IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A Review on the effectiveness of microsponges for Nosocomial Skin Infections

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Abstract

Nosocomial infections, acquired during hospital stays, pose a significant risk to patients. The resistance caused by the staphylococcus aureus bacteria and other organisms leads to the antibiotic and the therapeutic resistance causing the nosocomial or the surgical site infections. Effective skin preparation is crucial in preventing these infections. This study intended to determine the effectiveness of microsponges as a modern therapy for nosocomial skin infections. The microsponges, loaded with an antibacterial and antimicrobial agents, are designed to provide controlled release and prolonged antimicrobial activity. Preliminary results show promising potential in reducing bacterial colonization and preventing nosocomial infections. Microsponges are a potentially useful tool for enhancing patient safety in hospital environments because of their special qualities, which include controlled release and high medication loading capacity.

Keywords: Microsponges, Topical drug delivery system, Nosocomial skin infections, Antibacterial agents, Antimicrobial agents

Introduction

In medical settings, nosocomial skin infections might be concerning. These infections were picked up in a hospital or another type of healthcare setting. In order to stop the spread of these infections, it's critical that healthcare workers adhere to stringent cleanliness guidelines. Surgical site infections, cellulitis, methicillin resistant staphylococci aureus(MRSA) infections and pressure ulcers are a few common nosocomial skin conditions. These may be brought on by invasive procedures, weakened immune systems, or extended hospital stays, among other things. To stop these illnesses, it's critical that healthcare facilities implement infection control procedures[1]

Nosocomial skin infections are in fact frequently caused by Staphylococcus aureus. Cellulitis, abscesses, and surgical site infections are just a few of the skin illnesses that can be brought on by this particular strain of bacteria. These bacteria can resist multiple drugs, particularly Staphylococcus aureus. Effective infection control, hygiene practices have a major role in preventing Staphylococcus aureus infections in hospital settings[2].

Nosocomial infection types

Site infections during surgery (SSI)

2% to 5% of individuals experience nosocomial infections during surgical operations. The predominant cause of these infections, which are the second most common type of nosocomial infection, are mostly caused by bacteria staphylococci aureus. The infections that lead to SSI originate from the patient's endogenous microbiota. Depending on the procedures followed and the monitoring criteria used, the incidence may approach 20%[3].

Urinary tract infections related to catheter use (CAUTI)

Infections with CAUTI are prevalent nosocomial infections globally. Over 12% of infections reported in acute care hospitals in 2011 were UTIs, according to data. What causes CAUTIs in patients is their endogenous native microbiota. Because catheters don't drain well, some urine remains in the bladder, which helps to maintain the bacterial colony. This opens up a channel for germs to enter. Male patients may get orchitis, epididymitis, and prostatitis; female patients may experience meningitis, cystitis, and pyelonephritis[4].

Pneumonia linked to ventilators (VAP)

Nosocomial pneumonia, or VAP, affects 9–27% of individuals using mechanical assistance in their breathing. It typically happens 48 hours following tracheal incubation. Ventilation is linked to nosocomial pneumonia in 86% of case. Common signs of VAP include bronchial noises, fever, and leucopenia[5].

Introduction to microsponge technology

Microsponges are a potentially effective treatment for nosocomial skin infections in controlling these diseases. They provide a steady and regulated discharge of antimicrobial drugs, which is advantageous for treating and avoiding infections contracted in medical facilities. Microsponges that adhere to the skin can be used to apply antimicrobial chemicals locally and for a prolonged duration to the affected area. The formulation of the microsponge can be modified to include antimicrobial medicines, such as gentamicin, in order to efficiently target nosocomial skin infections. The antimicrobial drugs' therapeutic efficiency can be increased[6].

The powder form of Curcumin, which has been known to have anti-bacterial and anti-inflammatory properties that are complimentary to the wound healing process, was utilized in conjunction with gentamicin sulphate. Our decision to create topical Gentamicin sulphate microsponges in conjunction with curcuma longa was driven by the herb's accessibility, affordability, and capacity to decrease bacteria resistance to the antibiotic substitute. It was used in conjunction to lower microbial resistance and increase the activity of wound healing[7].

Background of Microsponges

The microsponge technology was invented in 1987, and the first patents for it were obtained by Advanced polymer system Inc. This company has created a number of technique modifications that are utilized in over the counter, prescription, and cosmetic products[8].

The constituents of microsponge therapeutic delivery system consists of small, spherical fragments with a large porous surface that resemble sponges or uniform., spherical, porous, highly cross-linked polymeric microspheres. It modify the release of medicine, minimize side effects, and enhance stability. It is made up of active compound-filled, microporous beads that are normally 10-25 microns in diameter[9].

