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MICROSPONGES DELIVERY SYSTEM (MDS); AND THEIR FORMULATION AND EVALUATION, METHOD OF PREPARATION

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ABSTRACT

The primary goal of the current review was to increase drug deposition in the skin by developing a microsponge based on oral and topical drug delivery systems, as well as by preparing microsponges and their delivery system (MDS). The tiny porous particles known as microsponges are composed of polymers. Microsponges do not cause bacterial growth; they are self-sterilizing. Microsponge preparation techniques include oil-in-oil emulsion solvent diffusion (O/O) employing polymers, vibrating orifice aerosol production and liquid liquid suspension. The quasi-emulsion solvent diffusion method is a practical approach to microsponge research. For eight hours, the microsponge's highest formulation was 86.76% and 84.25%, respectively. Its spherical shape and size ranged from 5 to 300 microns and it produced good amounts of oxiconazole nitrate, benzoyl peroxide, fluconazole and ketoprofen. Use of microsponges as a delivery mechanism in formulation goods such as tablets, creams, gels, liquid suspensions, or powders. The lowest dosage, increase efficacy, lessen adverse effects and alter drug release.

KEYWORDS

Microsponge, Methods of preparation, Evaluation, Compatibility study and Microsponge-based delivery systems.

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INTRODUCTION

Advance Polymer Systems, Inc. was granted the original patents for the 1987 development of microsponge technology[1]. Under the name transdermal delivery system (TDS), a number of reliable and respectable methods were created for systemic distribution through the skin. It has increased the safety and effectiveness of numerous medications that might be better absorbed through the skin. However, transdermal distribution is impractical for materials whose ultimate destination

is the skin[2]. When many medicine delivery technologies are employed to increase the efficacy and cost-effectiveness of treatment procedures, MDS drug delivery technology is developing quickly (Figure No.1)[3]. These efforts to produce novel drug carrier systems led to the development of microparticulate drug carriers[4]. The simplicity of construction and the ability to regulate drug release in multiple ways, including rate control, site control, or both, make multi-particulate systems crucial[5]. Because they are more likely to be dispersed evenly throughout the absorption site, multi-particle systems are anticipated to improve drug absorption. Several microparticulate systems have been developed and investigated for this purpose, including microspheres, microbeads, microcapsules, microballoons, and microsponges[6,7]. The microsponge system can stop substances from building up too much in the dermis and epidermis. These products, which have a comparatively high concentration of active chemicals, are topically applied to the user in traditional forms such as gels or lotions. A variety of active substances, including emollients, perfumes, essential oils, sunscreens, and anti-bacterial, anti-fungal, and anti-inflammatory compounds, can be entrapped by microsponges, which are polymeric delivery systems made up of porous microspheres[8].

Regarding medication diffusion or release from the vehicle and administration through the skin, there have been issues with traditional topical dose forms such lotions, creams, gels and powders. Because creams and lotions are quickly removed from the skin and release the drug from the base poorly, they frequently result in decreased drug bioavailability. Medicated powders for topical application have a limited residence period on the skin, while non-hydrophilic ointments are oily, oleaginous and inconvenient for patients. Gels are semi-solid systems where a three-dimensional network of interlacing particles or solvated macromolecules of the dispersed phase limit the mobility of the dispersion medium.

The semisolid condition results from increased viscosity brought on by interlacing and, in turn, internal friction. In order to create crystalline and amorphous areas throughout the system, a gel may also be made up of twisted, matted strands that are frequently bound together by greater Vander Waals forces. Drugs' residence time on the skin can be prolonged by using gel as a delivery mechanism, which will increase their bioavailability. Easy administration, non-greasy, patient compliance, long skin residence time, and improved drug release are just a few benefits of gel delivery systems[9]. Ergosterol production, which is necessary for the integrity of fungal cytoplasmic membranes, is inhibited by oxiconazole nitrate. Lanosterol 14-alpha demethylase, another name for the fungal cytochrome P450 51 enzyme, is destabilized by it[10]. This is essential to the fungus's cell membrane structure. Its blockage leads to cell lysis. Additionally, it has been demonstrated that oxiconazole inhibits DNA synthesis and lowers intracellular ATP levels. Oxiconazole can increase membrane permeability to zinc, increasing its cytotoxicity, just like other imidazole antifungals. The carrier system, which enables a controlled and localized release of the active drug in accordance with the particular needs of the therapy, also influences the drug's in-vivo fate in addition to its own characteristics. Controlling the medication delivery rate using a variety of contemporary technologies that require substantial study is currently the largest problem[11,12].

Delivery systems are therefore required in order to minimize the amount of time that an active ingredient penetrates the body through the skin while increasing the amount of time that it remains on the skin's surface or within the epidermis. Uncontrolled evaporation of the active ingredient, unpleasant odours and the use of unaesthetic vehicles-which can be greasy, sticky, and produce discolorations-are further possible issues with topical medication administration. These issues can lead to a lack of patient compliance[13-15].

A variety of techniques are used to create microsponges, including suspension polymerization in a liquid–liquid system and emulsion systems. Oil-in-water (o/w) is the most widely utilized

emulsion system, and the emulsion solvent diffusion (ESD) method is used to create the microsponges[16]. Both primary and secondary skin infections can be successfully treated with the topical antibiotic medication mugirocin (MP)[17]. MP has *in vitro* action against a variety of Gram-positive and certain Gram-negative bacteria and is generated by Pseudomonas fluorescens. Nevertheless, MP also prevents certain harmful fungi from growing in vitro, such as pityrosporum and a variety of dermatophytes[18].

By attaching itself to the enzyme isoleucyl-t-RNA synthetase, which stops isoleucine from being incorporated into proteins, MP limits the production of proteins by bacteria[19]. Cross-resistance between MP and other antibiotics is not an issue because of its distinct chemical structure and mode of action compared to other antibiotics used in clinical settings[20].

Monic acid, an inactive metabolite that is quickly eliminated in the urine, is created when MP enters the systemic circulation. Under occlusive dressings and in wounded skin, penetration into the deeper layers of the epidermis and dermis is improved. Currently available on the market, the mupirocin 2% ointment with polyethylene glycol is used three times a day and exhibits measurable activity. Due to their high viscosities, which cause them to be applied inappropriately to skin lesions, and the possibility of garment soiling from greasy residues, topical ointment formulations are less appealing to patients[21]. Novel formulations, such as creams, gels, and emulgels containing particulate drug carriers such microparticles and nanoparticles, could be created to improve patient acceptance and compliance.

These carriers could control the active's release and protection. Athlete's foot and acne can already be treated topically with benzoyl peroxide microsponges[22]. Their ability to load a large quantity of active elements onto the particle's surface and inside the particle itself is one of their defining characteristics. The ability of microsponge products to trap medications up to three times their weight sets them apart from other dermatological product kinds. The microsponge particle in the formulation protects the active payload, which is then delivered to the skin through controlled diffusion. One useful technique to increase effectiveness and lessen common discomfort is the gradual release of activities to the skin[23].

Microsponges have various advantages such as delivering the active ingredients at minimum dose, it has increased the efficacy and safety of several medications that may be better delivered through skin. TDS, however, is impractical for delivering compounds that are intended for the skin itself. Research on the controlled release of medications onto the epidermis with the guarantee that the medication stays mostly localized and does not significantly penetrate the systemic circulation has only lately been successfully tackled.

For the regulated and localized delivery of medications into the stratum corneum and underlying skin layers, without going past the epidermis, no effective delivery systems have been created. Furthermore, there are a number of issues with topical medication application, including ointments that are frequently unsightly, greasy, sticky and so forth, which frequently lead to patient noncompliance.

