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Microsponges: A Novel Approach Topical Drug Delivery System

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Abstract:

Microsponge is an Innovative Technique used to overcome conventional topical delivery system problems. Microsponge is developed as an Novel approach reduces drug amount and side effects. There are two methods of preparations 1.Liquid Liquid Suspension Polymerization and 2.Quasi Emulsion Solvent Diffusion Method. Mainly Quasi Emulsion Solvent Diffusion Method is used because Eudragit Polymers forms the best microsponges. Microsponges are highly porous, cross linked, polymeric microsperic system. Microsponge provides controlled drug release for prolong time. There are various applications of microsponges like in medicines, colon cancer, stomach ulcer, in Acne treatment, Antifungal can apply topically, in Melanoma, skin protection purpose, Diabetic wounds Treatment, Arthritis, Hyperpigmentation of skin, treat infected skin.

Key Words: Microsponge, controlled drug release, Eudragit polymer, Quasi emulsion Solvent diffusion method.

Introduction:

A Micro sponge drug delivery system (MDDS) is a patented, highly cross-linked, porous, polymeric microspheres polymeric system (10-25), consisting of porous microspheres particles consisting of a myriad of interconnecting voids within non-collapsible structures with a large porous surface that can entrap a wide range of actives (cosmetics, over-the-counter (OTC) skin care, sunscreens, and prescription products) and then to cause. A normal 25-mm sphere can contain up to 250000 holes, giving it a total pore volume of around 1 ml/g, and an internal pore structure that is 10 feet long. [1]

The skin cannot be penetrated by micro sponges, which can hold four times their weight in skin secretions. Instead, they gather in the skin's minuscule crevices and release the medicine there as the skin requires it. The micro sponge system can stop components from building up too much in the dermis and epidermis. These products often have a high concentration of active chemicals and are offered to the consumer in customary forms such creams, gels, or lotions. Micro sponges are porous microsphere-based polymeric delivery devices. They include a variety of active components that they can contain, including emollients, perfumes, essential oils, sunscreens, and anti-infective, anti-fungal, and anti-inflammatory medications. Compared to other technologies like microencapsulation and liposomes, the MDS has advantages. Typically, microcapsules are unable to regulate how quickly actives are released. The actives inside the microcapsules will be released once the wall is ruptured. Low payload, challenging formulation, limited chemical stability, and microbial instability are all problems for liposomes.[2]

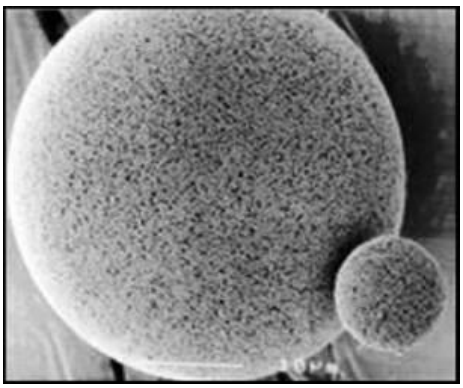

Figure- Microsponge

In order to reduce systemic exposure and minimise local cutaneous reactions to active pharmaceuticals, the Micro sponge Delivery System (MDS) technology has been used in topical drug solutions. This technology allows for the controlled release of active drugs into the skin. Micro sponges are made to effectively distribute pharmaceutically active ingredients at low doses while also improving stability, minimising side effects, and altering drug release profiles. [3]

History of Microsponges:

The initial patents for the micro sponge technology were given to Advanced Polymer Systems, Inc. by Won in 1987.US city of Redwood City, California This company created a wide range of technique modifications that are used for both cosmetic and over-the-counter (OTC) and prescription pharmaceutical items. Currently, Cardinal Health, Inc. has a licence to employ this intriguing technology in topical medicines to enable the controlled release of active pharmaceuticals into the skin and limit systemic exposure and local cutaneous reactions to active drugs**.**[4]

The following describe the properties of microsponges

1. Microsponges are stable at temperatures up to 130°C and over a wide pH range of 1 to 11.

2. Microsponges can absorb oil up to 6 times its weight.

3. Microsponge formulations are compatible with most vehicles and active ingredients.

4. Microsponge formulations have high entrapment efficiency upto 50 to 60%.

5. Microsponge formulations are free flowing and can be cost effective.

6. It provides continuous action up to 12 hours i.e., extended release.

7. They have superior formulation flexibility.

8. Microsponges are thermal, physically, and chemically stable.

9. Liquids can be converted into powders by improving material processing.

10. Microsponge formulations are self-sterilizing because the pores, which have an average size of 0.25 m, are too small for bacteria to enter. [5,6].

Methods of Preparation:

1. **Liquid Liquid Suspension Polymerization**

The suspension polymerization process is used to create the microsponges with porous microsphere bases. The immiscible monomers are first mixed with the active components in the appropriate solvent in this polymerization procedure, and then they are dispersed in aqueous phases that include off For the creation of suspension, surfactants or suspending agents are utilised. Then, the polymerization is triggered by raising the temperature, applying radiation, or adding a catalyst. Up until a reservoir form of a system with a spherical shape is created, polymerization proceeds. The solvent is eliminated during the polymerization process, leaving the microsponges.[7]

2. **Quasi–emulsion solvent diffusion:**

When the medication is responsive to the conditions of polymerization, the two-step technique is used. the microsponges created utilising a quasi-emulsion solvent diffusion process and the varied polymer amounts.[8]

In emulsion solvent diffusion, the drug and the good solvent have a stronger affinity than the good solvent and the unreliable firm. Even though the natural solvents are miscible, the medicine is dissolved in the healthy solid and the solution is distributed into the poor firm, forming emulsion droplets. From the emulsion particles, the healthy solvent gradually diffuses into the bad solvent stage, and the bad solvent then spreads into the droplets inside the cells where the drug crystallises.

The polymer is injected into an external aqueous phase in this two-step procedure, which usually includes a stabiliser like Along with the catalyst, plasticizer, and diffuser, polyvinyl alcohol (Porogen). After emulsification, the system is kept constantly agitated for two hours and, if necessary, kept at a higher temperature. A very porous microparticle known as a "Microsponge" causes porogen to diffuse into the surrounding media. The mixture is then filtered to remove the microsponges. The item has been cleaned and dried for 24 hours at 50°C in a vacuum oven [9]

