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Review Article

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MICROSPONGES: A PERSEPECTIVE APPROCH FOR TRANSDERMAL DELIVERY

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ABSTRACT

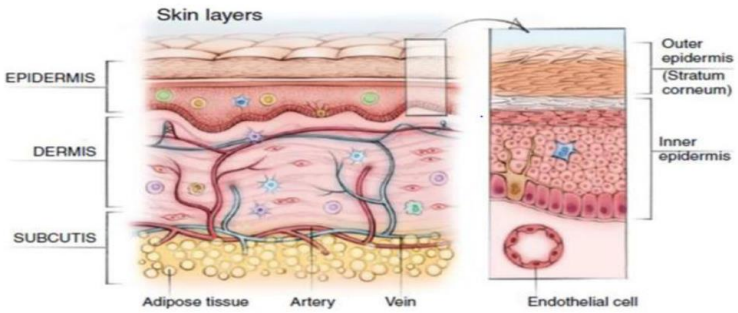
Transdermal drug delivery system (TDDS) is not practicable for delivery of materials whose final target is skin itself. Controlled release of drugs onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts is a challenging area of research. Microsponges are highly porous micro-sized particles with a unique ability for entrapping active pharmaceutical ingredients. To control the delivery rate of active agents to a predetermined site in human body has been one of the biggest challenges faced by scientists. Microsponge technology has many favorable characteristics which make it a versatile drug delivery vehicle. Microsponge delivery system (MDS) can entrap wide range of drugs and then release them into the skin over a time by diffusion mechanism to the skin. Microsponges can entrapped various type of drug and incorporated in formulation such as cream, powder, gels, and lotions. Microsponges can entrapped various type of drug and incorporated in formulation such as cream, powder, gels, and lotions. The present review describes microsponge technology including its preparation, characterization, programmable parameters and release mechanism of microsponge drug delivery system.

KEYWORDS: Microsponges, Controlled release, Transdermal delivery.

INTRODUCTION

Drug delivery systems (DDS) have various routes of administration, among which the oral route is the most commonly used. However, the oral route of DDS has several drawbacks such as pre-systemic elimination, first pass metabolism, and are prone to various drug interactions. As a result, various alternatives for this route of drug delivery have evolved. Transdermal drug delivery systems (TDDS) are a suitable alternative route for oral DDS as they have various advantages over other routes of drug delivery. TDDS is a self-contained, discrete dosage form that is applied to intact skin to deliver the drugs through the skin at a controlled rate to the systemic circulation. TDDS has good patient compliance and can bypass first-pass metabolism, providing a leading edge over the injectable and oral routes.[1] A new and innovative method for regulating release and delivering drugs to specific targets is the microsponge. Consequently, a large number of scientists and researchers are drawn to the microsponge drug delivery technology.[2] The pharmaceutical industry has demonstrated a strong interest in microparticulate medication delivery technologies. They make it possible for medication therapeutic efficacy to rise and for side effects to decrease. Given this, micro-sponges offer a novel form of porous polymer microspheres that can incorporate a variety of active chemicals.[3] Nowadays, sunscreens, prescription medications, over-the-counter (OTC) skin care products, and cosmetics all use micrsponges delivery technology.[4]

Anatomy of the skin[5]



- **Epidermis**[6] The epidermis is the outermost layer of the skin and varies in thickness with approximately 0.8 mm on the palms of the hands and soles of the feet. It consists of multi-layered regions of epithelial cells and the viable epidermis is often referred to as the epidermal layers below the stratum corneum. The cellular content of the epidermis consists predominantly of keratinocytes (approximately 95% of cells), with other cells of the epidermal layers including melanocytes, Langerhans cells and merkel cells. The stratum corneum is the most superficial layer of the epidermis. It is in direct contact with the external environment and its barrier properties may be partly related to its very high density (1.4 g/cm^3 in the dry state) and its low hydration of 15%–20%. The cells of the stratum corneum are composed mainly of insoluble keratins (70%) and lipid (20%). Water in the stratum corneum is associated with keratin in the corneocytes.

- **Dermis**[6]**:** The dermis is approximately 2–3 mm thick and consists of collagenous (70%) and elastin fibers which give strength and elasticity to the skin. Blood vessels found in the dermis provide nutrients for both the dermis and epidermis. Nerves, macrophages and lymphatic vessels are also present in the dermis layer, as depicted.