Potential characteristics of microsponges

1.Microsponges have excellent stability over pH ranges of 1to 11 and at higher temperatures(up to 130^0C).
2.Microsponges function effectively in a range of media and functions.
3.Microsponges have a notable trapping efficiency of 50–60%.
4.The microsponges are free-flowing.
5.Microsponges often have small pores (0.25µm), which hinder the entry of germs, microsponges don't need to be sterilized.

6. Microsponges do not cause allergies, irritability, mutagenicity, or toxicity.

7. Without drying out, Oil can be absorbed by microsponges up to six times their weight[10].

Characterization of the components trapped in microsponges

The majority of soluble or liquid substances may become trapped in the particles.

In order for actives to be entrapped in microsponges, they need to fulfill certain conditions.

1.It should be entirely soluble in polymer or able to become miscible when a small amount of a solvent that is water-immiscible is introduced.
2.It needs to hardly soluble or water insoluble.
3.Ought to have no effect on monomers.
4.Within their spherical structure, microsponges shouldn't collapse.
5.In the specified time frame, for the necessary release rate, active's microsponge payload and polymer design must be adjusted.
6.The material must exhibit stability while in touch with its catalyst and the circumstances of the polymerization[11].

Superiority compared to alternative medicinal compositions

More effective than lipo and nano formulations

Due to their high drug loading capacity, simple formulation method, controlled release, physical, chemical, and microbial stability, and compatibility with a wide range of medications (including Fluconazole, ibuprofen, ticonazole, ketoprofen, tertinonin, retinol, trolamine, acyclovir, and benzyl peroxide), microsponges are superior than microspheres, microencapsulation, niosomes, lipid nanoparticles, nanotubes, liposomes, and others[12].

Superior than traditional medicine formulations

For topical medication delivery, semi-solid or biphasic liquid solutions are typically offered. The medication is released onto the skin's outermost layer. These conventional formulations demonstrated quick drug releases that might potentially absorb and build up in the skin's dermis and epidermis layers. Side effects, irritability, and toxicity are caused by the drug's significant accumulation. The medication delivery method using microsponges solves these issues[13].

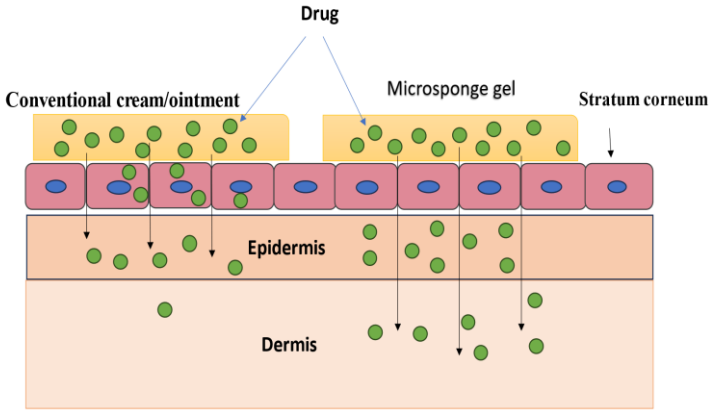
Benefits compared to creams

Ointments can be unsightly due to their stickiness, greasiness, and other characteristics, which makes patients less likely to comply. These vehicles' inadequate delivery system implies considerable dosages of active medications are required for effective therapy, which may irritate and trigger allergic reactions in heavy users. Topical formulations also include an unpleasant odour, the potential for medication incompatibility with the carriers, and an abnormally high active component evaporation rate. Microsponge technology is used to reduce the amount of an active component that enters the body transdermally and lengthen its time on the skins surface or in the epidermis[14].

The Strategy of Release via Microsponges

Release Mechanism Triggered by Temperature	The microsponges active components are viscous at room temperature. When applied topically, either by rubbing or by raising the temperature, which lowers the viscosity and allows the active medication to flow out of the skin more forcefully. The fluidity of the medication may occasionally be improved by raising the skin's temperature. Easily controlled medication release can be achieved by adjusting the temperature[15].
Systems activated by pressure	When compressed or rubbed, the microsponge system releases the material that has been trapped; the quantity released is dependent on the unique properties of the microsponge. The most suited microsponge for a certain application can be optimized by adjusting different process parameters and material types[16].

pH-driven discharge	This could have been accomplished via modifying the outer covering of the microsponges, which would enable pH-dependent release of active compounds traditional microsponges are enteric-coated with a polymer that facilitates the Ph response in order to produce pH microsponges. In research pertaining to pH, the USP spindle dissolution equipment is employed. If the pH falls from 3-8, release increases from 0% to 80%. To extend the drug's release duration, the pH may be changed for this reason[17].
Release caused by solubility	Drug release occurs when a porous system containing a watersoluble excipient is in contact with water. The ratio of partition between the medication and the external system is occasionally influenced by diffusion processes, which might impact release[18].