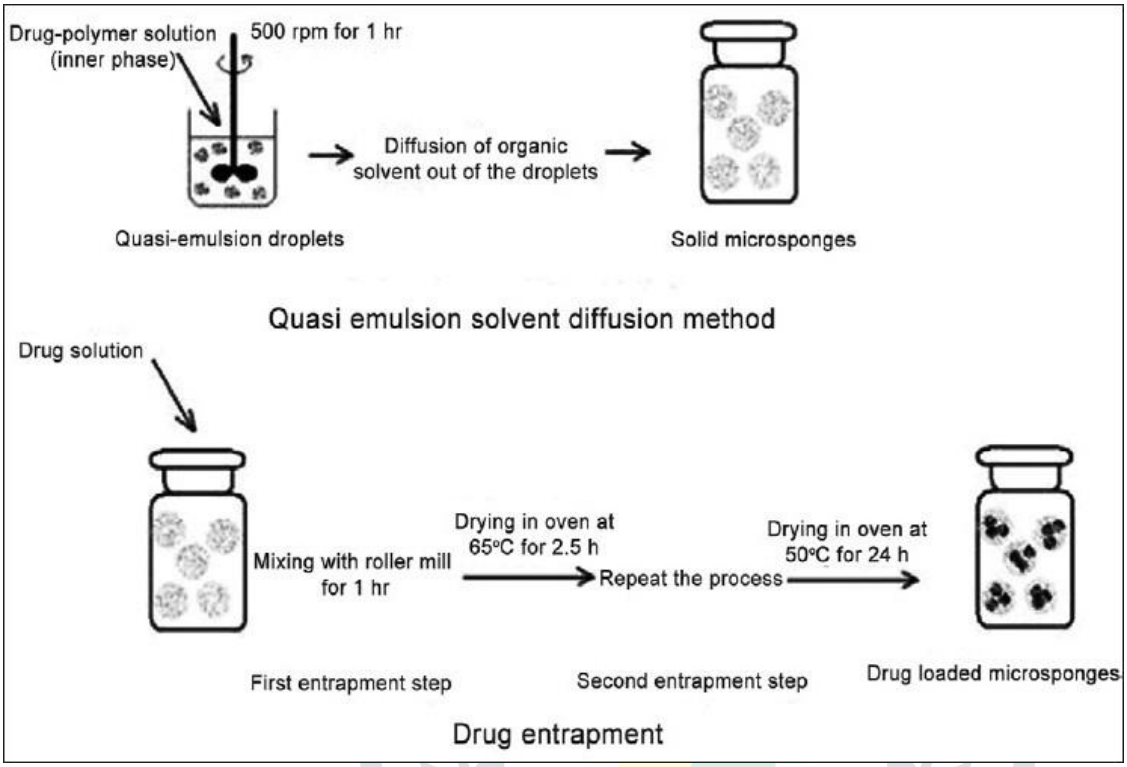

Figure- Quasi–emulsion solvent diffusion method

Limitations:

The preparation methods usually use the organic solvents as porogens, which pose an environmental hazard, as some may be highly inflammable, posing a safety hazard. In some cases, the traces of residual monomers have been observed, which may be toxic and hazardous to the health.[10]

Mechanism of action

The noncollapsible network of voids in the porous microspheres is extremely intricate. These systems are capable of absorbing a variety of active substances, including emollients, volatile oils, sunscreen, fragrances, and anti-infective and antifungal compounds.

The rate of release of active ingredients before they become trapped in the microspheres can be calculated based on a number of variables, including pore diameter, the degree of cross-linking of the polymers, and the concentration difference of the active ingredient between the microspheres and the vehicle in which these spheres are contained. This method is frequently used to manufacture topical agent formulations in a variety of different forms, such as gel, cream, or lotion. While applying the formulation topically to the targeted area of the skin, the active chemicals diffuse out of the spheres into the vehicle and then onto the skin. Numerous release triggers, including changes in pressure and temperature, pH, and solubility, might start the release. Due to their small size, the microsponges cannot penetrate the stratum corneum; as a result, they are maintained in the skin's surface and release the active chemicals gradually over time. The MDS offers better control over release rate, which may have an impression of the degree of skin irritancy that the topical treatment has caused. Microsponges technology, however, has a few limitations. It can only entrap active chemicals with specific characteristics.[11]

Microsponges' method of drug release

In reaction to one or more external triggers, a microsponge can be made to release the specified amount of active chemicals gradually over time.

Temperature:

Few encapsulated active compounds may be too viscous at room temperature to flow abruptly from microsponges onto the skin. The rate of flow also increases with an increase in skin warmth, which improves release.[12]

Pressure: Applying pressure or rubbing skin might cause microsponges to release their active component. The microsponge's resilience determines how much release occurs.[13]

Solubility: When water is present, chemicals such as antiseptics and deodorants that are water miscible in microsponges will release. Diffusion can also trigger the release, however taking into account the partition coefficient of the between the external system and the microsponges.[14]

PH Activating system:

By altering the coating on the microsponge, it is possible to start the pH-based release of the active. This has numerous uses for drug delivery.[15]

Applications of microsponges in medicine:

Various therapeutic uses for microsponges have been researched. It offers a brand-new carrier system that is appropriate for therapeutic agents and has the ability to alter and regulate how the medications release. The use of microsponges is rapidly developing, starting with topical treatments for a variety of skin conditions and diseases and progressing to oral formulations that deliver drugs orally at controlled release rates to specific areas.

Microsponges are crucial in the creation of a 3D porous scaffold for bone tissue engineering due to the safety and efficacy of the medication administration. Microsponges play a significant part in cardiovascular engineering because they are self-sterilizing by nature (because to their pore size), Microsponges, which are self-sterilizing by nature (because to their pore size), are also playing a significant role in cardiovascular engineering. Biodegradable graft material containing collagen microsponges is utilised to construct a patch for cardiovascular tissue regeneration surgery. [16,17]

Some improvements in microsponges, such as nanosponges, nanoferrosponges, and porous microbeads, are made by altering the processing methods. They can be utilised to transport siRNA and RNA as well as hydrophilic and hydrophobic medicines topically or orally. They can also be used to deliver gaseous particles for the treatment of malignant cells and to deliver siRNA. [18;19,20]

Colon cancer and microsponges:

To ensure a sustained release of the medicine and reduce toxicity, microsponges can also be utilised for oral drug delivery. To treat colon cancer, Othman et al. created microsponges based on Eudragit RS100 and 5-Fluorouracil. The anticancer compound 5-FU is effective against a variety of solid cancers. By boosting relative accumulation in the tumour areas, 5-FU activity can be improved. As a result, the toxicity also decreases. Utilizing the solvent diffusion method with oil in oil emulsions, microsponges were created. Release studies were conducted, and the pure 5-FU was discovered. whereas that from the microsponges was found to initially be an immediate burst release and subsequently a somewhat slow release up to 5 hours, it was discovered to be released in just 20 minutes. Cell viability tests have revealed that 5-FU with MS is more effective than 5-FU alone. Results indicate that 5-FU microsponges can take the place of 5-FU, an oral anticancer medication.[21]

Five microsponges are used to treat stomach ulcers:

In 2016, Charagonda et al. created the famotidine-loaded gastro-retentive microsponges for the treatment of stomach ulcers. By using a quasi-emulsion solvent diffusion process and various ratios of the polymer Eudragit RS100 and the stabiliser polyvinyl alcohol, floating microsponges were created. Regarding particle size, drug content, thermal stability, surface morphology, powder properties, and an in-vitro drug release investigation, the produced microsponges were assessed. Using USP Type II equipment, the in-vitro drug release behaviour was evaluated in an acidic medium (0.1N HCl). The microsponges were said to follow zero order kinetics and to release the medication in a sustained way for a duration of 12 hours.[22]

Acne microsponges:

One of the main skin issues, acne is connected to skin irritability. One of the most popular medications used to treat acne is benzoyl peroxide. To regulate the discharge of benzoyl peroxide onto the skin, Jelvehgari and his colleagues created benzoyl peroxide microsponges.

