



Microsponge as Novel Drug Delivery System: A Review

Pratima Jayasawal¹, N. G. Raghavendra Rao^{*2}, Vikas Jakhmola³

¹ Department of Pharmacy, GRD (PG) IMT, 214, Rajpur, Dehradun-248009, Uttarakhand, India.

² Department of Pharmaceutics, KIET School of Pharmacy, KIET Group of Institutions, Delhi-NCR, Meerut Road, Ghaziabad-201206, UP.

³ Department of Pharmacy, Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Dehradun- 248007, Uttarakhand, India

Address for Correspondence: N.G. Raghavendra Rao, raghavendra.rao@kiet.edu , drngraghu@gmail.com

Received:

21.12.2019

Accepted:

03.01.2021

Published:

10.01.2022

Keywords

Microsponge,
Microspheres,
Control release,
Target release,
Topical, Enhance
stability.

ABSTRACT: During the last few decades, pharmaceutical industry gave more importance to the controlled release of dosage forms like solid formulation, semi solid formulation, and topical preparation due to efficacy and patient compliance. Normal topical preparations have some disadvantages like unpleasant odour, greasiness, and skin irritation reported in study cases. Also many topical preparations fail to reach the systemic circulation in sufficient amounts in few cases. This problem is achieved by the present formulation as microsponge in the areas of research. MDS is a microscopic sphere capable of absorbing skin secretions, therefore reducing the oiliness of the skin. Microsponge having particle size of 10-25 microns in diameter, have wide range of entrapment of various ingredients in a single microsponges system and release them at desired rates. Microsponge is recent novel technique for control release and target specific drug delivery system. Microsponges are polymeric delivery system composed of porous microspheres. They are tiny sponge-like spherical particle with a large porous surface. Drug release in microsponge is done by the external stimuli like (pH, temperature, rubbing). It has several advantageous over the other topical preparations are non allergenic, non toxic, non irritant, non mutagenic. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects and modify drug release. © 2022 iGlobal Research and Publishing Foundation. All rights reserved.

Cite this article as: Jayasawal, P.; Rao, N.G.R.; Jakhmola, V. Microsponge as Novel Drug Delivery System: A Review. Indo Global J. Pharm. Sci., 2022; 12: 21-29. DOI: <http://doi.org/10.35652/IGJPS.2022.12002> .

INTRODUCTION

Microsponges are polymeric delivery systems composed of porous microspheres. They are tiny sponge-like spherical particles with a large porous surface. Moreover, they may enhance stability, reduce side effects and modify drug release favorably. Microsponge technology has many favorable characteristics, which make it a versatile drug delivery vehicle. Microsponge Systems are based on microscopic, polymer-based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as a gel, cream, liquid or powder. Microsponges delivery systems can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved aesthetic properties in an efficient manner.[1,2]

A Microsponge drug delivery system (MDDS) is a patented, highly cross-linked, porous, polymeric microspheres system (10-25 μ) consisting of porous microspheres particles consisting of a myriad of inter connecting voids within non-collapsible structures with a large porous surfactant can entrap wide range of actives (cosmetics, over-the-counter (OTC) skin care, sunscreens and prescription products) and then release them onto the skin over a time and in response to trigger. The size of the microsponges can be varied, usually from 5 – 300 μ m in diameter, depending upon the degree of smoothness or after-feel required for the end formula. A typical 25 μ m sphere can have up to 250000 pores and an internal pore structure equivalent to 10ft in length providing a total pore volume of about 1ml/g.

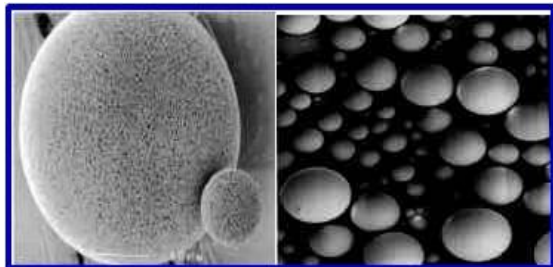


Figure 1: Microsponges Advantages of microsp sponge over other topical dosage forms.

HISTORY OF MICROSPONGE

The microsp sponge technology was developed by Won in 1987 and the original patents were assigned to Advanced Polymer Systems, Inc. This Company developed a large number of variations of the technique and applied those to cosmetic as well as OTC and prescription pharmaceutical products. At the present time, this interesting technology has been licensed to Cardinal Health, Inc., for use in topical products.[3]

ADVANTAGES OF MICROSPONGE DRUG DELIVERY SYSTEM: [4-6]

1. Microsponges are biologically safe and offer unique advantage of programmable release.
2. They offer entrapment of numerous ingredients and are believed to contribute elegance and enhanced formulation flexibility.
3. They have the capacity to absorb or load a high degree of active materials into the particle or onto its surface.
4. Microsponges are stable over a pH range of 1- 11 and upto temperature of 130°C.
5. They are self sterilizing as average pore size is 0.25 μm where bacteria cannot penetrate.
6. Microsponges are capable of absorbing skin secretions so reducing the oiliness of the skin upto 6 times of its weight.
7. With size 10-25 microns in diameter it is capable of entrapping the various ingredients in a single microsphere.
8. The drug releases in microsponges by the external stimuli like pH, temperature, and rubbing.
9. Microsponges have several advantages over topical preparations in being non-allergic, non-toxic, non-irritant and non-mutagenic.
10. Microsponges are thermal, physical and chemically stable.
11. These are compatible with the majority of vehicles and ingredients.
12. These systems have higher payload up to 50 to 60%.
13. Provides continuous action upto 12 hrs ie. extended release & improved product elegance.
14. It can amend bioavailability of same drugs & efficacy in treatment.

