characteristics of drugs. Microspheres are unable to control the drug's release rate manually. Once the outer wall is broken, the drug contained in Microspheres will exit from it [6]. In liposomes, fluttering of lesser drugs, difficulty in preparing deformities, limited chemical stability and microbial stability worsens, hence the need of the preservatives. In solid lipid nanoparticles, there are more benefits in topical drug delivery. Nanomaterial can easily enter systemic circulation by inhalation or injection, and probably through skin

absorption, especially if the skin is damaged [7]. Only once in the bloodstream, nanomaterials can be taken almost in the body and taken by the limbs and tissues including the brain, heart, liver, kidney, spleen, bone marrow and nervous system. Micro-sponge-based polymeric microsphere helps overcome problems related to superior technologies. Compared to conventional method, the microscope system can stop epidermis and excessive accumulation of material within the skin [8]. Furthermore, the MDS can reduce the irritation of skin irritating drug without reducing the effectiveness of the system. For example, MDS-benzoyl peroxide formulations have a minimal irritation by gradually delivering the active ingredient to the skin [9].

## 2. MICROSPONGES DELIVERY SYSTEM (MDS)

### 2.1 Overview of microsponges

Microsponges Delivery System (MDS) is porous, cross-linked, polymeric microspheres, polymeric systems, which include porous microsphere, which can entangle a wide range of drug and then release them into skin at one time and in response to trigger". Microsponges technology was developed In 1987, Won pioneered micro sponge system (MDS) technology, These patents include Advanced Polymer Systems, Inc. (United States) [10]. Microsponges are small sponges, like circular particles, in which there is no processed structure with a large cough surface through which the active ingredient is released in a controlled manner. The size of the microscope ranges from 5-300 $\mu$ m in diameter and in a specific 25 $\mu$ m area, the spacing of up to 250000 pores and an internal pore structure can be equal to 10 feet length, making it almost 1ml / gram for all embracing drug retention. The surface can be separated from 0.1 to 0.3 centimeters / grams in quantity of 20 to 500 m / g and 2 pore [11].

The Scanning electron microscopy of micro sponge particles shows that its internal structure is "bag of marbles". It is a unique technique for controlling release of topical agents, in which microporous pearls are normally 10-25 microns in diameter, loaded with active ingredients, which in turn result in them in a controlled manner into the skin at a time, including triggers rubbing, pH, friction moisture and ambient skin temperature [9]. When it is applied to the skin, drug release can be controlled through spread. This controlled release of active ingredient on the skin at the time has been done to provide enhanced product efficacy, tolerance, benignity benefits, and to reduce the irritability associated with powerful therapeutic agents such as retinoid or benzyl peroxide and the range of a comprehensive skin therapies [12].

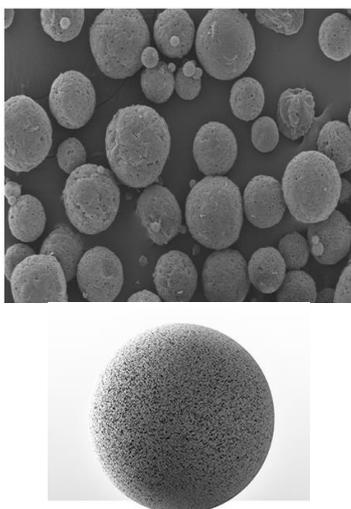


Fig 1: Structure of Microsponge

Microsponges have the ability to absorb or load high volume of active ingredients on the particle or its surface. Microsponges separate from other types of dermatology delivery systems, the ability to be active to activate its intensity up to 3 times. In the distinction, Micro-sponge technology allows a flat and constant rate of release, which reduces irritation in maintaining efficacy. Microsponges are able to absorb the secretion of the skin, so the skin glows down and shines from the skin [12]. MDS can prevent accumulation of ingredients within the skin. Potentially, they can reduce the irritation of skin irritating drugs, without reducing their efficacy [13]. Another advantage is the potential bacterial contamination of the material entrapped in the microsponge since the size of the pore diameter is lighter, the bacteria from 0.007 to 0.2 microns cannot penetrate into the digging structure of the microsponges[12]. Due to the trapping of drug molecules within the microscopic holes, the rate of solubilization of poorly water-soluble drug becomes improved. When the drug molecules are trapped in the pores, then the particle size is shortened due to the small aperture size (~ 0.07-0.25  $\mu$ m). As the particle size decreases, its surface area increases, which leads to increased drug solubility [14].

