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REVIEW ARTICLE

A REVIEW ON MICROSPONGE DRUG DELIVERY SYSTEM

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ABSTRACT:

The drug delivery technology landscape has become highly competitive and rapidly evolving. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. Peptides, proteins and DNA-based therapeutics cannot be effectively delivered by conventional means. A Microsponges delivery system is a highly cross-linked, porous, polymeric microsphere, polymeric system consisting of porous microspheres that can entrap and release them into the skin over a long period of time. This delivery system provides extended release with reduced irritation, better tolerance, improved thermal, physical and chemical stability. The main goal of any drug delivery system is to achieve desired concentration of the drug in blood or tissue, which is therapeutically effective and non-toxic for a prolonged period In the present study various methods for preparation of microsponges drug delivery system are studied. Various advantages are also given which shows the importance of this method for the delivery of drugs over the other drug delivery system. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. Microsponge technology offers entrapment of ingredients and is believed to contribute towards reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. In addition, numerous studies have confirmed that microsponge systems are non-irritating, nonmutagenic, non-allergenic, and non-toxic. Microsponges delivery technology is being used currently in cosmetics, over-the-counter (OTC) skin care, sunscreens and prescription products. One of the best feature of microsponge is it is self-sterilizing. This review is focused on method of preparation, characterization and application of microsponge.

Keywords: Microsponge, Control relaease, Target release, topical formulation, oral administration

INTRODUCTION:

A Microsponges Delivery System (MDS) is "Patented, highly cross-linked, porous, polymeric microspheres, polymeric system consisting of porous microspheres that can entrap wide range of actives and then release them into the skin over a time and in response to trigger". 10-25 microns in diameter.[1] Micro-sponge polymers possess the versatility to load a wide range of actives providing the benefits of enhanced product efficacy, mildness, tolerability, and extended wear to a wide range of skin therapies. Several predictable and reliable systems were developed for systemic drugs under the heading of transdermal delivery system (TDS) using the skin as portal of entry. It has improved the efficacy and safety of many drugs. But TDS is not practical for delivery of materials whose final target is skin itself. Thus the need exists for system to maximize amount of time that an active ingredient is present either on skin surface or within the epidermis, while minimizing its transdermal penetration in the body .[2, 3, 4]

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 favourable 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. MDS can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved aesthetic properties in an efficient manner. [5, 6, 7]

The microsponge 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 procedures and those are applied to the cosmetic as well as over-the-counter (OTC) and prescription pharmaceutical products. At the current time, this interesting technology has been licensed to Cardinal Health, Inc., for use in topical products. The scanning electron microscopy of the microsponge particle reveals that its internal structure as the "bag of marbles".

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The porosity is due to the interstitial spaces between the marbles. The interstitial pores can entrap many wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens, anti-infective and anti-inflammatory agents. [8, 9]

Benefits of microsponge drug delivery systems: [10, 11, 12]

- Enhanced product performance.
- Extended release.
- Diminish irritation and hence enhanced patient Compliance.
- Improved product elegancy.
- Improved oil control as it can absorb oil up to 6 times its weight without drying.
- Allows for novel product forms.
- Improves efficacy in treatment.
- Cure or control confirm more promptly.
- Improve control of condition.
- Improve bioavailability of same drugs
- Flexibility to develop novel product forms.
- Non-irritating, non-mutagenic, non-allergenic and non-toxic
- Improves stability, thermal, physical and chemical stability
- Allows incorporation of immiscible products.
- Improves material processing eg. liquid can be converted to powders

Limitations:

The preparation methods usually use 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 health.

Potential features of microsponge drug delivery system: [13, 14, 15, 16]

- Shows tolerable stability over pH ranging from 1 to 11 and at high temperatures (up to130°C).
- Reveal good compatibility with various vehicles and ingredients.
- High entrapment efficiency up to 50 to 60%.
- Are characterized by free flowing properties.
- The average pore size of microsponges is small (0.25 µm) in a way to prevent the penetration of bacteria, thus they do not need sterilization or addition of preservatives.
- Can absorb oil up to 6 times their weight without drying.