BENEFIT OF MICROSPONGE DRUG DELIVERY SYSTEM

1. Enhanced product performance.
2. Extended release.
3. Reduced irritation and hence improved patient Compliance.
4. Improved product elegance.
5. Improved oil control as it can absorb oil up to 6 times its weight without drying.
6. Improved formulation flexibility.
7. Improved thermal, physical, and chemical stability.
8. Flexibility to develop novel product forms.
9. Microsp sponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic [7,8].

CHARACTERISTICS OF ACTIVES MOIETIES THAT IS ENTRAPPED INTO MICROSPONGES

1. Active ingredients that are entrapped in microsp sponge can then be incorporated into many products such as creams, gels, powders, lotions and soaps.
2. Certain considerations are taken into account while, formulating the vehicle in order to achieve desired product characteristics:
3. It should be either fully miscible in monomer as well as capable of being made miscible by addition of small amount of a water immiscible solvent.
4. It should be inert to monomers and should not increase the viscosity of the mixture during formulation.
5. It should be water immiscible or nearly only slightly soluble.
6. It should not collapse spherical structure of the microsponges.
7. It should be stable in contact with polymerization catalyst and also in conditions of polymerization.
8. The solubility of actives in the vehicle must be limited.
9. If not, the vehicles will deplete the microsponges before the application.
10. Not more than 10 to 12% w/w microsponges must be incorporated into the vehicle in order to avoid cosmetic problems.
11. Payload and polymer design of the microsponges for the active must be optimized for required release rate for given period of time [9,10]

METHOD OF PREPARATION OF MICROSPONGE

Microsp sponge drug delivery system can be prepared in two ways, one-step process or by two-step process that is liquid-liquid suspension polymerization and quasi emulsion solvent diffusion techniques based that is based on physicochemical properties of drug to be loaded.

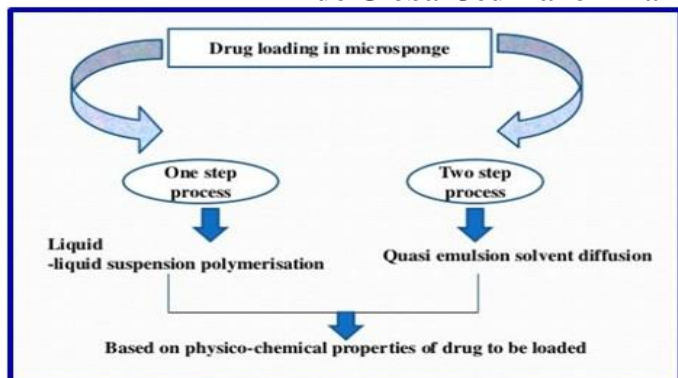


Fig 2: Preparation of Microsponge

1. Liquid-liquid suspension polymerization

The porous microspheres are prepared by suspension polymerization method in liquid-liquid systems. In this method the monomers which are immiscible are first dissolved along with active ingredients in a suitable solvent monomer and are then dispersed in the aqueous phases which consist of additives like surfactant, suspending agents to facilitate formation of suspension. The polymerization is then activated by increasing temperature or irradiation or by addition of catalyst. The polymerization process continues the formation of a reservoir type of system with spherical structure. After the polymerization process the solvent is removed leaving the spherical structured porous microspheres, i.e., microsponges [11-14].

The various steps involved in the preparation of microsponges are summarized as follows:

- Step 1:** Selection of monomer as well as combination of monomers.
- Step 2:** Formation of chain monomers as polymerization starts.
- Step 3:** Formations of ladders as a result of cross-linking between chain monomers.
- Step 4:** Folding of monomer ladder to form spherical particles.
- Step 5:** Agglomeration of microspheres leads to the production of bunches of microspheres.
- Step 6:** Binding of bunches to produce microsponges.

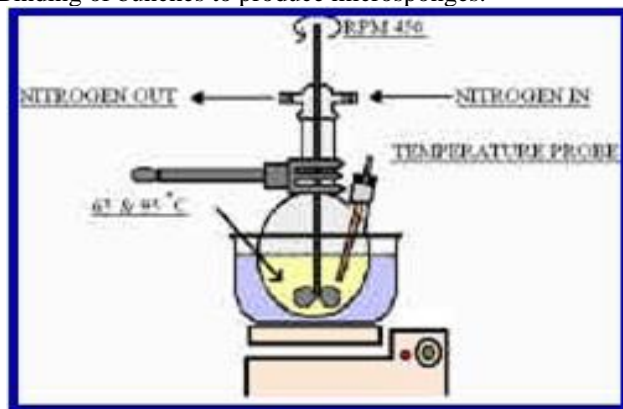


Fig 3: Reaction vessel for microsponge preparation by liquid-liquid suspension Polymerization.

