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# REVIEW ON MICROSPONGES

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## ABSTRACT

Microponage drug delivery system (MDDS) is an innovative approach designed to increase drug stability, bioavailability and controlled liberation. Microspongs are porous, polymer microphes that can meet active pharmaceutical ingredients (APIs) and can provide continuous or targeted drug release, reduce systemic side effects and improve medical results. This system is widely used to distribute antibacterial, fungicidic and anti -inflammatory agents in dermal, cosmetics and drugs. MDD provides many benefits, including an increase in drug loading capacity, low dosage frequency and improves the patient's compliance. The review examines synthesis, characterization, benefits and various applications of micropongs in modern drug delivery. In addition, it addresses today's challenges, recent progress and potential future development in the region. As research develops, MDD is expected to bring revolution in targeted therapy and individual medicine, which offers more effective and patient -friendly drug delivery solutions.

**KEYWORDS:** Microsponge, drug delivery system, sustained release, polymeric carrier, pharmaceutical innovation.

## INTRODUCTION

A microsponge delivery system (MDS) is a highly cross-linked, porous polymeric system made up of porous microspheres that can hold a variety of active chemicals, including anti-fungal, anti-infective, anti-inflammatory, and sunscreen.[1] The macroporous beads, or microsponges, have an active substance loaded therein and are usually 10–25 microns in diameter. Polymeric microspheres with pores are called microsponges, and they are mostly applied topically for extended periods of time. microsponges made of non-collapsible structures with porous surfaces that allow for the regulated release of active substances. Microsponges are porous microspheres with interconnected voids that range in size from 5 to 300 micrometers. They are spherical, homogeneous polymer particles.[2]

Microsponges are little spheres that have the ability to absorb skin secretions and lessen skin oiliness. Skin secretions may store four times the weight of spherical particles made up of clusters of even smaller spheres. The minuscule, innocuous, and unbreakable spheres known as microsponge particles are not able to penetrate the skin. Instead, they gather in the minuscule crevices of the skin and gradually release the medicine that is held there, as needed by the skin. The overabundance of component buildup in the dermis and epidermis can be avoided by using the microsponge system. It may be possible for the microsponge system to considerably lessen the irritation caused by medications that work without compromising their effectiveness.[3]

Won created the microsponge technique in 1987, and Advanced Polymer Systems, was given the original patents. This company created numerous variations of the techniques, which are used for both prescription and over-the-counter (OTC) pharmaceutical items in addition to cosmetics. As of right now, Cardinal Health, Inc. has a license to utilize this intriguing technology in topical medicines. The microsponge particle's interior structure is shown by scanning electron microscopy as a "bag of marbles."[4] Because microsponge delivery systems regulate the drug's transit through the stratum corneum and epidermis, they can prevent it from reaching the dermis, which contains numerous blood arteries. This could have positive effects.[5]

### Characterstic features of microsponges[6]

1. The pH range of pH 1–11 is stable for microsponges formulations.
2. Formulations for microsponges remain stable at temperatures as high as 130 °C.

3. The majority of microsponge formulations self-sterilize. hole size of 0.25 µm, which is impermeable to bacteria.
4. The majority of vehicles are suitable with microsponge compositions. and components.
5. Microsponge compositions can be economical and have a larger payload (50–60%) while remaining free-flowing.

**Advantages**[7,8,9]

1. Intelligent oil management: absorb up to six times its own weight without drying out
2. A more elegant product
3. Immiscible items can be incorporated with MDS.
4. Extended release
5. Formulas with less irritation
6. Permits innovative product forms
7. They are non-toxic, non-allergenic, non-mutagenic, and non-irritating.
8. Better-looking products
9. Extended release, 12-hour continuous action
10. Less annoyance and increased tolerance translate into wider customer approval
11. A more refined appearance that provides the goods a refined vibe
12. Enhances chemical, physical, thermal, and stability
13. Permits the addition of immiscible goods
14. Enhances material processing.
15. Increases treatment efficacy.
16. Stable up to temperature 130℃.
17. It increases the formulation's flexibility.
18. Microsponges don't cause allergies.
19. It improves patient adherence.
20. Drug is applied directly to the area or organs of interest.
21. The drug has a greater potential to load than other topical getting ready.