According to studies on drug release, the presence of nonencapsulated drugs may have caused the drug release to increase in the first four hours and then stabilise for the next seven. When these nonencapsulated drugs released completely, the drug release stabilised, indicating the release of the entrapped drugs.[23]

In order to achieve sustained release, Osmani et al. created microsponges containing cream of miconazole nitrate, an anti-acne drug. They used the quasi-emulsion solvent diffusion approach to create Eudragit RS-100 microsponges. A cream was added to prepared microsponges. Drug-loaded microsponges provided extended drug release of 78.28% up to 8 hours, according to research on drug release, but conventional creams ran out after 4 hours and released 83.09%. [24]

Antifungal microsponges formulation:

Anju et al. developed terbinafine hydrochloride microsponges as an antifungal agent. Drug-loaded microsponge based gel in vitro investigations were carried out and compare dusing the ordinary gel that contains a medication. The microsponge-loaded gel demonstrated the best sustained drug release for around 10 hours, whereas the drug-loaded plain gel demonstrated drug release of 96.65% up to 6 hours. In contrast to ordinary gels, terbinafine hydrochloride-loaded microsponge gels demonstrated sustained drug release.[25]

By employing the quasi-emulsion solvent diffusion approach, Dombe et al. created oxiconazole nitrate microsponges that were subsequently integrated into the gel. Another antifungal drug, oxiconazole nitrate, likewise has low aqueous solubility, side effects, and adverse reactions. The results demonstrated that this method of preparation was appropriate for making microsponges since the microsponges produced were discrete, spherical in shape, and had an excellent production yield of 61.44% to 80.45%. For 8 hours, 87.77% drug release was found to be the highest. The microsponge gel demonstrated the drug's regulated release over 12 hours.[26]

Melanoma microsponges:

For the treatment of melanoma and post-inflammatory hyperpigmentation, Grimes created microsponges containing 4% hydroquinone and 0.15% retinol (PIH). The microsponges.

Formulated to release hydroquinone over time while causing the least amount of skin irritation. An open-label investigation was conducted. When compared to baseline, improvements in illness symptoms and pigmentation intensity were observed to be statistically significant at weeks 4, 8, and 12 (p.001). At each appointment, the lesion area measurements dramatically improved (p .001). The formulation was well tolerated, and only one trial participant withdrew due to an allergic response that was not deemed to be serious.[27]

Using microsponges to treat diabetic wounds:

Nebivolol-loaded microsponges were created by Pandit et al. and then included in a gel to offer a sufficient moist wound care environment throughout the last phases of the procedure.wound closure. An antihypertensive medication called nebivolol causes vasodilation through the nitric oxide route, which lessens diabetic neuropathy and restores endothelial function in the body. diabetes injuries In vitro tests revealed that 80% of the medication was released within 8 hours. Due to the drug being trapped in its entrapped form within the formulation's porous structure, microsponge gel demonstrated delayed drug release Diabetic rats' wound healing and closure is observed.[28]

Skin protection with microsponges:

Sunscreens are used to protect against UV radiation, which can cause sunburns and a number of cancers, including malignant melanoma and basal carcinoma. To intensify the impact, It is possible to create microsponges. For the topical delivery of Oxybenzone, a broad-spectrum sunscreen ingredient, Pawar et al. produced microsponges. They used the quasiemulsion solvent diffusion approach to create it. Oxybenzone exhibits skin irritability, dermatitis, and systemic absorption in lotion and cream form. They used 32 factorial designs to maximise the impact of ethyl cellulose and dichloromethane before dispersing it in hydrogel to be tested further. The improved formulation's entrapment efficiency was discovered to be 96.9 0.52%.

The gel had a controlled release and wasn't irritating to the skin of the rats. It demonstrated the highest recovery during the creep recovery test, which is a sign of high elasticity. The formula had a higher sun protection factor and less toxicity and irritability.

in contrast to the one that is offered on the market. The marketed lotion had an SPF of 20, however the microsponge gel had an SPF of 25, which might be explained by the slower drug release from the microsponge gel, demonstrating longer oxybenzone retention.[29]

hyperpigmented microsponges:

Glabridin microsponge has been effectively created by Deshmukh et al. to treat hyperpigmentation problem. A quasiemulsion was used to prepare the microsponges.using the solvent diffusion method with ethyl cellulose as the polymer Regarding particle size, drug content, thermal stability, and FTIR spectroscopy, the produced microsponges were assessed. Mercury intrusion porosimetry was used to calculate the microsponges' porosity characteristics. The produced microsponges were mixed into the Carbopol gel for simple topical administration. The glabridin microsponge-based gel's ability to whiten the skin was tested on guinea pigs. In guinea pigs, UV B radiation was utilised to cause hyperpigmentation. The skin of the animal was examined histopathologically after the course of treatment. Animals treated with microsponge-based gel experienced an effective reduction in melanin density. Finally, writers demonstrated how well microsponges can treat hyperpigmentation problem.[30]

Arthritis microsponges:

Diclofenac delivery in arthritis has been examined using a topical microsponge application. The most used NSAID for treating pain and edoema is diclofenac arthritis and other musculoskeletal conditions, although oral administration is linked to issues such stomach discomfort and first pass metabolism. To solve these issues, topical formulations with diclofenac microsponges can be employed. To achieve a sustained release for arthritis therapy, Osmani et al. created a diclofenac diethylamine microsponges gel utilising a quasi-emulsion solvent diffusion approach. They compared their findings to the Voltaren Emulgel 1.16% w/w commercial formulation.