Due to their poor delivery system efficiency, these vehicles necessitate high concentrations of active drugs for effective therapy, which causes allergic responses and irritation in major users. Uncontrolled active ingredient evaporation, disagreeable Odor, and possible drug incompatibility with the carriers are further disadvantages of topical preparations. Topical medications in conventional formulations are designed to act on the skin's outermost layers.

When such products are applied, their active ingredients usually come out in a highly concentrated layer that improves stability, decreases adverse effects, and allows for the modification of medication release profiles[24].

Microsponge particles are minuscule, inert and unbreakable spheres that are unable to penetrate the epidermis. Instead, they gather in the skin's minuscule crevices and gradually release the

medicine that is trapped there when the skin requires it. The microsponge system can stop substances from building up too much in the dermis and epidermis. The microsponge system may be able to considerably lessen the irritation of medications that work well without sacrificing their effectiveness. The subsequent washing is then used to remove the empty spheres. These needs are met by the microsponge delivery technology, which has produced a new generation of innovative, highly effective, and well-tolerated medications[25].

The rapid advancement of drug delivery technology is being fueled by the new generation of medicines and biopharmaceuticals. The creation of new medications is insufficient for drug treatment in the present years. However, it also entails creating an appropriate medication delivery mechanism at the site of action. Controlling the medication delivery rate using a variety of contemporary technologies that have undergone much investigation is currently the largest problem[7].

Granules have been created to achieve targeted and prolonged release of medications in the colon, while other multiparticulate techniques include formulation in the form of pellets. Due to their tiny size, they offer numerous advantages over single-unit systems[26].

lessen adverse effects by modifying and targeting drug release, and it also shields the entrapped active ingredients from environmental and physical deterioration. Additionally, these can effectively deliver pharmaceutical active substances at the intended place at the lowest dose, hence reducing severe systemic side effects[27,28].

According to a recent assessment, microsponge provides a novel method to medication targeting because the active agent is not chemically modified and this system may be used to deliver drugs selectively to a wide range of chemically varied agents. Additionally, in vitro research has shown that the microsponge system speeds up the dissolving of medications that are insoluble in water[29].

Advantages of microsponge delivery system[30,31]

Oil may be absorbed by microsponges up to six times its weight without drying up.

It offers extended release, or continuous activity for up to 12 hours.

A more elegant product.

It can increase therapeutic efficacy and enhance patient compliance by reducing discomfort and improving tolerance.

They are more stable chemically, physically and thermally.

These don't cause irritation, mutagenesis, allergies, or toxicity.

Immiscible items can be incorporated thanks to MDS.

Their formulation flexibility is superior.

MDS is easier to construct, has a larger payload, and a wider range of chemical stability than competing technologies like liposomes and microencapsulation.

The ability to turn liquids into powders enhances material processing.

It is adaptable enough to create new product shapes.

MDS can increase the medications' bioavailability.

Compared to microcapsules, microsponges provide superior control over drug release. Typically, microcapsules are unable to regulate the active pharmaceutical ingredients' (API) rate of release. The API inside the microcapsules will be released as soon as the wall is broken[32].

Compared to liposomes, microsponges exhibit greater chemical stability, a larger payload, and simpler formulation. 3. Unlike ointments, microsponges may absorb skin secretions, which helps to make the skin less greasy and shiny. Because ointments are frequently unsightly, oily and sticky, patients are less likely to comply with them.

Characteristics of Microsponges

Microsponge formulations are compatible with the majority of vehicles and ingredients; • Microsponge formulations are self-sterilizing due to their average pore size of 0.25μm, which prevents bacteria from penetrating; Microsponge formulations have a higher payload (50 to 60%), are still free-flowing,

and can be economical. Microsponge formulations are stable over the pH range of 1 to 11[33].

It should either be completely miscible in monomer or able to be made so by adding a tiny quantity of a solvent that isn't soluble in water[34].

It should either be completely insoluble in water or very marginally soluble.

Monomers should not react with it.

To prevent aesthetic issues, the solubility of active ingredients in the vehicle must be kept to a minimum; a maximum of 10–12% w/w microsponges must be added. Otherwise, before the application, the vehicle will exhaust the microsponges.

Microsponges' spherical structure shouldn't disintegrate.

The active's microsponges' polymer payload and design must be tuned for the necessary release rate within the allotted time frame.

It must remain stable when in contact with the polymerization catalyst under polymerization conditions[34].

Drugs Explored in MDS

Kotoprofen
Benzyl peroxide
Retinol
Fluconazole
Ibuprofen
Tretinoin
Trolamine[35- 38].

METHODS OF PREPARATION OF MICROSPONGES

Liquid–liquid suspension polymerization

Monomers and the functional or active components, which are immiscible with water, are typically used to create a solution. After that, this phase is agitatedly suspended in an aqueous phase, which typically contains additives like dispersants and surfactants to aid in suspension. Activating the monomers by catalysis, raising the temperature, or irradiating them is how polymerization is accomplished once the suspension has distinct droplets of the appropriate size. Thousands of microsponges are grouped together like grapes to form a spherical structure as the polymerization process proceeds.

Choosing a monomer or a mix of monomers.

As polymerization starts, chain monomers are formed.

Ladder formations brought forth by cross-linking between chain monomers.

Agglomeration of microspheres, which results in the creation of microspheres; folding of the monomer ladder to create spherical particles. Clusters of tiny spheres

Microsponge binding to form bunches. A reservoir-type structure that opens at the surface through pores is created as a result of the polymerization process. Sometimes the pore network is formed during polymerization by using an inert solvent that is entirely miscible with monomer but immiscible with water. The liquid is extracted from the porous microspheres, or microsponges, following polymerization. The functional materials are then included by impregnating them into premade microsponges. Solvents can occasionally be utilized to incorporate active ingredients more quickly and effectively.

The microsponges serve as topical delivery systems for a range of useful compounds, such as rubefacients, anti-inflammatory, anti-acne, anti-purities and antifungal agents. A two-step procedure is employed when the medication is sensitive to the polymerization conditions. Under mild experimental conditions, the functional material replaces the substitute porogen used for the polymerization[39].

The solid particles produced by the polymerization process are extracted from the suspension after it is finished. After that, the particles undergo processing and washing to make them largely usable. Methacrylate and ethylene glycol dimethacrylate or styrene and divinylbenzene can be used as starting materials to create the microsponge products[40].

The microsponges with the corresponding composition, as indicated in table 2, were created with polyvinyl alcohol as a stabilizer and the polymers eudragit S-100 and L-100. At a stirring speed of 1500rpm, batches were created for various

drug:polymer ratios and polyvinyl alcohol concentrations. Eudragit S-100 and L-100 were used as polymers in a quasi-emulsion solvent diffusion process to create the microsponges carrying oxiconazole nitrate.

The medication is added to methyl alcohol and the polymer is added to ethyl alcohol to create the inner phase. Drug and polymer solutions were dissolved at 35°C using ultrasonication. This solution made inner phase. The PVA solution in water (external phase) was filled with the inner phase. The mixture is filtered to extract the microsponges after two hours of stirring at 1500rpm. Production yield (PY) is calculated by weighing the microsponges after they have been dried for 12 hours at 40°C in an air-heated oven[41].

Quasi-emulsion solvent diffusion method: (Top-down approach)

The premade polymer is the first step in this top-down method. In this process, two distinct phases-an interior phase and an exterior phase that resembled emulsions-formed a quasi-emulsion. With vigorous stirring, the drug-polymer solution's internal phase-made in a volatile solvent such as ethanol, acetone, or dichloromethane-was introduced to the exterior phase, which included the aqueous polyvinyl alcohol (PVA) solution. To promote plasticity, a sufficient quantity of triethylcitrate (TEC) was applied.