**Properties of material to be entrapped into microsponges**[10,11]

1. It should be either fully miscible in a monomer or capable of being made miscible by the addition of a small amount of a water-immiscible solvent.
2. It should be water immiscible or at most only slightly soluble

3. It should be inert to monomers and should not increase the viscosity of the mixture during formulation.
4. It should be stable when in contact with the polymerization catalyst and under conditions of polymerization.
5. The spherical structure of the microsponges should not collapse.
6. The solubility of actives in the vehicle must be limited.
7. Not more than 10 to 12% w/w microsponges must be incorporated into the vehicle in order to avoid cosmetic problems.
8. Payload and polymer design of the microsponges for the active must be optimized for required release rate for given. period of time.

**Drugs explored in microsponge delivery system**[12]

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

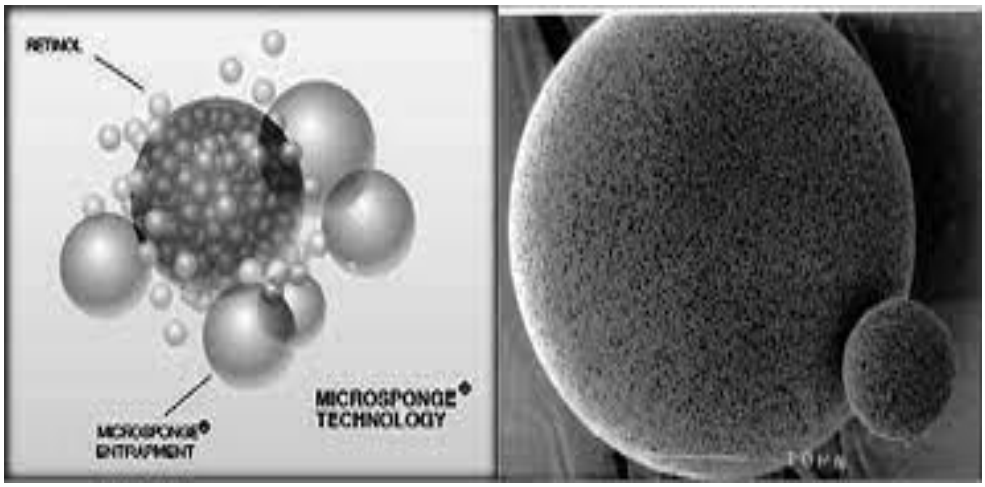


**Figure No. 01: SEM images of microsponges.**

**Preparation of microsponges**

There are two methods for loading drugs into microsponges: a one-step procedure called liquid-liquid suspension polymerization, or a two-step procedure called quasi emulsion solvent diffusion method. Both methods are based on a drug's physicochemical characteristics. If the medication is usually a non-polar, inactive substance, it will produce a porous material known as a porogen. Porogen medication that doesn't impede polymerization or becomes stable to free radicals and triggered by it.get caught up in the one-step procedure.[13]

- Liquid-liquid suspension polymerization
- Quasi-emulsion solvent diffusion.[14]
- Multiple-emulsion Solvent Diffusion
- Addition of Porogen
- Oil in Oil Emulsion Solvent Diffusion
- Lyophilization
- Ultrasound-Assisted Production
- Electrohydrodynamic Atomization Method.[15]

**1. Liquid-liquid suspension polymerization**

The active component and immiscible monomers are dissolved in the appropriate solvent monomers.

⇩

It distributed throughout aqueous phases with additions such as suspending agents and surfactants

⇩

Catalyst addition, radiation, or temperature increases can all initiate polymerization.

⇩

The process of polymerization is what keeps the spherical structure from falling apart.

⇩

Spherical porous microsponges are generated after the procedure solvent is withdrawn.[16]