According to drug release studies, gel releases 81.11% of the drug for just 4 hours, whereas microsponge-based gel releases the drug for up to 8 hours.[31]

Another study was conducted by Karthika et al., who developed microsponges with lornoxicam as the active ingredient for treating arthritis and turned them into tablets. They discovered sustained drug release, or 86%-96% to 12 hr.[32]

Shuhaib B. et al. created a mafenamic acid-loaded microsponge for topical application in the treatment of rheumatoid arthritis in 2018. Using a quasi-emulsion solvent, ethyl cellulose as the polymer and polyvinyl alcohol as the stabiliser, a drug-loaded microsponge was created.diffusion methodology The medication and excipients did not interact, according to the FTIR spectrum.Evaluations of the formed microsponges' manufacturing yield, drug content, entrapment effectiveness, and mean particle size were conducted. The prepared microsponge included light liquid paraffin emulgel and HPMC. Using a modified Keshary-Chein (K-C) cell, the In-vitro diffusion of medication across egg membrane was evaluated. The outcomes showed persistent drug diffusion over an 8-hour period. Finally, authors came to a conclusion about Mafenamic acid is more effectively delivered via a topical drug delivery method based on microsponges.[33]

Infected skin using microsponges:

In addition, lotions or gels containing microsponges are applied to the skin to treat conditions like eczema and atopic dermatitis. Mupirocin, an antibiotic substance applied topically for infection of the skin therapy. Mupirocin microsponges were developed by Amrutiya et al. for the long-lasting protection against skin infections. Utilizing the emulsion solvent diffusion approach, they created mupirocin microsponges, which they later put into an emulgel basis. Controlled release and drug deposition have been demonstrated in investigations on drug release utilising cellulose dialysis membrane.Studies on the abdomen skin of rats revealed that the medication remained detectably in the skin for up to 24 hours.Draize patch testing demonstrated the stability and skin-friendliness of improved compositions.The microsponge gel showed up to 10 hours of drug release, but the ointment showed up to 4 hours.[34]

Microsponge Evaluation Methodology:

In vitro techniques

Size and Size Distribution of Particles:

Both optical and electron microscopes can be used to measure particle size and size distribution.

The particle size has a significant impact on the formulation's stability and smoothness, making this a crucial stage. By controlling the particle size during polymerization, free-flowing powders with attractive properties can be produced. Using a laser light diffractometer or another suitable technology, one may determine the particle size of charged and unloaded microsponges. You can express the values (d50) as the mean size range for all formulations. Plotting cumulative percentage drug release from microsponges of various particle sizes against time will help researchers better understand the role that particle size plays in drug release.[35]

SPM Surface Topography and Morphology:

Several techniques, including photon for morphology and surface topography, several techniques have been applied, including correlation spectroscopy (PCS), scanning electron microscopy (SEM), transfer electron microscopy (TEM), etc. SEM is frequently employed to study the surface structure of prepared microsponges after they have been coated with gold-palladium at room temperature and in an argon atmosphere.

Calculating True Density:

An ultra-pycnometer can be used to assess the actual density of microsponges under Calculated from the mean of several determinations, helium gas[36]

Understanding Pore Structure:

Controlling the intensity of the active substance requires both the volume and diameter of the pores.and effectiveness's duration. The movement of active substances from microsponges to the medium that disperses the material is also influenced by pore diameter.

To investigate the relationship between pore diameter and amount and the frequency of Microsponges substance discharge, mercury porosimetry incursion may be utilised.

Intrusion-isotherms of extrusion are among the microsponges' porosity metrics. The distribution of pores, pore size distribution, pore surface area, average pore diameters, and pores are all determined via mercury intrusion porosimetry.

It is possible to determine volume, relative density, form, and morphology.Scanning for incremental bulk intrusions is mapped in opposition to pore diameters that show pore size distributions.Using the equation, the pore diameter of microsponges can be determined Washburn.[37,38]

Testing with **infrared (IR) technology** may also reveal chemical incompatibilities molecules. FT-IR with thin-layer chromatography (TLC).[39]

may also research how drugs interact with reaction enhancers.**X-ray diffraction** of powder (XRD) andDrug crystallinity can be examined using **Differential Scanning Colorimetry (DSC)** to determine how polymerization affects it.[40]

Resiliency:

Viscoelastic properties of microsponges can be modified to produce Depending on the needs of the initial formulation, weaker or stiffer beadlets may be produced.

The discharge rate tends to slow down with increased cross-linking. Therefore, by taking into account discharge as a property of temporal interconnection, the resilience of Microsponges is studied and optimised in accordance with the necessity.[41]

Composition of Polymers and Monomers:

Particle size, for example, affects the drug discharge from Microsponges the structure of polymers and drug charging. The polymer structure of the Microsponges Drug Delivery system can have an impact on the partition coefficient of the trapped drug between the vehicle and the Microsponges system, directly altering the trapped drug's frequency of discharge.

Plotting against time can be used to investigate drug release from microsponge structures made of different polymer architectures.cumulative percentage of drug discharge.

Methane methacrylate/ethylene glycol dimethacrylate structure produces pharmaceuticals at a slower rate and in fewer quantities overall than the styrene/divinylbenzene procedure.

The active ingredient's trapping properties and the vehicle it will be delivered in both have an impact on the choice of monomer. Various electrically priced or electrically varying polymers It might be possible to produce flexible active ingredient releases using hydrophobicity or lipophilicity. Various monomer mixtures will be assessed for compatibility with the medications by examining their drug discharge profile.[42]

Release Assessment:

Tests for Dissolution:

Dissolution discharge from microsponges

The USP XXIII dissolution instrument and a bespoke container made of 5 m stainless metal mesh can be used to study frequency. 150 rpm is the rotational speed. To achieve sink conditions, the dissolution medium is chosen while the solubility of the actives is taken into account. The samples from the dissolving medium were examined periodically using the appropriate analytical techniques[43].

Microsponge Drug Delivery System Recent Advances:

By modifying the methods used to build There have been numerous developments, including porous microbeads, nanosponges, and nano-ferrosponges. In contrast to polymeric micro- or nanosponges, -CD nanosponges have also been developed that work with both hydrophobic and hydrophilic medications. For the oral administration of dexamethasone, flurbiprofen, HCl doxorubicin, itraconazole, and serum albumin, these complex compounds have been studied as model drugs. The -CD was reacted with diphenyl chloride to create these The -CD molecule was cross-linked to produce nanosponges. Some scientists have mentioned the nanosponges as a helpful source for gas distribution. Additionally, researchers discovered that adding a cytotoxic to a nanosponge carrier system could increase the drug's effectiveness, suggesting that these carriers could be utilised to specifically target cancer cells.[44]

The self-performing carriers with greater resistance to the target region were created using a revolutionary technique called nanoferrosponge. The deepest tissue can be reached by the carriers thanks to their internal magnetic mechanism, which also causes the particle to be extracted from the magnetic material and fall into a porous system.[45]

The method to create porous microbeads was created as a result of the enhanced properties of porous microspheres. This technique (High Internal Phase Emulsion, HIPE) used a monomer that contained an internal aqueous phase, an interlinking agent, and a continuous oil phase [45]. Additionally, they noticed improved RNA stability and SiRNA's generally successful encapsulation procedure. The strategy might result in new therapeutic routes for siRNA administration.[46]

FUTURE POTENTIAL

Microsponge medication delivery technology offers potential future applications in several pharmaceutical applications because it offers specific qualities that make it simple to develop new product kinds, such as improved product quality and elegance, expanded release, improved drug release profile, lower discomfort, and improved physical, chemical, and thermal stability. The design of the oral peptide distribution system using a changeable polymer ratio will play the real function in the future. The Usage of biodegradable and erodible materials