Mechanism of drug release from microsponges gel

Elements influencing medication release from microsponges:

- The entrapped API's physicochemical properties.
- The physical characteristics of microsponges, including their volume and pore diameter.
- The characteristics of the vehicle utilized to distribute microsponges.
- Aspects such as the composition of the monomer and the pore features[19].

Various drugs impelled with microsponge technology:[20,21,22]

- Paracetamol (NSAID)
- Erythromycin (Anti-biotic)
- Mupirocin (Anti-bacterial)
- Curcumin (Anti-inflammatory)
- Ketoprofen (NSAID)

- Trolamine (Analgesic)
- Fluconazole (Anti-fungal)
- Tretinoin (Vitamin-A)
- Febuxostat (Anti-gout)
- Flurbiprofen (NSAID)
- Benzoyl peroxide (Anti-acne)

Composition of microsponges for Nosocomial skin infections:

According to reports, different polymers can construct microsponge "cages." Materials used to create topical or oral microsponges include polymers like polydivinyl benzene, polyhydroxyl butyrate, polylactic acid, Eudragit S-100, Eudragit RS-100, polyactide-co-glycolic acid, and Eudragit RS PO. Because Eudragit RS-100 is so versatile and can be used in so many different ways, it has become the most studied polymer. Eudragit RS PO formed a solid dispersion-like structure that improved the drug's solubility and controlled its release. The possibility of using polylactic acid and polylactide-co glycolic acid to transport proteins and peptides was investigated[3].

Because it is non-irritating, nontoxic, and nonallergenic, ethyl cellulose is employed as a foundation material for microsponges as well as in their engineering. There have been reports of using polydivinyl benzene, another polymer, to create permeable spheres by the liquid polymerization process[24].

It appears that pre-gelatinized starch and sugar are utilized as pore inducers to quicken the flow of medicines. In the quasi-emulsion diffusion approach, cellulose ethers and polyvinyl alcohol have been identified as emulsifies that maintain the aqueous phase's viscosity [25].

List of Polymers: Microsponges for nosocomial Infections are prepared using the following polymers[26]

- PHEMA
- Eudragit RS 100
- Ethylcellulose
- Polyvinyl alcohol
- Eudragit RL 100
- Acrylic polymer
- Polystrene
- Polydivinyl benzene
- Eudragit RS PO
- Carbapol 934
- polyhydroxyl butyrate

Methods for Preparing Microsponges[27]:

Two methods are available for loading drugs into the microsponges delivery system:

Single-step approach - Liquid-Liquid Polymerization technique

Double-step technique - Quasi-Emulsion Solvent diffusion technique

A. Liquid-Liquid Polymerization

Microsponges made of porous spheres are produced using the process of suspension polymerization. Throughout the aqueous stages of this polymerization process, which are composed of surfactants or suspending agents that aid in the formation of suspensions, the active ingredients are first mixed with the insoluble subunits in an appropriate solvent. After that, the polymerization is subjected to radiation, a catalyst is added, or the temperature is elevated. Polymerization is carried out continuously until a spherical structure is created. When the process is completed, the solvent is removed, then the formation of microsponges takes place[28].

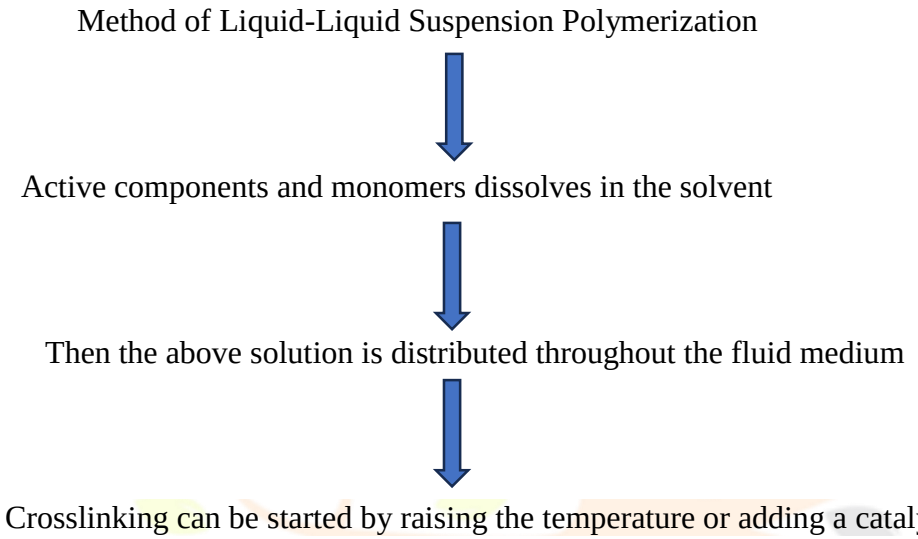


Fig 1- Liquid-Liquid Suspension Polymerization method

B. Quasi-emulsion diffusion technique

Preparing oral and topical microsponges is the usual purpose for this technique. The inner organic phase and the outer aqueous phase were formed by using above diffusion system . The medication dissolved by ultrasonography in a solution including the inner organic phase, ethyl alcohol, and dissolved polymer in ambient temperature. The outer phase is a water-based PVA solution. Prior to usage, the mixture is agitated and sieved[29]. Through dropwise mechanical stirring, the inner and outer phases were combined. A quasi-emulsion droplet was created during the stirring process, and solid microsponge cages were produced by the organic solvent continuing to evaporate. Filtered and dried for 12 hours, the prepared microsponges[30].

