

**MICROSPONGE-BASED TOPICAL DELIVERY SYSTEMS: A
VERSATILE APPROACH FOR ENHANCED THERAPIES****Mamatha G. T., Hithesh P.*, Mahalakshmi A. S. and Spoorthy R.**

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya

District, Karnataka, India-571422.

Article Received on
13 February 2025,Revised on 04 March 2025,
Accepted on 24 March 2025

DOI: 10.20959/wjpr20257-36092

***Corresponding Author****Hithesh P.**Department of
Pharmaceutics, Bharathi
College of Pharmacy,
Bharathinagara, Mandya
District, Karnataka, India-
571422.**ABSTRACT**

The microsphere delivery system is an advanced polymeric technology designed to enhance the effectiveness of topical drug delivery. It consists of highly cross linked, porous microspheres capable of entrapping active ingredients and releasing them gradually into the skin over an extended period. This sustained release mechanism offers several benefits, including prolonged drug action, reduced skin irritation, enhanced patient tolerance, and improved thermal, physical, and chemical stability of the formulation. Microspheres are manufactured using different techniques, such as suspension polymerization in a liquid-liquid system or emulsion-based methods. These techniques create porous structures that allow the controlled release of active ingredients. Due to their unique properties, microspheres are incorporated into various dermatological and cosmetic formulations, including creams, powders, gels, and lotions. Additionally, they can encapsulate a wide range of pharmaceutical and cosmetic agents, such as anti-inflammatory drugs, skin lightening agents, sunscreens, and anti-aging compounds. One of the key advantages of microspheres is their ability to improve drug penetration into the skin while minimizing irritation, making them highly beneficial for sensitive skin applications. Their sustained-release capability also ensures a prolonged therapeutic effect, reducing the need for frequent application. This review focuses on the technology of microspheres, covering their synthesis, advantages, characterization, evaluation, and drug release mechanisms in topical drug delivery systems.

KEYWORDS: Microsponge, Microsphere, Topical delivery, Versatile approach, Quasi emulsion solvent diffusion.

INTRODUCTION

Micro-sponges are polymeric, porous microspheres that are mostly applied topically over extended periods of time. In addition to improving stability, lowering side effects, and altering drug release profiles, micro sponge is made to effectively distribute a pharmaceutically active substance at the lowest possible dosage. The Micro sponge Drug Delivery System (MDDS) is a patented, highly cross-linked, porous polymeric microsphere system (10-25 μ) made up of porous microsphere particles with a large porous surface that can entrap a variety of actives (prescription medications, cosmetics, over-the-counter (OTC) skin care products, and sunscreens) and release them onto the skin over time and in response to triggers.^[1] Microsponge systems are built on tiny, polymer-based microspheres that have the ability to entrap or suspend a broad range of compounds. These microspheres can then be added to a prepared product, such as a liquid, gel, cream, or powder. Microsponge technology allows components to be trapped and is thought to help with less adverse effects, better stability, more elegance, and more formulation flexibility. Furthermore, a number of investigations have verified that Microsponge systems are non-toxic, non-irritating, non-mutagenic, and non-allergic.^[2] Topical formulations are uncontrolled evaporation of the active ingredient, an unpleasant odour, and possible medication incompatibilities with the carriers are the problems with topical preparations. The goal of conventional topical medication formulations is to target the skin's outermost layer. When applied, these products usually release their active chemicals, creating a highly concentrated coating that is quickly absorbed.^[3] Topical treatment for severe life intimidating skin fungal infections has come out as an efficient therapy occupying a high-flying position among the alternatives of treatment. Although, topical delivery has resulted in systemic absorption and skin irritation and hence failed to accomplish mycological eradication. Furthermore, in drug delivery, the topical administration of bioactive molecules is still a challenging area with the difficulty in controlling and determining the exact amount of drug reaching the different skin layers.^[4]

Advantages of topical drug delivery system

- Hepatic first pass metabolism, salivary metabolism and intestinal metabolism are avoided.
- Ease of usage makes it possible for patients to self-administer these systems.

- In case of an emergency, removing the patch at any point of time during therapy can instantly stop drug input.
- Since the composition of skin structurally and biologically is the same in almost all humans, there is minimal inter and intra patient variation.
- Drugs showing gastrointestinal irritation and absorption can be suitably administered through skin.
- Continuous, non-invasive infusion can be achieved for drugs with short biological half-life which would otherwise require frequent dosing.
- Due to reduced frequency of dosing, there is better patient compliance.
- Therapeutic failures associated with irregularities in dosing with conventional therapies can be avoided.^[5]

Disadvantages of topical drug delivery system

- Risk of burns if electrodes are used improperly
- Difficulty stabilizing the therapeutic agent in the vehicle
- Complexity of the drug release system
- Can be prolonged to administer
- Minor tingling, irritation and burning
- SC must be unbroken for effective drug penetration
- Impossible to use on a large area
- Can be disturb the cargo if high voltage is used
- Possibility of cell damage
- Relatively nonspecific.^[6]

Types of topical drug delivery system

1. Gels/Creams

It is applied topically to treat skin conditions such as seborrhoeic dermatitis, rosacea, and acne vulgaris. Several strategies have been used to improve medication penetration through the skin using vehicles or penetration enhancers, such as propylene glycol, fatty acids, or alcohols, in order to alleviate as for mentioned in the symptoms.

