



A Review on the Drug Delivery from Microsponges

¹Ibrahim Ali Usmani, ²Mrs. Anuradha K. Salunkhe,

¹M.Pharmacy, ²M.Pharmacy (Pharmaceutics),

¹Departments of Pharmaceutics,

¹Satara College of Pharmacy Satara, Satara, India

Abstract: Microsponges are polymeric delivery systems they made up of porous microspheres. They are small, round, sponge-like globular particles with a large porous surface. Microscopic scanning of fine needle-like particles showed that the internal structure was a "marble bag". Microsponges have high entrapment up to 50 to 60%, Stable in the pH range from 1 to 11, Stable up to 130°C temperature. Microsponges show many advantages over other technologies and delivery system like microsponges give better control of drug release than microcapsules and compare to liposomes microsponges have better chemical stability, higher load and easier formulation. Microsponges can be prepared by Liquid-Liquid Suspension Polymerization or Quasi-emulsion solvent diffusion method. Particle size determination, Scanning Electron Microscope study, loading efficiency, compatibility studies are used to characterize the microsponges. Drug can be released by sustained or timed release mechanism or by release on command such as temperature release, pH release. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to reduce side effects, enhance stability and modify drug release.

Index Terms: Controlled release, Drug delivery, Microsponge, Topical formulation.

INTRODUCTION:

In the recent years, the development of new microsphere-based drug delivery systems has been added to switch and control drug release behavior. By inserting it into the carrier system, you can change the therapeutic index and the duration of drug action.

In 1987, Won developed the micro-sponge technology and the original patent was obtained by Advanced Polymer Systems. Microsponges are polymeric delivery systems they made up of porous microspheres. They are small, round, sponge-like globular particles with a large porous surface. It also increases persistence, reduces side effects, and advantageously alters drug release. Microsphere technology has many beneficial properties that make it a flexible drug delivery tool. Microscopic scanning of fine needle-like particles showed that the internal structure was a "marble bag". Interstitial pores can trap a variety of active ingredients such as emollients, fragrances, essential oils and sunscreens, anti-infectious and anti-inflammatory agents. These entrained microsponges can be incorporated or formulated into products such as creams, lotions, powders, soaps, capsules, and tablets.

Microsponges can vary in size, but a typical 25 μm sphere can have up to 250,000 pores and an internal pore structure of about 10 feet, resulting in a total pore capacity of about 1 ml/g. The surface can be varied from 20 to 500 m²/g and 2 pore volume range from 0.1 to 0.3cm³/g. This results in a large reservoir within each 3 microsponge, which can be loaded with up to its own weight of active agent. A new protection problem is the possibility of bacterial contamination of substances entrapped within the microsponge. Since the diameter of the pore is smaller, microorganisms ranging in size from 0.007 to 0.2 microns cannot penetrate into the Warren microsponge structure.

Controlled release of drugs onto the epidermis with assurance that the drug remains primarily localized and does not enter the systemic circulation in significant amounts is a challenging area of research.

PROSPECTIVE FEATURES OF MICROSPONGES DRUG DELIVERY SYSTEM:

- 1) The microsponge formulation is stable in the pH range from 1 to 11.
- 2) The formulation of the micro-sponge is stable up to 130°C.
- 3) The micro-sponge formulation is compatible with most vehicles and materials.
- 4) The microsponge formulation is self-sterilizing because the average pore size is about 0.25 μm and bacteria cannot pass through the pores.
- 5) The microsponge formulation has high entrapment capacity up to 50 to 60%.

- 6) The microsponge formulation flows freely and can be cheap.
- 7) The fine particles of the micro-sponge formulation itself are too large to be absorbed into the skin, which can avoid the side effects of the microsponge adjuvants.
- 8) Microsponge formulations can be inexpensive even for cosmetic applications in mass markets where ingredient prices are important.

ADVANTAGES:

- 1) Advanced oil control, absorption up to 6 times to it's mass without aeration.
- 2) Enhances the elegance of the product.
- 3) Microsponge formulation allows the incorporation of unmixed products.
- 4) Microsponge formulation provides continuous action up to 12 hours.
- 5) Reduces irritation and improving tolerance improves patient compliance.
- 6) Microsponge formulation can increase the bioavailability of the drugs.
- 7) Enhanced product aesthetics
- 8) Better thermal, physical and chemical stability.
- 9) Excellent formulation flexibility.
- 10) Microsponge formulation allows the alliance of immiscible products.
- 11) Liquids can be transformed in to powders enhancing material processing.
- 12) It can also enhance the effectiveness of the treatment.

