Review Article **CODEN: IJPRNK** **ISSN: 2277-8713**
Upadhye Shashikant, IJPRBS, 2016; Volume 5(1): 152-166 **IJPRBS**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

A REVIEW ON MICROSPONGE DRUG DELIVERY SYSTEM

UPADHYE SHASHIKANT S., KOTHALI B.K., APTE A.K., PATIL A.A., DANOLE A.B.

Lecturer at Dr. J.J. Magdum Pharmacy College Jaysingpur, Tal- Shirol, Dist- Kolhapur, Pin-416101, Maharashtra, India

Accepted Date: 21/02/2016; Published Date: 27/02/2016

Abstract: The microsponges are polymeric delivery system composed of porous microspheres. They are tiny sponge-like spherical particle with a large porous surface. To control the delivery rate of the active agents to the predetermined site in the human body has been one of the biggest challenges faced by drug industry. The microsponge drug delivery technology holds a great promise for reaching the goal of controlled and site-specific drug delivery and hence, has attracted wide attention of researchers. Microsponges are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance stability, reduce side effects, and modify drug release profiles. MDS technology is being used currently in cosmetics, over the counter [OTC] skin care, sunscreens products. The present review focuses on different methods of preparation of microsponges, its release mechanisms, physical characterization of microsponges, applications of microsponges.

Keywords: Microsponge, Porous, over the counter

.

PAPER-QR CODE

Corresponding Author: MR. UPADHYE SHASHIKANT S.

Access Online On:

www.ijprbs.com

How to Cite This Article:

Upadhye Shashikant, IJPRBS, 2016; Volume 5(1): 152-166

INTRODUCTION

The Microsponges are the highly cross-linked, porous, patented, polymeric microspheres that acquire the flexibility to entrap the wide variety of the active ingredients that are mostly used for the prolonged topical administration & recently for the oral administration. On the outer layer of the skin the conventional topical preparations are supposed to work. These preparations release their active ingredient which produces the accumulation of drug that is rapidly absorbed on application. The application of the topical preparations suffers from several problems such as the ointments which are greasy & sticky in nature & also are aesthetically unappealing, which results into the lack of patient compliance. The topical preparations also have other drawbacks like the unpleasant odor, uncontrolled evaporation of the active ingredient & incompatibility of drugs with the vehicle. Hence, for the effective therapy these types of formulations high amount of active ingredient is required because of their low efficiency of the delivery system which results into the irritation & allergic reactions. Therefore there exists the need of such delivery system which can overcome these problems & thus microsponge delivery system can be used in this case. Microsponges are uniform, micro-porous polymeric beads, tiny & spherical in shape. It has the interconnected voids of the particle size ranges between 5-300µ. The microsponges have the network of pores which holds a active ingredient to provide the controlled release of it. The Micro-sponge polymers possess a versatility to load the wide range of the actives providing the benefits of enhanced product efficacy, tolerability, mildness & extended wear to the wide range of the skin therapies. The active ingredient is released in the controlled manner due to the porous surface of non-collapsible structure. The microsponge system has the high degree of the cross linking which results in the particle that is insoluble, inert & of the sufficient strength to withstand the high shear.

The microsponge delivery system is designed:

1] To enhance the stability,

2] To reduce side effects.

3] To deliver a pharmaceutically active ingredient efficiently at minimum dose,

4] To modify drug release profile,

The Microsponges are capable of absorbing the skin secretions which reduces the oiliness from the skin. It has the ability to load the wide range of the actives which provides the benefit of the enhanced product efficiency, mildness, tolerability etc. These microsponges are then further incorporated in to the formulations like lotions, gels, powder, ointments & creams. [1,2]

Advantages Of Microsponges over Conventional Formulations:

The conventional formulations of the topical drugs are intended to work on the outer layers of the skin. By producing the highly concentrated layer of the active ingredient that is rapidly absorbed, such products release their active ingredients upon application. When compared the microsponge system can prevent the excessive accumulation of the ingredients within the epidermis & the dermis. Potentially, the Microsponge system can significantly reduce the irritation of effective drugs without reducing their efficacy. For eg: By delivering the active ingredient gradually to the skin like MDS the Benzoyl peroxide formulations have the excellent efficacy with minimal irritation

