MICROSPONGE: A NOVEL DRUG DELIVERY SYSTEM

Abstract

Microsponges are tiny, spongy, spherical particles with surfaces that have tiny pores. Additionally, they can alter medication release, improve stability, and lessen unwanted effects. Based on tiny polymeric microspheres, microsponge systems may suspend or contain a variety of substances that can be added to products like gels, creams, liquids, or powders. The exterior is frequently porous, allowing material to continuously flow from the person. Microsponges are made to effectively disperse medicinal components with a little dosage, enhance medication release, and boost safety. As a result of the formula's lack of antibiotics and lower bacterial content, it is regarded as harmless. For this reason, it is a component of several sterile preparations, including ophthalmic, parenteral, and others. Here, we focus on providing an overview of the state-of-the-art in approach, planning, and microsponge technology, as well as the industrial design, use, and assessment of microsponges in a variety of forms. Although they have lately been used orally, microsponges are typically employed for aesthetic purposes.

Keywords: Polymer solution, Microsponge.

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I. MICROSPONGE

Points to be covered in this topic,

- Definition
- Ideal properties
- Preparation of microsponge
- Theory of drug release from microsponge
- Microsponge drug delivery system
- Advantages of microsponge based on drug delivery system
- Evaluation of microsponges
- Factor affecting drug release from microsponge

II. INTRODUCTION

Microsponge particles are small, immobile, non-destructive and do not penetrate the skin. Instead, they fill in small gaps and cracks in the skin and gradually release the drug when the skin needs it. The micro-sponge mechanism protects the dermis and epidermis from being too accumulated with substances. The micro-sponge technique reduces their irritation without reducing the effects of strong chemicals. In the next wash, the hollow balls are cleaned. In the past few years, the development of new chemical microsponge to modify and control drug release behavior has received a lot of attention. The clinical parameters of the drug and the duration of action can be changed by delivery. Consumer interest in skin care products and treatments is increasing due to the use of ingredients such as alpha-hydroxy acids and vitamins in cosmetics. These ingredients are especially beneficial for aging or damaged skin. Although helpful, many of these ingredients can be irritating. This irritation is characterized by burning, itching or redness and is often seen in people with sensitive skin. Models aware of this problem try to solve it in one of two ways. They reduce the cost of these components but sacrifice quality in the process. Microsponges are polymer delivery systems containing porous microspheres ranging in size from 5 to 300 µm. Microsponge is a porous material that can absorb many substances. They are small porous spheres with a large porous surface. They can also improve safety by changing drug delivery methods while reducing side effects. Microsponges are microporous materials that are often used for cosmetic purposes and more recently for oral care.

III. DEFINITION

Microsponges are small globules that can absorb skin secretions, thereby reducing the oil and shine of the skin. Microsponges are polymer delivery systems containing porous microspheres ranging in size from 5 to 300 µm. It is a granular distribution system containing microsponge, porous materials, which can capture various materials. They are small porous like spherical particles with large porous surface. They can also improve safety by changing drug release patterns while reducing side effects. Microsponges are microporous particles used mainly for cosmetic purposes and more recently for oral administration.

IV. IDEAL PROPERTIES OF MICROSPONGE DELIVERY SYSTEM (MDS)

1. The structure of the microsponge should not deteriorate, that is, it should preserve its structural integrity.
2. It should be slightly soluble in water.
3. It should be stable when exposed to polymerization catalysts and polymerization conditions.
4. The monomers used in the design should not be forgotten.
5. MDS should not increase the viscosity of the mixture during preparation.
6. The size of the microsponge is about 10 to 25 µm in diameter.

V. PREPARATION OF MICROSPONGES

According to the principles of the human body, there are two ways to package drugs into microsponges: one-step method (liquid-liquid suspension polymerization) or two-step method as discussed in liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques which are based on physicochemical properties of drug to be loaded. If the substance is mostly non-polar, it forms a porous structure called a porogen. Its chemical structure does not inhibit or activate polymerization and is stable against free radicals.