Drug delivery using polymers makes it possible to securely administer active ingredients. Considering that these permeable structures have alsoThe colon is an effective place for drug discharge since it has been studied for drug delivery through the pulmonary pathway, showing that these structures can demonstrate efficient drug discharge even in the absence of dissolved fluid.Additionally, these carriers must be developed for alternate drug delivery routes such parenteral and pulmonary channels. These ions can be utilised in the environment for stem cell culture and tissue regeneration. They can also be employed as a medium for cell culture.[47]

One of the most promising disciplines is tissue engineering since researchers think it can improve patients' quality of life. Vascular Tissue Engineering is one illustration. Expanded polytetrafluoroethylene (ePTFE) or Dacron, which is clinically utilised for reconstructing large-diameter arteries, including the aorta and iliac artery, is the standard method for doing this. They are not appropriate for small arteries since they are thought to be foreign bodies that could cause thrombosis. As a result, a bypass procedure is required, requiring additional surgical intervention. An innovative small-

caliber vascular graft made of polyglycolic acid (PGA) and poly-L-lactic acid (PLLA) fibres that were combined with collagen microsponge to form a vascular patch material was tested on dogs using the Scaffold Design approach.[48-52]

RNAi

RNA interference, often known as RNAi, is hypothesised to be an innate defence system that has developed to shield organisms from RNA viruses and cancer. Double stranded RNA (dsRNA) is a foreign substance that cells can identify. When this occurs, the enzyme Dicer is called upon to fragment the foreign RNA into siRNA. These RNA fragments measure about 22 nucleotides long. The target viral mRNA is subsequently bound by one strand of the siRNA.

to prevent its expression in a sequence-specific manner.

The delivery of siRNA to the target site faces a number of difficulties, including:

1. Administrative Barrier: Its limited permeability across the intestinal epithelium prevents it from being absorbed orally and entering the bloodstream.

2. Immune Response and Safety: In order to avoid being destroyed before reaching the target, the carrier must be non-immunogenic.

3. Providing a dose that is adequate without the need for repeated doses.

Due to prior difficulties, rolling circle transcription of a DNA template was thought to be the best delivery method to resolve these difficulties employing microsponge. Rolling circle transcription of circular DNA produces RNA polymers in a solution containing the RNA-producing enzyme RNA polymerase and the building blocks for RNA (nucleoside triphosphates, or NTPs). The result is the formation of lamellar sheets, wrinkled sheets with semi-spherical structures, and entangled and twisted fibrils. The RNAi micro sponges finally condense into 200 nm-diameter PEI-coated micro sponges with about 500,000 siRNA precursors each after the addition of poly cationic poly ethylenimine (PEI).[53,54].

Literature survey:

Drug	Polymer	Solvent	Method of preparation	Outcome	Reference
Fluconazole	Ethyl cellulose50	Triethanolamine	Quasi emulsion – solvent diffusion method.	Curcumin loaded microsponges successfully developed by quasi emulsion method for colon targeting for treating ulcerative colitis.	55
Tenofovir	Eudragit L-100.	Dichloromethane	Quasi emulsion – solvent diffusion method.	Increase the bioavailability of drugs.	56
5 - fluorouracil	Eudragit.	Eudragit RS100	Oil in oil emulsion solvent diffusion technique.	It shows sustained release action.	57
Valsartan	Ethyl cellulose.	Dichloroethane,	Quasi emulsion – solvent diffusion method.	Increase stability and minimum side effect.	58
Diclofenac sodium	Eudragit RS100,HPMC	Dichloromethane	Quasi – emulsion solvent	It shows a controlled-release drug.	59

			diffusion method .		
Terbinafine hydrochloride	Ethyl cellulose,	Dichloromethane	Quasi emulsion – solvent diffusion method.	Optimize sustained release of drug around a period of 10 hr was shown by F2 formulation.	60
Acetazolamide	Ethyl cellulose (EC)	Dichloromethane	Quasi emulsion – solvent diffusion method.	Stable acetazolamide microsponges was successfully prepared by this method.	61
Acyclovir	HPMC, EC.	Dichloromethane,	Quasi emulsion – solvent diffusion method.	Increase in drug release with increase in polymer concentration.	62
Voriconazole	Ethyl cellulose	Triethanolamine	Quasi emulsion – solvent diffusion method.	Voriconazole microsponges are effective carrier for topical drug delivery of drug.	63
Nystatin	Carbapol 974p, HPMCk4	Triethanolamine	Quasi emulsion – solvent diffusion method.	Microsponges based gel of Nystatin shows good release of drug as compared to Nystatin gel.	64
Eberconazole	Ethyl cellulose	Dichromethane, triethanolamine	Quasi emulsion – solvent diffusion method.	The developed microsponges gel formulations demonstrated controlled release of eberconazole.	65
Roxithromycin	Eudragit RL 100	Ethanol, Dichloromethane	Quasi emulsion – solvent diffusion method.	It is unique technology for controlled release of topical agents.	66
Ketoconazole	Ethylcelluollse N22	Dichloromethane,	Quasi emulsion – solvent diffusion method.	Drug release to continuous prolonged period of time by reducing frequency of application and side effects.	67
Miconazole	Eudragit RS 100	Ethanol, Dichloromethane	Quasi emulsion – solvent diffusion method.	This method is simple,reproducible & rapid gives prolong release of miconazole drug treat diaper dermatitis.	68
Itraconazole	Ethyl cellulose, Eudragit Rs 100.	Ethanol, methanol.	Quasi emulsion – solvent diffusion method. Liquid liquid suspension	Suitable external phase volume was found to be 100ml,suitable concentration of PVA 0.5%,internal phase 20ml,stirring speed	69