- **Hypodermis**[6]**:** The hypodermis or subcutaneous layer is the deepest layer of the skin and consists of a network of fat cells. It is the contact layer between the skin and the underlying tissues of the body, such as muscles and bone. Therefore, the major functions of the hypodermis are protection against physical shock, heat insulation and support and conductance of the vascular and neural signals of the skin. Hypodermis-resident fat cells account for approximately 50% of the body's fat with the other predominant cells of the hypodermis consisting of fibroblasts and macrophages.

Advantages of transdermal drug delivery[7]

The advantages of transdermal delivery over other delivery systems are as follows:

1. Transdermal drug delivery system enables the avoidance of first pass metabolism.
2. Reduced side effects when compared to the conventional drug delivery.
3. Constant plasma drug concentration is achieved.
4. Drug candidates with short half-life and low therapeutic index can be chosen.
5. In case drug toxicity the patches can be removed at any time.
6. Reduction of dosing frequency.
7. Enhancement of patient compliance.
8. It is possible that an equivalent therapeutic effect can be elicited via transdermal drug input with a lower daily dose of the drug that is necessary.

Disadvantages of transdermal drug delivery[8]

Some patients develop contact dermatitis at the site of application from one or more of the system components, necessitating discontinuation.

1. Higher cost.
2. Should not use ionic drug.
3. May cause allergic reactions.
4. A molecular weight less than 500 Da is essential.
5. Sufficient aqueous and lipid solubility, a log P (octanol/water) between 1 and 3 is required for permeate to transverse SC and underlying aqueous layers.
6. Transdermal therapy is feasible for certain potent drugs only.
7. Transdermal therapy is not feasible for ionic drugs.
8. It cannot deliver drug in pulsatile fashion.
9. Only relatively potent drugs are suitable candidates for transdermal delivery because of the natural limits of drug entry imposed by the skin's impermeability.

Types of transdermal drug delivery system[9]

a) Single layer drug in adhesive: In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and also responsible for the releasing the drug to the skin. The adhesive layer is surrounded by a temporary liner and a backing.

b) Multi -layer drug in adhesive: This type is also similar to the single layer but it contains an immediate drug-release layer and other layer will be a controlled release along with the adhesive layer. The adhesive layer is responsible for the releasing of the drug. This patch also has a temporary liner-layer and a permanent backing.

c) Vapour patch: The patch containing the adhesive layer not only serves to adhere the various surfaces together but also serves as to release the vapour. The vapour patches are new to the market, commonly used for releasing the essential oils in decongestion. Various other types of vapour patches are also available in the market which are used to improve the quality of sleep and reduces the cigarette smoking conditions.

d) Reservoir system: In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous or non-porous. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid polymer matrix. Hypoallergenic adhesive polymer can be applied as outer surface polymeric membrane which is compatible with drug.

e) Matrix system: the drug will disperse in the polymeric system.

i. **Drug-in-adhesive system:** This type of patch is formulated by mixing the drug with adhesive polymer to form drug reservoir. It then followed by spreading on an impervious backing layer by solvent casting or melting method. The top of the reservoir is protected by an unmediated adhesive polymer layer. It may further be categorized into single-layer and multi-layer drug-in-adhesive. The system is considered to be compatible with a wide variety of drugs. Moreover, the system is competent to deliver more than one drug in a single patch. It offers advantages in reduced size and thickness and improved conformability to the application site, helping drive patient preference.

ii. **Matrix-dispersion system**: The drug is dispersed homogenously in a hydrophilic or lipophilic polymer matrix. It is then altered into a medicated disc with the definite shape and thickness. This drug containing polymer disk is fixed on to an occlusive base plate in a compartment fabricated from a drug impermeable backing layer. Instead of applying the adhesive on the face of the drug reservoir, it is spread along with the circumference to form a strip of adhesive rim.

f) **Micro reservoir system:** The system consists of microscopic spheres of drug reservoirs which releases drug at a zero-order rate for maintaining constant drug levels. Micro reservoir system is a combination of reservoir and matrix-dispersion system. The aqueous solution of water-soluble polymer is mixed with drug to form a reservoir. It is then followed by dispersing the solution homogeneously using high shear mechanical force in a lipophilic polymer to form thousands of microscopic drug reservoirs. Cross linking agents are added to stabilize the thermodynamically unstable dispersion by in-situ cross-linking the polymer.