2. Quasi-emulsion solvent diffusion

Porous microspheres (microsponges) were also prepared by a quasi-emulsion solvent diffusion method (two-step process) using an internal phase containing polymer such as eudragit which is dissolved in ethyl alcohol. Then, the drug is slowly added to the polymer solution and dissolved under ultrasonication at 35°C and plasticizer such as triethylcitrate (TEC) was added in order to aid the plasticity. The inner phase is then poured into external phase containing polyvinyl alcohol and distilled water with continuous stirring for 2 hours. Then, the mixture was filtered to separate the microsponges. The product (microsponges) was washed and dried in an air-heated oven at 40°C for 12 hr. [11,12]

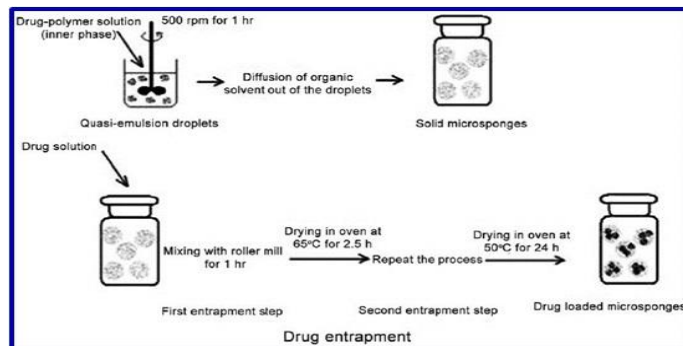


Fig 4: Various steps involved in Quasi-emulsion solvent diffusion method.

Drug release mechanism of microsponge: The active ingredient is added to the vehicle in an entrapped form. As the microsponge particles have an open structure (they do not have a continuous membrane surrounding them), the active is free to move in and out from the particles and into the vehicle until equilibrium is reached, when the vehicle becomes saturated. Once the finished product is applied to the skin, the active that is already in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated, therefore, disturbing the equilibrium. This will start a flow of the active from the microsponge particle into the vehicle, and from it to the skin, until the vehicle is either dried or absorbed. Even after that the microsponge particles retained on the surface of the stratum corneum will continue to gradually release the active to the skin, providing prolonged release over time. This proposed mechanism of action highlights the importance of formulating vehicles for use with microsponge entrapments. If the active 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 was added to the vehicle in a free form. Therefore, while formulating microsponge entrapments, it is important to design a vehicle that has minimal solubilizing power for the actives. This principle is contrary to the conventional formulation principles usually applied to topical products. For these conventional systems it is normally recommended to maximize the solubility of the active in the vehicle [15,16].

Accelerated or Triggered by following mechanism:

1. Pressure triggered systems: Microsponge releases the entrapped material when pressurized/rubbed.
2. Temperature triggered systems: It is possible to modulate the release of substances from the microsponge by modulation of temperature. That is viscous sunscreens were show a higher release when exposed to higher temperatures.
3. pH triggered systems: Triggering the pH-based release of the active can be achieved by modifying the coating on the microsponge.
4. Solubility triggered system: Microsponges loaded with water-soluble ingredients will release the ingredient in the presence of water. Perspiration can trigger the release rate of active ingredients [17,18]

Advantages over Conventional Formulations: Conventional formulations of topical drugs are intended to work on the outer layers of the skin. Such products release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed. When compared to the Microsponge system can prevent excessive accumulation of ingredients within the epidermis and the dermis. Potentially, the Microsponge system can reduce significantly the irritation of effective drugs without reducing their efficacy. For example, by delivering the active ingredient gradually to the skin like MDS Benzoyl peroxide formulations have excellent efficacy with minimal irritation [19-23] .

Advantages over Microencapsulation and Liposomes: The MDS has advantages over other technologies like microencapsulation and liposomes. Microcapsules cannot usually control the release rate of actives. Once the wall ruptured, the actives contents within microcapsules will be released. Liposomes suffer from lower payload, difficult formulation, limited chemical stability and microbial instability. While microsponge system in contrast to the above systems are stable over range of pH 1 to 11, temperature up to 130° C ; compatible with most vehicles and ingredients; self sterilizing as average pore size is 0.25 µm where bacteria cannot penetrate; higher payload (50 to 60%), still free flowing and can be cost effective [24-26] .

EVALUATION OF MICROSPONGE

1. Particle size determination

Particle size analysis of loaded and unloaded microsponges can be performed by laser light diffractometry or any other suitable method. The values can be expressed for all formulations, size range. Cumulative percentage drug release from microsponges of different particle size will be plotted against time to study effect of particle size on drug release. Particles larger than 30 µm can impart gritty feeling and hence particles of sizes between 10 and 25 µm are preferred to use in final topical formulation.