			polymerization method.	1000rpm,stirring hour 3hrs,drug/polymer ratio 1:4.	
Oxiconazole nitrate	Eudragit S-100, Eudragit L-100	Dichloromethane	Quasi emulsion – solvent diffusion method.	Compared to conventional formulation microsponge based gel remain on skin for more time.	70
Naproxen	Eudragit RS 100	Ethanol, Dichloromethane	Quasi emulsion – solvent diffusion method.	Formulation F10 and G3 have better results than other formulations chemically stable.	71
Lornoxicam	Ethyl cellulose, HPMC K200M	Ethanol, Dichloromethane	Quasi emulsion – solvent diffusion method.	Study represents successful optimization of lornoxicam loaded cellulosic microsponge gel & proved in vivo study for treatment of arthritis.	72
Famotidine	Eudragit S-100	-	Quasi emulsion – solvent diffusion method.	Drug delivery through polymer controlled drug delivery .	73
clotrimazole	Eudragit RL 100, Eudragit S 100, ethyl cellulose	Ethanol	Quasi emulsion – solvent diffusion method.	Formulations showed controlled release of drug through skin compared to marketed products.	74
Meloxicam	Eudragit	Dichlromethane	Quasi emulsion – solvent diffusion method.	In vitro release of MLX from gel was found to follow first order release kinetics .	75
Nicorandil	Eudragit RSPO, Eudragit RLPO, Eudragit S100, HPMC	Isopropyl alcohol, Dichloromethane	Quasi emulsion – solvent diffusion method.	HPMC & Eudragit polymer for controlled delivery system of drug upto 24hrs.	76
Baclofen	Eudragit RS100and RL 100	N hexane	Oil in oil emulsion solvent diffusion technique.	Microsponges successfully formed by this non aqueous emulsion method.	77
Dicyclomine	Eudragit RS100	Dichloromethane	Quasi emulsion – solvent diffusion method.	Colon specific tablets based on microsponges could provide effective local action.	78
Febuxostat	Eudragit RS100	Ethanol	Quasi emulsion – solvent diffusion method.	Study represents a new approach for preparation of modified	79

				microsponges with controlled release behaviour over prolong duration of time which may reduce side effects.	
Diclofenac sodium	Ethyl cellulose, carbapol 940	triethanolamine	Multiple emulsion technique	Unique technology for controlled drug release.	80
Luteolin	Eudragit RS100, ethyl cellulose.	Acetone	Quasi emulsion method.	A Luteloin gastro retentive microsponges with high production yield ,high drug content,high drug entrapment efficiency, and prolong in vivo flotability in the albino rat model was successfully developed.	81
Telmisartan	Eudragit E100, Eudragit 100	Methanol	Quasi emulsion – solvent diffusion method.	Telmisartan microsponges was successfully formulated and their tablet formulation proved to provide better release compared to marketed products.	82
Meloxicam	Eudragit (RS,100) and (E100)	Dichloromethane	Quasi emulsion – solvent diffusion method.	This method formation of microsponges could be by rapid diffusion of dichloromethane into aqueous method.	83
Clotrimazole	Eudragit RS 100, Eudragit RL 100, Eudragit S100, Ethyl cellulose	Ethanol	Quasi emulsion – solvent diffusion method.	Formulation has better potential of controlled release of drug through skin than marketed products.	84
Amphotericin B	Eudragit RS100	Dichloromethane	Quasi emulsion – solvent diffusion method.	The ratio of drug:polymer require to produce microsponges with good efficiency was found to be 1:3	85

References:

1. Jyoti and Kumar Sandeep, Innovative and Novel Strategy: Micro sponges for Topical Drug Delivery, Journal of Drug Delivery and Therapeutics, 2018: 28-34.
2. Deepak Sharma et.al., Recent Advancement: Microsponges DDS: A Review Pharmatutor. Universal Journal of pharmaceutical science and research,2015; 1(1):32-38.

3. Arijit gandhi,saugata jana,kalyan kumar sen,tailoring effect of microsponges for target drug delivery,journal of scientific and innovative research 2013;2(6):1073-1082.
4. Saripilli Rajeshwari, Vanapalli Swapna Microsponges as a Neoteric Cornucopia for Drug Delivery System, Int. J. Curr. Pharm. Research Vol 11, Issue 3, 4-12.
5. Parthiban K.G., Manivannan R., Krishnarajan D., Chandra S., Nidhin R. Microsponge Role In Novel Drug Delivery System. Intl. J. Pharm. Res. Devel, 2011; 3(4): 117-125.
6. Aritomi H., Yamasaki Y., Yamada K., Honda H, 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, 1996; 56(1): 49-56.
7. Jyoti, Kumar S, Innovative and novel strategy. Microsponges for Topical Drug Delivery. Journal of Drug Delivery and Therapeutics, 2018; 8(5): 28-34.
8. Anita Patel, Jayvadan Patel (2012), "Design Development and In vitro Evaluation of Sertaconazole Vaginal Tablet", Der Pharmacia Letter, Volume 4, Issue 2, pp. 418−427.
9. Tansel Comoglu, Nurs¸in Go¨nu¨, Tamer Baykara (2003), "Preparation and in vitro evaluation of modified release etteefen microsponges", Il Farmaco, Volume 58, pp. 101−106
10. Shital S. Patil, Vaishali Dandekar, Asawari Kale, S. D. Barhate. Microsponge Drug Delivery System: An Overview. European Journal of Pharmaceutical and Medical Research, 2016; 3(8): 212-221.
11. Mansurelahi SK, Koteswani P and Srinivasa PB. Microsponge As A Novel Drug Delivery System. International Journal of Pharmaceutical Review & Research, 2014; 4: 166-174.
12. Sato T, Kanke M, Schroeder G and Deluca P. Porous Biodegradable Microspheres for Controlled Drug Delivery. Assessment of Processing Conditions & Solvent RTechniques. Pharmaceutical Research, 1988; 5: 21-30.
13. Khopade AJ, Jain S and Jain NK: The microsphere. Easterern Pharmacist, 1996; 39: 49-53.
14. Guyot M and Fawaz F. Microsphere: Preparation & Physical Characteristics. Int J Pharmaceutics, 1998; 175: 61-74.
15. Christensen MS and Natch SJ. Invest. Dermato, 1983; 69: 282.
16. Osmani, R. A., Aloorkar, N. H., Ingale, D. J., Kulkarni, P. K., Hani, U., Bhosale, R. R., & Jayachandra Dev, D. Microsponges Based Novel Drug Delivery System For Augmented Arthritis Therapy. Saudi Pharmaceutical Journal: SPJ, 2015; 23(5): 562–572.
17. Tejashri, G., Amrita, B., & Darshana, J. Cyclodextrin Based Nanosponges for Pharmaceutical Use: A Review. Acta Pharmaceutica (Zagreb, Croatia), 2013; 63(3): 335–358.
18. 18. Chilajwar, S. V., Pednekar, P. P., Jadhav, K. R., Gupta, G. J., & Kadam, V. J. Cyclodextrin-Based Nanosponges: A Propitious Platform For Enhancing Drug Delivery. Expert Opinion on Drug Delivery, 2014; 11(1): 111–120.
19. Trotta, F., Zanetti, M., & Cavalli, R. Cyclodextrin-Based Nanosponges As Drug Carriers. Beilstein Journal of Organic Chemistry, 2012; 8: 2091–2099.
20. 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, 2011; 12(3): 989–1001.
21. Gupta, A., Tiwari, G., Tiwari, R., & Srivastava, R. Factorial Designed 5-FluorouracilLoaded Microsponges And Calcium Pectinate Beads Plugged In Hydroxypropyl Methylcellulose Capsules For Colorectal Cancer. International Journal of Pharmaceutical Investigation, 2015; 5(4): 234–246.
22. Charagonda S. Formulation and Evaluation of Famotidine Floating Microsponges. Int Res J Pharm, 2016; 7(4): 62-67.
23. Jelvehgari, M., Siahi-Shadbad, M. R., Azarmi, S., Martin, G. P., & Nokhodchi, A. The Microsponge Delivery System of Benzoyl Peroxide: Preparation, Characterization and Release Studies. International Journal of Pharmaceutics. 2006; 308(1–2): 124–132.
24. Osmani, R. A., Aloorkar, N. H., Kulkarni, A. S., Kulkarni, P. K., Hani, U., Thirumaleshwar, S., & Bhosale, R. R. Novel Cream Containing Microsponges of AntiAcne Agent: Formulation Development And Evaluation. Current Drug Delivery, 2015; 12(5): 504–516.
25. Bothiraja, C., Gholap, A. D., Shaikh, K. S., & Pawar, A. P. Investigation of Ethyl Cellulose Microsponge Gel for Topical Delivery of Eberconazole Nitrate for Fungal Therapy. Therapeutic Delivery, 2014; 5(7): 781–794.
26. Grimes, P. E. A Microsponge Formulation of Hydroquinone 4% and Retinol 0.15% in The Treatment of Melasma And Postinflammatory Hyperpigmentation. Cutis, 2004; 74(6): 362–368.
27. Gupta, A., Tiwari, G., Tiwari, R., & Srivastava, R. Factorial Designed 5-FluorouracilLoaded Microsponges and Calcium Pectinate Beads Plugged in Hydroxypropyl Methylcellulose Capsules For Colorectal Cancer. International Journal of Pharmaceutical Investigation, 2015; 5(4): 234–246.
28. Yang, Y., Ou, R., Guan, S., Ye, X., Hu, B., Zhang, Y., Li, Q. G. A Novel Drug Delivery Gel of Terbinafine Hydrochloride with High Penetration for External Use. Drug Delivery, 2015; 22(8): 1086–1093.