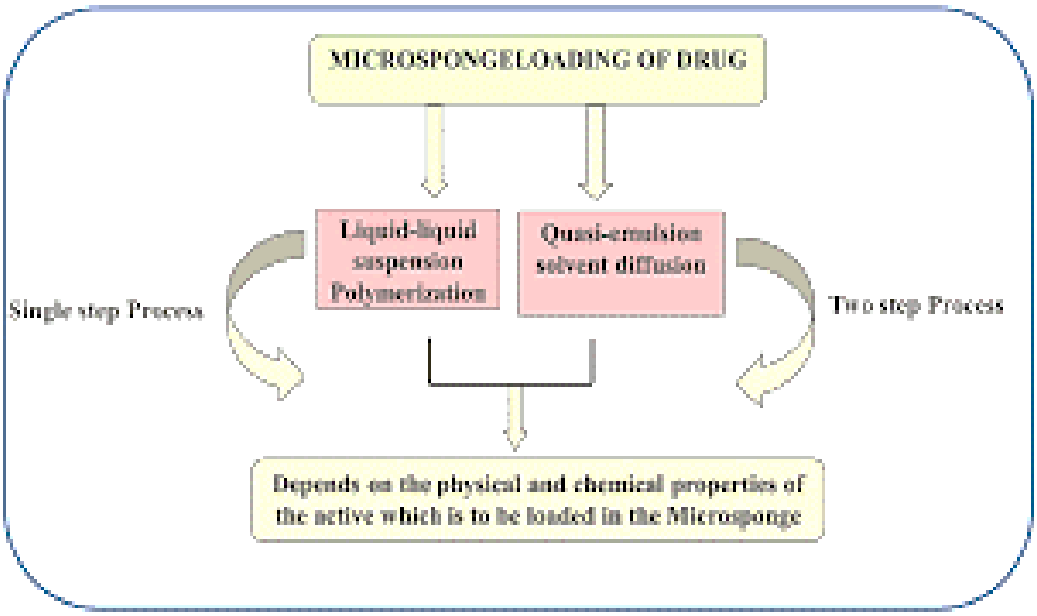

Figure 1: One Step and Two Step Preparation of Microsponges.

1. **Liquid-liquid Suspension Polymerization:** Typically, the product and the monomer are first dissolved in a suitable monomer solution. Following that, it is blended in the aqueous phase, which frequently incorporates extras like surfactants and dispersants to help stabilize the suspension. After the proper number and size of droplets have formed a suspension, the monomers are activated or catalyzed by high temperature or electricity to begin the polymerization process. As the polymerization process goes on, spherical structures made of tens of thousands of microscopic sponges that are grouped together like fruit to form a water web are created. (Hainey et al., 1991). After the polymerization is completed, the material is cleaned and stored.