ADVANTAGES OF MICROSPONGES OVER OTHER TECHNOLOGIES AND DELIVERY SYSTEM:

- 1) Micro-sponges give better control of drug release than microcapsules.
- 2) Microcapsule cannot usually control the discharge time of the API. Once the wall is ruptured, the API controlled in the microcapsules is released.
- 3) Compared to liposomes, microsponges have better chemical stability, higher load and easier formulation.
- 4) Compared to ointments, microsponges absorb skin secretions, reduce oiliness and pop out of the skin. Ointments are often aesthetically unappealing, greasy and sticky, resulting in poor patient compliance.

THE CHARACTERISTICS OF MATERIALS TO BE ENTRAPPED IN MICROSPONGES:

- 1) It must be completely soluble as a monomer or mixed with a solvent that is immiscible with water.
- 2) It must be immiscible with water or slightly soluble.
- 3) It must be inert with respect to the monomer so that it can react with other excipients in the composition.
- 4) It must be stable in contact with the polymerization catalyst and the polymerization medium.

PREPARATION OF MICROSPONGES:

The drug formulation loaded into the microsponge delivery system is completed in two ways: a one-step process or a two-step process, as discussed in the section on polymerization of a liquid-liquid suspension, and a quasi-emulsion diffusion method in a solvent based on the physicochemical properties of the loaded drug.

1) Liquid-liquid suspension polymerization:

The suspension polymerization process is used in preparation for creating porous microspheres in liquid-liquid systems. The monomer is first dissolved in the center of the active ingredient in the presence of a suitable monomeric solvent and then dispersed in an aqueous phase containing additives (surfactants, suspending agents, etc.) as shown in **Figure 1**.

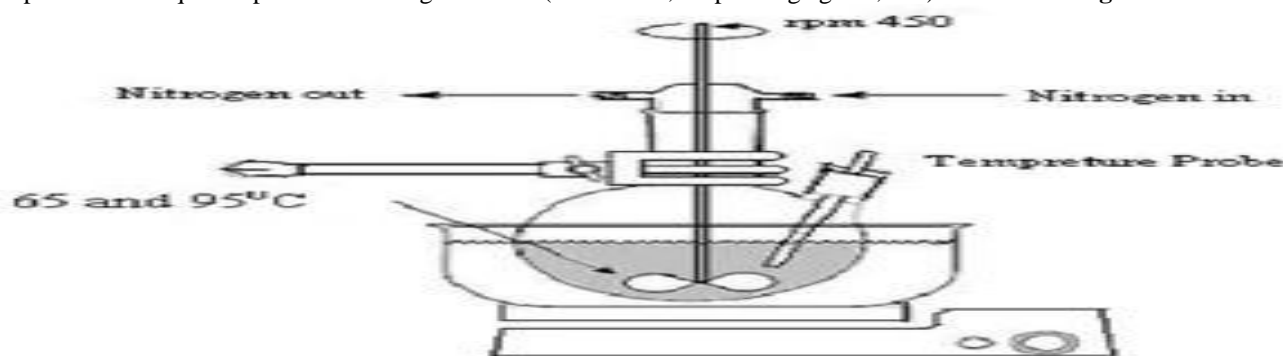


Figure 1: The microsponges developed by liquid-liquid suspension polymerization

2) Quasi-emulsion solvent diffusion:

Each micro-sponges were prepared by quasi-emulsion solvent diffusion process which consists of an external phase and inner phase as shown in **Figure 2**.