Micro-sponge drug delivery technology is far and wide for dermatology drug delivery products. But Micro-sponges drug delivery also extends its application in oral drug delivery, bone and tissue engineering in the investigation of illness and RNAi silencing [15].

Recent applications from Microsponges obtained from seaweed can help in the diagnosis of cardiovascular disease, cancer, HIV and other diseases, and a lot less cost than current diagnostic methods. Biomarkers are hidden in small sponges set in an array of pyramid-shaped funnels in the heart of the PBN microprocessor, which is in the shape of a credit card [16].

Nowadays, many Food and Drug Administration (FDA) - approved products such as Retin-A Micro® (0.1 or 0.04% tretinoin) and Carac (0.5% 5- fluorouracil) are used for acne treatment and actinic keratos [17].

### 2.2 Potential feature of Microsponges drug delivery system [18, 19].

- MDS are unbreakable on the range of pH 1-11.
- They are mostly affiliates with vehicles and excipients.
- Microsponges have increased the efficiency of trapping by 50 to 60%.
- They flow freely and are cost effective and have more sense of flexibility.
- Due to self-sterility, their average pore size is around 0.25 microns, while bacteria cannot Infiltration in the pores.
- These particles are deployed in the shape of the skin absorbing.
- Microsponges are microscopic spheres able to absorb skin secretion, therefore, to reduce oiliness and shine with skin.
- Microsponges formulation can absorb 6 times the weight of oil without drying.
- It provides 12 hours of continuous action, i.e. extended release.
- Microsponges are non-allergic, non-irritating, non-metagenic and non-toxic.

Microsponges particles themselves are very large, so they are complex to absorb in the skin and this protects these Microsponges materials by avoiding the side effects microsponges adjuncts. Microsponges formulations can also be cost effective for the use of cosmetic mass market

where the cost of materials is important [20]. Inequalities for other technologies like microencapsulation and liposomes, chemical stability in MDS, a wide range of high payloads and easy to prepare [21].

### 2.3 Advantages of micro sponge delivery systems [16, 22, and 23].

**Table 1: Advantages of micro sponge delivery systems**

S.No	Advantages	Comments
1.	High Surface Area	The total pore length of approximately 10 feet in 25 $\mu$ sphere can be around 1 mg / gram with the amount of quantity and can have up to 25,000 pore. It provides a broad surface area to trap high.
2.	Range	Microsponges can be prepared to regulate their properties and make them suitable for an accurate purpose. Various parameters can be converted into which particle size, pore characteristics and hardness are included.
3.	Simple Production Methodology	Production of such Microsponges is comparatively simple in scaling up and therefore has an advanced capacity for commercialization.
4.	Programmable Release	Pressure Triggered Systems Temperature Triggered Systems pH Triggered Systems Solubility Triggered Systems
5.	Safety of microsponges	Most of the polymers used in formulation are inactive and inability to cross through stratum corneum, their inability to increase their safety, apart from this, reduces the irritation of various actives and thus indicates its harmlessness.