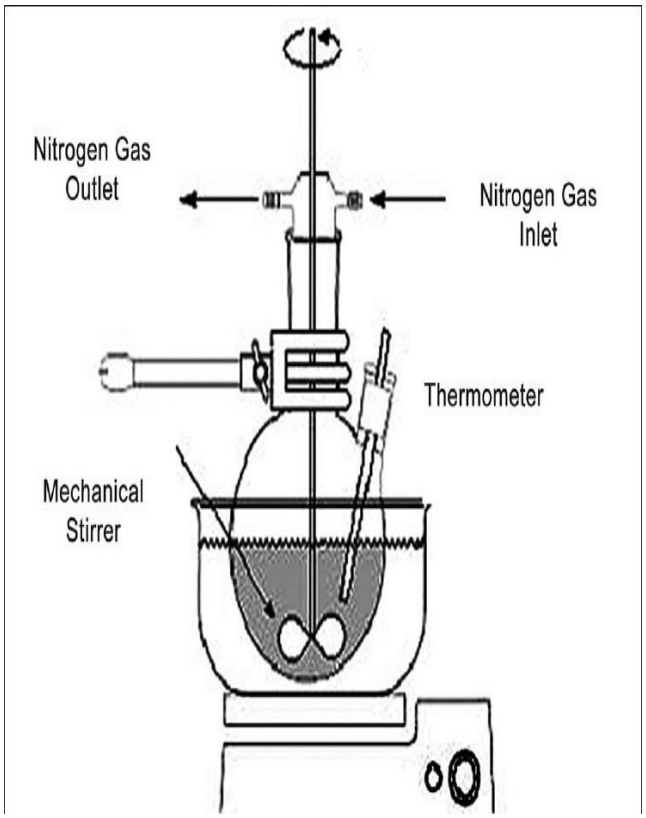

Figure 2: Formation of Suspension for Preparation of Liquid-Liquid Suspension Polymerization

2. **Quasi-Emulsion Solvent Diffusion:** Use the two-step approach when the medication is prone to the polymerization process. Polymer compounds dissolve in organic solvents (internal phase) as active molecules with various chemical compositions. The mixture was then continuously stirred while it was placed into the polyvinyl alcohol (external phase), enabling the solvent to evaporate before filtering to remove the microsponges. The resulting microsponges were further dried and stored in a desiccator to ensure complete removal.

3. **Water-Oil-Water Emulsion Solvent Diffusion:** This technique involves dispersing an internal aqueous phase with the emulsifier in an organic polymer liquid. A second emulsion was created by redistributing the water-in-oil emulsion in the aqueous phase that included PVA. Both water-soluble and water-insoluble compounds will be gathered in this manner.

4. **Oil-in-Oil Emulsion Solvent Diffusion:** This technique creates an emulsion with an interior phase that contains an organic solvent. In several preparations, dichloromethane is utilized as a volatile solvent. It is made of polylactide glycolic acid, a polymer containing 85 holes. To create a microsponge, the internal phase is continually mixed with the dispersion medium after being introduced dropwise.

5. **Addition of Porogen:** For this, the inner phase contains a porogen such sodium bicarbonate or hydrogen peroxide. The product is redistributed in the aqueous phase

containing PVA after the porogen is homogeneously diffused in the polymer solution. The addition of hydrogen peroxide causes the development of interconnecting holes that range in diameter from 5 to 20 m.