Characteristics of moieties that is entrapped in microsponges:[17, 18]

- Either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- Stable in contact with polymerization catalyst and conditions of polymerization**.**
- The spherical structure of microsponges should not collapse.
- Active ingredients that are entrapped in microsponge can then be incorporated into many products such as creams, gels, powders, lotions and soaps.
- The solubility of actives in the vehicle must be limited to avoid cosmetic problems; not more than 10 to 12% w/w microsponges must be incorporated into the vehicle. Otherwise the vehicle will deplete the microsponges before the application.
- Water immiscible or at most only slightly soluble.
- Inert to monomers.
- Payload and polymer design of the microsponges for the active must be optimized for required release rate for given period of time.

METHOD OF PREPARATION OF MICROSPONGE DRUG DELIVERY SYSTEM:

A Porogen drug neither hinders the polymerization process nor become activated by it and also it is stable to free radicals is entrapped with one-step process (liquid-liquid suspension polymerization). Microsponges are suitably prepared by the following methods:

1. Liquid-liquid suspension polymerization: [19, 20, 21]

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

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.

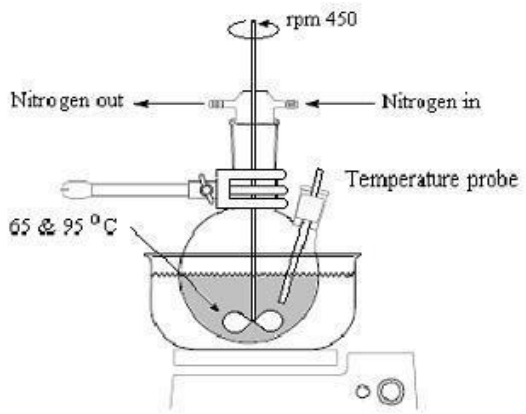

Figure 1: Microsponges preparations by liquid-liquid Suspension polymerization

2. Quasi-Emulsion Solvent Diffusion Method: [22, 23, 24]

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 RS 100 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 hours11. 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 hrs.

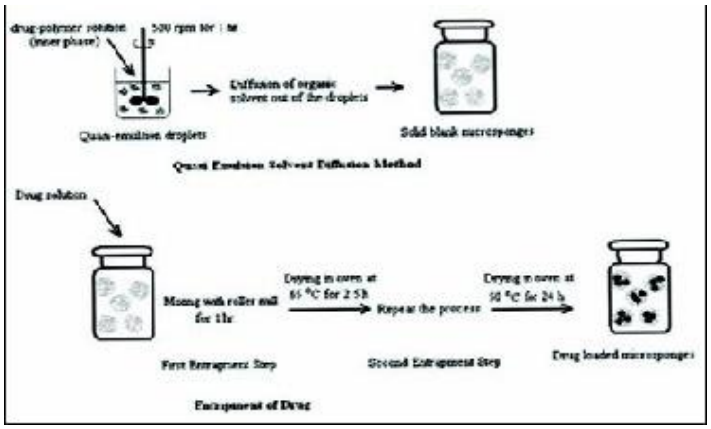

Figure 2: Preparation of microsponges by quasi emulsion solvent diffusion method

RELEASE MECHANISM OF MICROSPONGE: [25, 26]

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.

Accelerated or Triggered by following mechanism:

- Pressure triggered systems
- Temperature triggered systems
- pH triggered systems
- Solubility triggered system

FACTORS AFFECTING DRUG RELEASE FROM MICROSPONGE DELIVERY SYSTEM: [19]

- Physical properties of Microsponge system like pore diameter, pore volume, resiliency etc. Properties of vehicle in which the microsponges are finally dispersed.
- Pressure Rubbing/ pressure applied can release active ingredient from microsponges onto skin.
- Temperature change some entrapped actives can be too viscous at room temperature to flow spontaneously from microsponges onto the skin. Increased in skin temperature can result in an increased flow rate and hence release.
- Solubility Microsponges loaded with water-soluble ingredients like antiperspirants and antiseptics will release the ingredient in the presence of water. The release can also be activated by diffusion taking into consideration the partition coefficient of the ingredient between the microsponges and the outside system.