**Table 2: - Advantages of Microsponges over Other Formulations**

S.No	Advantages	Other Formulations	Microsponges formulation
1.	Advantages over Conventional Formulations	Conventional formulation actively produce a highly concentrated layer of active ingredient, which are rapidly absorbed.	MDS can prevent excessive accumulation of drugs within the skin. Potentially, the MDS can reduce the irritation of skin irritating active ingredient without significantly reducing their efficacy [9]s.
2.	Advantages over Microencapsulation and Liposomes	Microcapsules cannot do more often than controlling the release rate of activation. Once the wall is broken the activations contained within the microcapsules will be unconstrained.	In the inequality for Microencapsulation and Liposomes system, the Microsponges system prevents these limitations [9, 24].
3.	Advantages over Ointments	Ointments are often invisible, sleek and sticky from aesthetics, which often occur in lack of patient adherence. These vehicles require high concentrations of active agents for effective treatment because their delivery system has less efficiency, causing significant users to have irritation and allergic reactions.	The microscope system increases the maximum amount of time, which is an active ingredient on the skin surface or in epidermis, while reducing its transdermal penetration in the body [12, 25].

### 2.4 Category of drugs Explored in microsponges delivery system [26].

- Anti-Inflammatory
- Anti Fungals
- Anti-Acne
- Anti-Dandruffs
- Skin Depigmenting Agnts
- Sunscreens

- Antipruritics
- Rubefacients

### 2.5 Drug release mechanism of microsponges

Microsponges contain a large amount of porous microspheres, which have a complex network of interconnection with a non-compressed structure. The active ingredient is added to the trapped form in the vehicle. Once formulation is applied to the preferred area of the skin, the active ingredient spreads out of the spheres into vehicles and then on the skin, reduces the vehicle, which becomes

unsaturated, therefore, disturb the equilibrium. It will start the flow of particle from the micro-sponge into the vehicle, and from it to the skin, until the vehicle is dry or absorbed [12]. Even then, microsponge particles retaining to the surface of the stratum corneum will continue to activate the skin gradually, which will release over time for a long time. This proposed mechanism of action demonstrates the importance of building vehicles to trap micro-sponges. If the

active product is very soluble in their favorite vehicle during preparation, then the products will not get the desired benefits of release [12]. As a replacement, they will behave as active microsponge may intend to release active elements in quantity over time, in response to one or more of the following external triggers added in the vehicle in an open form. Pressure, temperature change and solubility etc [4].

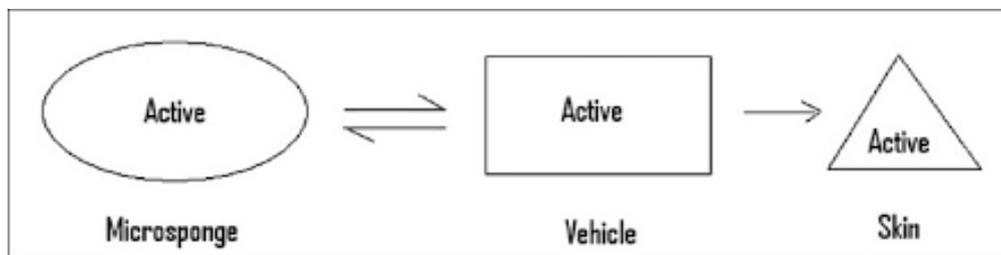


Fig. 2 Drug release from microsponge

### 2.5.1 Release triggers [14].

The release trigger is defined as a mechanism, which can be used to release or accelerate active agents from MDS. These mechanisms are given below:

Table 3: Drug release mechanism of microsponge

S.No	Release triggers	Drug release mechanism
1.	Pressure triggered systems	Rubbing or pressure is applied to the active ingredient can release from the microsponges into the skin.
2.	pH triggered systems	The coating on microsponges can be modified by triggering the pH-based release of activation.
3.	Temperature change triggered systems	At room temperature, some trapped active ingredients can be viscous to the sudden flow of the skin from the microsponges.
4.	Solubility triggered systems	Microsponges loaded with water-sweeping materials such as antiseptics and antiperspirants will issue components in the presence of Water.