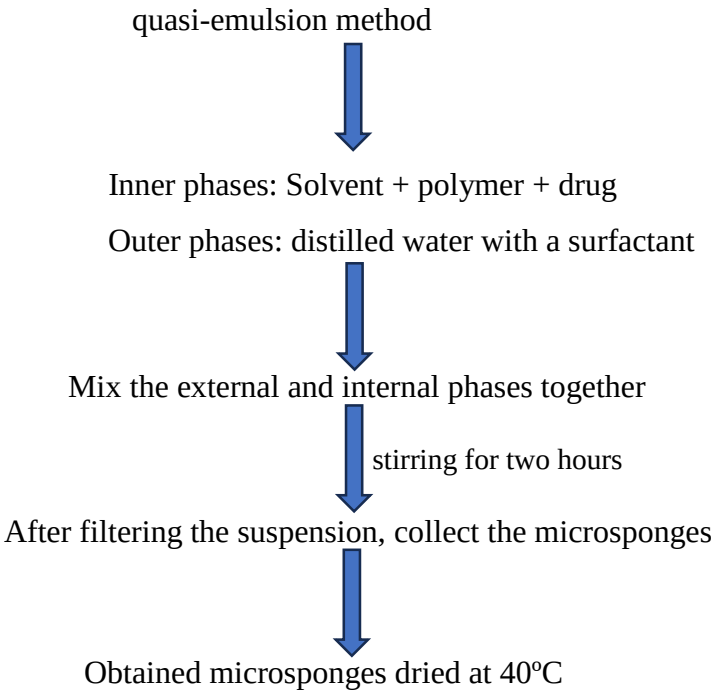


Fig 2 - Quasi-Emulsion Solvent Diffusion method

C. Production Assisted by Ultrasound:

Through modifications to liquid-liquid polymerization, this method was established. Cross-linking agent diphenyl carbonate and the monomer beta cyclodextrin (BCD) are used in the manufacture of the microsponges. To regulate the microparticle size, the mixture was heated and then sonicated. The resulting solution was allowed to cool before the end product was crushed into coarse particles and washed twice, once with ethanol and once with distilled water. The cross-linked β-CD's porous microparticles are useful for encapsulating medications. The possibility for harmful cross-linking agent residues to become trapped is a drawback of this approach [31].

D. Diffusion technique of multiple-emulsion solvent

Porous and biodegradable microspheres were intended to be produced using this method. The span was distributed in solution using an aqueous inner phase that contained stearyl amine. After that, polyvinyl alcohol is used to respread this w/o emulsion in water phase, creating a double emulsion. Capturing both soluble and insoluble actives is advantageous, as this approach demonstrates. Thermolabile compounds, such as proteins, can also be captured using this technique[32].

Evaluation of microsponges

1.Entrapment efficiency and total drug content

Ten milligrams of drug-loaded microsponges were introduced to a 10 milliliter solution of pH 7.4 methanolic phosphate buffer, which was constantly mixed[29]. A suitable dilution of 1ml of the previously mentioned sample was made with methanolic phosphate buffer solution, whose E1% value is 0.206. In comparison to the blank, the absorbance was measured at 428 nm[30].

Formula for total drug content

Drug content = Abs/E1%×dilution factor×100

Formula for entrapment efficacy

Entrapment efficacy% = Total drug content/amount of drug added × 100

2.pH determination

After producing the microsponges gel, the gel pH was determined by dipping the electrode tip into a pH meter. The result was noted after two minutes. The mean pH of the formulation was calculated after three measurements.

3.The degree of Viscosity

The measurement of viscosity in centripose, which reflects a fluid's resistance to flow, is a part of rheology. A Brookfield viscometer was used to measure the gels viscosity while different rpm and room temperature were used by spindle No 7.

4.Spreadability

The gel spreadability was evaluated by incorprating a weighted sample between two glass slides and adding 500g of weight to them for around five minutes, then the weight was removed. Spread circle lengths, both final and initial, served as standards for spreadability and were expressed in cm.

Characterization of microsponges

1.Analysis of particle size

Using the Malvern instruments limited master sizer 2000, the mean polydispersity index and mean particle size of each batch of microsponge was determined at 25ºC[34].