2. Morphology and surface topography of microsponges

Prepared microsponges can be coated with gold–palladium under an argon atmosphere at room temperature and then the

surface morphology of the microsponges can be studied by scanning electron microscopy (SEM). SEM of a fractured microsponge particle can also be taken to illustrate its ultra-structure.

3. Determination of loading efficiency and production yield

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

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

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 microsponge obtained.

$$\text{Production Yield Y} = \frac{\text{Practical mass of Microsponges}}{\text{Theoretical mass (Polymer + drug)}} \times 100$$

4. Characterization of pore structure

Pore volume and diameter are vital in controlling the intensity and duration of effectiveness of the active ingredient. Pore diameter also affects the migration of active ingredients from microsponges into the vehicle in which the material is dispersed. Mercury intrusion porosimetry can be employed to study effect of pore diameter and volume with rate of drug release from microsponges. Porosity parameters of microsponges such as intrusion– extrusion isotherms pore size distribution, total pore surface area, average pore diameters, interstitial void volume, percent porosity, percent porosity filled, shape and morphology of the pores, bulk and apparent density can be determined by using mercury intrusion porosimetry.

5. Dissolution tests

Dissolution release rate of microsponges can be studied by use of dissolution apparatus USP XXIII with a modified basket consisted of 5µm stainless steel mesh. The dissolution medium is selected while considering solubility of actives to ensure sink conditions. At various intervals the samples from the dissolution medium was analysed by suitable analytical methods.

6. Determination of true density

The true density of micro particles is measured using an ultracycnometer under helium gas and is calculated from a mean of repeated determinations

7. Resiliency (viscoelastic properties)

Resiliency (viscoelastic properties) of microsponges can be modified to produce beadlets that is softer or firmer according to the needs of the final formulation. Increased cross-linking tends to slow down the rate of release [27].

Other In-vitro studies are

Fourier transform infrared (FTIR) analysis [28]

FTIR spectra of the drug, physical mixture of drug and Eudragit RS-100, formulations FPRS1nFPRS4 were recorded in potassium bromide disc using a Shimadzu Model 8400 FTIR spectrometer to ascertain compatibility.

Differential scanning calorimetric (DSC) analysis[28]

Thermal analysis using DSC was carried out on drug, physical mixture of the drug and Eudragit RS-100; accurately weighed samples were loaded into aluminum pans and sealed. All samples were run at a heating rate of 20°C/min. over a temperature range 40-430°C.

Stability studies [29-30]

In pharmaceutical sense, stability is technically defined as the capacity of particular formulation in a specific container or closure system, to remain within its physical, chemical, microbiological, therapeutic and toxicological specification. Durability of a product may be defined as the capability of a particular formulation in a specific container to remain with the physical, chemical, microbiological, therapeutic and toxicological specification. Stability of Microsponge gel formulation on storage is of a great concern as it is the major resistance in the development of marketed preparations. The prepared formulation was tested for stability on storing them at 4 ± 1°C, 25 ± 2°C and 37 ± 5°C & RH (Relative Humidity) 75 %.

After one month and the three months, they were evaluated for the following parameters:

- Appearance, pH, Drug content analysis, Drug release profiles, Rheological properties etc.

Statistical analysis [28]

The data obtained from each experiment were subjected to statistical analysis by Student t-test and one-way analysis of variance (ANOVA) using Graph Pad InStat software. *P* < 0.05 was considered to be indicative of significance.

Safety considerations

Skin irritation studies in rabbits[31-32]

The scores for erythema totaled for intact and abraded skin for all rabbits at 24 and 72 h. The primary irritation index was calculated based on the sum of the scored reactions divided by 24 (two scoring intervals multiplied by two test parameters multiplied by six rabbits

Anti-inflammatory activity by ear edema measurement [33]

Experiments reported in this study were performed after approval by the Animal Ethics Committee of our College and were carried out in accordance with the CPCSA guidelines Anti inflammatory activity was done by Male Swiss mice (25–35 g) housed at 22±2 °C under a 12h light/12-h dark cycle and with access to food and water, which were performed during the light phase of the cycle. The animals were allowed to acclimate to the laboratory for at least 2 h before testing and were used only once. Edema was induced in the right ear by topical application of 0.1mg/ear of croton oil dissolved in 20µL of acetone. In house gels of FA containing free, entrapped drug and marketed gel were applied topically simultaneously with the croton oil. Ear thickness was measured before and 6 h after the induction of inflammation using a digital vernier caliper and reported

Primary Eye Irritation Study (Unwashed Eyes) [34]:

Test substance is instilled into one eye of each of 6 rabbits (unwashed eyes), The cornea, iris, and conjunctival tissue of the treated eyes are graded for irritation effects at 1, 24, 48 and 72 hr after instillation. Observation period may be extended for up to 21 days to evaluate the reversibility of the effects observed.

Other evaluation studies are

Oral toxicity studies in rats, Mutagenicity in bacteria, allergenicity in guinea pigs, Compatibility studies by (TLC) thin layer chromatography.