### 2.6 Formulation considerations

Action taken in microsponges drug distribution system can then be included in many products like as lotions, creams, soaps and powders. While preparing the vehicle, certain ideas are taken into consideration to achieve the selected product characteristics. Solubility of the active ingredients in the vehicle should be limited. If not the vehicle will reduce the activity of microsponges before the application [9]. To avoid cosmetic problems; in the vehicle more than 10% to 12% w / w microsponges should not be included. For active microsponges polymer designs and payloads should be optimized for the required release rate for the given time. When preparing suitable vehicles for a given application, some ideas should be kept in mind to achieve the desired product characteristics [27].

To prevent cosmetic problems, the powder load should be sufficient (not more than 10-12%) in the vehicle [28].

- The solubility of the active agent in the vehicle should be restricted; otherwise, the skin will actually reduce the polymer before it is applied to the skin.
- Polymer design and loading levels should be properly selected for the release of active agent during the given period.

### 2.7 Characteristics of materials that are entrapped in Microsponges [2, 29, 30]

- The materials should be erasable in water or should be slightly soluble.
- The material must not react with monomers and should maintain the viscosity of the mixture during preparation.
- In Monomer, the material should be fully miscible, as well as the miscible with small amounts of water, besides the immiscible solvent.
- The material should not break the spherical structure of the microsponges.
- Polymerization catalyst as well as in the conditions of polymerization, the material should remain constant.
- The active ingredient is trapped in microsponge then such products can be included in many products such as cream, gels, powder, lotions and soap.
- To avoid cosmetic problems, the solubility of activators in the vehicle should be limited; in the vehicle more than 10% to 12% w / w microsponges should not be included. Otherwise the vehicle will reduce microsponges before the application.

- Microsponges payloads and polymer designs should be optimized for the required release rate for the given period.

## 2.8 Safety considerations

Microsponge systems are made of famous used polymers with very low amounts of outstanding monomers, in addition, the high degree of cross-linking biologically disables them, as the body cannot biodegrade to reproduce them in other substances [31]. Animal statistics show that, after injection into the skin, MDS does not respond to any swelling by the body in response to its presence. Due to their size, these microspheres are very large, which pass through the stratum corneum. They are staying behind the surface of the skin, gradually releasing their material over time. This release pattern prevents excessive accumulation of active agents in epidermis and as a result, can increase the safety of topical drugs [32].

## 2.9 Method of Microsponges preparation

In the microsponges the drug loading can be done in two ways with one or two-stage process; for loading on the basis of physical-chemical properties of the drug [33]. If the drug is usually an inactive non-polar material, then it makes the porous structure fashionable, which is called porogen. Porogen drug, which neither interrupts polymerization nor activates it and stable for free radicals is entrapped with one-step process [9, 34].

## 2.10. Liquid-liquid suspension polymerization

The liquid-liquid suspension polymerization method is easily method for preparation of microsponges (one-step process). Polymerization done in the round bottom flask of styrene or methyl methacrylate. In their preparation, Non-polar active ingredients are dissolved with monomer in a suitable solvent immediately possible and then dispersed in aqueous phase this includes additives such as surfactant, suspended agents, etc. assistance in the formation of suspension. Once identified with the different droplets of the desired size after the suspension, polymerization is activated by monomer stimulant or increased temperature or radiation [35].

The various steps of microsponges preparation are summarized as follows: [36].

- Monomer selection or monomer combination.
- Monomer chain formation as polymerization begins.
- Ladders formations as a result of cross linking between chain monomers.
- Monomer ladder folding to form spherical particles.
- Microspheres agglomeration, which give rise to formation of bunches of microspheres.

- Microspheres bunch binding to form microsponges. [37].

In some cases, an inactive liquid with water is invisible, but it is used to create pore network during the completely erodable environment with monomers. After the conclusion of polymerization, the fluid is released to the porous microspheres, that is, the microsponge. Regression within the preformed microsponges, then include functional substances [25].