Discrete emulsion globules known as quasi-emulsion globules are created as a result of stirring. After that, the solvent was removed from these globules to create hard, insoluble microparticles, or microsponges. The mixture was sufficiently stirred, and the microsponges were separated by filtering. After that, an air-heated oven was used to dry the microsponges. The idea is that the organic solvent and water counter-diffusion into and out of the finely dispersed droplets of the drug's polymeric solution (dispersed phase) solidifies them in the aqueous phase. Drug and polymer solubility were reduced by the diffused aqueous phase in the droplets, which led to their co-precipitation. Further solidification was achieved through the diffusion of the organic phase, which produced matrix-type porous microspheres. The advantages of this method over liquid-liquid suspension polymerization were that the drug was exposed to less ambient conditions and that there were fewer solvent residues in the final product because the solvent was extracted because it was volatile or soluble in aqueous media[42,43,37].

Ethyl alcohol is used to dissolve Eudragit RS 100 in order to prepare the inner organic phase. The medication is then added to the mixture and dissolved at 35°C using ultrasonication. The polyvinyl alcohol solution in water (outer phase) is filled with the inner phase. To separate the microsponges, the mixture is filtered after being stirred for 60 minutes. For 12 hours, the microsponges are dried at 40°C in an air-heated oven (Figure No.4)[44].

Vibrating Orifice Aerosol Generator Method (VOAG)

Initially, lipid-bi-layered mesoporous silica particles (VOAG) were being produced using a vibrating orifice aerosol generator. The VOAG approach produced porous particles through heat deposition driven by surfactant microdroplet evaporation. First, a hydro-ethanolic combination of tetra-ethyl-orthosilicate was refluxed in diluted HCl to create a stock solution for the core particle. To create monodisperse droplets that were encased in microsponges, this stock solution was diluted with a solvent that contained surfactants and then swirled[45].

Electrohydrodynamic Atomization Method

In 2009, Pancholi et al. used this method to produce porous chitosan microspheres[46]. Bubbles were created by ultrasonifying the chitosan solution. The suspension was then electro-hydrodynamically vaporized after the bubble solution was perfused into a steel capillary using a syringe pump. The capillary's diameter was carefully selected to guarantee that each suspension bubble remained intact during passage.

The amount of chitosan in the test solution was the only factor that affected the voltage. In every instance, the flow rate and applied voltage produced the steady cone-jet mode, with the exception of the

maximum concentration, which was difficult to electrospray. A sodium hydroxide solution in water at a weight-volume ratio of 4% was used to cross-link the chitosan microspheres. 7. Combining the medicinal molecule with the monomer is a possibility. Experience is also necessary to control the pore and particle sizes of the microsponges produced using this method.

Oil-in-oil Emulsion Solvent Diffusion Method

Instead of employing the w/o/w approach, which included letting the water slowly evaporate while stirring, the oil-in-oil (o/o) emulsion was created by using a volatile organic liquid as the internal stage. 44 The internal phase was dichloro-methane, the exterior phase was span-85, a combination of dichloro-methane and fixed oil (Corn or Mineral) and the polymer was polylactic glycolic acid. The internal step was gradually added to the dispersion medium while being continuously stirred to create the microsponges. This technique was used to create 45 hydroxyzine HCl-loaded Eudragit RS-100 microsponges, utilizing liquid paraffin as the continuous medium and acetone as the dissolver[47].

Water-in-oil in Water (w/o/w) Emulsion Solvent Diffusion

This method is straightforward for creating biodegradable porous microspheres. This method used an internal aqueous phase to separate an emulsifying agent, such as span, polyethyleneimine, or spaced repetition, from an organic polymeric solution[48]. A double emulsion was then produced by dispersing the w/o emulsion in an external PVA-containing aqueous process. One advantage of this approach is entanglement[49]. Xanthan gum is an emulsifier that stabilizes the internal water-in-oil emulsion, according to several studies[50]. Although this method has the advantage of capturing both water-soluble and water-insoluble substances, a significant disadvantage is the use of water-insoluble surfactants, which may cause residues to remain inside the microsponges.

Differential scanning calorimetry (DSC) study

Nicorandil and the microsponge of batch F6 were subjected to various scanning calorimetry (DSC) tests (Shimadzu DSC-60, Tokyo Japan). A 40µL aluminum pan was filled with about 2 mg of the sample, which was then compressed in a dry air environment. After that, the pans were hermetically sealed and heated at a rate of 20ºC per minute throughout a temperature range of 40ºC to 400ºC.

Scanning electron microscopy (SEM) study

The chosen microsponges' intricate surface topography was examined with a scanning electron microscope (JEM-6400, Jeol Ltd, Japan). After utilizing double-coated adhesive tape to secure the microsponge sample to the specimen holder, it was vacuum-coated using a sputter coater for 5-10 minutes at 40mA, and then it was examined at 30Kv[51]. The gold coating had a thickness of 20nm.

Rheological Characterization

A controlled stress rheometer was used to test the rheological properties of the microsponge-loaded gel and blank gel (Viscotech Rheometer, Rheological Instruments AB, Lund, Sweden). Version 5.0 of the Stress Rheological Basic program was used to analyze the data. With a cone of 1.0∘ and a 25mm diameter, Acone and Plate Geometry was employed[52]. All measurements were performed in triplicate at 25°C and 37°C using a fresh sample for the test. Creep Recovery Exam. Samples were exposed to a set stress from LVR for 100 seconds and then given time to recover in a process known as creep recovery. The creep compliance, or J was time-stamped.

Skin Irritation Test

The commercial and placebo gels were compared to the optimized oxybenzone-loaded microsponge gel (M9) in a skin irritation test. To assess skin irritation, the current study was used on three groups of rats (n=6). After a seven-day acclimatization period, they were closely monitored to make sure they were suitable for the study. The test mice were housed in a restricted-access rodent facility with a 12-hour light/12-hour dark cycle, a temperature of 25 ± 2∘C and a humidity range of 60 to 90% RH. Each cage had drinking water, and the animals had labium access to a commercial rat food. Before the experiment, the region on each rat's back was shaved.

Commercial sunscreen lotion was applied to the second group of rats, while microsponge gel was put to the first group. The remaining rats were regarded as the control group. For 30 minutes, 0.5g of each test product was applied to each 25 x 25mm region. The rat's treated skin was finally cleaned with tap water. Both the treatment and control sites were covered and bandaged with cotton bandages, and the erythema was scored at 24 and 72 hours. After 24 and 72 hours, skin reactions were measured in the form of erythema. The Draize scale was used to record the mean erythemal scores, which ranged from 0 to 4[53].

As indicated in Table 3, the principal irritation index (PII) was computed and matched with the response category after the reactions of every formulation applied to the rat skin surface were assessed. Each rat's primary irritation score was determined. The number of observations for the treated sites was divided by the total of the erythema scores at 24 and 72 hours[54].

Evaluation Parameters of Microsponges

Particle size (Microscopy)

Loading efficiency and production yield

Compatibility studies

Particle Size Determination

Laser light diffractometry or any other appropriate technique can be used to analyze the particle sizes of loaded and unloaded microsponges. For every formulation, the values can be represented as the mean particle size range. 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 25µm are recommended for use in the final topical formulation because particles bigger than 30µm can give off a grainy texture[55].

Morphology and Surface Topography of Microsponges

Scanning electron microscopy (SEM) can be used to examine the surface morphology of prepared microsponges after they have been coated with gold-palladium at room temperature in an argon environment. A shattered microsponge particle's ultrastructure can also be shown using a scanning electron microscope[56].

Determination of Loading Efficiency and Production Yield

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

Loding efficiency= Actual Drug Content in Microspoges /Theoretical Drug content*100

Theoretical Drug Content The production yield of the microparticles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microsponge obtained.