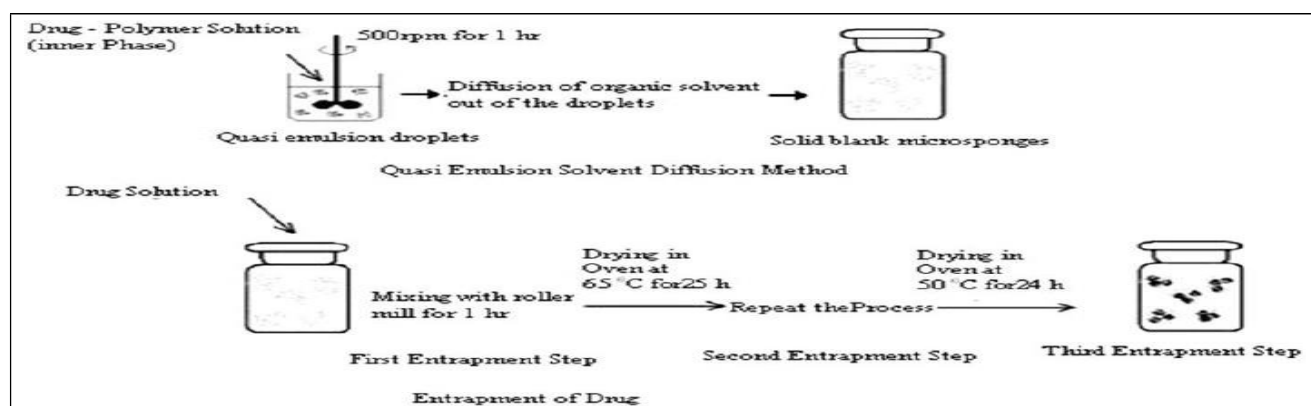


Figure 2: Quasi-emulsion solvent diffusion process

Steps involved are as follows:

- 1) Eudragit RS 100 was dissolved in a suitable solvent to form an internal phase such as Dichloromethane known as inner phase.
- 2) Then, drug was added to the inner phase and dissolved under ultrasonication at 35°C.
- 3) 0.5 ml of Dibutyl phthalate was added as a plasticizer.
- 4) Polyvinyl alcohol was added into the water in another container known as external phase.
- 5) Inner phase was added into the external phase with continuous stirring.
- 6) The mixture was stirred at 800-900 rpm and filtered to separate the microsponges, then dried for 12 hours in an air-heated oven at 40 °C.

HYPOTHETICAL MECHANISM OF ACTION:

- a) As the microsp sponge particles have an open structure (i.e., they do not have a continuous membrane surrounding them), the active ingredient is free to move in and out from the microsponges and into the vehicle until the vehicle reaches equilibrium, at which point it becomes saturated.
- b) Prepared microsponges are applied to the skin.
- c) The active ingredient that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore, disturbing the equilibrium.
- d) This will start a flow of the active ingredient from the microsp sponge particle into the vehicle, and from it to the skin, until the vehicle is either dried or absorbed.
- e) Even after that the microsp sponge particles retained on the surface of the stratum corneum will continue to gradually release the active ingredient to the skin, providing prolonged release over time.

The importance of developing vehicles for use with microsp sponge entrapments is highlighted by this proposed mechanism of action. If the active ingredient is too soluble in the desired vehicle during compounding of the finished products, the products will not provide the desired benefits of gradual release. Instead they will behave as if the active ingredient was added to the vehicle in a free form. As a result, whenever developing microsp sponge entrapments, it's essential to choose a vehicle with low solubilizing capacity for the active drug. This theory is completely contradictory to the traditional formulation concepts used in topical items. In these traditional systems, it is usually advised to choose a vehicle with high solubilizing capacity for the active drug. When using microsp sponge entrapments, some solubility of the active ingredient in the vehicle is acceptable, because the vehicle can provide the initial loading dose of the active ingredient until release from the microsp sponge is activated by the change in equilibrium from the polymer into the carrier. Another way to avoid undesirable premature leaching of the active ingredient from the microsp sponge polymer is to formulate the product with some free and some entrapped active ingredient, so the vehicle is pre-saturated. In this case there will not be any leaching of the active ingredient from the polymer during compounding. The rate of active ingredient release will ultimately depend not only on the partition coefficient of the active ingredient between the polymer and the vehicle (or the skin), but also on a few of the characteristics the beads (examples of these include surface area and mean pore diameter). Diffusion or other stimuli such as moisture, pH, friction or temperature may also be used to monitor the release.

EVALUATION OF MICROSPONGES:

1) Particle size determination:

Particle size analysis of loaded and unloaded microsponges can be performed using laser light diffraction or other suitable methods. The value (d50) can be expressed as the average of the measured value over all formulations. To investigate the effect of particle size on drug release, the percentage of cumulative drug release from microsponges with different particle sizes is plotted against time. Particles larger than 30 µm can have a gritty appearance, so particles between 10 and 25 µm are used in final topical formulation.