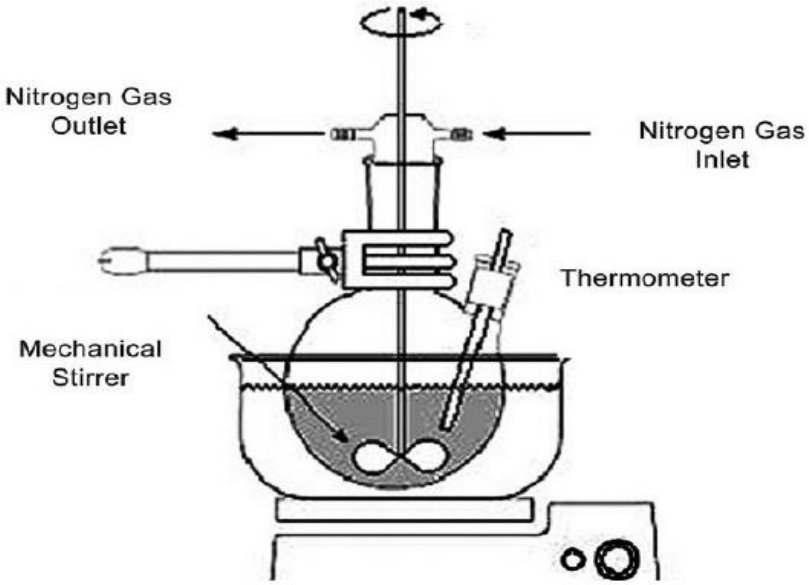


**Figure No. 02: Liquid liquid suspension polymerization method.**

### 2. Quasi-emulsion solvent diffusion

Two steps make up the quasi-emulsion solvent diffusion approach, which improves drug release sensitivity. Various polymer concentrations are used in this process. As this comprised of the internal phase and the exterior phase. Stage. Polymers like are present in the internal phase. Eudragit RS-100 (permeability reduced). This polymer is entrapping efficiency, cationic nature, and lack of biodegradability was discovered to rise as Eudragit levels rose. The RS-100.Polyvinyl alcohol makes up the exterior phase. (PVA) combined with pure water Phase inside the body that includes A solvent such as ethyl alcohol is used to dissolve Eudragit RS-100. so that the interior phase is ultrasonicated at 35 °C. distributed in the PVA solution-containing exterior phase under water. After stirring for an hour, the mixture is filtered. the solid microsponges can be obtained. This sturdy microsponge is dried in an oven at 35 °C- 40 °C for 12 hours. before use.[17]

### 3. Multiple-emulsion solvent diffusion

This unique method was used to create porous microspheres that are biodegradable. Using this technique, An organic polymeric solution contained an internal aqueous phase that was distributed and contained an emulsifying agent such as span, polyethyleneimine, and stearyl amine. To create a double emulsion, this water-in-oil emulsion was then again distributed in an external aqueous phase containing PVA.

The benefit of this approach is that it can trap both water-soluble and water-insoluble medications. Proteins and other thermolabile materials can be entrapped using it as well. Additionally, xanthan gum was described by some authors as an emulsifier to stabilize the internal w/o emulsion.

**4. Addition of porogen**

This method substituted a porogen, such as sodium bicarbonate or hydrogen peroxide, for the internal numerous emulsions. Because of this, The polymeric solution was used to dissolve the porogen, creating a single-phase system that was then re-dispersed in an aqueous phase that included PVA. Following the addition of an initiator to the multiple emulsion, the organic solvent was allowed to evaporate, leaving the microparticles behind to create microsponges 32. The addition of hydrogen peroxide caused pores with widths ranging from 5 to 20 μm to develop, which were equally distributed and linked.

**5. Oil in oil emulsion solvent diffusion**

As opposed to the w/o/w approach, volatile organic liquid was used to prepare the oil in oil (o/o) emulsion. interior phase that was continuously stirred while being allowed to progressively evaporate at a predetermined rate. According to reports, the method employed a mixture of fixed oil (corn or mineral) and dichloromethane containing span 85 as the exterior phase, polylactide glycolic acid as the polymer, and dichloromethane as the internal phase solvent. To create the microsponges, the internal phase was gradually introduced to the dispersion medium while being constantly stirred. This method was used to create hydroxyzine hydrogel-loaded Eudragit RS-100 microsponges, with liquid paraffin serving as the continuous medium and acetone serving as the dispersion solvent. Depending on the drug's physicochemical characteristics and the polymer used for fabrication of microsponges, the organic solvent and exterior phase selected.

**6. Lyophilization**

The process of lyophilization was employed to create porous microspheres from the gelation technique-produced microspheres. In Using this technique, the microspheres were lyophilized after being incubated in a chitosan hydrochloride solution. The rapid elimination of the solvent caused the microspheres to become porous. This technique is quick and efficient, but because the solvent is quickly eliminated, it has the drawback of creating broken or shrunken microparticles.

**7. Ultrasound-assisted production**

Through modification of liquid-liquid suspension polymerization, this technique was created. The tiny sponges are synthesis using diphenyl carbonate as the cross-linking agent and betacyclodextrin (BCD) as the monomer. The reaction mixture was heated and then sonicated to control the size of the microparticles. After allowing the reaction mixture to cool, the resulting product was ground into coarse particles and cleaned twice—once with distilled water and once with ethanol. The cross-linked β-CD's porous microparticles can effectively load medicines into them.