APPLICATIONS OF MICROSPONGES

Microsponges are used mostly for topical, oral administration as well as biopharmaceutical delivery. It offers the formulator a range of alternatives to develop drug and cosmetic products. These are developed to deliver an active ingredient efficiently at the low dose and Microsponge drug delivery system unique, novel and versatile and extremely attractive in cosmetic world.[35] Recent applications of micro sponge from sea weed were to detect the diseases and also micro sponge drug delivery in RNA silencing. Some applications of MDS are described as follows:

Applications [36]:

Actives	Application
Sunscreens	Long lasting product efficacy, with improved protection against sunburns and sun related injuries even at elevated concentration and with reduced irritancy and sensitization.
Anti-acne e.g. Benzoyl Peroxide	Maintained efficacy with decreased skin irritation and sensitization Maintained efficacy with decreased skin irritation and sensitization.
Anti-inflammatory e.g. hydrocortisone.	Long lasting activity with reduction of skin allergic response and dermatoses.
Anti-fungals	Sustained release of actives.
Anti-dandruffs e.g. zinc pyrithione, selenium sulfide	Reduced unpleasant odour with lowered irritation with extended safety and efficacy.
Antipruritics	Extended and improved activity.
Skin	Improved stabilization against oxidation

depigmenting agents	with improved efficacy and aesthetic appeal.
Rubefaciants	Prolonged activity with reduced irritancy greasiness and odour.

Microsponge delivery systems are used to enhance the safety, efficacy and aesthetic quality of topical, over-the counter ("OTC") and personal care products. Products under development or in the marketplace utilize the topical microsponge systems in three primary ways;

1. As reservoirs releasing active ingredients over an extended period of time.
2. As receptacles for absorbing undesirable substances, such as excess skin oils, or
3. As closed containers holding ingredients away from the skin for superficial action.

The resulting benefits include extended efficacy, reduced skin irritation, cosmetic elegance, formulation flexibility and improved product stability.

In Food Industry: Nanosponges are useful for masking, reduction and elimination of bitter components from fruit juices and other dietary products by selective combination of polymer and cross-linker.

Chemotherapy: Nanosponges have been studied as a potential delivery system for anticancer therapies in which enhancement of bioavailability and activity was seen in molecules such as Paclitaxel and Tamoxifen. Different cancer cells had been treated by nanosponges like breast cancer or fast acting glioma type with help of single dose of injections.

1. Microsponge for topical delivery

The Microsponge systems are based on microscopic, polymer-based microspheres that can bind, suspend or entrap a wide variety of substances and then be incorporated into a formulated product, such as a gel, cream, liquid or powder. A single Microsponge is as tiny as a particle of talcum powder, measuring less than one-thousandth of an inch in diameter. Like a true sponge, each microsphere consists of a myriad of interconnecting voids within a non-collapsible structure that can accept a wide variety of substances. The outer surface is typically porous, allowing the controlled flow of substances into and out of the sphere. Several primary characteristics, or parameters, of the Microsponge system can be defined during the production phase to obtain spheres that are tailored to specific product applications and vehicle compatibility. Microsponge systems are made of biologically inert polymers. Extensive safety studies have demonstrated that the polymers are non-irritating, non-mutagenic, non-allergenic, non-toxic and non-biodegradable. As a result, the human body cannot convert them into other substances or break them down. Although they are microscopic in size, these systems are too large to pass through the stratum corneum when incorporated into topical products. Benzoyl peroxide (BPO) is commonly

used in topical formulations for the treatment of acne, with skin irritation as a common side effect. It has been shown that controlled release of BPO from a delivery system to the skin could reduce the side effect while reducing percutaneous absorption. Therefore, microsponge delivery of Benzoyl peroxide was developed using an emulsion solvent diffusion method by adding an organic internal phase containing benzoyl peroxide, ethyl cellulose and dichloromethane into a stirred aqueous phase containing polyvinyl alcohol and by suspension polymerization of styrene and divinyl benzene. The prepared microsponges were dispersed in gel base and microsponge gels are evaluated for anti-bacterial and skin irritancy. The entrapped system released the drug at slower rate than the system containing free BPO. Topical delivery system with reduced irritancy was successfully developed [37-46].

2. Microsponge for oral delivery:

In oral applications, the microsponge system has been shown to increase the rate of solubilisation of poorly water soluble drugs by entrapping such drugs in the microsponge system's pores. As these pores are very small, the drug is in effect reduced to microscopic particles and the significant increase in the surface area thus greatly increases the rate of solubilisation. Controlled oral delivery of ibuprofen microsponges is achieved with an acrylic polymer, Eudragit RS, by changing their intraparticle density. Sustained release formulation of chlorpheniramine maleate, using powder-coated microsponges, is prepared by the dry impact blending method, for oral drug delivery. Controlled oral delivery of Ketoprofen prepared by quasi-emulsion solvent diffusion method with Eudragit RS 100 and afterwards tablets of microsponges were prepared by the direct compression method. Results indicated that compressibility was much improved in the physical mixture of the drug and polymer; due to the plastic deformation of the sponge-like microsponge structure, producing mechanically strong tablets. Colon-specific, controlled delivery of Flurbiprofen was conducted by using a commercial Microsponge 5640 system. In vitro studies exhibited that compression-coated colon-specific tablet formulations started to release the drug at the eighth hour, corresponding to the proximal colon arrival time, due to addition of the enzyme, following a modified release pattern, while the drug release from the colon-specific formulations prepared by pore plugging the microsponges showed an increase at the eighth hour, which was the point of time when the enzyme addition was made.