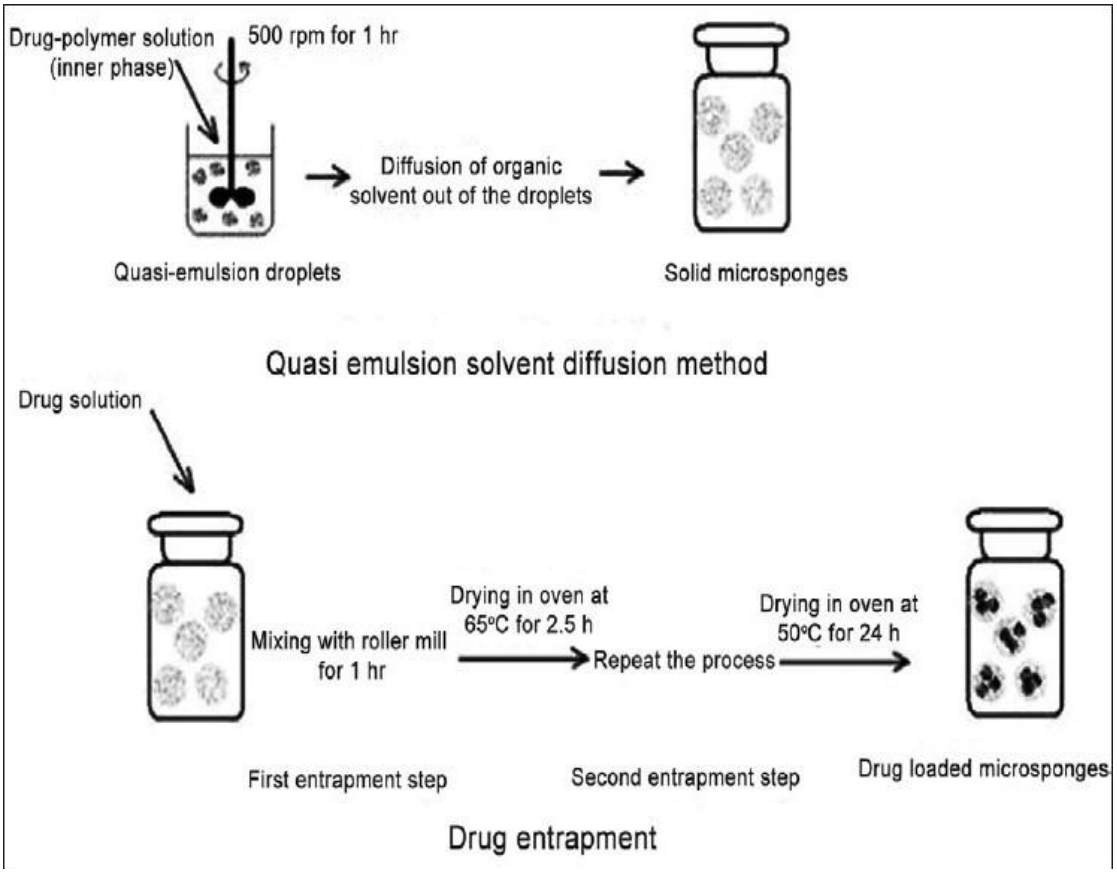

Figure 3: Preparation of Microsponges by the Quasi-Emulsion Solvent Diffusion Method

6. **Lyophilization:** In this method, the microspheres are converted into porous microspheres by rapid removal of the solvent, resulting in the formation of porous microspheres. This is done using chitosan hydrochloride. Microspheres were incubated in this solution and then lyophilized. Fragmentation and shrinkage of microparticles may occur due to rapid removal.

7. **Vibration-Hole Aerosol Generation Method:** The vibrating aerosol generation process mainly prepares lipid bilayer silica particles in suspension form. Prepare foundation beads with tetraethyl orthosilicate, ethanol, water and hydrochloric acid heated at reflux to prepare the solution. The solution is diluted with a solvent-containing surfactant and mixed again to obtain a dispersed droplet. The resulting microspheres are encapsulated in liposomes.

VI. DRUGS USED IN THE PREPARATION OF MICROSPONGES

- Paracetamol
- Miconazole
- Benzoyl peroxide

- Curcumin
- Ketoprofen
- Tretinoin
- Fluconazole
- Hydroquinone
- Acyclovir sodium
- Ibuprofen
- Retinol Prednisolone
- Erythromycin
- Indomethacin
- Mupirocin

VII. POLYMERS USED FOR THE PREPARATION OF MICROSPONGES

- Eudragit RS 100 and RL 100
- Ethyl cellulose
- Polystyrene
- Acrylic polymer
- PHEMA
- Carbopol 934

VIII. DRUG RELEASE MECHANISM FROM MICROSPONGES

Drug release from microsponges occurs in one or more response times. More external factors such as (temperature, pressure, pH and solubility)

1. **Pressure Friction or Pressure Releases:** Applying pressure or release can cause the release of drug from the microsponge onto the skin.

2. **Temperature:** Temperature fluctuations frequently have an impact on the synthesis of microsponge components. There is direct relationship between the flow and discharge process and skin temperature. The higher the skin temp, the increase in the flow and discharge of drug.

3. **pH Value:** Active ingredients can be released in accordance with the pH levels by altering the layer of micro sponges.

4. **Solubility:** Antibacterial and antifungal agents, which are hydrophilic active components, are present in microsponges and are released when they come into contact with water. The release can be done by diffusion, however the material's partition coefficient between the microsponge and the outside must be taken into consideration.