2) Scanning electron microscopy:

The processed microsponges can be plated with palladium-gold under argon atmosphere at normal room temperature and then the surface morphology of the microsponges can be confirmed using a Scanning Electron Microscope (SEM). SEM of damaged microsphere particles can also be used to describe the ultra-structure.

3) Determination of loading efficiency:

The loading efficiency (%) of microsponges can be calculated according to the below equation:

$$\text{Loading efficiency} = \frac{\text{Actual drug content in microsphere}}{\text{Theoretical drug content}} * 100$$

4) Determination of production yield:

The production yield of the micro particles can be determined by calculating accurately the initial weight of the raw materials and the last weight of the microsphere obtained.

$$\text{Production yield} = \frac{\text{Practical mass of microsphere}}{\text{Theoretical mass (drug+polymer)}} * 100$$

5) Determination of true density:

The true density of microsponges can be measured using an ultra-pycnometer under helium gas and is calculated from a mean of repeated determinations.

6) Compatibility studies:

Compatibility of drug with reaction adjuncts can be studied by thin layer Fourier Transform Infrared spectroscopy (FT-IR) and chromatography (TLC). X-ray diffraction (XRD) and Differential Scanning Calorimetry (DSC) methods are used to investigate the effect of polymerization on crystallinity of the drug.

7) Polymer/monomer composition:

Factors such as microsphere size, drug loading, and polymer composition govern the drug release from microspheres. Polymer composition of the microsponges drug delivery system can affect partition coefficient of the entrapped drug between the vehicle and the microsphere system and hence have direct influence on the release rate of entrapped drug. Plotting cumulative percent drug release against time can be used to investigate drug release from microsphere structures with various polymer compositions.

DRUG RELEASE MECHANISMS:

These programmable parameters can be effectively controlled to create microsphere delivery systems that release functional substances over time in response to one or more external stimuli. The release mechanisms of this system are mainly as follows:

1) Sustained or Timed Release: In the development of sustained-release microsponges, various physical and chemical parameters of the entrained active ingredients, such as volatility, viscosity and solubility will be investigated, while for polymer microsponges pore diameter, volume, and resiliency of the polymer microsponges are evaluated to give required sustained release effects.

2) Release on Command: Microsponges can be designed to release the given amounts of active ingredients over time in response to external stimuli.

a) Pressure Release: Microsphere system releases active ingredient when it is pressed or squeezed, this replenishes the quantity of entrapped active ingredient onto the skin. The amount of material released can also depend on the release of the sponge and the stability of the microsponges.

b) Temperature Release: The release of the active ingredients from the microsponges can be activated depending on the temperature. Active ingredients that linger a little at room temperature can be so thick that they cannot suddenly transfer from the microsphere to the skin. As the temperature of the skin rises, the flow rate is increased and thus release is also enhanced.

c) **pH Release:** An easier release of the pH-based active agent can be achieved by changing the coating of the microsp sponge.

d) **Solubility:** A microsponges filled with water-soluble substances such as antiseptics and antiperspirants releases substances in the presence of water. The discharge can also be activated by diffusion, taking into account the distribution coefficient of the material between the microsp sponge and the external system.

CONCLUSION:

Microsponges consider a new and creative ways to deliver active ingredients with full capabilities of these unique materials and provide enhanced safety, improved stability, reduced side effects from active ingredients, enhanced multifunctionality and improved ingredient compatibility. Microsponges have many advantages over existing conventional topical dosage forms for the treatment of tropical diseases; it is a unique technology for the controlled release of topical agents also use for oral as well as biopharmaceutical drug delivery. This shows advantages over other products by non-mutagenic, non-toxic, non-irritant. So, microsp sponge drug delivery system has great potential and is a very developing area which is needed to be explored in the future with most research study.

Table I. Applications along with advantages of MDDS

Sr. No	Application	Advantages
1.	Anti-acne: e.g. Benzoyl peroxide	Maintained efficiency with decreased skin irritation and sensitization.
2.	Anti-fungals: Itraconazole	Sustained release of active ingredient.
3.	Antipruritics: Sertaconazole	Extended and improved activity.
4.	Skin depigment agent: e.g. Hydroquinone	Enhanced stabilization alongside oxidation with improved efficacy.