2. Nano-colloidal carriers

The second generation of nano-sized lipid carriers used to transport hydrophilic and hydrophobic medications are called nano-structured lipid carriers, or NLCs. The addition of liquid lipid to the solid matrix improves the carrier's ability to load drugs and lowers the

frequency of drug expulsions, which is a disadvantage of solid lipid nano-carriers (SLNs). NLCs are appropriate carriers for topical drug delivery in a sustained/controlled manner for local or systemic usage since they are stable, biocompatible, and biodegradable.

3. Microneedles

By forming tiny holes in the skin, microneedles-2D-3D organised micro-projections that are less than 100 μ long improve the drug's permeability through the stratum corneum. It is a minimally invasive method that confuses the effects of transdermal patches and hypodermic needles to deliver drugs (proteins, peptides/polypeptides, vaccines, etc.) to the skin's viable epidermal zone. Superficial penetration and non-stimulation of nerves make microneedles a pain-free drug delivery device.

4. Hydrogels/modified hydrogels

A hydrogel is a network of hydrophilic polymer chains that can hold a large amount of water while maintaining a gel-like structure. It is widely used in pharmaceuticals, cosmetics, wound dressings, contact lenses, and biomedical applications. Thermo-sensitive hydrogels are a novel class of formulations that exhibit physical state changes in response to stimuli. These are colloidal hydrophilic polymeric (natural or synthetic) systems that shift from a sol to a gel state in response to temperature changes.

5. Rapid dissolving tablets (RDT)

Rapid-dissolving tablets (RDTs), also called orally disintegrating tablets (ODTs) or fast-melt tablets are designed to dissolve quickly in the mouth without needing water. The tablets contained bio adhesive polymers (hydroxypropyl cellulose, low substituted hydroxyethyl cellulose, polyvinylpyrrolidone; PVP, PVA, PEO, chitosan, carrageenan, etc.), sugar-alcohol/saccharides (glycerol, arabitol, sorbitol, maltitol, xylitol, etc.), and API (antimicrobial, antiviral, anti-migraine, anti-Parkinson, contraceptives, hormones, etc.).

6. Pressure sensitive adhesives

Simple, self-applying, stable, and reversible delivery systems, pressure sensitive adhesives are made to release the medication from the formulation for extended lengths of time following a single application. Under light pressure, these formulations readily stick to the biological surface and can be removed when treatment is finished or if an unpleasant reaction occurs.

7. Soft-gelatin capsules

Soft gelatin capsules are discrete solid dosage forms with a hermetically sealed shell that contain semi-solid or liquid medication. Soft gelatine capsules are used pharmaceutically to improve the drug's bio-performance due to their stability, biocompatibility, and biodegradable nature.

8. Suspensions

A suspension is a liquid dosage form where fine solid particles are dispersed in a liquid medium. It requires suspending agents to maintain uniform dispersion and wetting agents to help disperse hydrophobic drugs. Flocculating agents prevent caking, while preservatives inhibit microbial growth. Proper viscosity control ensures easy pouring while preventing rapid sedimentation. Suspensions are used in oral, topical, parenteral, and ophthalmic formulations for better patient compliance.

9. Colloidal carriers

Lipophilic medications can be topically administered into the posterior part of the eye using microemulsion-based eye drops. Transparent and thermodynamically stable, microemulsions are made up of tiny disperse phase droplets scattered across a dispersion medium. Microemulsions are an appealing delivery system for ocular administration due to their inherent qualities, particular architectures, and delayed release characteristics.

10. Contact lens

Translucent biomimetic contact lens carrier designed to improve drug loading and offer a longer-lasting and consistent release of medication. Recognitive polymeric hydrogel made of silicon, carbon, and organic-based polymer chains was used to create the soft contact lens.^[7]

Route of penetration

According to figure, a drug molecule may diffuse through shunts, especially those provided by the rather widely dispersed hair follicles and eccrine glands, or it may pass through the epidermis itself during the process of percutaneous permeation. Drug molecules may enter the skin by sweat ducts or hair follicles during the first transitory diffusion stage, after which they are absorbed by the sebaceous glands and follicular epithelium. When a steady state has been reached the diffusion through the intact stratum corneum becomes the primary pathway for transdermal permeation.^[8]

Microsponges drug delivery system

Micro-sponges are microscopic, spherical particles made of porous microspheres that resemble sponges. These are tiny, polymer-based microspheres that have the ability to suspend or trap a broad range of materials. They can then be added to a prepared product, such as a gel, cream, liquid, or powder. Microsponge technology is a versatile medication delivery method because of its many advantageous features. They efficiently boost the effectiveness of topically active drugs while improving safety, product stability, and aesthetic qualities. One of the most difficult problems facing pharmaceutical scientists has been regulating the rate at which active ingredients are delivered to a specific location in the human body. Using the skin as a conduit, a number of dependable and predictable systems have been created for systemic medication delivery of drug using skin as the portal of entry.^[9]