Microsponges Production Yield=Practical Mass of Microsponges/Theoretical Mass (Polymer + Drug) X 100[57].

Compatibility Studies

Thin layer chromatography (TLC) and Fourier transform infrared spectroscopy (FT-IR) can be used to investigate a drug's compatibility with reaction adjuncts[58]. Differential Scanning Colorimetry (DSC) and powder X-ray diffraction (XRD) can be used to examine the impact of polymerization on the drug's crystallinity[59]. For DSC, 5 mg samples can be precisely weighed into aluminum pans, sealed, and heated at a rate of 15 °C per minute throughout a temperature range of 25°C to 430°C in a nitrogen atmosphere[60,61].

Oral drug delivery

For oral drug delivery, a microsponge system has various benefits, including: Providing oral controlled delivery to the lower gastrointestinal tract (GIT) and preserving the active components in a protected environment.

By trapping poorly soluble medications in their porous structure, microsponge devices increase their solubility.

Because the microsponge's porous structure is so tiny, the medications it traps will be reduced to minuscule particles with a larger surface area, which will boost the solubilization rate.

Because the microsponge system takes a lot longer to move through the colon, maximize the amount of medication that is absorbed. The creation of microsponges loaded with medications for topical application has been the subject of numerous

investigations[62]. Used the quasi-emulsion solvent diffusion approach to load paracetamol into eudragit RS 100-based microsponges to create colon-specific formulations. Microsponges were compressed and coated with a pectin:hydroxypropyl methylcellulose (HPMC) mixture before being tableted.

All of the formulations underwent *in vitro* drug release experiments, and the outcomes were assessed both statistically and kinetically. The study found that although the release data matched the Higuchi matrix, the primary mechanism of drug release from microsponges was diffusion. According to *in vitro* tests, the drug release from compression-coated colon-specific tablet formulations began at the sixth hour, which corresponded to the arrival time at the proximal colon[63]. Investigated the feasibility of creating a microsponge based on eudragit loaded with dicyclomine using a quasi-emulsion solvent diffusion approach for colonic administration. The drug's compatibility with different formulation ingredients was investigated. SEM was used to illustrate the microsponges' surface morphology and form.

In the study, ketoprofen served as a model medication for the systemic drug distribution of microsponges. Using Eudragit RS 100, ketoprofen microsponges were made using the quasi-emulsion solvent diffusion method. Direct compression was then used to create tablets of the microsponges. To find the ideal pressure value for tablet compression, several pressure values were applied to the mass of tablet powder. The results showed that compressibility was significantly better than the physical combination of the medication and polymer; microsponges create mechanically robust tablets because of the plastic deformation of their sponge-like structure[37].

Microsponges for Topical Delivery

Microscopic, polymer-based microspheres that may bind, suspend, or entrap a wide range of compounds are the foundation of microsponge systems. These microspheres can then be added to a prepared product, such as a gel, cream, liquid, or powder. Each microsphere is composed of numerous interconnected gaps within a non-collapsible framework that can absorb a wide range of chemicals, much like a real sponge. Because the outer surface is usually porous, materials can enter and exit the sphere under controlled conditions. In order to create spheres that are suited to particular product applications and vehicle compatibility, a number of key features, or parameters, of the microsponge system can be specified during the production stage.

Topical formulations containing benzoyl peroxide (BPO) are frequently used to treat athletes' foot and acne. Controlled release of BPO from a delivery system to the skin has been demonstrated to lessen skin irritation, a typical side effect, while also lowering percutaneous absorption[63]. Despite the fact that topical drugs can cause severe skin irritation, particularly in individuals with sensitive skin, they are frequently used to treat skin disorders and even in cosmetics[64]. Numerous dependable and predictable systems for systemic drugs have been developed using the Transdermal Delivery System (TDS), which primarily employs the epidermis[65].

With this technique, the medication is injected gradually into the epidermis with the expectation that it will remain primarily localized, have minimal impact on the skin, and not significantly alter the body's circulation[66,67]. Several topical medications with microsphere bases that have been tested for effectiveness and protection in the management of dermatological conditions[68].

Microsponge-based Delivery Systems for Bone and Tissue Engineering

Pre-polymerized polymethylmethacrylate powders and liquid methylmethacrylate monomer were combined with two aqueous dispersions of calcium-deficient hydroxyapatite powders and a-tricalcium phosphate grains to create bone-substitute compounds. The finished composites functioned as microsponges and seemed porous[69]. Based on the biodegradation of the sponge matrix, the basic fibroblast growth factor (bFGF) integrated into a collagen sponge sheet was released in the mouse sub-cutis and shown dose-dependent local angiogenic activity.

In the mouse ischemic hind leg, intramuscular injection of collagen microsponges containing bFGF resulted in a substantial increase in blood flow that would not have been possible with bolus injection of bFGF. These findings point to the importance and potential therapeutic benefits of type I collagen as a bFGF reservoir[70]. For cardiovascular tissue transplantation, a biodegradable graft material comprising collagen microsponge was created since it would allow the autologous vessel tissue to regenerate[71]. A three-dimensional culture of human skin fibroblasts was conducted using a thin biodegradable hybrid mesh of naturally occurring collagen and synthetic poly (DL-lactic-co-glycolic acid) (PLGA).

Collagen microsponges that resembled webs were created in the holes of a PLGA-knit mesh to create the hybrid mesh[72]. Our biodegradable polymer and collagen microsponge were combined to create a tissue-engineered patch that demonstrated good in situ regeneration at the venous and arterial walls. This suggests that the patch could be employed as a novel surgical material for cardiovascular system repair[73].

Drug release studies

The membrane surface was treated with 2.5, 5 and 10% benzoyl peroxide lotions that included either freely diffused or trapped in the microsponge system after silastic membranes were placed in static diffusion cells. The cell was supplied with a distilled water/acetone (1:1) receptor fluid, which was kept at 25°C. A water/acetone mixture was chosen as the receptor fluid to provide sufficient "sink" conditions because BPO is extremely poorly soluble in either water or regular saline. This was done after initial tests revealed that the mixture did not interact with the membrane or the mixtures placed on the "donor" side. As previously described, drug flux through the membrane was measured by regularly removing the receptor phase and using HPLC to analyze the % content[42].

Kinetics of release

The amount of drug released vs time was used to ascertain the drug release mechanism and examine the variations in release profiles among microsponges. The following mathematical models were used to assess the release data:

Q=K1 tn or log kl+n log t ……. Equation (1)

Where Q is the amount of the released at time (h), n is a diffusion exponent which indicates the release mechanism and k1 is a constant characteristic of the drug–polymer interaction. From the slope and intercept of the plot of log Q versus log t, kinetic parameters n and k1 were calculated for comparison purposes, the data was also subjected to Equation (2), which may be considered a simple, Higuchi type equation.

Q=k2t0:5+C ……Equation (2)

Equation (2), for release data dependent on the square root of time, would give a straight-line release profile, with k2 presented as a root time dissolution rate constant and C as a constant[74].

***In vitro* drug release study**

Diffusion research *in vitro* the gel was examined in vitro over the egg membrane that was removed using strong HCl. Phosphate buffered saline (PBS) at pH 7.4 was used to fill the receptor compartments and an excised egg membrane was used for the study. A 30ml receptor compartment Franz diffusion cell with an effective area of 4.52cm² was set up on a thermostatic magnetic stirrer and the temperature was kept at 37˚C throughout the duration of the investigation. For the diffusion investigation employing a diffusion cell, certain batches of drug microsponge gel (MGI, MGII, and M. F.) were utilized. At certain times, 1 ml aliquots were taken out and replaced with an equivalent volume of the receptor media.