Table II. List of Marketed Products Using Microsponge Drug Delivery System

Product name	Content & Advantages	Manufacturer
Retin-A-Micro™	Topical treatment of acne vulgaris with 0.1 to 0.04 percent tretinoin entrapped in MDS. To allow for the inclusion of the active ingredient, tretinoin, in an aqueous gel, this formulation utilized proprietary methyl methacrylate/glycol dimethacrylate cross-polymer porous microspheres.	Ortho-McNeil Pharmaceutical, Inc.
Carac cream, 0.5%	Carac cream contains 0.5% fluorouracil, with 0.35% being incorporated into a patented porous microsphere (Microsponge) composed of methyl methacrylate / glycol dimethacrylate cross-polymer and dimethicone. Carac is a once-a-day topical prescription product for the treatment of actinic keratoses, a common pre-cancerous skin condition caused by over-exposure to the sun. The product has a number of advantages over the existing topical therapies, including less irritation with shorter duration of therapy and reduced dosage frequency.	Dermik Laboratories, Inc. Berwyn, PA 19312 USA
Line eliminator dual retinol facial treatment	Lightweight cream with a retinol (pure Vitamin A) in MDS, delivers both immediate and time-released wrinkle-fighting action.	Avon
Retinol cream	To maintain the efficacy of vitamin A, the retinol molecule is held in the microsponge system. This allows maximise the retinol dosage while minimising irritation. Retinol is a vitamin A derivative used topically to keep skin, hair, and mucous membranes healthy.	Biomedic
Retinol 15 night cream	A nighttime treatment cream with Microsponge technology using a stabilized formula of pure retinol and vitamin A. Continued use of Retinol 15 will result in the visible diminishment of fine lines and wrinkles, a noticeable improvement in skin discolorations due to aging, and enhanced skin smoothness.	Sothys
EpiQuin- micro	The Microsponges system uses microscopic reservoirs that entrap hydroquinone and retinol. These ingredients are steadily released into the skin by the microsponges throughout the day. This allows the skin to be exposed to hydroquinone and retinol over time, which significantly reduce skin irritation.	Skin Medica Inc
Sports cream RS and XS	Topical analgesic, anti-inflammatory, and anti-irritant actives in a Microsponge Delivery System (MDS) for musculoskeletal disorders.	Embil Pharmaceutical Co. Ltd