PHYSICAL CHARACTERIZATION OF MICROSPONGE DRUG DELIVERY SYSTEM:

Particle size and shape: [27]

Free-flowing powders with fine aesthetic attributes are possible to obtain by controlling the size of particles during polymerization. Particle size analysis of loaded and unloaded microsponges can be performed by laser light diffractometry or any other suitable method. The values (d50) can be expressed for all formulations as mean 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. Particle larger than 30 µm can impart gritty feeling and hence particles of sizes between10 and 25 µm are preferred to use in final topical formulation.

The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). Both can be used to determine the shape and outer structure of microparticles. LM provides a control over coating parameters in case of double walled microparticles. Conflocal fluorescence microscopy is used for the structure characterization of multiple walled microparticles. Laser light scattering and multi size coulter counter other than instrumental methods, which can be used for the characterization of size, shape and morphology of the microparticles (microsponges).

Morphology and surface topography of microsponges: [28]

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.

Determination of loading efficiency and production yield: [29]

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.

$$\text{Production Yield} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical Mass (Polymer + Drug)}} \times 100$$

Compatibility studies: [30]

Compatibility of drug with reaction adjuncts can be studied by thin layer chromatography (TLC) and Fourier Transform Infra-red spectroscopy (FT-IR). Effect of polymerization on crystallinity of the drug can be studied by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC). For DSC approximately 5 mg samples can be accurately weighed into aluminum pans and sealed and can be run at a heating rate of 15 C/min over a temperature range 25–430 C in atmosphere of nitrogen.

Resiliency (viscoelastic properties): [31]

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.

Drug release kinetics: [32]

The dissolution profile of each formulation have been subjected to various models such as Zero order kinetics (percentage drug release against time), First order kinetics (log percentage drug unreleased against time), Higuchi (percentage drug released against square root of time) and Korsemeyer-Peppas (log percent drug released against log of time) were applied to assess the kinetics of drug release from prepared microsponges.

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.

Determination of true density: [33]

The true density of micro particles and BPO was measured using an ultra-pycnometer under helium gas and was calculated from a mean of repeated determinations.

Characterization of pore structure: [34]

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, shape and morphology of the pores, bulk and apparent density can be determined by using mercury intrusion porosimetry.

WORK DONE ON MICROSPONGES DRUG DELIVERY SYSTEM:

Karthika et al fabricated microsponges drug delivery system using the drug Lornoxicam. They prepared the formulation using Quasi emulsion solvent diffusion method Eudragit RS 100. The effects of drug to polymer ratios on physical characteristics of the microsponges were investigated. Lornoxicam is a Non-steroidal anti-

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inflammatory drug used for the treatment of various inflammatory diseases. This study presents a new approach based on microsponge drug delivery system. [35]

John et al formulated microsponges drug delivery system using anti-inflammatory gels of Flucinolone Acetonide Entrapped in Eudragit. They prepared the formulation using Quasi emulsion solvent diffusion method Eudragit RS 100. The main aim to produce Flucinolone Acetonide microsponges was to control the release of drug to the skin. [36]

Vikas et al prepared microsponges drug delivery system using the dicyclomine. They prepared the formulation using Quasi emulsion solvent diffusion method Eudragit RS 100. Process parameters were modulated to optimize the formulation. Shape and surface morphology of the microsponges were examined using scanning electron microscopy. [37]

Saboji et al formulated microsponges drug delivery system using the drug ketoconazole. They prepared the formulation using Quasi emulsion solvent diffusion method Eudragit RS 100.The The physical characterization showed that microsponge formulation MS IV and MS VI showed a better loading efficiency and production yield. The microsponge ketoconazole gel formulations showed an appropriate drug release profile and also bring remarkable decrease on gel application for fungal treatment. [38]

Ramani Gade et al design and development of Hydroxyzine hydrochloride controlled release tablets based on microsponges. These are prepared by oil in oil emulsion solvent diffusion method using acetone as dispersing solvent. Hydroxyzine hydrochloride is an anti-histaminic drug used in the treatment of urticaria and pruritus. Thickness, hardness, friability, % drug content and invitro release studies were done on microsponge tablets. [39]