Routes of drug penetration[10]

Figure shows a diagrammatic representation of the trans epidermal and transappendegeal pathways, which are the two potential routes of drug penetration across the intact epidermis. Molecules traverse the stratum corneum—a multilayered, multicellular barrier with a variable architectural style—as part of the trans epidermal pathway. One may refer to trans epidermal penetration as intra- or intercellular. Hydrophilic or polar solutes can be transported intracellularly through corneocytes, which are terminally differentiated keratinocytes. Diffusion of lipophilic or non-polar solutes through the continuous lipid matrix is made possible via transport via intercellular gaps. Molecules go through sweat glands and across hair follicles via the transpendial pathway.

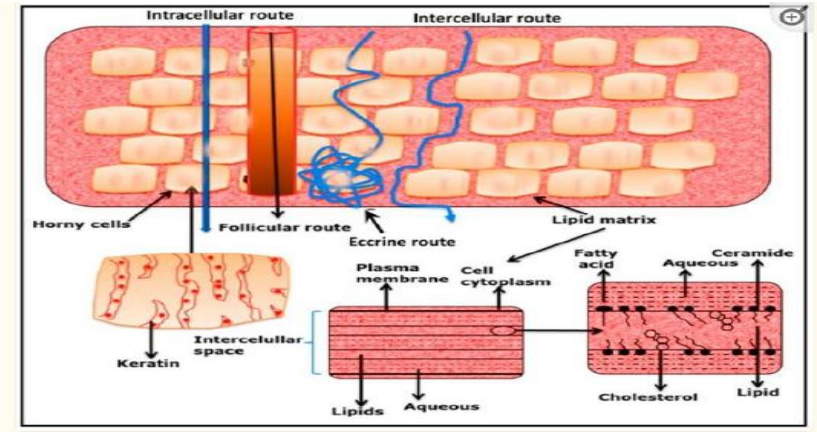


Fig. No: Different route of transdermal drug delivery.

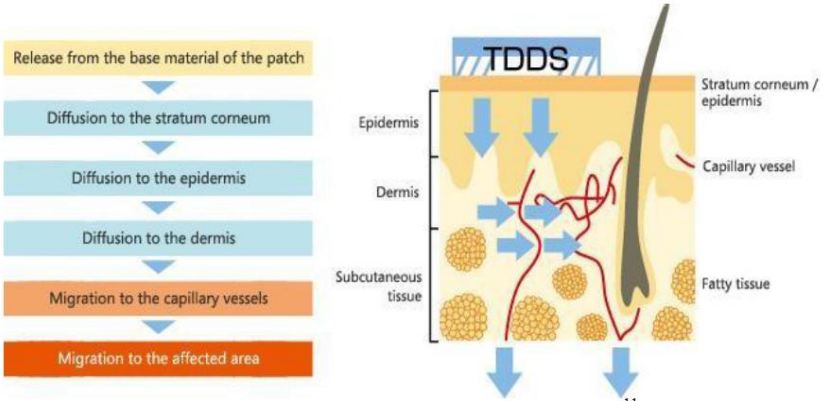


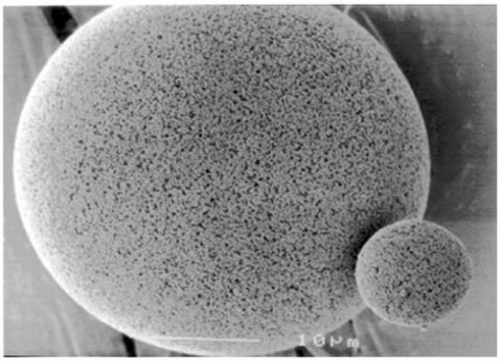
Fig. No: mechanism of transdermal drug delivery.[11]

Transdermal permeation of a drug delivery system based on the

1. Permeation of drug by feasible epidermis
2. Sorption through stratum corneum
3. Take up of the drug moiety through the capillary system in the dermal papillary layer

Microsponges drug delivery system[12]

Microsponges are tiny, sponge-like spherical particles that are composed of porous microspheres. They are microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as a gel, cream, liquid or powder. Microsponge technology has many favorable characteristics, which make it a versatile drug delivery vehicle. It can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved aesthetic properties in an efficient manner. To control the delivery rate of active agents to a predetermined site in the human body has been one of the biggest challenges faced by pharmaceutical scientists. Several predictable and reliable systems have been developed for systemic delivery of drugs using the skin as portal of entry.