Table III. Updated Research about Microsponges

Sr. No.	Research Paper Information	Research Work
(1)	Formulation and Evaluation of Microsponge Drug Delivery System Using Indomethacin [Mahajan.A.G.et.al, 2011]	Microsponges loaded with Indomethacin was prepared by Quasi emulsion solvent diffusion method by changing drug polymer ratio (3:1, 4:1, 5:1) and process was optimized and which consists of Eudragit RS 100, pH independent release polymer and PVA, stabilizer or emulsifier. In-vitro dissolution study indicated that the release of Indomethacin varied according to the concentration of matrix forming polymer.
(2)	Preparation and Evaluation of Microsponge Loaded Controlled Release Topical Gel of Acyclovir Sodium [Chandramouli.Y.et.al, 2012]	The prepared microsponges incorporated into the gel and evaluation studies are carried out such as viscosity, pH, drug content, spreadability, in-vitro release. The formed Microsponges formulation of gel, displayed viscosity- 206.72 Ps, spreadability- 11.75g cm/s and drug content- 92.37%. Microsponges of Acyclovir sodium gel displayed a satisfactory drug release profile.
(3)	A novel strategy for ophthalmic drug delivery system containing ketotifen. [Kumar.J.R.et.al, 2013]	Microsponge containing ketotifen drug with three different proportions of ethyl cellulose and drug were obtained successfully using Quasi-emulsion solvent diffusion method. These formulations were studied for particle size and physical characterization. These microsponges enriched gel formulation were prepared by using 2 and 3 % w/w of SCMC and studied for viscosity, pH, gel strength, spreadability, bioadhesive force, drug content, in vitro release, HPLC and SEM analysis. The optimized formulations were able to release the drug up to 8 hours.
(4)	Assessing the viability of microsponges as gastro retentive drug delivery system of curcumin: optimization and pharmacokinetics [Arya.P.et.al, 2014]	Floating microsponges loaded with curcumin were prepared by quasi emulsion solvent diffusion method. The effect of different levels of ethyl cellulose and polyvinyl alcohol concentration, selected as independent variables was determined on the % entrapment efficiency, % buoyancy and % cumulative drug release. The optimized formulation (MS5) demonstrated favourable % entrapment efficiency (90.7 ± 1.7), % buoyancy (82.0 ± 2.0) and % cumulative drug release (85.2 ± 1.07) with maximum desirability factor of 0.816. SEM revealed spherical and porous microsponges. This study presents a new approach based on floating ability of microsponges for treatment of gastric cancer.
(5)	Formulation and Evaluation of Optimized Oxybenzone Microsponge Gel for Topical Delivery [Pawar.A.P.et.al, 2015]	Prepared Oxybenzone loaded microsponge gel for enhanced sun safety factor along reduce toxicity. Microsponges of Oxybenzone prepared by Quasi-emulsion solvent diffusion method. The 3^2 factorial designs were used to optimize the property of ethyl cellulose and dichloromethane. The optimized microsponges were incorporated into the hydro-gel and evaluated. It displayed the improved sun defense factor correlated with the marketed formulation by lower toxicity and irritation.
(6)	Microsponge Based Drug Delivery System for Augmented Gastroparesis Therapy: Formulation Development and Evaluation [Osmani.R.M.et.al, 2015]	Prepared a microsponge based novel dosage form for sustained delivery of Domperidone by taking Eudragit RS-100 with different drug to polymer ratios to produce microsponges and it was also developed via a Quasi-emulsion solvent diffusion process. DSC and FT-IR results showed there have been no chemical interactions between drugs and polymers. Sphere-shaped in form with porous surface microsponges were revealed by SEM micrographs and had 104 ± 0.22 micro meter mean particle size. An in vitro release rate study of CUR microsponges filled into capsule shells for drug release was carried out.
(7)	Microsponges Based Novel Drug Delivery System for Augmented Arthritis Therapy [Osmani.R.M.et.al, 2015]	Microsponges containing diethylamine diclofenac gel were formulated and evaluated to provide sustained release for arthritis therapy. Quasi-emulsion solvent diffusion method was used to prepare Microsponges containing diethylamine diclofenac with various drug-polymer ratios, characterized by SEM, DSC, FT-IR, XRPD and particle size analysis and evaluated for morphology, drug loading, and in-vitro drug release and also ex-vivo diffusion. The microsponges were then incorporated in gel; which showed a sticky modulus along the lateral pseudoplastic behavior.
(8)	Formation and Evaluation of Famotidine Floating Microsponges	Floating microsponges containing famotidine were designed to increase site-specific absorption of drug for peptic ulcer therapy. Microsponges prepared by Modified quasi-emulsion solvent diffusion