Mahajan et al formulated microsponges drug delivery system using the drug Indomethacin. They prepared the formulation using Quasi emulsion solvent diffusion method Eudragit RS 100, pH independent release retardant polymer and polymer, stabilizer by changing the drug polymer ration. They evaluated micromeritic properties, drug content, encapsulation efficiency and particle size. They did the characterization for formulation by DSC, X-Ray diffraction and SEM.[40]

PHARMACEUTICAL UTILIZATION OF MICROSPONGES:

Microsponge delivery systems are used to enhance the safety, effectiveness and aesthetic quality of topical prescription, over-the-counter and personal care products. Microsponges can be used in variety of applications. It is used mostly for topical and recently for oral administration. Several patents have reported that it can be used as an excipients due to its high loading capacity and sustained release ability.

Long lasting Coloured Cosmetics: [41, 42]

Colours entrapped in microsponges may be used in a variety of coloured cosmetic products such as rouge or lipsticks to make them long lasting. As stated above, microsponges help in uniform spreading and improving covering power. Thus, colored cosmetics formulated with microsponges would be highly elegant.

For topical administration: [43, 44]

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 is commonly used in topical formulations for the treatment of acne, with skin irritation as a common side effect.

For oral administration: [45]

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.

For Bone and Tissue Engineering: [46, 47]

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.

RECENT DEVELOPMENTS IN MICROSPONGE DRUG DELIVERY SYSTEM: [48]

Various advances were made by modifying the methods to form Nanosponges, nanoferrosponges and porous micro beads. β - CD nanosponges were also developed that can be used for hydrophobic as well as hydrophilic drugs, in contrast to polymeric micro or nanosponges.

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These advanced systems were studied for oral administration of dexamethasone, Flurbiprofen, doxorubicin hydrochloride, itraconazole and serum albumin as model drug. These nanosponges were developed by cross- linking the β CD molecule by reacting the β-CD with biphenyl carbonate. Some researchers also observed the nanosponges as good carrier for the delivery of gases. Researchers also observed that incorporating a cytotoxic in a nanosponge carrier system can increase the potency of the drug suggesting that these carriers can be potentially used for targeting the cancerous cells.

CONCLUSION

The microsponge delivery technology of controlled release system in which active pharmaceutical ingredient is loaded in the macro porous beads and initiates reduction in side effects with improved therapeutic efficacy. 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. This technology is being used currently in cosmetics, over-the-counter skin care, sunscreens, and prescription products. This kind of drug delivery technology may lead to a better understanding of the healing of several diseases. Hence, the microsponge-based drug delivery technology is likely to become a valuable drug delivery matrix substance for various therapeutic applications in the future.

Ease manufacturing, simple ingredients and wide range actives can be entrapped along with a programmable release make microsponges extremely attractive. It is originally developed for topical delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, antipruritics, rubefacients etc. Microsponge Delivery System holds a promising future in various pharmaceutical applications in the coming years as they have unique properties like enhanced product performance and elegancy, extended release, reduced irritation, improved thermal, physical, and chemical stability so flexible to develop novel product forms. Researchers are continuously trying to develop a drug delivery system which is cost effective and having better therapeutic efficacy. The technology showed such promises to meet researchers expectations. numerous studies reveal that microsponge systems are non-irritating, non-mutagenic, non-allergenic, and non-toxic. A Microsponge Delivery System can entrap wide range of actives and then release them onto the skin over a time and in response to trigger. It is a unique technology for the controlled release of topical agents and consists of microporous beads loaded with active agent and also use for oral as well as biopharmaceutical drug delivery. A Microsponge Delivery System can release its active ingredient on a time mode and also in response to other stimuli. Thus microsponge has got a lot of potential and is a very emerging field which is needed to be explored.