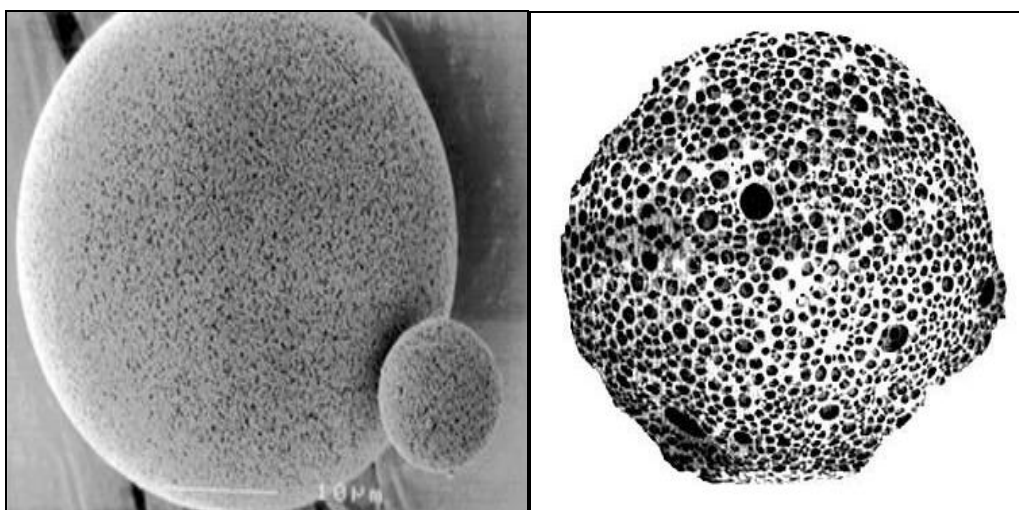


Fig. No. 1: Microscopic structure of microsponge.

A proprietary, highly cross-linked, porous, polymeric microsphere system called a Microsponges Delivery System (MDS) is made up of porous microspheres that have the ability to imprison a variety of active ingredients and then release them into the skin gradually and in reaction to a trigger. With the capacity to load a broad variety of active ingredients, these microsponge polymers provide a variety of skin therapies the advantages of increased product efficacy, mildness, tolerability, and prolonged wear. Under the umbrella of transdermal delivery systems (TDS), which use the skin as a portal of entry, a number of dependable and predictable systems for systemic medications were created. Numerous medications' safety and effectiveness have increased as a result. 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.^[10]

Benefits of micro sponge technology

- Enhanced product performance.
- Extended release.
- Reduced irritation and hence improved patient compliance.
- Improved product elegance.
- 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.
- In contrast to other technologies like microencapsulation and liposomes, MDS has wide range of chemical stability, higher payload and are easy to formulate.
- Microsponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.^[11]

Characteristic of Microsponge material

1. Microsponges are stable over the extended pH range from 1 to 11 and constant up 130°C.
2. Microsponges are friendly with many of excipients and no require of sterilization.
3. About 50 to 60 % drug may possibly be entrapped in micro sponges, and gives good flowing properties.
4. These are still molecules without any allergy, irritation and toxicity.
5. It must 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.
6. It must be water immiscible or at most only slightly soluble.
7. It must be inert to monomers and should not increase the viscosity of the mixture throughout formulation.
8. It must be stable when in contact with the polymerization catalyst and under environment of polymerization.
9. The spherical structure of the micro sponges must not collapse.^[12]

Advantages of micro sponge

- Microsponge delivery system allows the incorporation of immiscible products
- It shows extended drug release, continuous action up to 12 hours. It reduced formulas of irritation
- Advanced oil control, without drying it absorb up to six times its weight Improved product elegance

- It allows novel product form
- These microsponges are non-toxic, non-mutagenic, non-irritating, non-allergenic
- Microsponges improves bio availability of the same drugs
- It improves control of condition
- It improves efficacy in treatment
- It improves processing of materials Eg: liquid can be converted to powders.^[13]

Application of microsponges

Topical application

The substance that enters the skin to deliver a specific drug is known as a topical delivery system. The transfer of topical medications across the skin's barrier is a challenge. Topical delivery encompasses two product categories: internal and exterior topicals.

External topicals

External topicals are applied externally to cutaneous tissues by covering the afflicted area with a spray, spread, or other method.

Internal topicals

Topicals applied locally to the anorectal tissues, vaginally, or orally on the mucous membranes are known as internal topicals. Topical preparations are usually used for localized effects at the site of application because they enable drug penetration into the underlying layers of skin or mucous membranes. Although some unintended drug absorption may occur, it typically occurs in little quantities and at subtherapeutic levels.^[14]

Release mechanism of microsphere

Several factors, including the physicochemical characteristics of the active ingredient and the cutaneous environment, can be changed to regulate the release of a medication from microsponges. As was previously mentioned, the vehicle that dissolves the polymer has a significant impact on the active agent's exit from the system. The concentration of the active ingredient in the polymer and the vehicle are initially in balance. The MDS releases additional active agent in response to the demand generated by the equilibrium shift as the concentration of the active agent from the vehicle diminishes in the skin. A method like this causes the active ingredient to be released onto the skin steadily and continuously. Furthermore, the MDS can serve as a depot, which, even after the skin has absorbed or dried the carrier, keeps releasing the active ingredient to the skin. Researchers evaluated the

features of the reported microsphere-based intradermal drug delivery systems using mupirocin, phenol, hydroxyzine hydrochloride, Glabridin, and benzoyl peroxide as model drugs. They found that diffusion was the primary drug release mechanism and that the microsphere preparation could speed up drug release.^[15]