3. Microsponge for Bone and Tissue Engineering

Bone-substitute Compounds were obtained by mixing pre polymerized powders of polymethyl methacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium deficient hydroxyapatite powders. The final composites appeared to be porous and acted as microsponges. Basic fibroblast growth factor (bFGF) incorporated in a collagen sponge sheet was sustained released in the mouse sub-cutis according to the biodegradation of the sponge matrix, and exhibited local angiogenic activity in a dose-dependent manner. The injection

of collagen microsponges incorporating bFGF induced a significant increase in the blood flow, in the murine ischemic hind limb, which could never have been attained by the bolus injection of bFGF. These results suggest the significance and therapeutic utility of the type I collagen as a reservoir of bFGF. Recent advances in microsphere drug delivery system: Various advances were made by modifying the methods to form Nan sponges, nanofersponges and porous micro beads. β - CD microsponges were also developed that can be used for hydrophobic as well as hydrophilic drugs, in contrast to polymeric micro or microsponges. These advanced systems were studied for oral administration of dexamethasone, Flurbiprofen, doxorubicin hydrochloride, itraconazole and serum albumin as model drug. These microsponges were developed by cross- linking the β CD molecule by reacting the β -CD with biphenyl carbonate. Some researchers also observed the microsponges as good carrier for the delivery of gases. Researchers also observed that incorporating a cytotoxic in a microsphere carrier system can increase the potency of the drug suggesting that these carriers can be potentially used for targeting the cancerous cells [47-48].

Marketed Formulation of Microsponges: [49]

Product Name	Manufacturer	Advantages
Retinol cream	Biomedic	Microsphere system helps to maximize retinol dosage while reducing the possibility of irritation. Retinol is a topical vitamin A derivative which helps maintain healthy skin, hair and mucous membranes.
Dermalogica oil control lotion	John & Ginger Dermalogica skin care products.	Microsphere technology has exclusive skin response complex soothes and purifies, provides effective skin hydration, without adding excess oil.
Oil free matte block spf 20	Dermalogica.	Microsphere technology absorbs oil, maintaining an all-day matte finish and preventing shine without any powdery residue. Oil free formula contains soothing Green Tea to help calm inflammation caused by breakouts. Contains no artificial fragrance or color.
Retin-A-Micro	Ortho-McNeil Pharmaceutical, Inc.	0.1% and 0.04% tretinoin entrapped in MDS for topical treatment of acne vulgaris. This formulation uses patented methyl

		methacrylate/ glycol dimethacrylate cross-polymer porous microspheres (MICROSPONGE® System) to enable inclusion of the active ingredient, tretinoin, in an aqueous gel.
Epi Quin Micro	SkinMedica Inc	The Microsphere ® system uses microscopic reservoirs that entrap hydroquinone and retinol. This provides the skin with continuous exposure to hydroquinone and retinol over time, which may minimize skin irritation.
Carac Cream, 0.5%	Dermik Laboratories, Inc.	Carac Cream contains 0.5 % fluorouracil, with 0.35% being incorporated into a patented porous microsphere (Microsphere) 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 (AK), a common pre-cancerous skin condition caused by over-exposure to the sun.

FUTURE IMPACT OF MICROSPONGE DRUG DELIVERY SYSTEM

Microsphere is one of the novel drug delivery systems, for the topical preparations for drug delivery through skin. Not only it is limited to the topical preparations it shown its activity in colon targeting by the use of natural polymers, also shown its activity in biopharmaceuticals i.e. it is useful in drug delivery systems in various forms. Main advantage is that liquids can be transformed into free flowing powders. Its produce less toxic, non greasiness, non irritant, it requires less amount of drug due to delayed release. Normal topical preparations shows toxic reactions, incompatibilities, unpleasant odour, etc. by this microsphere products are advantageous some products are already approved and available in market; several products under development.

CONCLUSION

A Microsphere Delivery System can entrap wide range of actives and then release them onto the skin over a time and in response to trigger. Microsphere drug delivery has become highly competitive and rapidly evolving technology and more

and more research are carrying out to optimize cost effectiveness and efficacy of therapy. With demand for innovative and highly efficient Pharmaceutical as well as Cosmetic products, the market holds considerable potential for Microsponge technology and the versatility they offer. Microsponge can be effectively incorporated into topical drug delivery system for retention of dosage form on skin, and also use for oral delivery of drugs using bio erodible polymers, especially for colon specific delivery and controlled release drug delivery system thus improving patient compliance by providing site specific drug delivery system and prolonging dosage intervals. Therefore, microsponge has got a lot of potential and is a very emerging field which is needed to be explored. Microsponges constitute a significant part by virtue of their small size and efficient carrier characteristics. So microsponge drug delivery system has got a lot of potential and is a very emerging field which is needed to be explored in the future with most research study.