IX. PROPERTIES OF MICROSPONGES

In addition, research studies were conducted to determine the following in prepared microsponges:

- Particle size
- Product yield
- Loading Efficiency
- Surface topography
- In vitro Release studies

1. **Particle Size:** Particle size of microsponge is assessed by a light microscope or electron microscope. Particle size affects the performance of design. Factors affecting size are chemical Polymer ratio and emulsifier concentration. As that drug: Polymer ratio increases, the particle size decreases, and the increase in emulsifier concentration results in larger particles. The size was determined using a light microscope and a micrometer level spread a small piece of microsponge in a clean glass, put liquid paraffin on it, and cover it with a lid.

   100 Particles Are Measured For Each Batch To Determine The Average Particle Size.

2. **Product Yield:** The Drug To Polymer Ratio Will Also Have An Impact On Production Efficiency; A Higher Drug To Polymer Ratio Will Result In Higher Production Efficiency.

   Production Efficiency /Production Capacity = Actual Amount / Theoretical Amount X 100.

3. **Loading Efficiency:** Depending On The Characteristics Of The Microsponge, The Amount Of Drug Loaded Depends On Physicochemical Factors. The Drugs Can Be Transported Via Two Methods: Active Or Passive. The Most Effective Charging Method Is Passive.

   Drug Loading Efficiency Is Measured As:

   Drug Loading Efficiency = Drug Loading / Theoretical Drug Loading X 100.

   Surface Topography

   Topography Employs A Variety Of Methods, Including Transmission Electron And Scanning Electron Microscopy (Sem). (Tem) Microscopy, Etc. It Is Common Practice To Prepare Microsponges Using Sem.

4. **In Vitro Release Studies:** Utilizing A Dissolving Apparatus Usp Xxiii Fitted With New Baskets Having 5 M Stainless Steel Mesh, In Vitro Released tests were carried out. The rate of dissolution was determined at 37 °C and 150 rpm. The solubility of the active substance influences the choice of the dissolving media.

X. APPLICATION AREA OF MICROSPONGE

Microsponges finds its uses in pharmaceutical preparations and cosmetic industry. Sunscreens, specialist peels, and a range of moisturizers are commercial products that employ microsponge delivery.

1. Topical Drug Delivery using Microsponge Technology

- Topical treatments with benzoyl peroxide (BPO) are frequently used to treat acne and Hong Kong foot. Reduced adverse effects can be achieved by managing the skin's absorption of BPO using the microsponge delivery method.
- Mupirocin is an antibiotic for the skin that is used topically in a microsponge-based formulation to cause drug release. Comparing the microsponge delivery system's absorption of mupirocin in the skin to that of traditional mupirocin gel and commercially available mupirocin shows that this method of administration is effective for treating primary and secondary skin disorders..

2. Microsponges for Oral Application: The drug is controlled by the microsponge system as it travels from the mouth through the digestive tract, where it is then released in the gut after coming into contact with certain enzymes. It has been demonstrated that the microsponge system improves the decomposition of toxic substances by trapping them inside of their pores. One of such example, Ketoprofen was administered orally using the semi-emulsion solvent diffusion technique using Eudragit RS100, and then micro sponge tablets were made using the direct compression method. The compressibility of the physical combination of the drug and polymer was extremely good due to the plastic deformation of the drug and polymer due to sponge-like microspheres structure.

3. Microsponges for Bone and Tissue Engineering: Pre-made polymethyl methacrylate monomer powder was combined with two different kinds of water-dispersed calcium-deficient particles, tricalcium phosphate and hydroxyapatite, to create bone-like composites. The finished substance has a porous appearance and develops like a little sponge.

By combining two kinds of water-dispersed calcium-deficient particles, tricalcium phosphate and hydroxyapatite, with pre-prepared polymethyl methacrylate monomer powder, bone-like composites were created. The finished substance resembles a little sponge and is permeable to the eye.

XI. KEY FEATURES OF MICROSPONGE DELIVERY SYSTEM

- At pH 1 to 11, microsponges are stable. Up to 1300 C, they are thermally stable.
- The average pore size is 0.25um, so there is no need to add preservatives to the milk as it is bacterially resistant and has antibacterial characteristics.
- Microsponges are more affordable compared to other drug delivery methods.
- The majority of additives and media are compatible with them..
- Microsponges are a very fine, free-flowing powder but possess a high bearing capacity (50–65% by weight).
- It possesses good oil management and oil absorption capacity.
- New products can be easily developed.