The drawback of this technique is that it may trap potentially hazardous cross-linking agent residues.

**8. Electrohydrodynamic atomization method**

Using this technique, porous chitosan microspheres were created. Bubbles were created by sonicating a chitosan solution, and the resulting bubble Using a syringe pump, the suspension was pulled into a syringe, perfused through a steel capillary, and then electrohydrodynamic atomization was applied. The capillary's diameter was selected to hold onto every bubble in the suspension as it passed through it. The concentration of chitosan in the solution is the only factor that affects the voltage employed in the studies. In every instance, the steady cone jet mode was achieved through the application of voltage and flow rate, with the exception of the difficult-to-electrospray cases where the greatest concentration was utilized. A 4% w/v sodium hydroxide aqueous solution was used to cross-link the chitosan microspheres.[15]

**Mechanism of drug release from microsponges**

Drug release from microsponges happened gradually in response to one or more outside factors, including pH, pressure, temperature, and solubility.[13]

**1. Release caused by pressure**

The fluid is released by the mechanism when the microsponges are pressed or squeezed. The microsponge's resilience determines how much release occurs.

**2. Temperature-dependent release**

Temperature release: The release of active substances is also influenced by temperature. The stuff trapped can occasionally be extremely viscous.Like sunscreens, it cannot fully diffuse out of the microsphere at ambient temperature. When they warm up from the sun or from skin temperature, their viscosity decreases and their flow rate increases.

### 3. pH-triggered release

The microsponges' covering can be altered to alter the release of actives in response to pH. To create conventional microsponges, a polymer that confers pH responsiveness is entericcoated on them.microsponges that react to pH. A dye that is very soluble in water is employed to conduct the investigations. To conduct experiments pertaining to pH, the USP spindle dissolution apparatus is utilized. Release increases from 0% to 80% when the pH is raised from 3 to 8. Therefore, pH can be changed to speed up the drug's release.

### 4. Release caused by solubility

Water miscible chemicals such as antiseptics, deodorants, and antiperspirants are loaded into microsponges, which release the API only in existence of an aqueous media, which depends on how well the external medium dissolves the API and how gradient in concentration it is. Diffusion can potentially cause the release to occur by changing the components' partition coefficient between the outer media and the microsponge.[18]

### Factor affecting mechanism of drug release

- Entrapped actives' chemical and physical characteristics.
- The physical characteristics of a microsponge system, such as resilience, pore volume, and diameter. characteristics of the vehicle that eventually disperses the microsponges.
- Particle size, pore properties, resilience, and monomer compositions are all programmable parameters. Microsponges can be made to release a specific amount of actives in response to pressure, temperature, and solubility of actives, among other external triggers.
- The active substance in microsponges can be released onto skin by applying pressure or rubbing.
- Changes in temperature. At room temperature, some entrapped actives may be too viscous to flow from microsponges onto skin naturally.Raising the temperature of the skin can raise the flow rate and, thus, the release.
- Dissolvability When water is present, microsponges containing water-soluble substances, such as antiperspirants and antiseptics, will release the substance. Diffusion, which takes into account the ingredient's partition coefficient between the microsponges and the external system, can also initiate the release.[19]