A Microsponges Delivery System (MDS) is a patented, highly cross-linked, porous, polymeric microsphere system consisting of porous microspheres that can entrap a wide range of actives and then release them into the skin over time and in response to a trigger. These micro-sponge polymers possess the versatility to load a wide range of actives providing the benefits of enhanced product efficacy, mildness, tolerability, and extended wear to a wide range of skin therapies. Several predictable and reliable systems were developed for systemic drugs under the heading of transdermal delivery system (TDS) using the skin as portal of entry. It has improved the efficacy and safety of many drugs. However, TDS is not practical for delivery of materials whose final target is skin itself. Thus, there is a need for a system to maximize the amount of time that an active ingredient is present either on the skin surface or within the epidermis, while minimizing its transdermal penetration in the body.[13]

Benefits of microsponge technology[14]

Microsponge technology offers:

- Enhanced product performance.
- Extended release.
- Reduced irritation and hence improved patient compliance.
- Improved product elegancy.
- Improved oil control as it can absorb oil up to 6 times its weight without drying.
- Improved formulation flexibility
- Improved thermal, physical, and chemical stability.
- Flexibility to develop novel product forms.
- Microsponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.

Characteristics of material

- Most liquid or soluble ingredients can be entrapped in the particles. Activates that can be entrapped in micro -sponges must meet following requirements,
- It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers.
- It should be stable in contact with polymerization catalyst and conditions of polymerization.[15]

Advantages of microsponges[16]

1. Advanced oil control, absorb up to 6 times its weight without drying Improved product elegancy.
2. MDS allows the incorporation of immiscible products.
3. Extended release
4. Reduced irritation formulas
5. Allows novel product form
6. These are non-irritating, non-mutagenic, non-allergenic and non-toxic.
7. Improved product aesthetics
8. Extended release, continuous action up to 12 hours
9. Reduced irritation,
10. Better tolerance means broader consumer acceptance.

Release mechanism of microsponge

The microsponge particles have an open structure, which means that they do not have a continuous membrane surrounding them. This allows the active ingredient to move freely in and out of the particles and into the vehicle until equilibrium is reached. Once the finished product is applied to the skin, the active ingredient that is already in the vehicle will be absorbed into the skin, depleting the vehicle and disturbing the equilibrium.[17] This will cause the active ingredient to flow from the microsponge particle into the vehicle and then into the skin until the vehicle is either dried or absorbed. Even after that, the microsponge particles retained on the surface of the stratum corneum will continue to gradually release the active ingredient to the skin, providing prolonged release over time. This mechanism of action emphasizes the importance of formulating vehicles for use with microsponge entrapments. If the active

ingredient is too soluble in the desired vehicle during compounding of the finished products, the products will not provide the desired benefits of gradual release.[18]

Method of preparation of microsponge drug delivery system[19]

A drug neither hinders the polymerization process nor become activated by it and also it is stable to free radicals is entrapped with one-step process (liquid liquid suspension polymerization). Micro sponges are suitably prepared by the following methods:

1. Liquid-liquid suspension polymerization
2. Quasi-Emulsion Solvent Diffusion Method

1. Liquid-liquid suspension polymerization:

The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems. In this method the monomers which are immiscible are first dissolved along with active ingredients in a suitable solvent monomer and are then dispersed in the aqueous phases which consist of additives like surfactant, suspending agents to facilitate formation of suspension. The polymerization is then activated by increasing temperature or irradiation or by addition of catalyst. The polymerization process continues the formation of a reservoir type of system with spherical structure. After the polymerization processes, the solvent is removed leaving the spherical structured porous microspheres, i.e., micro sponges. The various steps involved in the preparation of micro sponges are summarized as follows:

Step 1: Selection of monomer as well as combination of monomers.