XII. ADVANTAGES

1. Advantages Over Traditional Formula: Topical topology, because its chemical formula is designed to be applied to the skin. These products generate a thick, dense coating after

application, when their active components are released. It avoids the mixing of ingredients in the dermis and epidermis, unlike microsponge. Microsponge technology assist in decreasing strong medications' irritability without affecting their effects.

2. **Advantages Over Ointments:** Typically, cosmetic products are greasy, sticky, etc. are inadequate, and patients seldom ever adhere to them. Due to their improper medication usage, which results in discomfort and is unsuitable for many users, these gadgets require active medication to function effectively. The uncontrolled evaporation of the active substances, the scent, and the incompatibility of the medicine with the carrier are additional drawbacks of cosmetics.

XIII. MICROSPONGE DRUG DELIVERY SYSTEM

The Microsponge Delivery System (MDS) is a blend of porous polymers with porous microspheres that may hold a variety of ingredients, including anti-inflammatory, antifungal, antibacterial, etc. They are only employed to extend the shelf life of cosmetics. Microsponges are tiny, spherical, spongy particles that interact heavily with the surface's irregularity. Their sizes can vary, most frequently in diameter. Depending on the degree of slumber, 5 to 300 m. Additionally, they are appropriate for cosmetic usage because they can improve stability, lessen adverse effects, alter medication release, and manage the rate of release. Therefore, formulation factors like the drug:polymer ratio and mixing/mixing speed may be tuned to produce optimal microsponges.

Microsponges are versatile that make them adaptable in drug delivery. Many substances, which can be made into gels, creams, liquids, or powders for topical application, can be removed or trapped by microsponges. In response to various stimuli (pH, friction and temperature), the formula rapidly releases its contents when it is applied to the skin. Microsponges can be utilized to treat oral disorders, according to recent studies. It has been demonstrated that utilizing chemicals in the microsponge system's pores improves the separation of substances that are not soluble in water.

Advantages of Microsponge based Delivery System

Microsponge drug delivery systems are a type of drug delivery technology that offers several advantages in the field of pharmaceuticals and skincare. Here are some of the key advantages:

1. **Controlled Release:** Microsponges are porous microspheres that can encapsulate drugs. They allow for controlled and sustained release of the drug over an extended period of time. This controlled release helps in maintaining a constant drug concentration in the bloodstream, reducing the need for frequent dosing and minimizing side effects.

2. **Improved Drug Stability:** Microsponges can protect drugs from degradation due to light, heat, or chemical reactions. This enhanced stability can extend the shelf life of pharmaceutical products and ensure the drug remains effective for longer periods.

3. **Reduced Side Effects:** Controlled drug release minimizes the peak concentrations of the drug in the bloodstream, which can reduce side effects and improve patient compliance. It also helps in avoiding the toxic effects associated with high drug concentrations.

4. **Targeted Delivery:** Microsponges can be designed to release drugs at specific sites in the body, allowing for targeted drug delivery. This is particularly useful for drugs that need to be delivered to a particular organ or tissue.

5. **Enhanced Bioavailability:** Some drugs have poor solubility, which can limit their absorption in the body. Microsponges can improve drug solubility and bioavailability by dispersing the drug in a more easily absorbed form.

6. **Reduced Dosage Frequency:** Because of the sustained release capabilities of microsponges, patients often need to take medications less frequently. This can improve patient compliance and overall treatment outcomes.

7. **Versatility:** Microsponges can be used for various types of drugs, including both hydrophilic and hydrophobic compounds. They can also be employed for topical, oral, or parenteral drug delivery.

8. **Minimized Irritation:** In topical formulations, microsponges can help reduce skin irritation caused by certain drugs by controlling their release and reducing direct contact with the skin.