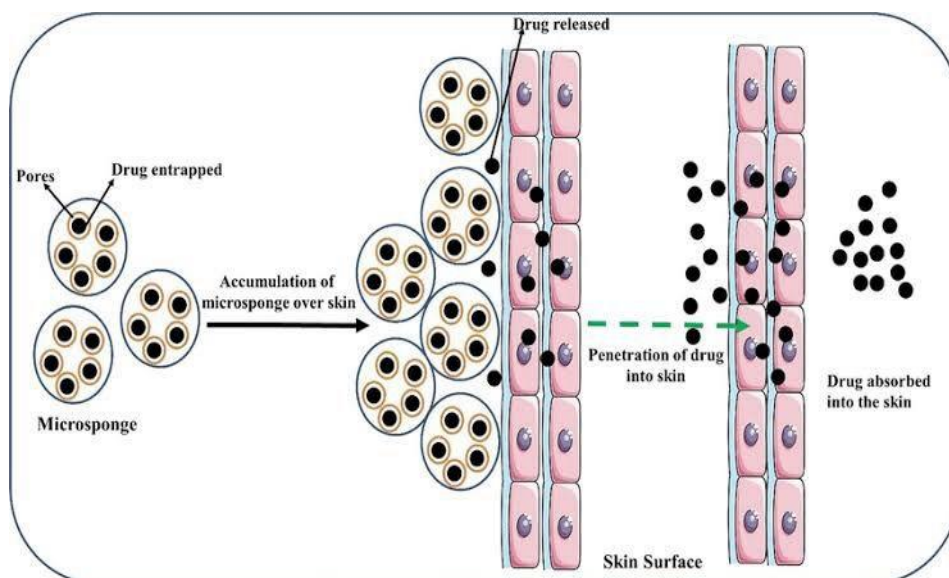


Fig. No. 2: representation of release mechanism of microsphere.

Preparation of microspheres

Drug loading in microspheres can take place in two ways, by one-step or two-step process; based on physicochemical properties of drug to be loaded. If the drug is typically an inert non-polar material, it will create the porous structure which is called as porogen. Porogen drug, which neither hinders the polymerization nor become activated by it and stable to free radicals, is entrapped with one-step process.

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.^[16]

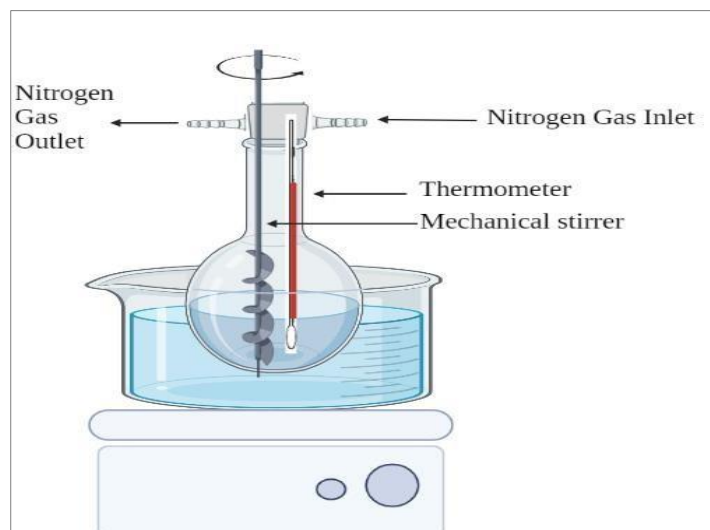


Fig. No. 3: representation of Liquid–liquid suspension polymerization method.

Quasi-Emulsion solvent diffusion method

A quasi-emulsion solvent diffusion approach (two-step procedure) was also used to create porous microspheres, or micro sponges, utilising an internal phase that included a polymer soaked in ethyl alcohol. After that, the medication is gradually added to the polymer solution, dissolved by ultrasonication at 35 °C, and plasticiser is added to promote plasticity. The outer phase, which contains distilled water and polyvinyl alcohol, is then filled with the inner phase while being constantly stirred for two hours¹¹. The micro-sponges were then separated from the mixture by filtering. The item (micro-sponges) was cleaned and dried for 12 hours at 40°C in an air-heated oven.^[17]