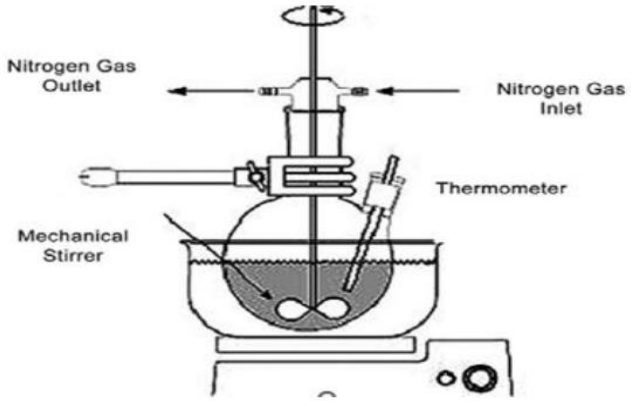
Step 2: Formation of chain monomers as polymerization starts.

Step 3: Formations of ladders as a result of cross-linking between chain monomers.

Step 4: Folding of monomer ladder to form spherical particles.

Step 5: Agglomeration of microspheres leads to the production of bunches of microspheres.

Step 6: Binding of bunches to produce micro sponges.[20]



2. Quasi-Emulsion solvent diffusion method

Porous microspheres (Micro sponges) were also prepared by a quasi-emulsion solvent diffusion method (two-step process) using an internal phase containing polymer which is dissolved in ethyl alcohol. Then, the drug is slowly added to the polymer solution and dissolved under ultrasonication at 35ºC and plasticizer was added in order to aid the plasticity. The inner phase is then poured into external phase containing polyvinyl alcohol and distilled water with continuous stirring for 2 hours11. Then, the mixture was filtered to separate the micro-sponges. The product (Micro-sponges) was washed and dried in an air heated oven at 40°C for 12 hrs.[21]

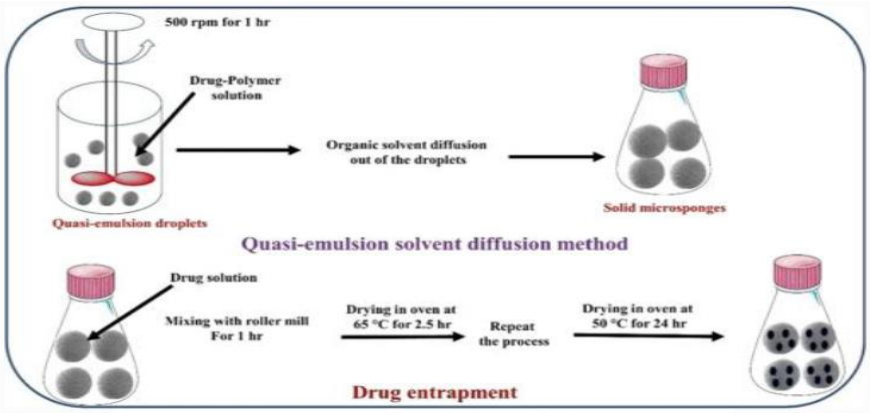


Fig. No: Quasi emulsion solvent diffusion method.

Physical characterization of microsponge drug delivery system

1. Particle size and shape

The sentence you provided can be rephrased as follows: By controlling the size of particles during polymerization, it is possible to obtain free-flowing powders with fine aesthetic attributes. Laser light diffractometry or any other suitable method can be used to perform particle size analysis of loaded and unloaded micro-sponges. The values (d50) can be expressed for all formulations as mean size range. To study the effect of particle size on drug release, cumulative percentage drug release from micro-sponges of different particle size will be plotted against time. Particles larger than 30 µm can impart a gritty feeling, hence particles of sizes between 10 and 25 µm are preferred for use in the final topical formulation. Conventional light microscopy (LM) and scanning electron microscopy (SEM) are the most widely used procedures to visualize microparticles. Both can be used to determine the shape and outer structure of microparticles. LM provides control over coating parameters in case of double-walled microparticles. Confocal fluorescence microscopy is used for the structure characterization of multiple-walled microparticles. Laser light scattering and multi-size coulter counter are other instrumental methods that can be used for the characterization of size, shape, and morphology of the microparticles (micro-sponges).[22]

2. Morphology and Surface topography of microsponges

Microsponges that have been prepared can be coated with gold-palladium under an argon atmosphere at room temperature. The surface morphology of the micro-sponges can then be studied using scanning electron microscopy (SEM). Additionally, SEM of a fractured microsponge particle can be taken to illustrate its ultra-structure.[23]