ACKNOWLEDGEMENT

Authors are special thanks to **Sri. Sardar Raja Singh Sir**, Chairman and **Mrs. Lata Gupta Madam**, Director Admin, GRD (PG) Institute of Management and Technology, Dehradun, providing the facilities to publish this research work. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The authors have no conflict of interest.

FUNDING SOURCE

The author (s) received no financial support for the research, authorship or publication of this article.

DATA AVAILABILITY

Not declared

REFERENCES

1. Shivani Nanda, Mandeep Kaur, Nikhil Sood, Sahil Nagpal. Microsponge drug delivery system: an overview, World Journal of Pharmacy and Pharmaceutical Sciences, Volume 2, Issue 3, 1032-1043.
2. Aity S., et al., Microsponges: A novel strategy for drug delivery system. J Adv Pharm Technol Res, 2010. 1(3): p. 90- 283.
3. Chadawar V, and J. Shaji, Microsponge delivery system. Curr Drug Deliv, 2007. 4(2): p. 9-123
4. Kydonieus AF, and Berner B. Transdermal Delivery of Drugs, CRC Press, Boca Raton, 1987.
5. Nacht S. and Kantz M., (1992), The Microsponge: A Novel Topical Programmable Delivery System. Chapter 15, In: Topical Drug Delivery Systems. Edited by David W. O. and Anfon H. A. Volume 42, pp 299-325.
6. Won R., Sep. 1987, United States Patent No. 4,690,825, 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 ingredient as a porogen.
7. Embil K, Nacht S, 1996. The microsponge® delivery system (MDS): a topical delivery system with reduced irritancy

incorporating multiple triggering mechanisms for the release of actives. J. Microencapsul. 13, 575–588.

8. Shivani Nanda, Mandeep Kaur, Nikhil Sood, Sahil Nagpal, Microsponge drug delivery system: an overview, World Journal of Pharmacy and Pharmaceutical Sciences, Volume 2, Issue 3, 1032-1043.
9. Brunton LL, Lazo JS, Parker KL. Goodman and Gilman's 'The Pharmacological Basis of Therapeutics'. 11th Edition. (2006) P. 1021.
10. Cooke CIET, Flora of Presidency of Bombay, Published under the authority of Secretary of State for Council (1903). Charde et al / International Journal of Advances in Pharmaceutics 2 (6) 2013: 70 .
11. Vyas SP, Khar RK, Targeted and Controlled Drug Delivery- Novel Carrier System: New Delhi, CBS Publication. 2002,453.
12. Neelam Jain, Pramod Kumar Sharma, Arunabha Banik. Recent advances on microsponge delivery system, International Journal of Pharmaceutical Sciences Review and Research, Volume 8, Issue 2, May – June 2011
13. Comoglu T, Gonul N, Baykara T. Preparation and in vitro evaluation of modified release ketoprofenmicrosponges, II Farmaco, 58, 2003, 101-106.
14. Namrata Jadhav, Vruti Patel, Siddhesh Mungekar, Manisha Karpe, Vilasrao Kadam, Microsponge delivery system: an updated review, current status and future prospects, World Journal of Pharmacy and Pharmaceutical Sciences, Volume 2, Issue 6, 6463-6485.
15. Christensen MS, Natch SJ. Invest. Dermatol. 1983;69:282.
16. Jelvehgari M, Siah-Shadbad MR, Azarmi S, Gary P, Martin, Nokhodchi A. The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies. International Journal of Pharmaceutics 2006;308:124-132.
17. Tansel C, Baykara T. The effects of pressure and direct compression on tableting of microsponges. Int. J. Pharm. 2002;242:191-195.
18. Ruckenstein E, Hong L. Concentrated emulsion polymerization pathway to hydrophobic And hydrophilic microsponge molecular reservoirs. Chem. Mater. 1992;4:1032-1037.
19. Chadawar V, Shaji J. Microsponge delivery system. Current Drug Delivery 2007;4:123-129.
20. Martin A, Swarbrick J, and Cammarrata A. In: Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences. 3rdEd., 1991 pp. 527.
21. Emanuele AD, Dinarvand R. Preparation, Characterization and Drug Release from Thermo responsive Microspheres. International Journal of Pharmaceutics.1995, 237-242.
22. Kilicarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of Verapamil HCl loaded microspheres. Int. J. Pharm. 252, 2003, 99–109.
23. Jayaweera DM. Medicinal Plants (Indigenous and Exotic) used in Ceylon. Part-2. A Publication of the Natural Sciences Council of Srilanka. Colombo (1980).
24. D'souza JI. In-vitro Antibacterial and Skin Irritation Studies of Microsponges of Benzoyl Peroxide. Indian Drugs. 2001, 38(7): 23.
25. Barkai A, Pathak V, Benita S. Polyacrylate (Eudragit retard) microspheres for oral controlled release of nifedipine. I. Formulation design and process optimization. Drug Dev. Ind. Pharm. 1990; 16:2057-2075.
26. D'souza JI, The Microsponge Drug Delivery System: For Delivering an Active Ingredient by Controlled Time Release. Pharma. info.net, 2008, 6 (3): 62.
27. Sarat CPM, Ajay M, Nagendra BB, Prathyusha P, Audinarayana N, Bhaskar RK. Microsponge Drug Delivery System. A Review. J. Pharm. Res.2011; 4(5): 1381-1384.