29. Pawar, A. P., Gholap, A. P., Kuchekar, A. B., Bothiraja, C., & Mali, A. J. Formulation And Evaluation of Optimized Oxybenzone Microsponge Gel For Topical Delivery. Journal of Drug Delivery, 2015; 261068.
30. Deshmukh K, Poddar SS. Tyrosinase Inhibitor-Loaded Microsponge Drug Delivery System: New Approach for Hyperpigmentation Disorders. J of Microencapsulation. 2012; 29(6): 559-568.
31. Osmani, R. A., Aloorkar, N. H., Ingale, D. J., Kulkarni, P. K., Hani, U., Bhosale, R. R., & Jayachandra Dev, D. Microsponges Based Novel Drug Delivery System For Augmented Arthritis Therapy. Saudi Pharmaceutical Journal: SPJ, 2015; 23(5): 562–572.
32. Hadi, M. A., Rao, N. G., & Rao, A. S. Formulation and Evaluation of Mini-TabletsFilled-Pulsincap Delivery of Lornoxicam in the Chronotherapeutic Treatment of Rheumatoid Arthritis. Pakistan Journal of Pharmaceutical Sciences, 2015; 28(1): 185–193.
33. Shuhaib B, Suja C. Studies on Formulation and Characterization of Topical Emulgel Containing Microsponges of Mefenamic Acid. Eur J Pharma Medi Res, 2019; 6(1): 314-326.
34. Amrutiya, N., Bajaj, A., & Madan, M. Development of Microsponges for Topical Delivery of Mupirocin. AAPS Pharm Sci Tech, 2009; 10(2): 402–409.
35. Martin A, Swarbrick J, Cammarata A (1991), "In: Physical PharmacyPhysical Chemical Principles in Pharmaceutical Sciences, 3rd ed.", Volume 527.
36. Emanuele AD, Dinarvand R (1995), "Preparation, characterization and drug release from thermoresponsive microspheres", Int. Journal of Pharmaceutics, pp. 237−242.
37. Washburn EW (1921), "Note on a method of determining the distribution of pore sizes in a porous material", Proc Natl Acad Sci, Volume 7, Issue 4, pp. 115−116.
38. Orr Jr (1969), "Application of mercury penetration to material analysis", Powder Technol., Volume 3, pp. 117– 123.
39. Anderson DL, Cheng CH, Nacht S (1994), "Flow characteristics of loosely compacted macroporous microsponge polymeric systems", Powder technology, Volume 78, pp. 15−18.
40. Ford JL, Timmins P (1989), "Pharmaceutical Thermal AnalysisTechniques and Applications", Ellis Horwood Ltd., Chichester.
41. Barkai A, Pathak V, Benita S (1990), "Polyacrylate (Eudragit retard) microspheres for oral controlled release of nifedipine. I.Formulation design and process optimization", Drug Dev. Ind. Pharm., Volume 16, pp. 2057−2075.
42. Chowdary KPR, Rao YS (2004), "Mucoadhesive Microspheres for Controlled Drug Delivery", Biol. Pharm. Bull, 27(11), pp. 1717−1724.
43. Shobha Rani, R Hiremath, "Textbook of industrial pharmacy", Universities Press Private Limited, pp. 44−45.
44. Trotta F, Cavalli R, Tumiatti W (2006), "Cyclodextrin-based nanosponges for drug delivery", J Incl Phenom Macrocyclic Chem., Volume 56, pp. 209−213.
45. Hu SH, Liu TY, Liu DM (2007), "Nano-ferrosponges for controlled drug release", J Control Release, Volume 121, Issue 3, pp. 181−189.
46. Lee JB, Hong J, Bonner DK (2012), "Self-assembled RNA interference microsponges for efficient siRNA delivery", Nat Mater, Volume 11, Issue 4, pp. 316−322.
47. Srivastava R, Pathak K (2012), "Microsponges: a futuristic approach for oral drug delivery", Expert Opin. Drug Deliv., 9(7), pp. 863−878.
48. Gu L, (2017) A Combination RNAi-Chemotherapy Layer by Layer Nano particle for Systemic Targeting of KRAS/P53 with Cisplatin to Treat Non–Small Cell Lung Cancer. Clinical Cancer Research 23(23): 7312-7323.
49. Han S, H Kim, JB Lee (2017) Library siRNA-generating RNA nano sponges for gene silencing by complementary rolling circle transcription. Scientific Reports 7(1): 10005.
50. Lee JB, Jinkee Hong, Daniel K, Bonner, Zhiyong (2012) Self-assembled RNA interference micro sponges for efficient siRNA delivery. Nature materials 11(4): 316-322.
51. Roh YH, Deng JZ, Dreaden EC, Park JH, Yun DS, et al. (2016) A multi-RNAi microsponge platform for simultaneous controlled delivery of multiple small interfering RNAs. Angewandte Chemie International Edition 55(10): 3347-3351.
52. Roh YH, Lee JB, Shopsowitz KE, Dreaden EC, Morton SW, et al. (2014) Layer-by-layer assembled antisense DNA microsponge particles for efficient delivery of cancer therapeutics. ACS nano 8(10): 9767-9780.
53. Shopsowitz KE, Young H, Zhou J D, Stephen, Paula T (2014) Composite RNAi-Microsponges Form through Self Assembly of the Organic and Inorganic Products of Transcription. Small 10(8): 1623-1633.
54. Tatiparti K, Sau S, Kashaw SK, Iyer AK (2017) SiRNA delivery strategies: a comprehensive review of recent developments. Nano materials 7(4): 77.
55. Swamykannu Dineshmohan,Vandagiri Rama mohan Gupta.Formulation and Characterization of Fluconazole as Topical Gel by Porous Microparticle Based Drug Delivery System.AJPR,2018,8(5) 2249-3387.