3. Determination of loading efficiency

The loading efficiency (%) of the micro-sponges can be calculated according to the following Equation: The production yield of the micro particles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microsponge obtained.[24]

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

4. Interaction studies by using FTIR spectroscopy

The drug - excipients interaction were studied using Fourier transform infrared spectrophotometer (FTIR). IR spectra for drug and powdered microsponges were recorded in a Fourier transform infrared spectrophotometer (FTIR 1615, Perkin Elmer, USA) with Potassium Bromide (KBr) pellets. The spectra were scanned over the 3600 to 400 cm-1 range.[25]

5. Resiliency (Viscoelastic properties)

The viscoelastic properties of micro sponges can be adjusted to create beadlets that are either softer or firmer, depending on the requirements of the final product. When the cross-linking is increased, the rate of release tends to slow down.[26]

6. Drug release kinetics

Different models such as Zero order kinetics, First order kinetics, Higuchi, and Korsemeyer-Peppas were used to evaluate the kinetics of drug release from the prepared microsponges by analyzing the dissolution profile of each formulation. Zero order kinetics measures the percentage drug release against time, First order kinetics measures log percentage drug unreleased against time, Higuchi measures percentage drug released against square root of time, and Korsemeyer-Peppas measures log percent drug released against log of time.[27]

7. Dissolution tests

The rate at which microsponges dissolve can be studied using the USP XXIII dissolution apparatus, which has a modified basket consisting of 5µm stainless steel mesh. The dissolution medium is selected based on the solubility of the actives to ensure sink conditions. Samples from the dissolution medium are analyzed at various intervals using appropriate analytical methods.[28]

8. Determination of true density

The true density of micro particles and BPO was determined by using an ultra-pycnometer under helium gas. The mean of repeated measurements was used to calculate the true density.[29]

9. Characterization of pore structure

The intensity and duration of effectiveness of the active ingredient are controlled by the pore volume and diameter. Pore diameter also affects the migration of active ingredients from microsponges into the vehicle in which the material is dispersed. Mercury intrusion porosimeter can be used to study the effect of pore diameter and volume on the rate of drug release from Microsponges. Porosity parameters of Microsponges, such as intrusion-extrusion isotherms, pore size distribution, total pore surface area, average pore diameters, shape, and morphology of the pores, bulk and apparent density, can be determined by using mercury intrusion porosimeter.[30]

10. Stability study

The stability testing is done to guarantee the quality, safety, and effectiveness of the active medication ingredient in dosage forms throughout storage. For a duration of six months in a stability chamber, Microsponges gel formulations were kept in tightly closed, amber-colored glass containers sealed with

aluminum foil at three different temperatures: room temperature (25°C±2°C/60%RH±5%), refrigerator temperature (4.0 °C±1. 0 °C), and accelerated temperature (40°C±2°C/75% RH ± 5%). The samples were taken out at the end of the first, second, third, and six months to assess the in-vitro drug release, pH, entrapment efficiency, and drug concentration.[31]

11. Drug content

Drug concentration in Microsponges gel was measured by HPLC. By accurately weighing 5 gm and dissolving it in 50 ml of Microsponges gel in purified water, the amount of drug present in the gel was determined using sonication with phosphate buffer at pH 7.4. Sonication for 15 minutes and heating for 5 minutes. The test was conducted into the triplicate, and the average percentage of drug content was calculated.[32]

The % drug content of Microsponges preparation was determined by using following formula

%drug content = Sample absorbance /standard absorbance

Pharmaceutical utilization of microsponges

Microsponge delivery systems are utilized to improve the safety, efficacy, and aesthetic quality of topical prescription, over-the-counter, and personal care products. Microsponges have a wide range of applications and are primarily used for topical administration, but recently they have also been used for oral administration. According to several patents, micro-sponges can be used as excipients due to their high loading capacity and sustained release ability.