2.Scanning electron microscope

Palladium-gold coating can be applied to already prepared microsponges at room temperature in an argon environment to study surface topography and morphology[8]. By scanning the microsponges, the surface morphology can be identified.use of electron microscopy (SEM). Another way to show the ultra-structure of a broken microsponges particle is by SEM[35].

3.Infrared spectroscopy with Fourier transform (FTIR)

KBr pellets were used to perform Fourier transform infrared spectroscopy on drug and polymer loaded microsponges samples, utilizing a infrared spectrophotometer, in the 4000–400 cm^{-1} range[36].

4.Calibration using differential scanning

Thermodynamic characteristics and thermal properties of the medication were evaluated with a scanning calorimetry study. One technique for obtaining a thermogram involved sealing a sample weighing about 5mg and heating it in a nitrogen atmosphere at a flow rate of 10ml/min at a rate of 10ºC/min over a temperature range of 40-200ºC[37].

5.Study of X-ray diffraction

Using a crystal monochromater and CuKα radiation with a wavelength of 1.5405 A°, an X-ray diffractometer (Seimens, Model D5000, Germany) was used to capture the diffraction patterns[19]. The device was running at 20 amps of current and 45 mV of voltage. In terms of 2 θ, at 5-10ºC/min, diffraction patterns were run to characterize the crystal and physical condition of FLZ[38].

6.Establishing the porosity parameters

Mercury intrusion porosimetry was used to determine porosity percentage, bulk, apparent density, average pore diameters, total cumulative value, and other pore-related metrics[37]. Pressure was applied incrementally to a small

sample of the microsponge immersed in mercury within a cell. The amount of mercury in the measured cell appeared to decrease as the pressure increased because more mercury was driven into the microsponge's even smaller pores[39].

7.Diffusion Examination

Utilizing a franz diffusion cell the amount of medication released from microsponges. Membranes made of synthetic (cellulose acetate and silastic) and animal(mouse, rat belly, and mucin) skin are used to investigate drug release and penetration profiles[28].The donar compartment membranes was subjected to microsponge formulation in oder to conduct diffusion experiments by using phosphate buffer as a dissolving solution at 37^0 C in the receptor compartment[40].

8.Analysis of Microsponges' Stability

The international committee of Harmonization's guidelines are followed in the expediated stability evaluations. At 50±2°C, 25^0±2^0C/60±5RH, and 40^0±2^0C/75±5 RH, stability tests are performed on the formulations. Every 15, 30 and 45 days, the physiochemical properties of formulations- which are stored in glass bottles or vials- are evaluated[41].

Microsponge applications

Products for oral, over the counter, personal care, and topical have improved safety, effectiveness, and aesthetic quality as a outcome of creation of microsponge delivery system.

In Application to topical medications:

Topical dose formulations, including emulgel, cream, and powder, are combined with different drug-loaded microsponges. It decreases application frequency by lengthening the duration of medication residence in the dermis and epidermis. By utilizing biocompatible, inert, non-toxic polymers, negative effects are also decreased[42].

The following conditions can be treated with topical drug delivery: hyperpigmentation disorder (Glabridin microsponges); anti-acne (Benzoyl peroxide microsponges); rheumatoid arthritis (Mefenamic acid microsponges); psoriasis (Clobetasol propionate microsponges); diabetic wound healing (Nebivolol microsponges[43].

Table-1: Topical applications of Microsponges

Drug	Dosage form	Method of preparation	References
Acyclovir sodium	Carbopol 934 gel	Quasi emulsion solvent dispersal	Chandramouli et al., 2012[44]
Glabridin	Carbopol gel	Quasi emulsion solvent dispersal	Deshmukh et al., 2012[45]
Oxybenzone	HPMC hydrogel	Quasi emulsion solvent dispersal	Pawar et al., 2015[46]
Mafenamic acid	Emulgel	Quasi emulsion dispersal	shuhaib B. et al, 2018[47]

Metronidazole	Plain Carbopol gel	w/o/w solvent emulsion evaporation	P. mahesh kumar et al.,[48]
sertaconazole nitrate	Carbopol 934 gel	Quasi emulsion solvent dispersal	Pandey et al., 2015[37]
Fluconazole	Carbopol 934 gel	Quasi emulsion solvent dispersal	Moin et al., 2016

Oral medication administration using microsponges

Because of its ease of use, great ability to dissolve a wide variety of medications, and low toxicity, the buccal ingestion is thought to be the popular method of application. Oral administration, however, is not recommended for medications with short half-lives, those that are broken down by stomach acid or bile juice, or those that are best absorbed through the colon. As a result, controlled release drug delivery systems were created. Microsponges were filled with a variety of medications for regulated drug administration.Microsponges have a prolonged lag time due to their porous shape, which can shield the medication from the stomach's acidic environment[49].