9. **Tailored Release Profiles:** Microsponges can be customized to achieve specific release profiles, such as zero-order, first-order, or pulsatile release, depending on the therapeutic needs of the drug.

10. **Compatibility:** Microsponges are generally biocompatible and can be incorporated into various pharmaceutical dosage forms, including creams, gels, lotions, and oral capsules.

11. **Long-Lasting Effects:** The prolonged release of drugs from microsponges can lead to longer-lasting therapeutic effects, making them suitable for chronic conditions or medications that require sustained action.

12. **Improved Patient Experience:** By reducing the frequency of drug administration and minimizing side effects, microsponge drug delivery systems can enhance the overall patient experience and compliance with treatment regimens.

While microsponge drug delivery systems offer numerous advantages, it's essential to consider factors like formulation design, manufacturing, and specific drug characteristics when developing and utilizing this technology to ensure its effectiveness and,safety.

XIV. EVALUATION METHOD OF MICROSPONGE

1. **Particle Size Evaluation:** Laser diffraction or other appropriate techniques can be used to determine the size of microsponges. The average dimensions for all formulations will

be shown as the value (d50). Sizes between 10 and 25 µm are used in the final formulation since particles larger than 30 µm seem sandy.

2. **Morphology and Surface Topography:** The morphology of microsponges is studied using a variety of methods, including photon correlation spectroscopy (PCS), transmission electron spectroscopy (TEM), and scanning electron microscopy (SEM).

3. **Determination of Loading Efficiency:** The loading efficiency (%) of the microsponges can be calculated as follows:-

$$\textbf{Loading efficiency} = \frac{\textbf{Actual Drug content in microsponges}}{\textbf{Theoretical drug content}} \times \textbf{100}$$

4. **Determination of Production Yield:** The production yield of the microsponges can be determined by:

$$\textbf{Production yield} = \frac{\textbf{Practical mass of microsponges}}{\textbf{Therotical mass (polymer+ drug)}} \times \textbf{100}$$

5. **Determination of True Density:** In the presence of helium, the actual density of microsponges may be determined using a pycnometer and is many orders of magnitude higher. may be determined using the average.

6. **Compatibility Study:** Thin Layer Chromatography (TLC) and Fourier Transform Infrared Spectroscopy (FT-IR) are two techniques that can be used in this study. By using differential scanning calorimetry and powder X-ray diffraction (XRD), it is possible to examine how polymerization affects crystallinity.

7. **Release Evaluation:** Contamination and other elements (such as humidity, pH, friction, and temperature) can regulate the discharge of microsponges. The product's quality is raised with this version.

8. **Resiliency:** To produce bullets, softer or harder microsponges can have their viscoelastic characteristics changed to suit the final formulation's requirements. The output will decrease as the number of connections increases.

9. **Stability Study:** Gel formulations are tested for safety according to ICH specifications. Collect the gel in clean, painted, collapsible aluminum tubes and store in several replicates in a vacuum chamber at 40 ± 2 °C and 75 ± 5% relative humidity. Changes in gel shape, pH, and in vitro release profile were evaluated at 30, 60, and 90-day intervals.

Table 1: List of Marketed Products based on Microsponges

Product Name	Pharmaceutical Uses	Manufacturer
Glycolic Acid Moisturizer w/SPF 15	Anti-Wrinkles, soothing	AMCOL Health & Beauty Solution
Retin A Micro	Acne vulgaris	Ortho-McNeil Pharmaceutical, Inc
Line Eliminator Dual Retinol Facial Treatment	Anti-wrinkle	Avon
Retinol 15 Night cream	Anti-wrinkles	Sothys
Retinol cream	Helps maintain healthy skin	Biomedic
EpiQuin Micro	Hyper pigmentation	SkinMedicaInc
Sports cream RS and XS	Anti-inflammatory	Embil Pharmaceutical Co. Ltd.
Salicylic Peel 20	Excellent exfoliation	Biophora
Oil free matte block SPF 20	Sunscreen	Dermalogica
Lactrex™12%	Moisturizing Cream	SDR Pharmaceuticals, Inc
Ultra Guard	Protects baby’s skin	Scott Paper Company

XV. DRUG RELEASE MECHANISM FROM MICROSPONGES

It causes a slow release of one or more external stimuli or components contained in microsponges.