- **Microsponge for topical delivery**

Microsponge systems are microscopic, polymer-based microspheres that can bind, suspend, or entrap a wide variety of substances and then be incorporated into a formulated product, such as a gel, cream, liquid, or powder. Each microsphere is as tiny as a particle of talcum powder, measuring less than one-thousandth of an inch in diameter. Like a true sponge, each microsphere consists of a myriad of interconnecting voids within a non-collapsible structure that can accept a wide variety of substances. The outer surface is typically porous, allowing the controlled flow of substances into and out of the sphere. Several primary characteristics, or parameters, of the Microsponge system can be defined during the production phase to obtain spheres that are tailored to specific product applications and vehicle compatibility. Microsponge systems are made of biologically inert polymers, which have been extensively studied for safety and found to be non-irritating, non-mutagenic, non-allergenic, non-toxic, and non-biodegradable[1] As a result, the human body cannot convert them into other substances or break them down. Although they are microscopic in size, these systems are too large to pass through the stratum corneum when incorporated into topical products. Microsponge delivery of Benzoyl peroxide (BPO) was developed using an emulsion solvent diffusion method by adding an organic internal phase containing benzoyl peroxide, ethyl cellulose, and dichloromethane into a stirred aqueous phase containing polyvinyl alcohol and by suspension polymerization of styrene and divinyl benzene. This method of delivery has been shown to reduce the side effects of BPO, such as skin irritation, while reducing percutaneous absorption.[33]

- **Microsponge for oral delivery**

The microsponge system has been shown to increase the rate of solubilization of poorly water-soluble drugs by entrapping such drugs in the microsponge system's pores. The drug is reduced to microscopic particles due to the small size of these pores, which greatly increases the surface area and thus the rate of solubilization. The controlled oral delivery of ibuprofen micro-sponges is achieved with an acrylic polymer, Eudragit RS, by changing their intraparticle density. Chlorpheniramine maleate sustained release formulation, using powder-coated micro-sponges, is prepared by the dry impact blending method for oral drug delivery. Ketoprofen controlled oral delivery is prepared by quasi-emulsion solvent diffusion method with Eudragit RS 100, and afterwards tablets of microsponges are prepared by the direct compression method. The compressibility is much improved in the physical mixture of the drug and polymer due to the plastic deformation of the sponge-like microsponge structure, producing mechanically strong tablets. Colon-specific, controlled delivery of flurbiprofen is conducted by using a commercial Microsponge 5640 system. In vitro studies exhibited that compression-coated colon-specific tablet formulations started to release the drug at the eighth hour, corresponding to the proximal colon arrival time, due to the addition of the enzyme, following a modified release pattern, while the drug release from the colon-specific formulations prepared by pore plugging the Microsponges showed an increase at the eighth hour, which was the point of time when the enzyme addition was made.[34]

- **Long lasting colored cosmetics**

Microsponges can be used to enhance the longevity of colored cosmetic products such as rouge or lipsticks.[35] Microsponges help in uniform spreading and improving covering power, making colored cosmetics formulated with micro-sponges highly elegant.[36]

- **For Bone and Tissue engineering**

Bone-substitute compounds were created by mixing pre-polymerized powders of polymethyl-methacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium deficient hydroxyl apatite powders. The final composites were porous and acted as Microsponges. Basic fibroblast growth factor was incorporated in a collagen sponge sheet and was released in the mouse sub-cutis according to the biodegradation of the sponge matrix, exhibiting local angiogenic activity in a dose-dependent manner.[37] The injection of collagen Microsponges incorporating

basic fibroblast growth factor induced a significant increase in the blood flow in the murine ischemic hind limb, which could not have been achieved by the bolus injection of basic fibroblast growth factor. These results suggest the therapeutic utility of type I collagen as a reservoir of basic fibroblast growth factor.[38]

CONCLUSION

Microsponge delivery technology is a controlled release system in which the active pharmaceutical ingredient is loaded in macro porous beads, initiating a reduction in side effects with improved therapeutic efficacy. Microsponges can be effectively incorporated into topical drug delivery systems for retention of dosage form on skin and also used for oral delivery of drugs using bio erodible polymers, especially for colon-specific delivery and controlled-release drug delivery systems, thus improving patient compliance by providing site-specific drug delivery systems and prolonging dosage intervals.

This technology is currently being used in cosmetics, over-the-counter skin care, sunscreens, and prescription products. This kind of drug delivery technology may lead to a better understanding of the healing of several diseases. Hence, the microsponge-based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future.