Table-2: Oral administration of Microsponges

Drug	Type of dosage form	Preparation method	References
Curcumin	Capsule and Carbopol 934P gel	Quasi emulsion solvent dispersal	Bhatia et al., 2018[29]
Diclofenac	Tablet-colon targeted	Quasi emulsion solvent dispersal	Janakidevi et al., 2018
Famotidine	Gastro-retentive	Quasi emulsion solvent dispersal	Charagonda et al, 2016[50]
Flurbiprofen	Tablet-colon targeted	Quasi emulsion solvent dispersal	Orlu et al., 2006[27]

Use of microsponge in tissue and bone engineering

Prior to polymerizing, tricalcium phosphate grins and powdered calcium-deficient hydroxyapatite were mixed in two aqueous mixures, with liquid methyl methylacrylate monomer to form compounds that resemble bone. The completed composites appeared to be porous, like microscopic sponges. In accordance with the sponge matrix biodegradation, a collagen sponge sheet containing simple fibroblast growth factor was retained and released in the mouse sub-cuts, demonstrating dose-dependent local genic activity[51].

With regard to cardiovascular engineering

The process of creating a sustainable substance using adoptive seeding of cells is intricate, intrusive, and it entails a danger of disease. A biodegradable graft material containing collagen microsponges has been developed to solve these issues and allows autologous vascular tissue to regenerate[52]. This substance was examined both with and without precellularization to see if it could speed up in situ cellularization using autologous endothelium and smooth muscle cells. The canine pulmonary arterial trunk was patched using poly(lactic-co-glycolic acid)-collagen patches, which are a biodegradable scaffold combined with collagen microsponge to create a vascular patch

material with (n=10) or without (n=10) autologous vascular cellularization. Assessments of the histology and biochemistry were carried between two and six months following the implantation[53].

MDS-assisted diabetic wound healing

In order to maintain the wound's moisture throughout the latter phases of healing, nebivolol- loaded MDS were produced by pandit et al., and then encapsulated in gel.Nebivolol is an antihypertensive medication that dilates blood vessels. The NO(nitric oxide) route improves the functionally of endothelial cells in diabetic wounds and reduces diabetic neuropathy. Approximately 80% of the medication was released after 8 hours, according to an in vitro test. The microsponge gel has caused the drug's release to be slowed down. The porosity quality of the mixture allows diabetic rats to repair wounds quickly[54].

MDS in the psoriasis

Psoriasis is a skin condition that is characterized by persistent inflammation. It lowers the quality of life for the ill individual. Psoriasis treatment using MDS has also been investigated. The medication mometasone furoate is made using the emulsion solvent difusion process.Inflammatory and itchy conditions like psoriasis are treated with methotreasone furoate. The quasi-emulsion diffusion technique is used to generate MDS[55]. Emission patterns indicated a first burst effect in a biphasic delivery. In first hour, the medication was released upto 29–36% and eight hours later, 77-85% of the drug was released. Because clobetasol propionate has a continuous release, microsponges have been used for psoriasis treatment to minimize the risk . In contrast to the typical form, which lasts 2.5 hours, drug release may last up to 12 hours. Encapsulated in a dendrimer, dithranol microsponge gel is effective when used topically and beneficial for psoriasis[56].

MDS as a fungal inhibitor

The solvent diffusion method of quasi-emulsion was applied by Tavva et al. to create MDS of the antifungal medication terbinafne hydrochloride. The conventional gel and the microsponge-based gel were evaluated in vitro. For a maximum of 10 hours, the medication-loaded microsponge gels exhibited optimal drug release, whereas for the maximum of six hours 96.65% of the medication was retained in the drug loaded-plain gel. Drug release duration of microsponge loaded gel was longer than that of conventional gels[57].

MDS in cases of melanoma

Hydroquinone MDS was developed by Grimes PE with 4% hydroquinone and 0.15 percent retinol for the therapy. associated with post-inflammatory hyperpigmentation (PIH) and melanoma. The development of MDS, which releases hydroquinone, aimed to administer medication for a extended period of time with minimal skin irritation. An open-label experiment was agreed upon. Weeks four, eight, and twelve showed statistically significant improvements in illness symptoms and pigmentation intensity when compared to the baseline ($p<0.001$). With every visit, there was a significant improvement in both the colorimetry measurements and the ($p<0.001$) lesion area. Only one patient stopped therapy because of little allergic reaction, indicating that the technique was well tolerated[58].

MDS in the treatment of colon cancer

Oral medications' long-term release and toxicity can both be reduced with MDS. 5- Fluorouracil MDS based on Eudragit RS 100 was developed by Gupta and associates as a colon cancer treatment. 5-FU is a versatile treatment option for a wide variety of solid tumor types. If 5-FU is present in tumors at a greater relative concentration, it

may be more effective. The toxicity level decreases as a consequence. MDS was created via oil-in-oil diffusion of solvent emulsion. This was determined whereas pure 5-FU releases in roughly 20 minutes, the MDS extends the release period to almost 5 hours. Research has shown that 5-FU loaded with MDS is superior to 5-FU on its own in terms of cell viability[59].