Advantages of Microsponges over Microencapsulation and Liposomes:

The MDS has the advantages over the other technologies like the microencapsulation & liposomes. The Microcapsules cannot usually control the release rate of the actives. The actives contained within microcapsules will be released, once the wall is ruptured. The Liposomes suffer from the lower payload, limited chemical stability and microbial instability, difficult formulation. While the microsponge system in contrast to the above systems are stable over the range of pH 1 - 11, the temperature up to 130 ^{0}C, compatible with most of the vehicles & ingredients, self sterilizing as the average pore size is 0.25 µm where the bacteria cannot penetrate, higher payload [50 - 60%] still the free flowing & can be cost effective. [3-6]

Characteristics of materials that are entrapped in the Microsponges:

The Most liquids or the soluble ingredients can be entrapped in the particles. The Actives that can be entrapped in the microsponges must meet following requirements,

a] It should be inert to monomers.

b] It should be water immiscible or at most only slightly soluble.

c] It should be stable in contact with polymerization catalyst and conditions of polymerization.

d] It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent. [7]

Potential features /Characteristics of Microsponges:

i] Microsponge formulations have higher payload [50 to 60%], still free flowing and can be

cost effective.

ii]Microsponge formulations are compatible with most vehicles and ingredients;

iii] Microsponge formulations are stable at the temperature up to 130oC;

iv] Microsponge formulations are stable over range of pH 1 to 11;

v] Microsponge formulations are self sterilizing as their average pore size is 0.25µm where

bacteria cannot penetrate [8]

Polymers used in MDDS:

Various polymers can be used for the preparation of microsponge, such as the Polystyrene, Ethyl cellulose, PHEMA, Eudragit RS 100 & acrylic polymers etc.[9-10]

Methods of preparation of Microsponges:

Liquid-liquid suspension polymerization

By suspension polymerization method in the liquid-liquid system, the porous microspheres are prepared. The monomers which are immiscible are first dissolved along with the active ingredients in the suitable solvent monomer & then are dispersed in to aqueous phases which consist of the additives like the suspending agent, surfactant to facilitate the formation of the suspension, in this method. By increasing temperature or irradiation or by addition of catalyst, the polymerization is then activated. After the polymerization process the solvent is removed by leaving the spherical structure porous microspheres, that is microsponges [11-13]

Quasi-emulsion solvent diffusion

By the quasi-emulsion solvent diffusion method [Two-step process], the porous microsponges were also prepared, by using an internal phase containing polymer which is dissolved in the solvent. The drug is then slowly added to the polymer solution & dissolved under the ultra-sonication at 35^0C & plasticizer such as the TEC [triethylcitrate] was added in order to aid the plasticity. Into external phase containing polyvinyl alcohol and distilled water, the inner phase is then poured with continuous stirring for 2 hours. Further, the 11 mixture was filtered to separate the microsponges. Then the microsponges were washed & dried in the air-heated oven at 40^0C for 12 hours. [14-15]

Hypothetical mechanism of action of Microsponge

To the vehicle in an entrapped form, the active ingredient is added. The microsponge particles have an open structure [that is, they do not have a continuous membrane surrounding] the active is free to move in & out from the particles & into the vehicle until equilibrium is reached when the vehicle becomes saturated. 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, once the finished product is applied to the skin, This will start the flow of a active from the microsponge particle into a vehicle, & from it to the skin, until the vehicle is either dried or absorbed. Even after that the microsponge particles that are retained on the surface of the stratum corneum will continue to gradually release the active to the skin by providing the prolonged release over the time. This proposed mechanism of the action highlights the importance of the formulating vehicles for use with the microsponge entrapments. If the active is too soluble in the desired vehicle during the compounding of the finished products the products will not provide the desired benefits of the gradual release. Instead of, they will behave as if the active was added to the vehicle in the free form. Hence, while formulating the microsponge entrapments it is important to design the vehicle that has the minimal solubilizing power for the actives. This principle is contrary to the conventional formulation principles usually applied to the topical products. For this conventional system it is normally recommended to maximize the solubility of the active in to the vehicle [16-17]

RELEASE MECHANISMS

The Microsponges can be designed to release the given amount of the active ingredients over the time in response to one or more external triggers.