The receptor media was used to appropriately dilute the aliquots. Over the course of 12 hours, release studies were conducted at regular intervals. Samples were taken out and examined at 261 nm using a UV spectrophotometer (Dynamica, Halo DB-20)[75,76].

United States Pharmacopeial (USP) dissolution equipment with a modified basket made of 5m stainless steel mesh at 37°C can be used for in vitro release experiments. To guarantee sink conditions, the release medium is chosen according on the formulation type-topical or oral-while taking the active components' solubility into account. At

regular intervals, sample aliquots are taken out of the medium and examined using an appropriate analytical technique. Franz diffusion cells can be used to measure the release of drugs from topical preparations (such as creams, lotions, and emulgels) that contain microsponges.

The dialysis membrane is positioned between the cell's two chambers. The donor side of the Franz cell has a fixed quantity of formulation mounted on it. A circulating jacket is used to continuously stir and regulate the receptor medium. Samples are taken out at various times and examined using an appropriate assay technique[77,42]. The release data is fitted to various kinetic models in order to ascertain the drug release kinetics and look into its mechanism from microsponges. First order, zero order, Higuchi, and Korsmeyer Peppas models are the kinetic models that are employed[78,79,80,74]. The determination coefficient (R2) values were used to assess the goodness of fit.

Factors affecting of the morphology of benzoyl peroxide microsponges

In topical formulations, benzoyl peroxide is frequently used to treat the majority of acne types and, more recently, athlete's foot. It is a first-line topical treatment for acne vulgaris and is better than antibiotics since the bacteria do not get resistant to it. Its bactericidal action also makes it preferable to keratolytic drugs. Its use, however, may result in mild dryness and skin irritation. The amount of BPO in the product is thought to be correlated with the level of irritation[81]. Benzoyl peroxide encapsulation has been demonstrated to significantly lessen negative effects[82].

For instance, it has been demonstrated that the controlled release of BPO decreased skin irritation since the drug's formulation release rate was lowered[82,83,36]. As a method for regulated release, the enclosed form has drawn more and more attention[84]. Microsponge administration is one method utilized to delay the release of active chemicals from topical formulations[42].

Recently, conducted a thorough assessment of this technique. Microsponges are porous microsphere-based delivery devices for polymers. They are tiny, spherical particles that resemble sponges and are made up of a broad porous surface and a multitude of interconnected spaces. Depending on their level of smoothness, these microsponges can range in diameter from 5 to 300mm. However, it might be feasible to create nanosponge drug delivery devices by refining formulation factors like the drug: polymer ratio and agitation/stirring rate. The average microsponge bead is a sphere around 25mm in size, with up to 250,000 holes, an average internal pore structure of 10 feet in length, and an average pore volume of roughly 1 millilitre per gram[85].

The pore volume ranges from 0.1 to 0.3 cm3/g, while the surface can vary from 20 to 500m2/g. Benzoyl peroxide microsponge formulations that have been prepared can obviously extend the amount of time that the active component stays on the skin's surface or in the epidermis while reducing the amount of time that it penetrates the dermis and, consequently, enters the body. In an effective and innovative distribution system, this technology offers maximum efficacy, minimal irritancy, prolonged product stability and enhanced aesthetic qualities.

Factors Affecting the Release of Drug from Microsponge

The physicochemical characterisation of the microsponge is an essential stage in the design and production of these multifunctional microcarriers. The morphological characteristics and porosity of microsponges are investigated using a variety of complementary techniques, including HPLC, FTIR, DSC, PXRD and SEM[86]. The many physicochemical components of microsponges must be analyzed by scientists using appropriate methods because the physicochemical characteristics of any carrier are crucial in influencing drug loading and release behaviors at a particular target. This idea runs counter to the conventional formulation principles used in topical treatments. For these traditional methods, increasing the active medication's solubility in the vehicle is usually advised[87].

It is strongly advised that the active chemicals used in microsponge entrapment be sufficiently soluble in the vehicle to allow the vehicle to provide the last loading dose of the substances prior to their release from the microsponge. By changing the balance between the polymer and the carrier, this is made possible[88]. Another tactic to reduce the unintentional leaching of the active ingredients is to produce the microsponge polymer with both free and trapped active ingredients, creating a pre-saturated vehicle. Diffusion or other stimuli, including steam, pH, friction, or temperature, may affect the release rate in addition to the partition coefficient between the polymer and the vehicle[89,77]. Illustrates a number of variables that could affect the drug's release from the microsponge.

Temperature

At room temperature, some encapsulated active ingredients could be too viscous to move quickly from microsponges to the skin. A increased flow rate brought on by an increase in skin warmth results in enhanced release.

Pressure

The active chemical may be delivered onto the skin by pressing or rubbing microsponges. The amount of release is determined by the microsponge's strength.

Solubility

When microsponges containing unintended chemicals, such deodorants and antiseptics, come into touch with water, they release their contents. Diffusion can potentially start the release, however it's important to take into account the partition coefficient between the microsponges and the outside environment.

pH triggered systems

When microsponges containing unintended chemicals, such deodorants and antiseptics, come into touch with water, they release their contents. Diffusion can potentially start the release, however it's important to take into account the partition coefficient between the microsponges and the outside environment.

Table No.1: Examples of microsponge drug delivery with their formulations[74,90,91]

S.No	Microsponge delivery systems	Drug	Disease
1	Gels	Benzoyl peroxide	Anti-Acne Treatment
2	Gels	Fluconazole	Inflammation
3	Gels	Mupirocin	Antibacterial Activity
4	Gels	Diclofenac sodium	Inflammation
5	Gels	Acyclovir	Viral infections
6	Gels	Hydroxyzine HCL	Urticaria and atopic dermatitis
7	Gels	Terbinafine	Anti-fungal
8	Lotions	Benzoyl Peroxide	Anti-Acne Tretment
9	Creams	Hydroquinone and Retionl	Melanoma
10	Tablets	Indomethacin	Inflammation
11	Tablets	Paracetamol	Anti-pyretic
12	Tablets	Chlorpheniramine maleate	Hay Fever
13	Tablets	Ketoprofen	Musculoskeletal pain
14	Tablets	Fenofibrate	Gout
15	Tablets	Dicylomine	Anticholinergic
16	Tablets	Meloxicam	Arthritis
17	Implants	Poly (DL-lactic-co glycolic acid)	Skin tissue engineering
18	Injection	Basic Fibroblastperoxide	Growth factor
19	Other	Mefenamic acid	Rheumatoid arthritis
20	Other	Ibuprofen	NSAID