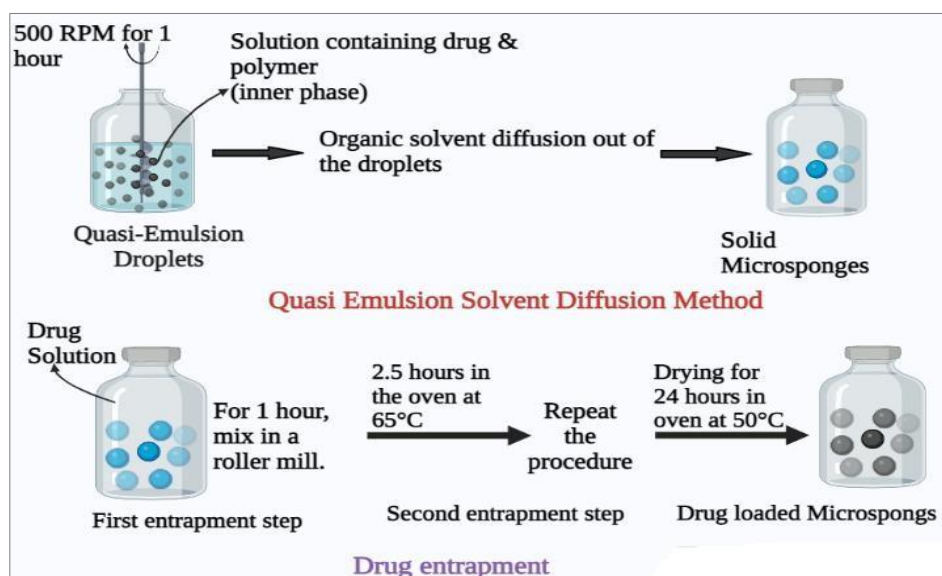


Fig. No. 4: representation of Quasi-emulsion solvent diffusion method.

Physical characterization of microsphere drug delivery system

1. Production yield

Production yield of microspheres was determined by formula mentioned below.^[18]

$$\text{Production yield (PY)} = \frac{\text{practical mass of microspheres}}{\text{Theoretical mass (polymer + drug)}} \times 100$$

2. Morphology and Surface topography of microspheres

Gold-palladium can be applied to prepared microspheres at room temperature in an argon environment. Scanning electron microscopy (SEM) can then be used to examine the microspheres' surface morphology. Furthermore, a shattered microsphere particle's ultrastructure can be shown via SEM.^[19]

3. Differential scanning calorimetry (DSC)

Using a differential scanning calorimeter (Mettler Toledo) DSC 821e equipped with an intercooler, the DDEA microsphere formulation's thermogram was acquired. To calibrate the DSC enthalpy and temperature scale, an indium standard was suggested. Microsphere samples were hermetically stored in an aluminium pan and heated between 10 and 200 °C at a steady rate of 10 °C per minute. An inert atmosphere was maintained by purging nitrogen at a rate of 10 millilitres per minute.^[20]

4. Determination of loading efficiency

The following formula can be used to determine the microspheres' loading efficiency (%).^[21]

$$\text{Loading efficiency} = \frac{\text{Actual Drug Content in Microsponge}}{\text{Theoretical Drug Content}} \times 100$$

5. Particle size determination

Particle size analysis of loaded and unloaded microsponges is done using laser light diffractometry or any other appropriate technique. All formulas and sizes of the values can be expressed. To investigate the impact of particle size on drug release, the cumulative percentage of drug release from microsponges with varying particle sizes will be plotted versus time. Particles between 10 and 25 μm are recommended for use in the final topical formulation because particles bigger than 30 μm can give off a grainy feeling.^[22]

6. Scanning electron microscope study

The produced microsponges can be coated with gold palladium at room temperature in an argon environment for morphology and surface topography. Scanning electron microscopy (SME) can then be used to examine the microsponges' surface morphology. The ultrastructure of a shattered microsponge particle can be obtained via SEM.^[23]

7. Dissolution Studies

Using a modified basket made of 5 μm stainless steel mesh, dissolution apparatus (USP XXIII) can be used to study the dissolution profile of microsponges. The rotational speed is 150 rpm. 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.^[24]

8. Drug release kinetics

The amount of drug released vs time was used to ascertain the drug release mechanism and examine the variations in release profiles between microsponges. The following mathematical models were used to analyse the release data.^[25]

$$Q = k_1 t^n \quad \text{OR} \quad \log Q = \log k_1 + n \log t$$

9. Determination of true density

Using helium gas and an ultra-pycnometer, real densities of BPO and microparticles were ascertained. True density was determined by taking the average of several readings.^[26]

10. Stability study

The purpose of stability testing is to ensure that the active pharmaceutical ingredient in dosage forms remains effective, safe, and of high quality throughout storage. Microsponges gel compositions were stored in firmly sealed, amber-coloured glass containers covered with aluminium foil at three distinct temperatures for six months in a stability chamber: at room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$), fridge temperature ($4^{\circ}\text{C} \pm 2^{\circ}\text{C}$), the accelerated temperature ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}/75\% \text{ RH} \pm 5\%$) and the ambient temperature ($40^{\circ}\text{C} \pm 1.0^{\circ}\text{C}$). To evaluate the in-vitro drug release, pH, entrapment efficiency, and drug concentration, the samples were removed at the conclusion of the first, second, third, and sixth months.^[27]