Microsponges are an attractive drug delivery system due to their ease of manufacturing, simple ingredients, and ability to entrap a wide range of actives with a programmable release. Originally developed for topical delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, antipruritic, rubefacients, etc., the Microsponge Delivery System holds a promising future in various pharmaceutical applications in the coming years as they have unique properties like enhanced product performance and elegance, extended release, reduced irritation, improved thermal, physical, and chemical stability, making them flexible to develop novel product forms. Researchers are continuously trying to develop a drug delivery system that is cost-effective and has better therapeutic efficacy. The technology has shown such promises to meet researchers' expectations. Numerous studies reveal that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic. A Microsponge Delivery System can entrap a wide range of actives and then release them onto the skin over time and in response to triggers. It is a unique technology for the controlled release of topical agents and consists of microporous beads loaded with active agents and can also be used for oral as well as biopharmaceutical drug delivery. A Microsponge Delivery System can release its active ingredient on a time mode and also in response to other stimuli. Thus, Microsponges have a lot of potential and are a very emerging field that needs to be explored.

Review of litrature

1 **Shyam sunder mandava** *et al*., (2012), Transdermal drug delivery system (TDS) is not practically for delivery of materials whose final target is skin itself. Application topical agents generally offer many problems such as rashes, skin irritancy and burning sensation etc due to higher percutaneous absorption of drugs on the skin. Some conventional dosage e.g., gels and ointments which are often aesthetically unappealing, greasiness and stickiness etc. that often result into lack of patient compliance. For reduce this side effects, microsponge technology offers many advantages over the conventional drug delivery. The microsponge based drug delivery system is a unique technology for controlled release and enhanced drug deposition in the skin while minimizing transdermal penetration of topically active agents. Microsponge delivery system (MDS) can provide increased efficacy for topically active agents with enhanced safety, extended product stability, enhanced formulation flexibility, reduced side effects and improved aesthetic properties in an efficient and novel manner. MDS technology is being used currently in cosmetics, over-the-counter skin care, sunscreen and prescription products.[39]

2 **Gautam Singhvi *et al*., (2018),** Microsponges are the spherical particles ranging from 5 to 300 μm in size. These are further made up of clusters of smaller spheres. They are designed for delivering the drug efficiently at a comparatively lesser dose and enhancing the stability, modifying the drug release profile and minimizing the side effects. Microsponge drug delivery system decrease transdermal invasion of the active ingredient into the skin while increasing the time the drug remains on the skin surface or within the epidermis. Preparation of the microsponges includes two techniques: Liquid–liquid suspension polymerization and Quasi-emulsion solvent diffusion method. Their characterization and evaluation can be done in many ways like particle-size measurement and porosity, morphology, true density determination, analyzing the rheological properties, and dissolution studies. Present work focuses on the detailed study of the microsponge drug delivery system. This will help the reader to get all the information regarding the microsponge delivery systems.[40]

3 **D.J. Ingale *et al., (2012),*** Transdermal drug delivery system (TDDS) is not practicable for delivery of materials whose final target is skin itself. Controlled release of drugs onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts is a challenging area of research. Microsponges are highly porous micro-sized particles with a unique ability for entrapping active pharmaceutical ingredients. To control the delivery

rate of active agents to a predetermined site in human body has been one of the biggest challenges faced by scientists. Microsponges are safe biologically and offer unique advantage of programmable release. This technology offers entrapment of ingredients and is believed to contribute towards reduced side effects, improved stability, increased elegance and enhanced formulation flexibility. This technology is being used for topical formulations and also for oral administration. The present review describes microsponge technology including its preparation, characterization, programmable parameters and release mechanism of microsponge drug delivery system.[41]

4 **Urvashi B. Patel *et al.*,(2018)** Microsponge is recent novel technique for control release and target specific drug delivery system. Therefore many scientist or researcher attracted towards the microsponge drug delivery system. Also Microsponge technology has been introduced in topical drug products to facilitate the controlled release of active drug into the skin in order to reduce systemic exposure and minimize local cutaneous reactions to active drugs. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. Transdermal drug delivery system (TDS) is not practically for delivery of materials whose final target is skin itself. Application topical agents generally offer many problems such as rashes, skin irritancy and burning sensation etc due to higher percutaneous absorption of drugs on the skin. Some conventional dosage e.g., gels and ointments which are often aesthetically unappealing, greasiness and stickiness etc. that often result into lack of patient compliance.[42]

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