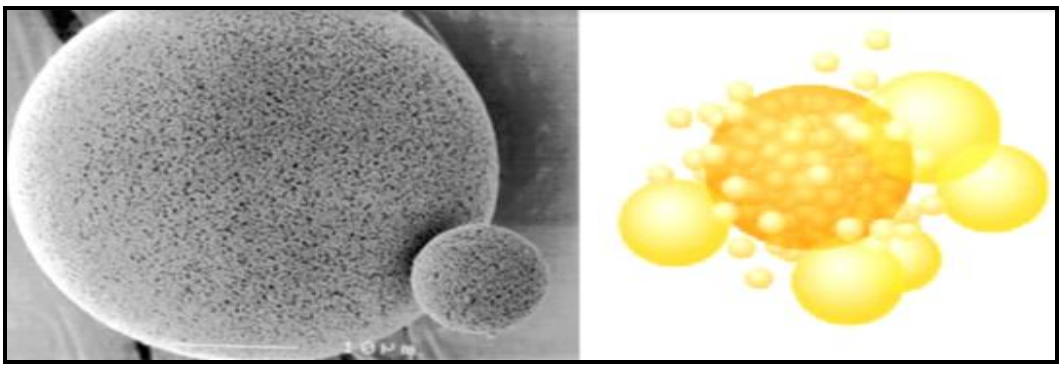

Figure No.1: Entrapment Microsponges

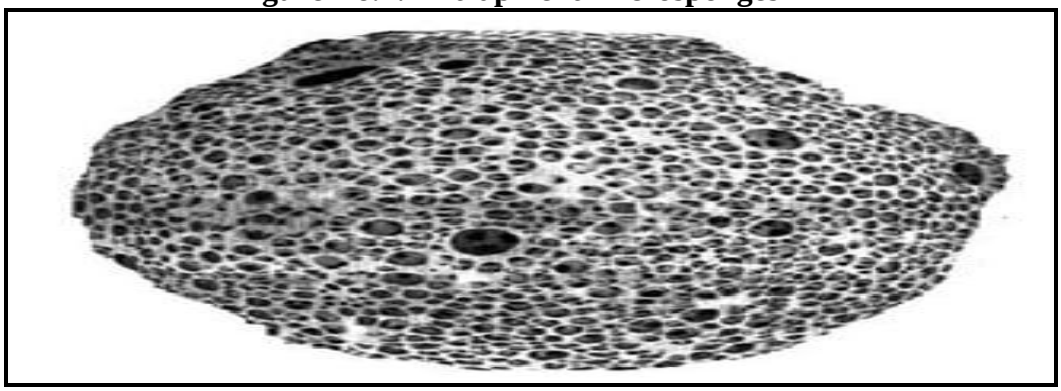

Figure No.2: Highly porous nature of a microsponge

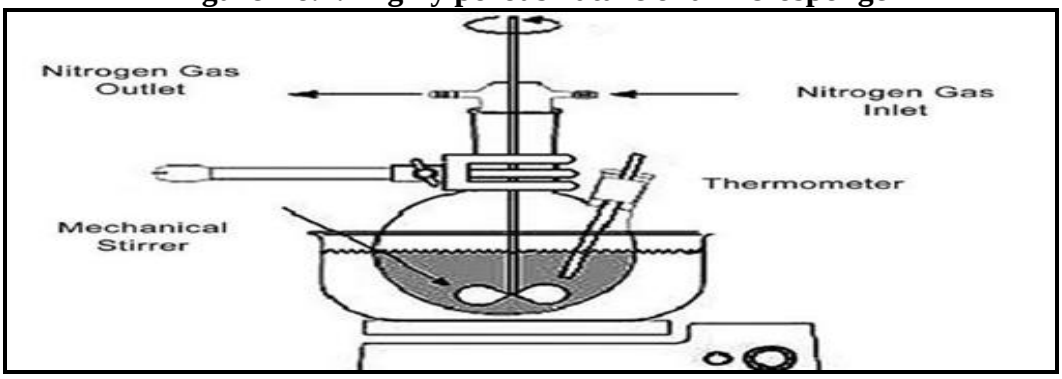

Figure No.3: Liquid-liquid suspension Polymerization of Microsponge

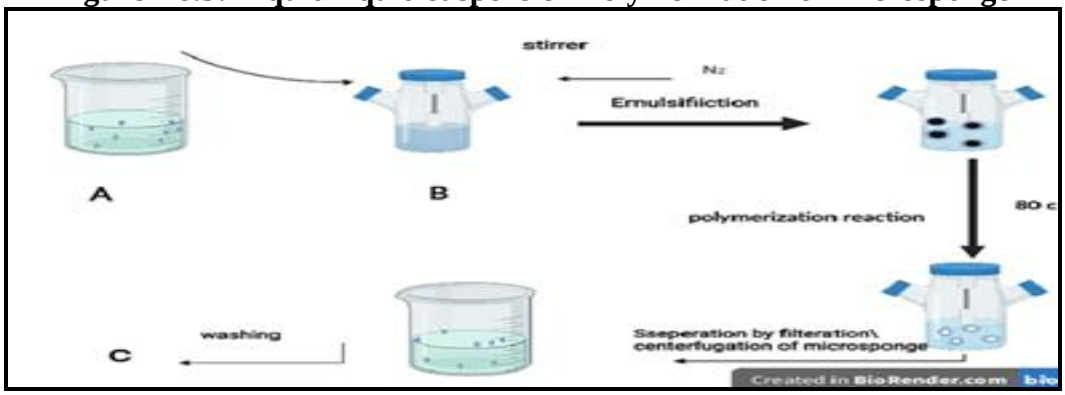

Figure No.4: Quasi-Emulsion solvent diffusion of microsponges

Figure No.5: Vibrating orifice Aerosol Generator

CONCLUSION

The market has a lot of promise for microsponge technology and its versatility because of the need for pharmaceutical products that are both creative and highly efficient. Formulators may fully utilize the potential of these special materials, which offer increased safety, stability, less active side effects, increased multifunctionality and improved ingredient compatibility, as they think of innovative and creative ways to deliver active ingredients. As a result, the microsponge drug delivery system is a highly new and promising sector that requires further research and development. Initially created for topical administration of medications such as anti-inflammatory, anti-fungal, anti-acne, anti-dandruff, antipruritic, rubefacients, etc., MDS has expanded its use to include oral drug delivery as well as bone and tissue engineering. As a result, future developments in controlled drug delivery systems will likely rely heavily on the microsponge drug delivery system. The goal of creating the polymeric microsponges delivery system (MDS) was to increase curcumin's bioavailability, decrease the frequency of administration, and distribute it continuously for a long time. Curcumin microsponges were thus made in the current work using a quick, easy and repeatable quasi-emulsion solvent diffusion approach. Studies using FTIR, DSC, SEM and XRD were used to characterize the formulation.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Won R. Method for delivering an active ingredient by controlled time release utilizing a novel delivery vehicle which can be prepared by a process utilizing the active ingredients as a Porogen, *US, Patent No. 4690825*, 1987.
2. Kydonieus A F. Transdermal delivery of drugs, *CRC Press, Boca Raton*, 1987, 205.
3. Patra J K, Das G, Campos E V R, Rodriguez-Torres M D P, Acosta-Torres L S, *et al*. Nano based drug delivery systems: Recent developments and future prospects, *J Nanobiotechnology*, 16(1), 2018, 71.
4. Kita K. Drug delivery vehicles with improved encapsulation efficiency: Taking advantage of specific drug-carrier interactions, *Expert Opin Drug Deliv*, 8(3), 2011, 329-342.
5. Singh K, Biharee A, Jain A K. Recent advancement of polymersomes as drug delivery carrier, *Curr Pharm Des*, 28(20), 2022, 1621-1631.