Microsponge for topical delivery

Microsponge delivery systems (MDS) are innovative, porous polymer-based microspheres designed for controlled and sustained drug release in topical formulations. These microscopic sponges can entrap active ingredients, gradually releasing them upon application to enhance efficacy while minimizing side effects. They offer several advantages, such as prolonged drug action, improved stability, reduced skin irritation, and better patient compliance due to their lightweight, non-greasy texture. Microsponge technology is widely used in dermatology for acne treatments, anti-aging products, sunscreens, and moisturizers. For the topically active sunscreen compounds, a unique delivery mechanism is now needed. Microsponge is a spongelike porous polymeric structure with prolonged drug release that ranges in size from 10 to 25 μm . With less irritation, mutagenicity, allergenicity, and adverse effects, it provides a higher medication payload and stability for topical applications. Microsponge has gained widespread recognition in the contemporary topical product period due to these excessive benefits.^[28]

Microsponge for oral delivery

Conventional dosage forms used orally typically release the active ingredient into the gastrointestinal fluid, and the drug's physicochemical characteristics determine how well it is absorbed from the different parts of the gastrointestinal tract (GIT). The vast majority of pharmaceutical formulations that are sold commercially are immediate-release medicines, which may cause the active ingredient to be poorly absorbed or the substance to be eliminated from the body before the next dose. As a result, these formulations might deprive users of the active agent's therapeutic benefits. By lowering the frequency of dosages, permitting gastric bypass or site-specific distribution, boosting the active compound's

effectiveness, and enhancing safety by lowering side effects and breakthrough symptoms, controlled drug delivery systems can help address these problems. The field of medication delivery technology is now fiercely competitive and changing quickly. An increasing number of delivery system advancements are being combined to maximise the therapy's effectiveness and affordability. The microparticulate drug carrier technique was developed as a result of these efforts to create innovative drug carrier systems.^[29]

Bone substitutes

Pre-polymerized polymethylmethacrylate and liquid methyl methacrylate monomer powders were combined with two aqueous dispersions of calcium-deficient hydroxyapatite (CDHA) powders and α -tricalcium phosphate (α -TCP) grains to create bone-substitute compounds. It seemed that the finished composites were permeable. The resultant composites' osteo-conductivity and osteo-conductivity were evaluated *in vivo* by implanting them in rabbits. Inside the pores where the inorganic powders had been deposited, new trabecular bone was seen to form. The resulting material exhibits good osteointegration rate, biocompatibility, and osteogenesis qualities.^[30]

Recently reported research work in microsp sponge drug delivery system

SI No	AUTHOR	DRUG	METHOD	REMARKS
1.	ThavvaVE <i>et al.</i> , (2019)	Terbinafine HCl	Liquid-liquid suspension polymerization	From the production yields of Terbinafine hydrochloride microsp sponge formulations, it was indicated that increasing the drug: polymer ratio to some extent increased the production yield. The release rate was high during the first two hours then the microsponges were able to sustain the release of THCI for more than 8 h in most formulations by combination of different PVA concentration. ^[31]
2.	Rafat S, <i>et al.</i> , (2019)	Clobetasol Propionate	Cold method	Clobetasol propionate of microsp sponge containing 5, 10, and 20 mg/g of, Clobetasol propionate being low-, medium- and high-Gel, in microsp sponge gel, clobetasol propionate of 6.5% each of Carbopol 934 and gave homogeneity, good consistency, optimum pH of 7.2. ^[32]
3.	Syal S <i>et al.</i> , (2020)	Havan Ash	Quasi-emulsion solvent diffusion	The formulation F3 has better results than other F1, F2, and F4 formulations. F3 have its appearance

			method	silver colour, consistency very good, Grittiness, homogeneity good, pH 6.3, Microsponge become highly competitive and rapidly evolving technology and more research are carrying out to optimize cost effectiveness and efficacy of the therapy. ^[33]
4.	Tomar MK <i>et al.</i> , (2022)	Clarithromycin	Quasi-emulsion solvent diffusion method	The F3 microsponge formulation showed a high production yield, drug content, and encapsulation efficiency with varying polymer concentrations. It released a significant amount of drug over 8 hours. The gel prepared with F3 microsponges was transparent, homogeneous, and had ideal physical properties, including good spread ability and viscosity. The formulation exhibited high viscosity and excellent dispersibility. ^[34]
5.	Hamid Hussain <i>et al.</i> , (2014)	Diclofenac sodium	Quasi emulsion technique	Increasing the drug/polymer ratio improved the yield significantly, with a notable change in particle size, which increased initially but decreased after a certain ratio. The gel showed a stable pH and good spread ability, with viscosity values within an optimal range. The cumulative drug release varied, reflecting different release profiles based on the polymer concentration. This variation in release indicates a tailored approach for drug delivery. ^[35]
6.	Alaa Khattab <i>et al.</i> , (2022)	Tazarotene	Emulsion solvent diffusion	Increasing the drug/polymer ratio enhanced the yield and caused an increase in particle size, which stabilized after reaching a certain concentration. The gel maintained a neutral pH, exhibited good spread ability, and showed viscosity within an optimal range. The cumulative drug release varied significantly, indicating different release profiles depending on the drug/polymer ratio. This demonstrates the formulation's potential for tailored drug delivery. ^[36]
7.	Farhana Sultan <i>et al.</i> , (2021)	Luliconazole	Quasi-emulsion solvent diffusion method	FG1 exhibited controlled drug release over 12 hours, slightly lower than FG2. The LCZ gel formulation with microsponges showed the best