MDS for arthritic conditions

Diclofenac is a medication that has been explored for the treatment of arthritis using a microsponge. Because of its link to gastrointestinal irritation and first pass metabolism, diclofenac is the most frequently recommended nonsteroidal anti-inflammatory medicine (NSAID) for the treatment of pain and swelling associated with musculoskeletal illnesses, especially arthritis.These worries can be allayed with a topical medication that contains diclofenac MDS. To create MDS gels with diclofenac diethylamine that would have a sustained release for the treatment of arthritis, Osmani and colleagues applied a quasi-emulsion diffusion methodology. They contrasted their results with the 1.16 percent w/w Voltaren Emulgel sold in stores. The microsponge-based gel delivered the medication throughout 4 hours, although the gel only released 81.11% of the medication in that time[60].

MDS incorporating lornoxicam was developed by Hadi et al. as the active ingredient used to treat arthritis and combined them into tablets, discovering that the drug's release occurred over an extended period of time, spanning from 86% to 96% to 12 hours[61].

Current developments in the medication delivery method using microsponge:

Nanosponges, nanoferrosponges, and porous microbeads were created by varying the techniques, leading to several advancements. Beta - Unlike polymeric micro- or nanosponges, CD nanosponges can be utilized for the water-loving and water-hating medicines[62]. Dextamethasone, doxorubicin hydrochloride, flurbiprofen, serum albumin, itraconazole,was investigated for oral administration using these sophisticated systems as model drugs[63].

Table-3: Marketed formulations of Microsponge[8,14,17,19,64,65]

Name of the product	Manufacturer	Advantages
Carac Cream	Dermik laboratories .Inc	Microsponge formulation of dimethicone and methyl methacrylate/ glycol dimethacrylate crosspolymer, holds 0.35% of the 0.5% flurouracil present in carac cream. Prescription medicine carac is used to treat actinic keratosis, a precancerous skin disease caused by prolonged sun exposure. The treatment is used topically once daily.
Salicylic Peels 20 and 30	Ontario's Biophora Medical Skincare	Salicylic acid 20%, Microsponge Technology, Deep BHA peeling agent (for use only by professionals), will greatly reduce acne, pigmentation, and fine line problems. This enzyme dissolves irritation and unclogs pores with ease. This

		treatment successfully treats acne, leaving the complexion incredibly clear and smooth.
EpiQuin Micro	SkinMedica, Inc.	Hydroquinone and retinol are captured in minute reservoirs by the Microsponge® technology. These substances are progressively released into the skin by the microsponges throughout the course of the day. This gradually exposes the skin to hydroquinone and retinol continuously, potentially reducing skin irritation. A prescription moisturizing fading cream called EpiQuin Micro lessens the effects of melasma, post-inflammatory hyperpigmentation, and sun lentigines. Help with sun spots, age spots, and facial discolouration as well.
Retinol 15 Night Cream: Retinol cream	Biomedical, Sothys	A stable blend of pure vitamin A and retinol combined with microsponge technology makes up this nighttime therapeutic lotion. Retinol 15 can help with gaining-related skin discolorations, fine lines, wrinkles, and smoother, more youthful-looking skin when used consistently.
Oil Prevention Lotion	Fountain Cosmetics	This thin lotion uses microsponge technology to absorb oil will take away shine for hours. In order to facilitate recovery, the naturally antibiotic Skin Response Complex reduces stiffness and inflammation. greasy skin problems, acne-prone
Moisturizing Cream, LactrexTM 12%	SDR Pharmaceuticals, Inc. 07821, Andover, NJ, United States of America	12% lactic acid is present in LactrexTM 12% Moisturizing Cream as ammonium lactate, a neutral ammonium salt. The use of Microsponge® technology allows for pleasant application and prolonged moisturization. In addition, glycerin—a naturally occurring humectant—and water are included in LactrexTM to help hydrate and soothe dry, flaky, cracked skin.
Matte oil-free block with SPF20	USA's Dermalogica, LIC	With a healthy matte finish, this undetectable, oil-free sunscreen prevents UV ray damage to the skin while also managing oil production. Utilizing microsponge technology in its formulation, Oil Free Matte Block eliminates shine by absorbing oil and leaving behind no powdery residue.
XS and RS Sportscream	The Embil Pharmaceuticals	To treat musculoskeletal issues, anti-inflammatory, topical analgesic and counterirritant properties are combined with microsponge delivery technology.