**Advantages:** For drug loading one-step or two-step methods can be modified appropriately.

**Disadvantages:** Possible trapping of unreacted monomers and solvent traces, monomers require long time to react to non-uniform structure; requires two-step methods for thermodynamic sensitive drugs require less drug-loading capability.

### 2.10.1. Quasi-emulsion solvent diffusion

In quasi-emulsion solvent diffusion method (two steps process), of microsponges formulation an internal phase is used containing polymer such as eudragit RS100, which is dissolved in ethyl alcohol and external phase include polyvinyl alcohol and distilled water [38].

Different steps have been summarized in the preparation of microsponges by quasi-emulsion solvent diffusion method: [24].

- The internal phase which containing polymer such as eudragit RS 100 dissolved in ethyl alcohol.
- The drug is gradually added to internal phase (polymer solution) then dissolved under ultrasonication at 35°C and added plasticizer such as triethylcitrate (TEC) in order to aid the plasticity.
- The external phase which containing polyvinyl alcohol dissolved in distilled water.
- The internal phase is then poured into external phase (polyvinyl alcohol and distilled water) with continuous stirring for 2 hours.
- Then, separate the microsponges after mixture filtered.
- The microsponges washed and dried in an air heated oven at 40°C for 12 hr [37].

**Advantages:** No monomer entrapment, Low solvent traces, High drug loading, No exposure of drug to ambient condition, Size of microsponges can be easily controlled by controlling the stirring, Spherical particles.

**Disadvantages:** Probable entrapment of unreacted monomers and solvent traces, Non uniform structure, requires a long time for the reaction of monomers, requires two-step method for thermo sensitive drugs that has low drug-loading efficiency.

**Table 4: Characterization parameters of microsponges:**

Characterization parameter	Methods	Remarks
Particle size determination of microsponges	Microscopy diffractometry method used for Particle size analysis of loaded and unloaded microsponges. To study the effect of particle size on drug release, cumulative percentage drugs should be issued from time to time with various particle size microsponges.	For all formulations, the value of 50% size can be used as the mean size range [20].
Morphology of microsponges	Internal and external morphology can be studied by scanning electron microscopy (SEM).	The prepared microsponges are coated with gold-palladium under the argon atmosphere at room temperature and then studied [39].
Production yield of microsponges	Production yield of micro particle can certainly be achieved by calculating the initial weight of raw material and can be done based on the final weight of the microsponges obtained.	Production yield = [Practical mass of microsponges/Theoretical mass (polymer + drug)] × 100 [40].
Entrapment efficiency of microsponges	Loading efficiency of drug determine by Drug extraction Method.	Entrapment efficiency (%) = [Actual drug content/Theoretical Drug content] × 100 [41].
Pore structure of microsponges	For controlling the power and duration of the effectiveness of the active ingredient the pore volume and diameter are important. The pore diameter affects the active component of the micro-sponge in the vehicle in which the material is dispersed. Mercury intrusion can be employed to study the effect of pore diameter and quantity with drug release rate from porosimetry microsponges.	Pore structure is determined by Using Washburn [42].
Resiliency of microsponges	According to the requirements of the final formulation, the flexibility of microsponges can be modified to produce soft or firmer beadlets. The rise in cross-linking reduces the rate of release.	No optimized method has been developed to determine the Resiliency of the micro particles [43].
Drug content of microsponges	Drug content in microsponges determine by Drug extraction Method.	These carriers have better drug loading, thus they provide better drug content [44].
Drug release study of microsponges	Drug release study in microsponges determine by USP apparatus II.	When studied for oral use, the rotation speed is 100 rpm; Temperature is maintained at 37 ± 0.5 ° C on various physical pH for a fixed time period [45].