56. Ravinder.Naik Eslavath,Vasudha Bakshi. Formulation Development and In Vitro Release Studies of Tenofovir- containing Microsponges.INNOSC,2019, 2(16)-24.
57. Mahmoud H Othman,Gamal M Zayad.Preparation and Evaluation of 5- Flurouracil Loaded Microsponges for Treatment of Colon Cancer.JCST,2017,8(1),307-313.
58. Madhuri Desavathu ,Raghuveer Pathuri Design ,Development and Characterization of Valsartan Microsponges by Quasi Emulsion Technique and the impact of stirring rate on Microsponge Formulation.JAPS,2017,7(01)193-198.
59. Rajashri B Ambikar,Ashok.V.Bhosale.Development and Characterization of Diclofenac Sodium Loaded Eudragit RS100 Polymeric Microsponges Incorporated into In Situ Gel for Opthalmic Drug Delivery System.IJPPS.2021;13(9).
60. Anju.V.S,M.A.Kuriachan.Formulation& Evaluation of Terbinafine Hydrochloride Loaded Microsponges Based Gel For Topical Sustained Delivery.IJPPR.2017;vol:10,Isssue 2.
61. Manar.M.Obieadallah,A.M.Abdel.Mageed. Ocular administration of Acetazolamide Microsponges In situ Gel Formulations.SPJ,2018,698.
62. V.Dinesh .Kumar,Sumit.Kr.Jaiswal.The Microsponge delivery system of Acyclovir:Preparation Characterization In- Vitro Evaluation.SRL,2011,Vol 3,Issue 5,115-124.
63. Swamikannu Dinesh Mohan,Vandagiri Rama Mohan Gupta . Microsponge Based drug delivery system of voriconazole for fungal infection: Formulation development & In vitro Evaluation.JDTT.2019,vol 9,issue 3,369-378.
64. Ashwini.S.Bansode,Vaishnavi .B.Kute.Formulation ,Development & Evaluation of Microsponge loaded topical Gel of Nystatin.JDDT,2019,vol 9,issue 2-s,451-461.
65. Chellampillai.Bothraja,Amol.D.Gholap.Investigation of ethyl cellulose microsponge gel for topical delivery of eberconazole nitrate for fungal therapy.FSG.2014 vol5,issue 7,781-794.
66. Pankaj Sharma,Rakesh Kumar Raut.Formulation & Evaluation of Gel loaded microsponges of Roxithromycin for topical drug delivery.IOSR.2019;vol9,issue5,14-22.
67. V.Pavani,M.Vinod.Design Formulation & In- vitro Evaluation of microsponge based gel for topical delivery of ketoconazole.IJPSR.2017;vol 8,issue10,4222-4229.
68. Neha Gulati,Neha Tomar.Miconazole Microsponge Based Topical delivery system for diaper dermatitis.Ars. Pharma.2016;57(2),77-87.
69. Pooja .A.Patil,Vijay.R.Chakote.New era in the drug delivery system :Formulation & Evaluation of Microsponges of Itraconazole.IJSR.2018;vol9,issue1
70. Vishal Yadav,Prakash Jadhav.Formulation and Evaluation of Microsponge Gel for Topical Delivery of Antifungal Drugs.IJAP,2017;issue 4,30-37.
71. Rajurkar VG,Tambe AB . Topical Anti-inflammatory Gels of Naproxen Entrapped in Eudragit Based Microsponge Delivery System. JACE 2015;5(2).
72. Yetenge He ,Khadija Majid.F).Formulation & characterization of Iornoxicam -loaded cellulosic microsponge gel for possible applications in Arthritis.SPJ,2020,994-1003.
73. Shireesha charagonda,Ramya Deepthi puligilla.Formulation & Evaluation of Famotidine floating Microsponges.IRJP,2016; 7(4),2230-8407.
74. Vishal Yadav,Prakash Yadav.Formulation and Evaluation of Microsponges Gel For Topical Delivery of Antifungal Drug.IJAP,2017,9(4) 30-37.
75. Roaa.A.Nief,Ahmed.A.Hussein. Preparation &Evaluation of Meloxicam Microsponges as Transdermal Delivery System.IJPS,2014.23(2).
76. S.S.Patel,M.R.Patel.Formulation and Evaluation of Microsponge based Nicorandil Sustained Released Tablet.JSR .2017;9(3)285-296.
77. Faten.Q.Ibraheem,Fatima.J.AL.Gawhari.Preparation & In- vitro Evaluation of Baclofen as an oral microsponge Tablets.IJPS.2019,28(1),75-90.
78. Vikas.Jain,Ranjit Singh. Dicyclomine -loaded Eudragit based Microsponge with Potential for Colonic Delivery : Preparation and Characterization.IJPR,2010, 9(1),67-72.
79. Pawar.P.G,Darekar.A.B. Formulation Development and Evaluation Of Febuxostat Loaded Microsponges.IJRAT.2019 7(5),2321-9637.
80. Hamid Hussain,Archana Dhyani. Formulation & Evaluation of gel loaded Microsponges of Diclofenac sodium for topical delivery.TPI,2013, 3(10),58-63.
81. Mahammad Jafar,Mohammad sajjad Ahmad Khan,Mohammmad Salahuddin.Preparation and In vitro-In Vivo Evaluation of Luteloin Loaded Gastroretentive Microsponge for Eradication for Helicobacter Pylori Infections.MDPI,2021vol 13,2094.

82. Muder AL Haydar.Formulation of telmisartan microsponges tablets and In Vitro Evaluation of dissolution profile.KJPS 2015 vol 9.
83. Roaa A.Nief,Ahmed A.Hussein.Preparation & Evaluation of Meloxicam Microsponges as Transdermal Delivery System.IJPS,2014. 23(2).
84. Markand Mehta,Ashish Panchal.Formulation & In Vitro Evaluation of controlled release microsponge gel for topical delivery of clotrimazole.IJAP,2012,2(2),93-101.
85. S.G .Killedar,D.A.Bhagwat. Development and Characterization of Microsponges of Amphotericin - B for Topical Drug Delivery .RJPBCS.2019,10(1),1288.