6. Asghar L F, Chandran S. Multiparticulate formulation approach to colon specific drug delivery: Current perspectives, *J Pharm Pharm Sci*, 9(3), 2006, 327-338.
7. Jose S, Prema M T, Chacko A J, Thomas A C, Souto E B. Colon specific chitosan microspheres for chronotherapy of chronic stable angina, *Colloids Surf B Biointerfaces,* 83(2), 2011, 277-283.
8. Pandey P, Jain V, Mahajan S C. A review: Microsponge drug delivery system, *Int J Biopharm*, 4, 2013, 225-230.
9. Sharma S, Pawar S, Jain U K. Development and evaluation of topical gel of curcumin from different combination of polymers formulation and evaluation of herbal gel, *Int J Pharm Pharm Sci*, 4(4), 2012, 452-456.
10. https://www.drugbank.ca/drugs/DB00239. [Last accessed on 10 Jan 2017.
11. Shaha V, Jain H, Jethva K, Patel P. Microsponge drug delivery: A review, *Int. J. Res. Pharm. Sci*, 1(2), 2010, 212-218.
12. Kydonieus A F, Berner B. Transdermal delivery of drugs, *CRC Press, Raton*, 1987.
13. Madgassi S, Touitou E. Novel cosmetic delivery systems, Cosmetic science and technology series, *Marcel Dekker Inc. USA,* 19, 1999.
14. Benita S. Microencapsulation: Methods and industrial applications, Drugs and Pharmaceutical Sciences Series, *Marcel Dekker, New York,* 23, 1996.
15. Osborne O W, Amann A H. Topical drug delivery formulation, *Marcel Dekker Inc, New York and Basel*, 1990, 308-309.
16. Comoglu T, Gonul N, Baykara T. Preparation and *in vitro* evaluation of modified release ketoprofen microsponges, *Il Farmaco,* 58(2), 2003, 101-106.
17. Pappa K A. The clinical development of mupirocin, *J Am Acad Dermatol,* 22(5Pt1), 1990, 873-879.
18. Ward A, Campoli-Richards D M. Mupirocin: review of its antibacterial activity, pharmacokinetic properties and therapeu tic use, *Drugs*, 32(5), 1986, 425-444.
19. Conly J M, Johnston B L. Mupirocin- are we in danger of losing it? *Can J Infect Dis*, 13(3), 2002, 157-159.
20. Parenti M A, Hatfield S M, Leyden J J. Mupirocin: A topical antibiotic with a unique structure and mechanism of action, *Clin Pharm*, 6(10), 1987, 761-769.
21. Gisby J, Bryant J. Efficacy of a new cream formulation of mupirocin: Comparison with oral and topical agents in experi mental skin infections, *Antimicrob Agents Chemother,* 44(2), 2000, 255-260.
22. Jelvehgari M, Siahi-Shabad M R, Azarmi S, Martin G P, Nokhodchi A. The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies, *Int J Pharm*, 308(1-2), 2006, 124-132.
23. Pradhan S K. Microsponges as the versatile tool for drug delivery system, *Int. J. Res. Pharm. Chem*, 1(2), 2011, 243-258.
24. Nacht S, Kantz M. The microsponge: A novel topical programmable delivery system, *Top. Drug Deliv. Syst*, 42, 1992, 299-325. Nokhodchi A, Jelvehgari M, Siahi M R, Mozafari M R. Factors affecting the morphology of benzoyl peroxide microsponges, *Micron*, 38(8), 2007, 834-840.
25. Nacht S, Kantz M. The microsponge: A novel topical programmable delivery system, *Top Drug Deliv Syst*, 42, 1992, 299-325.
26. Dey N S, Majumdar S, Rao M. Multiparticulate drug delivery systems for controlled release, *Trop. J. Pharm. Res,* 7(3), 2008, 1067.
27. Jain V, Singh R. Dicyclomine-loaded Eudragit®-based microsponge with potential for colonic delivery: Preparation and characterization, *Tropical J. Pharm. Res,* 9(1), 2010, 67-72.
28. Orlu M, Araman A. Design and evaluation of colon specific drug delivery system

containing flurbiprofen microsponges, *Int. J. Pharm,* 318(1-2), 2006, 103-117.

29. Harsh S, Patel K, Upadhyay U M. Formulation and evaluation of controlled release colon targeted micro sponge of Aceclofenac, *Pharma. Inno. J,* 3(10), 2014, 81-87.
30. Vyas S P, Khar R K. Targeted and controlled drug delivery- Novel carrier system, *CBS Publication, New Delhi,* 1st Edition, 2002, 453.
31. Embil K, Nacht S. The microsponge delivery system (MDS): A topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives, *J. Microencapsulation,* 308, 1996, 124-132.
32. Kaity S, Maiti S, Ghosh A K, Pal D, Ghosh B S. Microsponges: A novel strategy for drug delivery system, *J. Adv. Pharm. Technol. Res,* 1(3), 2010, 283-290.
33. D'souza J I, Masvekar R R, Pattekari P P, Pudi S R, More H N. Microspongic delivery of fluconazole for topical application, *Indo-Japanese Int. Conference on Adv. Pharm. Res. and Tech,* 2004, 76.
34. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Control of prolonged drug release and compression properties of ibuprofen microsponges with acrylic polymer, Eudragitrs, by changing their intraparticle porosity, *Chemical and Pharmaceutical Bulletin,* 40(1), 1992, 196-201.
35. D' souza J I, Masvekar R R, Pattekari P P, Pudi S R, More H N. Microspongic delivery of fluconazole for topical application, *1st Indo- Japanese International Conference on Advances in Pharmaceutical Research and Technology, Mumbai, India,* 2005.
36. Wester R C, Patel R, Nacht S, Leydan J, Malendres J, Maibch H. Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy, *J. Am. Acad. Dermatol,* 24(5Pt1), 1991, 720-726.
37. Tansel C, *et al*. Preparation and *in vitro* evaluation of modified release ketoprofen microsponge II, *Farmaco,* 58(2), 2003, 101-106.
38. Aritomi H, Yamasaki Y, Yamada K, Honda H and Koshi M. Development of sustained release formulation of chlorpheniramine maleate using powder coated microsponges prepared by dry impact blending method, *Journal of Pharmaceutical Sciences and Technology,* 56(1), 1996, 49-56.
39. Won R. Two step method for preparation of controlled release formulations, *(Palo Alto, CA) United States Patent 5145675,* 1992.
40. Hainey P, Huxham I M, Rowatt B, Sherrington D C. Synthesis and ultrastructural studies, of styrene-divinylbenzene polyhipe polymers, *Macromolecules,* 24(1), 1991, 117-121.
41. Makwana R, Patel H, Patel V. Photostability enhancement of miconazole nitrate by microsponge formulation, *Int J Curr Trends Pharm Res,* 2, 2014, 437-458.
42. Jelvehgari M, Siahi-Shadbad M R, Azarmi S, Gary P, Martin, Nokhodchi A. The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies, *International Journal of Pharmaceutics,* 308(1-2), 2006, 124-132.
43. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Control of prolonged drug release and compression properties of ibuprofen microsponges with acrylic polymer, Eudragit RS, Changing their intraparticle porosity, *Chemical and Pharmaceutical Bulletin,* 40(1), 1992, 196-201.
44. Orlu M, Cevher E, Araman A. Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges, *Int J Pharm,* 318(1-2), 2006, 103-117.
45. Ramaiya A. Detecting torsional motion of kinesin motor proteins using birefringent microspheres and high-resolution optical tweezers, *Universitat Tubingen,* 2018.