## 2.11 Applications of microsponges system

Microsponges are mostly used for topical delivery and are used for oral and simultaneous biopharmaceutical delivery. Many patents have reported that due to its high loading capacity and continuous release capacity it can be used as an excipient. This formulation offers many options for developing pharmaceutical and cosmetic products [12]. Microsponges are deliberately able to give a drug active ingredient in a minimal amount efficiently and increase stability, reduce side effects, and modify drug releases. Over-the-counter products that include the micro-sponge drug delivery system include many moisturizers, special renaissance products and sunscreens [25].

### 2.11.1 Microsponge for topical delivery

The purpose of topical formulations is to provide drug to the outer layers of the skin. Conventional topical formulations producing an extremely concentrated layer of active ingredient in skin that is speedily absorbed [12]. However, micro sponge systems are deliberately able to efficiently deliver a drug active ingredient on a minimum dose. They

consist of non-organized structures with porous surfaces through which active content is released in a controlled manner. Therefore, such systems can avert unwarranted accumulation of active ingredients within the epidermis and the dermis, thus they can show that reducing irritation and side effects due to drugs without reducing their efficacy decreases [13]. In addition to improving drug release and side effects, microsponges is also capable of increasing the stability of many drugs. The drug loaded porous microsponges can be further is incorporated into cream, lotions or powder. Microsponges are used for the topical delivery of many drugs and cosmetic agents [15]. In product or market placements, product uses topical microsponges system in three primary ways: [46, 24, and 47].

- As closed containers investment ingredients away from the skin for superficial action.
- As reservoirs releasing active ingredients over an extensive period of time.
- As receptacles for absorbing uninvited substances, such as more skin oils.

Table 5: Microsponge formulation

Drugs	Comments
Dicyclomine	Eudragit based microsponges were prepared by using a quasi-emulsion solvent diffusion method, filled with Dicyclomine. The cumulative release for microsponges for more than 8 hours ranged from 59 to 86%.
Flurbiprofen	Microsponge system containing flurbiprofen was formulated for the colonic delivery of the drug for targeted action [26].
Benzylperoxide	BPO loaded Ethyl cellulose MDS was prepared which was capable to release of BPO into the skin. And it has been shown that the BPO can reduce the effect of controlled release on the skin from the delivery system, while percutaneous absorption can be reduced.
Fluocinolone acetonide	FA entrapped micro porous micro particles (microsponges) were formulated to control the release of drug to the skin, which reduces the skin irritation and produce controlled release of active medicament [26.]
Hydroquinone (HQ)	HQ 4% with retinol 0.15% entrapped in microsponge reservoirs was developed for the treatment of melasma and PIH. Microsponges were used to release HQ gradually to prolong exposure to treatment and to minimize skin irritation [12].
Aceclofenac	Aceclofenac loaded microsponge are prepared by using quasiemulsion solvent diffusion method. It is incorporated in gel base and various parameters are studied.

### 2.11.2 Microsponge Technology in Cosmetics

An exciting application of microsponge technology can be found in oral cosmetics, such as as to sustain the release of volatile ingredients, thus increasing the duration of the 'fresh feel'. Microsponges of such volatile ingredients may be effortlessly incorporated in tooth pastes or mouthwashes [36]. Microsponges may be used in a variety of coloured cosmetic products such as rouge or lipsticks to make them long lasting by using colour entrapment in microsponge. As mentioned above, Microsponges helps in dismantling uniforms and improves covering power. Thus, the colorful cosmetics prepared with microsponges will be very elegant [48].

Marketed formulation using MDS include skin products that can absorb large amounts of excess of skin oil from the surface of the skin, while the skin looks beautiful on the surface. These products include conditioners, skin cleansing, moisturizers, oil control lotions, razor, deodorant, lipsticks, powder, makeup, and eye shadow; Which provides many advantages, including improved chemical and physical stability, better available concentrations, controlled release of active ingredients, brief skin irritation and sensitization, and exclusive touch properties [49].