**Recent studied done on microsonges**

**Table No. 01: Recent studies done on the microsponges drug delivery system.**

| Author | Drug used | Polymer used | Solvent used | Method of preparation | Results |
|---|---|---|---|---|---|
| Vinita *et al.*, (2023) | Resveratrol | Eudragit RL 100 | n-hexane, propylene glycol and triethanolamine. | Oil in Oil Emulsion Solvent Diffusion | high polymer concentrations showed delayed release of drug.[20] |
| Lagnajit *et al.*, (2022) | Tinidazole | HPMC | Dichloromethane | Quasi emulsion solvent diffusion method | microsponges were releases the drug up-to 12 hrs.[21] |
| Anjali *et al.*, (2021) | Aceclofenac | Ethyl cellulose | Ethanol | Quasi emulsion solvent diffusion method | The optimized gel showed controlled release of 71. 33% in 8 h.[22] |
| Shubhangi *et al.*,(2019) | Isoxsuprine Hydrochloride | ethyl cellulose | ethanol, chloroform | Quasi emulsion solvent diffusion method | The cumulative percentage drug release (% CDR) of isoxsuprine hydrochloride after 8 hr. was found between the ranges of 91.97% to 98.78%.[23] |
| Swamikannu *et al.*,(2019) | Voriconazole | ethyl cellulose 50 cps | polyvinyl alcohol | Quasi emulsion solvent diffusion method | Prepared microsponges shows controlled release of drug.[24] |
| Manar *et al.*, (2018) | Acetazolamide | Ethyl cellulose | Ethanol, toluene, dichloromethane | Quasi emulsion solvent diffusion method | The free drug showed about 67.8% of cumulative release after one hour whereas the microsponges formulations showed 6.36–37.87% drug release after one hour.[25] |
| Meenakshi *et al.*,(2018) | Curcumin | Ethyl cellulose | Polyvinyl alcohol, propylene glycol | Quasi emulsion solvent diffusion method | It showed 93.2% release of curcumin in 8 h.[26] |
| Pooja *et al.*, (2018) | Itraconazole | Eudragit RS 100, ethyl cellulose | Ethanol, dichloromethane | Quasi emulsion diffusion method | The percentage drug release after 8 hrs is found to be 91.62%.[27] |
| Ashlesha *et al.*, (2016) | Nebivolol | Eudragit RS 100 | Liquid paraffin | Oil in oil emulsion solvent diffusion | Eudragit RS 100 is chemically, methacrylic acid-ethyl acrylate copolymer (1:1) which |

| | | | | | |
|---|---|---|---|---|---|
| | | | | method | contributed to exhibit delayed action of drug release. Hence, increased polymer concentration extended drug diffusion time, achieving sustained action of NB through microsponges.[28] |
| Neha *et al*., (2016) | Miconazole | Eudragit RS 100 | Ethanol, dichloromethane | Quasi emulsion solvent diffusion method | formulations revealed the release rate within the range of 67%±0.09 to 80.6%± 0.68 at the end of 12 hours.[29] |
| Rishabh *et al*., (2012) | Meloxicam | Eudragit RS 100 | Dichloromethane | Quasi emulsion solvent diffusion method | It shows %EE = 98.73, %CDR = 97.32.[30] |
| Swetha *et al.*, (2011) | Etodolac | Eudragit RS 100,Ethyl cellulose | Polyvinyl alcohol | Quasi emulsion solvent diffusion method | Maximum drug release among the formulations containing etodolac and ethyl cellulose was found to be 99.3%within 8 h.[31] |
| Vikas *et al., (2010)* | Dicyclomine | Eudragit RS 100 | Polyvinyl alcohol | Quasi emulsion solvent diffusion method | Cumulative release for the microsponges over 8 hours ranged from 59 - 86 %.[32] |
| Netal *et al.*, (2009) | Mupirocin | Ethyl cellulose | Polyvinyl alcohol, dichloromethane | Quasi emulsion solvent diffusion method | Therapeutic drug concentration were maintained up to 24 h on skin.[33] |
| Orlu *et al.*, (2006) | Flurbiprofen | Eudragit RS 100 | Polyvinyl alcohol | Quasi emulsion solvent diffusion | The drug release at 8$^{th}$ hour was found to be 87.5%.[34] |
| Tansel *et al.*, (2002) | Ketoprofen | Eudragit RS 100 | Ethyl alcohol | Quasi emulsion solvent diffusion method | It was observed that when drug amount increased, particle size of the microsponges increased.[35] |

**Evaluation of microsponges**

**1. Particle Size and Size distribution**

Testing methods for particle size distribution include microfluidic resistive pulse detection, laser diffraction, and electro zone, sieve analysis, dynamic light scattering, air permeability diameter, single-particle optical detection, and nanoparticle tracking analysis. Particle size analysis is a technique used to assess and report data regarding the range and size of a

particular set of particles that influence formulation texture and material representation. Particle size distribution control enhances the powder's free-flowing qualities and reduces agglomerates or polymerization during handling, packing, quality control testing, and product development. It is possible to analyze the particle sizes of loaded and unloaded microsponges using laser light diffractometry, mean size range, and cumulative percentage of drug release from microsponges with varying particle sizes.[36]

### 2. Morphology and Surface topography of microsponge

After the prepared microsponge has been coated with gold–palladium at room temperature in an argon environment, scanning An image of a broken Microsponge particle's ultra-structure can also be obtained using SEM.[37]

### 3. Loading efficiency and production yield

The following formula can be used to determine the loading efficiency (%) of the microsponges:

$$\text{Loading efficiency} = \frac{\text{Actual Drug Content in Microsponge}}{\text{Therotical Drug Content}} \quad \text{Eqn no.(1)}$$