46. Gan Y, Zhang Y, Cheng D, Shetty A, Rathi P, Katarki N, *et al*. An open-source benchmark suite for microservices and their hardware-software implications for cloud and edge systems, *Proceedings of the Twenty-Fourth International Conference on Architectural Support for Programming Langauges and Operating Systems*, 2019, 3-18.
47. Zaki Rizkalla C M, Latif Aziz R, Soliman I I. *In vitro* and *in vivo* evaluation of hydroxyzine hydrochloride microsponges for topical delivery, *AAPS Pharm Sci Tech*, 12(3), 2011, 989-1001.
48. Rosenhek I. 2008.
49. Rawat A, Majumder Q H, Ahsan F. Inhalable large porous micro- spheres of low molecular weight heparin: *In vitro* and *in vivo* evaluation, *J Control Release*, 128(3), 2008, 224-232.
50. Maiti S, Kaity S, Ray S, Sa B. Development and evaluation of xanthan gum-facilitated ethyl cellulose microsponges for controlled percutaneous delivery of diclofenac sodium, *Acta Pharm*, 61(3), 2011, 257-270.
51. Hiremath J G, Valluru R, Jaiprakash N, Katta S, Matad P. Pharmaceutical aspects of nicorandil, *Int. J. Pharmacy Pharm. Sci*, 2(4), 2010, 24-29.
52. Mitkari B V, Korde S A, Mahadik K R, Kokare C R. Formulation and evaluation of topical liposomal gel for flu conazole, *Indian Journal of Pharmaceutical Education and Research*, 44(4), 2010, 324-333.
53. Campbell R L, Bruce R D. Comparative dermatotox icology, I. Direct comparison of rabbit and human primary skin irritation responses to isopropylmyristate, *Toxicology and Applied Pharmacology*, 59(3), 1981, 555-563.
54. Mishra A K, Mishra A, Ghosh A K, Chattopadhyay P. Evaluation of skin irritation of herbal O/W sunscreen cream on rat model, *IJPI's Journal of Pharmaceutics and Cosmetology*, 1(5), 2011, 220-226.
55. Chadawar V, Shaji J. Microsponge delivery system, *Current Drug Delivery*, 4(2), 2007, 123-129.
56. Nacht S, Katz M. The microsponge: A novel topical programmable delivery system, *Topical Drug Delivery Formulations, Marcel Dekker, New York*, 1990, 299-325.
57. Kilicarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres, *Int. J. Pharm*, 252(1-2), 2003, 99-109.
58. Anderson D L, Cheng C H, Nacht S. Flow characteristics of loosely compacted macroporous microsponge polymeric systems, *Powder Technology*, 78(1), 1994, 15-18.
59. Ford J L, Timmins P. Pharmaceutical thermal analysis- Techniques and applications, *Ellis Horwood Ltd, Chichester*, 1989, 313.
60. Jones D S, Pearce K J. Investigation of the effects of some process variables on microencapsulation of propranolol HCl by solvent evaporation method, *Int J. Pharm*, 118(2), 1995, 99-205.
61. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y, Furuyama S. Characterization of polymorphs of tranilast anhydrate and tranilast monohydrate when crystallized by two solvent change spherical crystallization techniques, *J. Pharm. Sci*, 80(5), 1991, 472-478.
62. Jain V, Singh R. Dicyclomine-loaded eudragit®-based microsponge with potential for colonic delivery: Preparation and characterization, *Trop. J. Pharm. Res*, 9(1), 2010, 67-72.
63. D'souza J I. *In vitro* antibacterial and skin irritation studies of microsponges of benzoyl peroxide, *Ind Drugs*, 38(7), 2001, 104-109.
64. Farris P K. Cosmeceuticals and cosmetic practice, *John Wiley and Sons*, 2013.
65. Kydonieus A F, Berner B. Transdermal delivery of drugs, *CRC Press*, 1987.
66. Dimatteo R, Darling N J, Segura T. In situ forming injectable hydrogels for drug

delivery and wound repair, *Adv Drug Deliv Rev*, 127, 2018, 167-184.
67. Lammers T, Aime S, Hennink W E, Storm G, Kiessling F. Theranostic nanomedicine, *Acc Chem Res,* 44(10), 2011, 1029-1038.
68. Chadawar V, Shaji J. Microsponge delivery system, *Curr Drug Deliv,* 4(2), 2007, 123-129.
69. Chen G, Ushida T, Tateishi T. A Biodegradable hybrid sponge nested with collagen microsponges, *J Biomed Mater Res,* 51(2), 2000, 273-279.
70. Kanematsu A, Marui A, Yamamoto S, Ozeki M, Hirano Y, Yamamoto M, *et al*. Type I collagen can function as a reservoir of basic fibroblast growth factor, *J Control Release,* 99(2), 2004, 281-292.
71. Iwai S, Sawa Y, Ichikawa H, Taketani S, Uchimura E, Chen G, *et al*. Biodegradable polymer with collagen microsponge serves as a new bioengineered cardiovascular prosthesis, *J Thorac Cardiovasc Surg,* 128(3), 2004, 472-479.
72. Chen G, Sato T, Ohgushi H, Ushida T, Tateishi T, Tanaka J. Culturing of skin fibroblasts in a thin PLGA–collagen hybrid mesh, *Biomaterials,* 26(15), 2005, 2559-2566.
73. Iwai S, Sawa Y, Taketani S, Torikai K, Hirakawa K, Matsuda H. Novel tissue-engineered biodegradable material for reconstruction of vascular wall, *Ann Thorac Surg,* 80(5), 2005, 1821-1827.
74. Peppas N A. Analysis of Fickian and non-Fickian drug release from polymers, *Pharm. Acta Helv,* 60(4), 1985, 110-111.
75. Riyaz Ali M Osmani, Aloorkar N H, Ingale D J, Kulkarni P K, Umme Hani, Bhosale R R, *et al*. Microsponge based novel drug delivery system for augmented arthritis therapy, *Saudi Pharm J,* 23(5), 2015, 562-572.
76. Ravi R, Senthil Kumar S K, Parthiban S. Formulation and evaluation of the microsponge gel for an anti acne agent for the treatment of acne, *Int J Pharm Sci Res,* 3(1), 2013, 32-38.
77. Embil K, Nacht S. The microsponge drug delivery system (MDS): A topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives, *J. Microencaps,* 13(5), 1996, 575-588.
78. Higuchi T. Mechanism of sustained-action medication theoretical analysis of rate of release of solid drugs dispersed in solid matrices, *J. Pharm. Sci,* 52(12), 1963, 1145-1149.
79. Wagner J G. Interpretation of percent dissolved-time plots derived from *in vitro* testing of conventional tablets and capsules, *J. Pharm. Sci,* 58(10), 1969, 1253-1257.
80. Korsmeyer R W, Gurny R, Doelker E, Buri P, Peppas N A. Mechanisms of solute release from porous hydrophilic polymers, *Int. J. Pharm,* 15(1), 1983, 25-35.
81. Fulton J E, Bradley S. Studies on the mechanism of action of topical benzoyl peroxide in acne vulgaris, *J. Cutan. Pathol,* 1(5), 1974, 191-194.
82. Arabi H, Hashemi S A, Fooladi M. Microencapsulation of alloporinol by solvent evaporation and controlled release investigation of drugs, *J. Microencapsul,* 13(5), 1996, 527-535.
83. Lorenzetti O J, Wernet T, Mcdonald T. Some comparisons of benzoyl peroxide formulations, *J. Soc. Cosmet. Chem,* 28, 1977, 533-549.
84. Puranik P K, Manekar N C, Dorle A K. Preparation and evaluation of abietic acid microcapsules by a solvent evaporation technique, *J. Micro encapsul,* 9, 1992, 425-435.
85. Chadawar V, Shaji J. Microsponge delivery, *Current Drug Deliv,* 4, 2007, 123-129.
86. Mahant S, Kumar S, Nanda S, Rao R. Microsponges for dermato- logical applications: Perspectives and challenges, *Asian J Pharm Sci,* 15(3), 2020, 273-291.

87. Pifferi G, Santoro P, Pedrani M. Quality and functionality of excipients, *Farmaco,* 54(1-2), 1999, 1-14.
88. Tekade R. Drug delivery systems, *Academic Press*, 1st Edition, 2019, 792.
89. Kaity S, Maiti S, Ghosh A K, Pal D, Ghosh A, Banerjee S. Microsponges: A novel strategy for drug delivery system, *J Adv Pharm Technol Res,* 1(3), 2010, 283-290.
90. Guoping C, Takashi S, Hajime O, Takashi U, Tetsuya T, Junzo T. Culturing of skin fibroblasts in a thin PLGA-collagen hybrid mesh, *Biomaterials,* 26(15), 2005, 2559-2566.
91. Gangadharappa H V, Gupta V, Sarat C P M, Shivakumar H G. Current trends in microsponge drug delivery system, *Current Drug Delivery*, 10(4), 2013, 453-465.

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