### 2.11.3 Microsponge for oral delivery

In oral applications, the MDS has been shown to increase the rate of solubilization of the system of poorly soluble drugs by trapping in such drugs in pores. Since this pore is very small, particles are influenced in drug and a significant increase in surface area thus increases the rate of many solubilizations [50]. It has been shown that the microsponges system enhances the solubilization of drugs,

which are poorly soluble in trapping these drugs in these pores [51].

A microsponges system gives many benefits for oral drug delivery, such as:

- Protect active ingredients in a limited environment and provide oral controlled delivery in the lower part of the gastrointestinal tract (GIT).
- Microsponges systems raise the solubility of poorly soluble drug by trapping these drugs in these porous structures.
- Since the porous structure of the microsponge is very small in size, the trapping drugs are dense for the micro particles with high surface area, and as a result, the rate of solubilization improves.
- Maximize the amount of drugs that are absorbed, as long as the microsponges system moves through the intestine to increase significantly.

### 2.11.4 Microsponges in biopharmaceuticals delivery

MDS is employed for both in tissue engineering as well as the delivery of biopharmaceuticals. Collagen microsponges have been studied with biodegradable polymers, which act as a new bioengineered cardiovascular prosthesis. Tabata *et al.* has been studied type I collagen can act as a reservoir of basic fibroblastic growth factor. Chain et al, the expansion of biodegradable porous scaffolding for tissue engineering has also been studied [52].

Table 5: List of some marketed products of microsphere drug delivery system

Product	Name Manufacturer	Advantages
Carac Cream	Dermik Laboratories, Inc. Berwyn , PA 19312 USA	Carac creams contain 0.5% fl uorouracil; Patented porous microsphere with 0.35% was included in the methyl methacrylate / glycol dimethacrylate cross polymers and dimethicon. Factors are the topical prescription product for treatment of actinic keratosis (AK), which is due to the condition of normal pre-cancerous skin, due to which the sun is caused by instability [26].
Retin-A-Micro	Ortho-McNeil Pharmaceutical, Inc.	In a retin-A-Micro 0.1% and 0.04% tretinoin, a patent was trapped in porous microsphere, which included active ingredient in aqueous gel, methyl methacrylate / glycol dimethacrylate cross-polymer to include traitinoin. This formulation is used for topical treatment of acne vulgaris [21].
Salicylic Peel 20 & 30	Biophora	Salicylic acid 20%, Micro-sponge technology has excellent exemption and is used for skin resistant to more resistant skin types. It will appreciably recover pigmentation, fine lines and acne concerns. Salicylic acid runs effortlessly throughout Pierce, while reducing inflammation they are taken out. This treatment effectively protects acne from the amazingly smooth and clear skin texture [11].
Line Eliminator Dual Retinol Facial Treatment.	Avon	Two-system wrinkle action, both immediate and timely released. Obviously, fine lines, wrinkles, and skin color seem to be related to aging [26].
Micro Peel Plus /Acne Peel	Biomedic	The MicroPeel @ Plus procedure stimulate cell turn in excess of from first to last the application of salicylic acid in the form of microcrystals using MDS. Micro peel Plus forcefully releases the skin of all dead cells by defeat other surface chemical peels, while not harming the skin [21].
Retinol cream, Retinol 15 Night cream	Biomedic, Sothys	A night-time treatment cream with microsphere technology using pure static, a stable formula of vitamin A. Continuous use of retinol 15 will result in fine lines and wrinkles, a noticeable improvement in the skin discolorations due to aging, and enhanced skin smoothness [26].
Lactrex™ 12% Moisturizing Cream (Pentewar RS <i>et al</i> , 2014).	SDR Pharmaceuticals, Inc., Andover , NJ , U.S.A. 07821	Microsphere® technology has been included for effortless application and for long lasting moisturization. Lactrex™ includes water and glycerin, a natural humectants help moisturize soft and dry, flaky, broken skin [52].
EpiQuin Micro	SkinMedica Inc	Microspheres continuously release these ingredients in the skin throughout the day. It provides skin with constant contact of hydroquinone and retinol over time, thereby reducing skin irritation. EpiQuin Micro A Recipe Moisturizing Fading Cream That Reduces Effect. These conditions are known as melasma, after inflammatory hyper pigmentation or solar lactagens. Also help in age spots, sun spots and facial discoloration [18].
Oil free matte block spf20	Dermalogica	This imperceptible oil-free sunscreen shields the skin from damaging UV sun rays while controlling oil production, giving a healthy matte finish. Designed with micro-sponge technology, the oil-free matte block absorbs oil and can prevent brightness without any powder residues [32]
Sportscream RS and XS	Embil Pharmaceutical Co. Ltd.	For the management of musculoskeletal conditions, timely analgesic anti-inflammatory and counter-hibernation activated in a Microsphere delivery system (MDS) [53].
Oil Control Lotion	Fountain Cosmetics	With feature-load lotion prepared with oil-absorbing micro-sponge technology, eliminate the shine for hours. Complex shoulder swelling and stiffness to promote antibiotic skin retention therapy naturally Acne-prone, oily skin condition [40].
Ultra Guard	Scott Paper compony	Microspheres system, which includes dimethicone to help protect a child's skin with diaper rash. The new wipes contain a skin protector that helps keep moisture and trouble from the skin of the baby. The solution is free of alcohol, is hypoallergenic and contains dimethicone, a component found in baby cream, lotions and skin protector [41].
Aramis fragrances	Aramis Inc.	Microsphere formulation are available in the form of ultra-light powder, it can easily take the aroma oil because of its suitable size. While the free-wide powder maintains the feature where the release is controlled due to moisture and temperature [52].