By precisely calculating the beginning weight of the raw materials and the final weight of the microsponge obtained, the production yield of the microparticles can be ascertained.

$$\frac{\text{Practical Mass of Microsponges} \times 100}{\text{Therotical Mass}} \quad \text{Eqn no.(2).}[38]$$

### 4. Determination of true density

Using helium gas and an ultra-pycnometer, true density can be determined as the average of several measurements.[39]

### 5. 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. Impact of Differential scanning calorimetry (DSC) and powder X-ray diffraction (XRD) can be used to study the effects of polymerization on the drug's crystallinity 26, 27, 28. About 5 mg of samples can be precisely

weighed, placed into aluminum pans, sealed, and heated at a rate of 5 °C per minute in a nitrogen atmosphere to a temperature range of 25–4300 °C for DSC.[40]

**6. Dissolution studies**

Using a modified basket made of USP XXIII dissolving apparatus, the dissolution profile of microsponges can be examined. stainless steel mesh measuring 5µm. There is a 150 rpm rotational speed. In order to guarantee sink conditions, the dissolution medium is chosen while taking the actives' solubility into account. At different periods, samples from the dissolution medium can be examined using an appropriate analytical technique.[41]

**7. Resiliency**

Microsponges resilience, or viscoelastic qualities, can be changed to create beadlets that are stiffer or softer depending on what the final composition requires. a rise in cross-linking tends to decrease the pace of discharge.[42]

**8. Release study**

Diffusion or another triggering mechanism, such as friction, temperature, pH, or moisture, can control the release of microsponge. This method of release has been applied to enhance the visual appeal of products.[43]

**Polymers used in microsponges**

- Eudragit RS 100 and RL 100
- Ethylcellulose
- Polystyrene
- Acrylic polymer
- PHEMA
- Carbopol 934.[44]

**Applications of microsponges**

Topical prescription, over-the-counter, and personal care products are improved in terms of safety, efficacy, and aesthetic quality by the use of microsponge delivery systems. There are several applications for microsponges. Mostly applied topically, it has recently been administered orally as well. Thanks to its high loading capacity and prolonged release ability, it has been reported in several patents that it can be utilized as an excipient. It provides a variety of options for formulators to create pharmaceutical and cosmetic products.

Microsponges are intended to increase stability, lessen adverse effects, alter medication release, and effectively administer a pharmaceutical active component at the lowest possible amount. The microsponge medication delivery method is found in several over-the-counter moisturizers, specific rejuvenation products, and sunscreens.[45]

**Application of microsponges with respect to their advantages[10,46]**

**Table No. 02: Application of microsponges with their advantages.**

| Sl. no | Application | Advantage |
|---|---|---|
| 1. | Sunscreens | Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization |
| 2. | Anti-acne<br>e.g. Benzoyl peroxide | Maintained efficacy with decreased skin irritation and sensitization |
| 3. | Anti-inflammatory<br>e.g. hydrocortisone | Long lasting activity with reduction of skin allergic response and dermatoses. |
| 4. | Anti-dandruffs<br>e.g. zinc pyrithione, selenium sulfide | reduced unpleasant odour with lowered irritation with extended safety and efficacy |
| 5. | Antipruritics | Extended and improved activity. |
| 6. | Skin depigmenting agents e.g. hydroquinone | Improved stabilization against oxidation with improved efficacy and aesthetic appeal. |

**Future prospect**

The most recent cutting-edge technology is called Microsponge, and it was primarily developed for oral and topical administration systems. The microsponge drug delivery system has unique qualities that include improved product performance and present exciting potential in the near future for a variety of pharmaceutical applications. elegance, longer release, better drug release profile, less irritability, better physical, chemical, and thermal stability, and the potential to create new product shapes with flexibility. Future microsponge carrier systems have been identified to have applications in cosmetics. The formulation's adaptability allows for its employment in a variety of contexts and creates a new avenue for the drug delivery system.

## CONCLUSION

The microsponge delivery system has a number of benefits, features, and uses. Because MDS are non-toxic, non-irritating, and non-mutagenic, they have numerous advantages over other products. The distribution technique for microsponges could improve our knowledge of how various diseases recover. MDS is now utilized in cosmetic industries, prescription drugs,

over-the-counter skin care products, and sunscreens. MDS is flexible and has a lot of potential; it is employed in tissue engineering and colon-specific delivery.

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