				controlled release and followed zero-order kinetics. The formulation demonstrated effective drug diffusion over time. It holds promise for treating fungal infections like tinea pedis, tinea cruris, and tinea corporis. ^[37]
8.	FarsanaT <i>et al.</i> , (2023)	azithromycin	Emulsion solvent diffusion method	The gel formulation was subjected to in vitro drug release studies in pH 6.8 PBS, demonstrating an extended drug release for approximately 24 hours. Additionally, antimicrobial studies were conducted using <i>S. aureus</i> in a nutrient agar medium over a 24-hour period. The formulated microsphere gel exhibited promising antibacterial activity. ^[38]
9.	Rajashri b. Ambikar <i>et al.</i> , (2021)	Diclofenac sodium	quasi solvent diffusion method	The DSER4 microsphere formulation demonstrated good production yield, entrapment efficiency, and drug release over time, with an optimal particle size. When incorporated into an in-situ gel, it showed sustained drug release and strong gelling capacity. Rheological studies confirmed the gel transitioned effectively under physiological conditions. The gel formed a firm structure, ensuring prolonged drug delivery. ^[39]
10.	Archana Dhyani <i>et al.</i> , (2025)	Atenolol	Oil in oil emulsion diffusion method	The microspheres exhibited a particle size range with entrapment efficiencies. The percentage yield varied while cumulative drug release. The microsphere-loaded gel had a pH, with viscosity range. ^[40]

CONCLUSION

The present review conclude that Microsphere Topical Delivery System (MTDS) represents a significant advancement in dermatological and cosmetic formulations, offering controlled and sustained drug release, enhanced stability, and reduced side effects. Its unique porous structure allows for improved drug loading, targeted delivery, and minimized irritation, making it highly suitable for topical applications such as acne treatment, anti-aging formulations, and wound healing. Hence, the microsphere drug delivery technology is probably going to develop into a useful drug delivery matrix material for a number of therapeutic uses in the future.

REFERENCES

1. Shrivastava S, Kumar D, Dubey CK, Singh SP, Khinchi MP. A review: microsphere-an effective drug delivery system. "Asian J. Pharm. Res.", Mar. 1, 2017; 1-08.
2. Patel A, Upadhyay P, Trivedi J, Shah S, Patel J. Microspheres as the versatile tool for Topical route: A Review. "Int. J. Pharm. Sci. Res.", Sep. 1, 2012; 3(9): 2926.
3. Mandava SS, Thavva V. Novel approach: microsphere drug delivery system. "Int. J. Pharm. Sci. Res.", Apr. 1, 2012; 3(4): 967.
4. Moin A, Deb TK, Osmani RA, Bhosale RR, Hani U. Fabrication, characterization, and evaluation of microsphere delivery system for facilitated fungal therapy. J Basic Clin Pharm., Mar. 2016; 7(2): 39.
5. Patel AV, Shah BN. Transdermal drug delivery system: A review. Pharma Science Monitor, Jan. 1, 2018; 9(1).
6. Jeong WY, Kwon M, Choi HE, Kim KS. Recent advances in transdermal drug delivery systems: A review. Biomaterials research, Jul. 28, 2021; 25(1): 24.
7. Singh Malik D, Mital N, Kaur G. Topical drug delivery systems: a patent review. Expert opinion on therapeutic patents, 2016 Feb 1; 26(2): 213-28.
8. Tanwar H, Sachdeva R. Transdermal drug delivery system: A review. "Int. J. Pharm. Sci. Res.", 2016 Jun 1; 7(6): 2274.
9. Kappor D, Patel M, Vyas RB, Lad C, Tyagi BL. A review on microsphere drug delivery system J. Drug Deliv. Ther, 2014; 14, 4(5): 29-35.
10. Aloorkar NH, Kulkarni AS, Ingale DJ, Patil RA. Microspheres as innovative drug delivery systems. Int J Pharm Sci Nanotechnol, 2012; 5(1): 1597-606.
11. Osmani RA, Aloorkar NH, Kulkarni AS, Harkare BR, Bhosale RR. A new cornucopia in topical drug delivery: microsphere technology. Asian J Pharm Sci Technol, 2014; 4: 48-60.
12. Shukla A, Garg A, Garg S. Application of microsphere technique in topical drug delivery system. Asian Journal of Biomaterial Research, 2016; 2(4): 120-6.
13. Ravi G, Ravi V, Bose PS, Saritha D. MICROSPHERES—A comprehensive review: success and challenges. Am. J. Pharm. Res., 2019; 9(07).
14. Patil PB, Datir SK, Saudagar RB. A review on topical gels as drug delivery system. J Drug Deliv Ther., 2019; 9(3): 989-94.
15. Mahant S, Kumar S, Nanda S, Rao R. Microspheres for dermatological applications: Perspectives and challenges. "Asian J. Pharm. Sci.", 2020 May 1; 15(3): 273-91.