Table 6: PATENT INFORMATION

September 1, 1987	Won R of Advanced Polymer Systems, Inc.	Received (US Patent 4,690,825) for Developing method to deliver an active ingredient by controlled time release using a novel delivery vehicle that can be prepared by a process utilizing the active ingredient as a porogen [53]
September 8, 1992,	Won R of Advanced Polymer Systems, In	Received (US Patent 5,145,675) for developing a two-step method for the preparation of controlled release formulation [53].
July 23, 2006	Advanced Polymer Systems, Inc. and subsidiaries ("APS" or the "Company")	Use MDS and related proprietary technologies to increase the effectiveness of security, beauty and topical prescriptions on personal care products such as counter ("OTC") and vitamin-A, tretinoin and 5-fluorouracil. .

Dean JR et al, US Patent Number Received 4863856 There are highly cross-linked collagen matrices for the development of weighted collagen microsponges, which is intended for use in fusion organisms in the reactor system. The pore structure of the surface of microsponges is an open dose for the size and size of the pore, which is suitable for stabilizing a range of bio active material.

### 3. CONCLUSIONS

The Microsponges Drug Delivery System is a novel strategy that regulates the delivery rate of active agents with less skin irritation and continues the drug during extended periods of time. They are stable over a wide range of pH (1-11) and temperature (up to 130° C), and are compatible with most vehicles and materials. Because the average pore diameter is less than 0.25 µm, bacteria cannot penetrate these structures and reach their contents; Therefore, they are self-sterilizing and do not need any preservatives. Topical MDS can be used to prevent drug penetration into the subcutaneous layer and reduce skin irritancy. In doing so, this system can provide maximum effectiveness for therapeutic active agents, reducing their irritability and increasing their safety, increase product stability in a skilled and novel way. Apart from this, MDS can also be cost effective for the use of cosmetic and MDS offering high drug loading efficiency compared to other conventional dosage forms. Thus microsphere approach can be successfully utilized to improve the pharmacokinetics and therapeutic efficacy, simultaneously reducing irritability and toxicity of various highly potent drugs.

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**Abbreviations:** MDS- microsphere drug delivery system, BPO- benzoyl peroxide

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