28. Shobha rani R Hiremath, Text book of industrial pharmacy, published by universities press private limited, pg.no.44-45.
29. Microspheres by shobha rani R Hiremath N Sree Harsha, Text book of industrial pharmacy, pg.no.126.
30. Netal Amrutiya, Amrita Bajaj, and Madhu Madan Development of Microsponges for Topical Delivery of Mupirocin ,AAPS Pharm Sci Tech, Vol. 10, No. 2, June 2009, 402-409.
31. Vikas Jain and Ranjit Singh, Dicyclomine-loaded Eudragit®-based Microsponge with Potential for Colonic Delivery: Preparation and Characterization, Tropical Journal of Pharmaceutical Research, February 2010; 9 (1): 67-72.
32. Sato T, Kanke M, Schroeder G, Deluca P. Porous biodegradable microspheres for controlled drug delivery. I: Assessment of processing conditions and solvent removal techniques. Pharm Res. 1988; 5:21-30.
33. Netal Amrutiya, Amrita Bajaj, and Madhu Madan, Development of Microsponges for Topical Delivery of Mupirocin, AAPS PharmSciTech, Vol. 10, No. 2, June 2009,402-409.
34. Netal Amrutiya, Amrita Bajaj, and Madhu Madan, Development of Microsponges for Topical Delivery of Mupirocin, AAPS Pharm Sci Tech, Vol. 10, No. 2, June 2009,402-409.
35. Aloorkar NH, Kulkarni AS, Ingale DJ and Patil RA, Microsponges as Innovative Drug Delivery Systems, International Journal of pharmaceutical Sciences and Nanotechnology, Vol 5, Issue 1, April – June 2012
36. D'souza JI, More HN (2008). Topical Anti-Inflammatory Gels of Fluocinolone Acetonide Entrapped in Eudragit Based Microsponge Delivery System. Res J Pharm Tech 1(4):502-506.
37. Neelam Jain, Pramod Kumar Sharma, Arunabha Banik, Recent advances on microsponge delivery system, International Journal of Pharmaceutical Sciences Review and Research, Vol 8, Issue 2, May – June 2011.
38. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Control of prolonged drug release and compression properties of ibuprofen microsponges with acrylic polymer, eudragit RS, by changing their intraparticle density, Chem Pharm Bull, 40, 1992, 196-201.
39. D'souza JI, The Microsponge Drug Delivery System: For Delivering an Active Ingredient by Controlled Time Release. Pharma. info.net, 2008, 6 (3): 62-69.
40. Sarat CPM., Ajay M, Nagendra BB, Prathyusha P, Audinarayana N, Bhaskar RK. Microsponge Drug Delivery System. A Review. J. Pharm. Res.2011; 4(5): 1381-1384.
41. D'souza JI. *In-vitro* Antibacterial and Skin Irritation Studies of Microsponges of Benzoyl Peroxide. Indian Drugs. 2001, 38(7): 23-32.
42. Wester R, Patel R, Natch S, Leyden J, Melendres J, Maibach H. Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy, J. Am. Acad. Derm., 1991, 24, 720-726.
43. John I. D'souza, Jagdish K. Saboji, Suresh G. Killedar, Harinath N. More "Design and Evaluation of Benzoyl Peroxide Microsponges to Enhance Therapeutic Efficacy in Acne Treatment", Accepted for presentation in 20th FAPA Congress, Bangkok, Thailand , Nov Dec 3, 2004: 28-36.
44. Jain V, Singh R, Dicyclomine-loaded eudragit based microsponge with potential for colonic delivery Preparation and characterization. Tropical Journal of Pharmaceutical Research, 9(1): 2010: 67-72.
45. Mine Orlu, Erdal Cevher, Ahmet Araman Design and evaluation of colon specific drug delivery system containing Flurbiprofen microsponges, International Journal of Pharmaceutics, 318 (2006) 103–117.
46. Shaheen SZ, Bolla K, Vasu K&Singara CMA. Antimicrobial activity of the fruit extracts of Cocciniaindica. African Journal of Biotechnology Vol. 8(24) (2009). P. 7073-7079.
47. Park WH, Lee SJ and Moon HI. Antimalarial Activity of a New Stilbene Glycoside from Parthenocissustricuspidata in Mice. Antimicrobial Agents and Chemotherapy. 52(9) (2008): 3451–3453.
48. Trotta F, Cavalli R, Tumiatti W. Cyclodextrin-based nanosponges for drug delivery. J Inc Phenom Macro cyclic Che2006; 56:209-213.
49. Rajeshree M, Patel H and Patel V: Microsponges for the topical drug delivery system. International Journal of Pharm & Tech. 2014; 5: 2839-2851.