Retinol Dual Facial Treatment with Line Eliminator	Avon Products, Inc., UK	Instantaneous and time-released wrinkle-fighting action is provided by a retinol(vitamin A) as an effective cream for microsponge system, dualsystem. reduces the visibility of aging-related wrinkles, fine lines, and skin discolorations.
Micro Peel Plus / Acne Removal	Southern Africa's Biomedical Imporium	Through the use of Microsponge ® technology to apply salicylic acid in the form of microcrystals, the MicroPeel ® Plus method promotes cell turnover. These microcrystals precisely target the parts of the skin that require enhancement. The MicroPeel Plus operates much better than other superficial chemical peels since it removes all dead skin cells without causing any skin harm.

Table-4: Patent applications for microsponges

Patent number	Inventor	Publication Date	Technique Developed
US5725869	Ray et al.	1998	A polymer and plasticizer-containing organic solvent is combined with an aqueous solution comprising one or more emulsifiers to create an oil-in-water emulsion that is then solvent-evaporated to create microsponges. The microspheres are ideally containing a component to be dispensed via controlled release[66].
US6395300	Straub et al	2000	In order to enhance a drugs solubility in aqueous settings, pharmaceuticals are administered in the form of porous matrix microparticles. For drugs with poor water solubility, this is particularly true. Parenterally administred or encased in tablets or capsules for oral administration, microparticles of the porous drug matrix are reconstitited in the necessary from using an aqueous medium and normal techniques[67].
US7426776B2	Franklin et al.	2008	The invention is related to a process for producing a nonwoven fabric with microsponges[68].
EP2317989A2	Shubhas Balaram	2009	An ethyl cellulose and tretinoin microparticle with significant porosity and therapeutic efficacy[69].

	Bhowmick et al.		
US20140102991	Euginea P. et al	2014	Despite tremendous advancements in the synthesis of nanocomposite materials, integrating several components with distinct functions continues to be a significant difficulty. This limits the control over the features of the nanocomposite[70].

Future directions of medication delivery using microsponge

The drug delivery technique of microsponges has a promising future because of its unique porosity system features and wide range of pharmaceutical uses. Peptide oral administration is going to be big problem for this medication delivery technology in the future. The number of polymer ratios can be changed and applied, and drug loaded MDS can be delivered via the core. As a result, future developments for the medication delivery method using microsponges seems quite promising[71].

MDS devices may be looked into for tissue engineering in the near future. There is great potential for tissue engineering to enhance quality of patients life. vascular tissue engineering is one among them. In order to reconstruct larger diameter arteries, the conventional approach uses an extended form of polytetrafuoroethylene, which is utilized therapeutically. However, this method is not appropriate for small arteries since the body views them as alien material, which might result in thrombosis. Consequently, a bypass technique is required[72].

Using the Scafold design process, a new planned vascular graft with microscopic caliber composed of polylactic acid and polyglycolic acid was created. Microsponge was then used to design the vascular patches, which tested on dogs. Additionally, the dogs full and trouble-free healing following the graft-which is composed of a biodegradable polymer-reduced the requirement for an anti-thrombic drug. The actual difficulty in employing microsponge technology for medicine delivery in future is obtaining shell system of active drugs in the future[73].

The development of novel product shapes is feasible with MDS, a novel drug delivery technology that offers unique qualities like reduced irritation, improved chemical, physical, thermal stability, longer release, and improved medication release profile. Tissue engineering, controlled oral medication delivery are more applications for biodegradable polymers. In terms of formulation, it offers many advantages. For MDS, more medication delivery techniques including pulmonary and parenteral must be developed. These advancements made it possible for scholars to use them in many conditions. New directions for drug distribution are also made possible by these formulation advances. Because of this, it is anticipated that drug delivery technology based on microsponges will one day be a practical medication delivery matrix material for therapeutic uses[74].

Conclusion

Since nosocomial infections and antibiotic resistance are becoming more common, it is becoming harder for infection control committees and healthcare executives to accomplish the goal of eliminating intervals. However, by following the sensible and health care delivery guidelines set forth by infection control committees and

preventing the spread of these infections through the appropriate use of antibiotics, the resistance in emerging microorganisms to antibiotics can be easily minimized. Healthcare facilities can adopt an efficient WHO-supervised surveillance system to develop infection control programs. Public education about these endemic infections, enhanced waste management, biosafety training for hospital staff, and healthcare reforms can all help lower the rate of nosocomial infections.

A novel technique for the control and cure of nosocomial skin infections is microsponge drug delivery technology, as this technique release the active ingredients in a controlled-manner from microporous beads by minimizing the adverse effects without sacrificing product's medicinal efficacy. Finally it is determined that microsponge delivery technology, which entraps its constituents, reduces the nosocomial and the other skin related infections by improving stability, elegance, and formulation flexibility. Furthermore, a great deal of research has established that microsponges delivery technology are non-mutagenic, non-toxic and non-allergic.

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