	[Puligilla.R.D.et.al, 2016]	process. Buoyancy center and multiple cumulative drug releases. Half of the retention efficiency was 88.3%, center buoyancy 76.4%, and the cumulative multiple drug release was 86.9% for the formulation. This study revealed a substitution approach that supports the floating capacity of the microsponges for ulcer management.
(9)	Design, development and evaluation of celecoxib-loaded micro sponge-based topical gel formulation [Kadam.V.et.al, 2016]	Microsponges loaded with celecoxib were prepared by quasi emulsion solvent diffusion method. Microsponges of optimized batch were spherical, fine and free flowing. The optimized formulation showed % practical yield of 72.84 ± 1.34 , % entrapment efficiency of 82.4 ± 1.48 and mean particle size of $26.4 \mu\text{m}$. The optimized batch incorporated in gel showed pH of 6.1, 12.35 grams-cm/sec of spreadability, 99.06 % of drug content and 68.1 % drug release. Skin permeation studies concluded that the drug was released in a controlled manner for a period of 12 hours.
(10)	Assessing the bioadhesivity of Acconon MC 8-2 EP/NF for gastroretention of floating microsponges of loratadine and achieving controlled drug delivery [Singh.S.et.al, 2016]	Gastroretentive floating loratadine microsponges were formulated by using quasi emulsion solvent diffusion method. The amount of ethyl cellulose (EC) and polyvinyl alcohol (PVA) were selected as independent variables while particle size, entrapment efficiency and %CDR were designated as dependent variables. The formulation (F1) with least particle size of $54 \pm 2.37\mu\text{m}$, entrapment efficiency of 65.98 ± 2.21 % and CDR of $88.15 \pm 1.59\%$ at 8 h that followed zero order release kinetics was selected as optimized formulation. F1 was re-fabricated as bioadhesive microsponges (BF1) using Acconon MC 8-2 and assessed. The particle size of BF1 increased to $84 \pm 2.29 \mu\text{m}$ whereas the entrapment efficiency lowered to $55.19 \pm 1.36\%$ in comparison to F1.
(11)	Formulation and evaluation of micro sponge gel for Topical Delivery of Antifungal Drug [Yadav.V.et.al, 2017]	By use of polymer Eudragit S-100 and Eudragit L-100 microsponges were prepared by quasi-emulsion solvent diffusion process. All the prepared microsponges were run through production yield, encapsulation efficiency, particle size analysis, and in-vitro drug release studies. The prepared microsponges were incorporated into gel formulation for topical delivery. The study of pH value, spreadability, active ingredient content, viscosity and in-vitro diffusion were evaluated of gel formulation and compared with commercially available formulations. The drug and excipient compatibility was confirmed by Fourier Transform Infrared Radiation measurement (FT-IR) and Differential Scanning Calorimetry (DSC).
(12)	Formulation and optimization of bupropion HCL microsponges by 2^3 factorial design [Muralidhar.P.et.al, 2017]	The rationale of the present study was to formulate & optimize the floating Bupropion HCl microsponges by 2^3 factorial design. The concentration of ethyl cellulose, polyvinyl alcohol and Dichloromethane were selected as independent variables. Floating lag time & % drug release were selected as independent variables. Optimized formulation studies showed satisfactory in vitro drug release for more than 16 h with less than 1 min floating lag time. Based on simulation (by DoE software) most economical batch (optimized) decided which were in desired range.
(13)	Development and Evaluation of Terbinafine Hydrochloride Polymeric Microsponges for Topical Drug Delivery [Mahaparale.P.R.et.al, 2018]	Microsponges formulated with ethyl cellulose containing terbinafine hydrochloride were prepared by the Quasi-emulsion solvent diffusion process, and the resulting microsponges morphology by scanning an electron microscope was found to be porous and spherical. Evaluated the drug content, pH value, viscosity and in-vitro drug release from the optimized microsponges formulation were incorporated into the Carbopol gel. It was found that the release of dosage form is sustained by gel microsponges compared to commercially available products and pure drug gel.
(14)	Studies on Formulation and Characterization of Topical Emulgel Containing Microsponges of Mefenamic Acid [Shuhaib.B.et.al, 2018]	Microsponges loaded with Mefenamic acid were prepared by Quasi-emulsion solvent diffusion process. Preformulation study showed no interaction between pure drug and the different polymers used which was revealed by using FTIR. The prepared microsponges were evaluated for their drug content, production yield, mean particle size & entrapment efficiency, Effect of formulation variable was studied. The micro sponge containing 0.5 gm of poly vinyl alcohol, 0.6 gm of ethyl cellulose and 5ml ethanol were compared to the other formulation prepared. The best microsponges incorporated into emulgel. The topical emulgel was evaluated for their organoleptic characters, spreadability, viscosity, drug content and drug release studies.

(15)	Preparation and Characterization of Itraconazole Microsponges Using Eudragit RSPO and Study the Effect of Stirring on the Formation of Microsponges [Singh.D.J.et.al, 2019]	Formulation of microsponges loaded with Itraconazole prepared by using Quasi-emulsion solvent diffusion process. The particle size of the resulting microsponges were revealed in the range of 78.43 to 23.18 μm . Scanning electron microscopic images of microsponges revealed that they were spherical with pores. As the ratio of drug polymers increased, it was found that production yield, drug content and entrapment efficiency increased while the drug to polymer ratio has opposite effects on particle size, the particle size decreases with increasing drug to polymer ratio.
(16)	Formulation and Evaluation of Linalool loaded Microsponges for topical delivery [Pawar.V.et.al, 2020]	Microsponges loaded with linalool were prepared by quasi emulsion solvent diffusion method by using Eudragit RS100 as polymers. The prepared microsponges were characterized by SEM, FTIR, % drug loading and % entrapment efficiency, particle size, zeta potential. Microsponges were further incorporated into cream formulation for topical delivery. Prepared cream formulation was evaluated for physical parameters like pH, spreadability and in-vitro drug diffusion study. Cream loaded with Linalool microsponges showed desirable physical parameters and in-vitro drug diffusion i.e. 92% in 9hrs. Antifungal activity of prepared formulation cream was done against <i>Candida albicans</i> , which showed zone of inhibition i.e. 1.7 cm.

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