16. D'souza JI, More HN. Topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsphere delivery system *Res J Pharm Technol*, 2008; 1(4): 502-6.
17. Vikrant K, Nikam DR, Somwanshi SB, Gaware VM, Kotade KB, Dhamak KB, Khadse AN, Kashid VA. Microparticles: a novel approach to enhance the drug delivery-a review *Int J Phys Res Appl*, 2011; 3(8): 170-83.
18. Moin A, Deb TK, Osmani RA, Bhosale RR, Hani U. Fabrication, characterization, and evaluation of microsphere delivery system for facilitated fungal therapy. *J Basic Clin Pharm.*, 2016 Mar; 7(2): 39.
19. Saurabh Kumar, Tyagi LK, and Dashrath Singh. Microsphere delivery system (MDS): A unique technology for delivery of active ingredients. *Int J Phys Res Appl*, 2011; 2(12): 3069-3080.
20. Osmani RA, Aloorkar NH, Ingale DJ, Kulkarni PK, Hani U, Bhosale RR, Dev DJ. Microspheres based novel drug delivery system for augmented arthritis therapy. *Saudi Pharm J.*, 2015 Oct 1; 23(5): 562-72.
21. Vitthal P, Anuradha S. A review on microspheres drug delivery system. *IJRAR-Int. J. Res. Anal. Rev. (IJRAR)*, E-ISSN. 2020: 2348-1269.
22. Emanuele AD, Dinarvand R. Preparation, Characterization and Drug Release from Thermo responsive Microspheres. *Int J Pharma*, 1995; 237-42.
23. Orr JRC. Application of mercury penetration to material analysis. *Powder Technol*, 1969; 3: 117-123.
24. Saurabh Kumar, Tyagi LK, and Dashrath Singh. Microsphere delivery system (MDS): A unique technology for delivery of active ingredients. *IJPSR*, 2011; 2(12): 3069-3080.
25. Jayaweera DM: Medicinal Plants (Indigenous and exotic) used in Ceylon. Part-II. A Publication of the Natural Sciences Council of Sri Lanka, Colombo 1980.
26. Sato T, Kanke M, Schroeder G, Deluca P: Porous biodegradable microspheres for controlled drug delivery. Assessment of processing conditions and solvent removal techniques. *Pharm Res.*, 1988; 5: 21-30.
27. Patel EK and Oswal RJ. Nanosphere and Microspheres, a Novel Drug Delivery System *Int. Res. J. Pharm*, 2012; 2(2): 238.
28. Bhura MR, Bhagat KA, Shah SK. Formulation and evaluation of topical nanoemulgel of adapalene. *World J. Pharm. Res.*, 2015; 3: 1013-24.
29. Pawar AP, Gholap AP, Kuchekar AB, Bothiraja C, Mali AJ. Formulation and evaluation of optimized oxybenzone microsphere gel for topical delivery. "*J. Drug Deliv.*", 2015; 2015(1): 261068.

30. Srivastava R, Pathak K. Microsponges: a futuristic approach for oral drug delivery. Expert opinion on drug delivery, Jul. 1, 2012; 9(7): 863-78.
31. Patel UB, Patel HM, Shah CN, Barse R. A review-Recent research on microsphere a novel new drug delivery system. Int J Adv Pharm., 2018; 7(03): 10-6.
32. Thavva VE, Baratam SR. Formulation and evaluation of Terbinafine hydrochloride microsphere gel. Int J Appl Pharm., 2019; 11(6): 78-85.
33. Rafat S, Singh LV. Formulation and evaluation of microspheres gel for topical use., 2017; 4(2): 244-52.
34. Syal S, Pandit V, Ankalgi AD, Verma CP, Ashawat MS. Formulation and evaluation of microspheres gel of Havan ash for the Treatment of Acne. J Drug Deliv Ther., 2020; 10(6): 74-85.
35. Tomar MK, Pahwa S, Tyagi LK, Gupta C, Maan P, Sethi VA. Formulation, characterization and antibacterial study of microsphere-loaded gel of Clarithromycin for topical drug delivery: Drug Deliv Lett., 2022; 12(2): 122-34.
36. Hussain H, Dhyani A, Juyal D, Bahuguna A. Formulation and evaluation of gel-loaded microspheres of diclofenac sodium for topical delivery. The Pharma Innovation, Dec. 1, 2014; 3(10, Part B): 58.
37. Khattab A, Nattouf A. Microsphere based gel as a simple and valuable strategy for formulating and releasing Tazarotene in a controlled manner. Scientific Reports, Jul 6, 2022; 12(1): 11414.
38. Sultan F, Chopra H, Sharma GK. Formulation and evaluation of luliconazole microspheres loaded gel for topical delivery. Res J Pharm Technol, Nov. 1, 2021; 14(11): 5775-80.
39. Farsana T, Geetha VS, Jumana KK, Mubashira NP. Formulation development and evaluation of antimicrobial drug loaded microspheres for topical drug delivery. World J Pharm Res., 2023 May 20.
40. Ambikar RB, Bhosale AV. Development and characterization of diclofenac sodium loaded Eudragit Rs100 polymeric microsphere incorporated into in situ gel for ophthalmic drug delivery system. Int J Pharm Pharm Sci., 2021; 13(9): 63-9.
41. Dhyani A, Kumar G. Development and Characterization of Atenolol Based Microsphere Gel for Ophthalmic Delivery. Ind. J. Pharm. Edu. Res., 2025; 59(1s): s114-20.