1. **Temperature-Triggered Release:** When the temperature fluctuates throughout this process, active substances are released into the body. Some chemicals flow exceedingly viscous at ambient temperature without disrupting porous structures. But when a substance is put to the skin, the skin's warmth raises the pressure, which releases the medicine.

2. **Pressure-Triggered Release:** When the dosage form is rubbed against the skin with this device, the tiny sponge releases the medicine that was contained within. Numerous characteristics of the microsponge, such as its method, strength, and material type, affect how much of the medicine is delivered.

3. **Solubility Triggered Release:** When exposed to water, porous systems containing water-soluble excipients release medicines. Diffusion mechanisms include the drug's distribution coefficient and, occasionally, outside forces that cause its release.

4. **ph Triggered Release:** By altering the layer of the microsponge to achieve the pH function, the medicine is released using this way when the pH changes.

5. **Hypothetical Drug Release Mechanism:** The medication is enclosed and then put to the carrier. The medicine can enter and depart the microsponge system with the carrier because of its open structure up until it is stabilized. The carrier becomes chemically saturated as a result. The carrier becomes unsaturated and unstable when the formulation is applied to the skin. The medicine will flow from the carrier to the skin until the carrier

dries or is absorbed in order to achieve this equilibrium. Active chemicals are then progressively released from the micro-sponge on the stratum corneum's surface over time. Carriers are crucial in the production of microsponges because they promote and allow for gradual absorption of the active substances. Therefore, the carrier must be selected in a way that decreases the solubility of the constituents. In order to avoid the medication from prematurely leaking from the polymer, the dosage form will contain both free and embedded drug moieties.

XVI. FACTORS AFFECTING DRUG RELEASE BY MICROSPONGES

- Physicochemical properties of embedded API.
- Physical parameters of microsponges such as pore size, volume, particle size, and flexibility.
- Properties of micro sponge dispersion carrier.
- Pore properties, monomer composition, etc.

A recent innovation in drug delivery systems and more recently in oral control is the use of microsponges. It offers a lot of benefits. A modest quantity of medication may be delivered to the region with the help of well-designed microsponges, which also improve safety, lessen adverse effects, and regulate drug release. The key future issue is to create oral peptide delivery methods using various polymer kinds. The use of microsponges for medicine delivery would be fantastic. In the upcoming years, the development of microsponge drug delivery systems that can regulate release rates for certain body areas will be furthered, with important consequences for health. Many microsponge products have already received regulatory approval; many more are now being developed and evaluated.

XVII. FUTURE PROSPECTS

The recent development of microsponges for oral medication delivery systems makes them novel technologies for drug delivery systems. It offers a lot of benefits. A modest quantity of medication may be delivered to the region with the help of well-designed microsponges, which also improve safety, lessen adverse effects, and regulate drug release. Creating a delivery mechanism for oral peptide administration using various polymers is the key future challenge. The use of microsponges for medicine delivery would be fantastic. Many microsponge products have been approved; many more are currently in the development and evaluation stages. The search for microsponge drug delivery systems that can control the rate of release to specific parts of the body will be further refined in the upcoming years, with significant therapeutic implications.

XVIII. CONCLUSION

A new device called the microsponge delivery system regulates the discharge of microporous beads that contain active chemicals that can lessen adverse effects and regulate treatments. It is thought that microsponge medication delivery systems enable for entrance of their medicines while reducing side effects, enhancing safety, increasing elegance, and simplifying design. The microsponge system is neither allergic, poisonous, irritating, or mutagenic. The technique is being utilized in sunscreens, OTC (over-the-counter) skin care

products, cosmetics, and medications. Modern medication delivery technologies can help us learn how to treat a wide range of illnesses and disorders.

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