REFERENCES:

1. Nacht S and Kantz M. The Microsponges, A Novel Topical Programmable Delivery System. Chapter 15, In, Topical Drug Delivery System. Edited by David WO and Anfon HA, 42, 1992, 299-325.
2. Kirti Deshmukh, Sushilkumar S Poddar. Solid porous microsphere: emerging trend in pharmaceutical technology. Int J Pharm Bio Sci, 2(1), 2011, 364-377.
3. Patel SB, Patel HJ and Seth AK. Microsponge drug delivery system: an overview. J Global Pharm Tech, 2(8), 2010, 1-9.
4. Viral Shaha, Hitesh Jain, Jethva Krishna1, Pramit Patel. Microsponge drug delivery: A Review. Int. J. Res. Pharm. Sci, 1(2), 2010, 212-218.
5. 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.
6. Aity, S., et al., Microsponges: A novel strategy for drug delivery system. J Adv Pharm Technol Res, 2010. 1(3): p. 90-283.
7. Chadawar, V. and J. Shaji, Microsponge delivery system. Curr Drug Deliv, 2007 4(2): 9-123.
8. 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.
9. Won R: Method for delivering an active ingredient by controlled time release utilizing a novel delivery vehicle which can be prepared by a process utilizing the active ingredients as a Porogen. 1987; US Patent No. 4690825.
10. Patidar K, Soni M, Saxena C, Soni P, Sharma DK. Microspongea versatile vesicular approach for transdermal drug delivery system. *J Global Pharm Tec*, 2(3), 2010, 154-164.
11. N.H. Aloorkar, A.S. Kulkarni, D.J. Ingale and R.A. Patil, Microsponges as Innovative Drug Delivery Systems, International Journal of pharmaceutical Sciences and Nonotechnology, 5(1), 2012.
12. D'souza J.I., More H.N. Topical Anti-Inflammatory Gels of Fluocinolone Acetonide Entrapped in Eudragit Based Microsponge Delivery System. Res J Pharm Tech 1(4), 2008,502-506.
13. Hibah Aldawsari and Shaimaa M. Badr-Eldin, Microsponges as promising vehicle for drug delivery and targeting: Preparation, characterization and applications, African Journal of Pharmacy and Pharmacology, 3(1), 2001, 873-881.
14. 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. J. Pharm. Sci.Technol. 56(1), 1996, 49-56.
15. Jain V, Singh R. Design and characterization of colon-specific drug delivery system containing paracetamol microsponges. Arch. Pharm. Res. 34, 2011, 733-740.
16. Vyas SP, Khar RK. Targeted and controlled drug delivery: novel carrier systems. CBS Publications, 1st ed., New Delhi, 453, 2002.
17. Swetha, Gopal Rao, Venkata Ramana K, Niyaz Basha B and Koti Reddy V. Formulation and *in-vitro* evaluation of etodolac entrapped in microsponge based drug delivery system. *Int J Pharma*, 1(2), 2011, 73-80.
18. Santanu Kaity, Sabyasachi Maiti, Ashoke Kumar Ghosh,Subham Banerjee. Microsponge: A novel strategy for drug delivery system. *J. Adv. Pharma. Tech. Res*, 1(3), 2010, 283-290.

 ISSN: 2250-1177 CODEN (USA): JDDTAO

19. Panwar AS, Yadav CS, Yadav P, Darwhekar GN, Jain DK, Panwar MS, Agrawal A. Microsponge a novel carrier for cosmetics. JGPT, 3(7), 2011, 15-24.
20. Vikrant K, Nikam, RT Dolas, Somwanshi SB, Gaware VM, Kotade KB, Dhamak KB, Khadse AN and Kashid VA. Microparticles: a novel approach to enhance the drug delivery - a review. IJPRD, 3(8), 2011, 170- 183.
21. Brunton LL, Lazo JS, Parker KL. Goodman and Gilman's 'ThePharmacological Basis of Therapeutics'. 11th Edition. 2006, 1021.
22. John I D' Souza and Harinath N. Topical anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. Research J Pharm and Tech, 1(4), 2008, 502.
23. Comoglu T, Gonul N, Baykara T, Preparation and in vitro evaluation of modified release ketoprofen microsponges, II, Farmaco, 58, 2003, 101-106.
24. 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.
25. Khopade AJ, Jain S, Jain NK, The microsponge, Eastern Pharmacist, 1996, 49-53.
26. Christensen MS, Natch SJ. Invest. Dermato. 1983;69:282.
27. Vikrant K, Nikam, RT Dolas, Somwanshi SB, Gaware VM, Kotade KB, Dhamak KB, Khadse AN and Kashid VA. Microparticles: a novel approach to enhance the drug delivery - a review. IJPRD, 3(8), 2011, 170- 183.
28. Madhu Sharma, Baibhav Joshi. Microsponges: A comprehensive Review. The Global J Pharm Res, 1(3), 2012, 359-377.
29. Saurabh Kumar, Tyagi LK, and Dashrath Singh. Microsponge delivery system (MDS): A unique technology for delivery of active ingredients. IJPSR, 2(12), 2011, 3069-3080.
30. Patel EK and Oswal RJ. Nanosponge and micro sponges: A novel drug delivery system. Int J Res in Pharm and Chem, 2(2), 2012, 237-244.
31. Saroj Kumar Pradhan. Microsponges as the versatile tool for drug delivery system. IJRPC, 1(2), 2011, 243-258.
32. Swetha, Gopal Rao, Venkata Ramana K, Niyaz Basha B and Koti Reddy V. Formulation and in-vitro evaluation of etodolac entrapped in microsponge based drug delivery system. Int J Pharma, 1(2), 2011, 73-80.
33. Kawashima YNT, Takeuchi HH, Tomoaki IY. Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity. *Chemical & pharmaceutical bulletin*, 40(1), 1992, 196-201.
34. Patel EK and Oswal RJ. Nanosponge and Microsponges, a Navel Drug Delivery System. *International Journal of Research in Pharmacy*, 2(2), 2012, 238.
35. Ramani Gade, Anitha Makineni, Aparna A, Krishna Keerthi B, TEGK Murthy, Chandu Babu Rao, Sreekant Nama. Design and development of Hydroxyzine hydrochloride controlled release tablets based on microsponges, *Caribbean Journal of Science and Technology*, 1, 2013, 172.
36. Karthika R, Elango K, Ramesh Kumar K, Rahul K. Formulation and evaluation of lornoxicam microsponges tablets for the treatment of arthritis. *International Journal of Pharmaceutical Innovations*, 3(2), 2013, 29.
37. Saboji JK, Manvi FV, Gadad AP and Patel BD. Formulation and evaluation of ketoconazole microsponges gel by quassi emulsion solvent diffusion. *Journal of Cell and Tissue Research*, 2(1), 2011, 26-31.
38. Jangde R. Microsponges for colon targeted drug delivery system, An overview. *Asian J Pharm Tech*, 1(4), 2011, 89.
39. Jain N, Kumar Pramod Sharma, Banik Arunabha. Recent advances on microsponges delivery system. *International journal of Pharmaceutical Sciences Review and Research*, 8(2), 2011, 16.
40. Jain V, Singh R. Dicyclomine-loaded Eudragit-based Microspongewith Potential for Colonic Delivery, Preparation and Characterization. *Tropical Journal of Pharmaceutical Research*, 9(1), 2010, 67-72.
41. Bhumika Sharma, Arvind Sharma. Future prospect of nanotechnology in development of anti-ageing formulations. Int J Pharm Pharm Sci, 4(3), 2012, 57-66.
42. Rekha U, Manjula BP. Formulation and evaluation of microsponges for topical drug delivery of mometasone furoate. Int J Pharm Pharm Sci, 3(4), 2010, 133-137.
43. D'souza JI, The Microsponge Drug Delivery System: For Delivering an Active Ingredient by Controlled Time Release. Pharma. info.net, 2008, 6 (3): 62.
44. Sarat C. P. M., Ajay M., Nagendra B.B., Prathyusha P., Audinarayana N., Bhaskar R.K.Microsponge Drug Delivery System . A Review. J. Pharm. Res.2011; 4(5): 1381-1384.
45. D'souza JI. In-vitro Antibacterial and Skin Irritation Studies of Microsponges of Benzoyl Peroxide. Indian Drugs. 2001, 38(7): 23.
46. Wester R., Patel R., Natch S., Leyden J., Melendres J., Maibach H., Controlled release of benzoyl peroxide from aporous microsphere polymeric system can reduce topical irritancy, J. Am. Acad. Derm., 1991, 24, 720-726.
47. 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, 200428.
48. Trotta F, Cavalli R, Tumiatti W. Cyclodextrin-based nanosponges for drugdelivery. J Inc Phenom Macro cyclic Chem. 2006; 56:209-13.

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