I] Temperature change

Some of the entrapped actives can be too viscous at the room temperature to flow spontaneously from the microsponges onto the skin. The increase in skin temperature can result in the increased flow rate & hence release. For eg, the viscous sunscreens were found to show the higher release from the microsponges when exposed to the higher temperatures, thus the sunscreen would be released from the microsponge only upon exposure to the heat from the sun.

II] Pressure

The Microsponge system releases the entrapped material by rubbing or by applying pressure can release active ingredient from the microsponges onto the skin. The amount released

depends upon the various characteristics of the sponge. By varying different process variables & the type of material the microsponge is best suited for the given application may be optimized. When compared with the mineral oil containing microcapsules the mineral oil containing microsponge showed much more softening effect. The duration of the emolliency was also much more for the microsponge systems.

III] PH triggered systems

By triggering the pH-based release of the active can be achieved by modifying a coating on the microsponge. It has many applications in the drug delivery.

IV] Solubility

The microsponges loaded with the water-soluble ingredients like the anti-prespirants & antiseptics will release the ingredient in presence of the water. The release can also be activated by diffusion taking into the consideration that the partition coefficient of the ingredient between the microsponges & the outside system. The sustained release microsponges can also be developed. The various factors that are to be considered during development of such formulations includes the physical & chemical properties of the entrapped actives. The physical properties of microsponge system like the pore volume, pore diameter, resiliency etc. The properties of the vehicle in which the microsponges are finally dispersed. The pore characteristics, particle size, resiliency & monomer compositions can be considered as programmable parameters & microsponges can be designed to release the given amount of the actives in response to the one or more external triggers like, temperature, pressure & solubility of the actives. [3,18-20]

PHYSICAL CHARACTERIZATION OF MICROSPONGES

I] The Morphology & surface topography of microsponges: For the morphology & surface topography the prepared microsponges can be coated with the gold–palladium under an argon atmosphere at the room temperature & then the surface morphology of the microsponges can be studied by the SEM [Scanning Electron Microscopy]. The SEM of the fractured microsponge particle can also be taken to illustrate its ultra structure.

II] The Determination of true density: By using an ultra-pycnometer under helium gas & is calculated from the mean of repeated determinations, the true density of microparticles is measured.

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

IV] The Determination of loading efficiency & production yield: The loading efficiency [%] of the microsponges can be calculated according to this following equation:

$$\text{Loading Efficiency} = \frac{\text{Actual drug Content in Microsponges}}{\text{Theoretical Drug Content}} \times 100 \quad \ldots\ldots 1$$

The production yield of the microparticles can be determined by calculating the accurate initial weight of the raw materials & the last weight of the microsponge obtained.

$$\text{Production Yield} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical mass [Polymer + Drug]}} \times 100 \quad \ldots\ldots 2$$

V] The Dissolution tests: By use of dissolution apparatus USP XXIII with a modified basket consisted of 5µm stainless steel mesh, the dissolution profile of the microsponges can be studied. The rotation speed is 150 rpm. The dissolution medium is selected while considering the solubility of the actives to ensure the sink conditions. The samples from the dissolution medium can be analysed by the suitable analytical method at various intervals.

VI] The Compatibility studies: By TLC [Thin layer chromatography] & FT-IR [Fourier Transform Infra-red spectroscopy] the compatibility of drug with reaction adjuncts can be studied. The effect of polymerization on the crystallinity of the drug can be studied by the powder X-ray diffraction [XRD] & DSC [Differential Scanning Colorimetry]. For the DSC approximately the 5mg samples can be accurately weighed into the aluminum pans & sealed & can be run at the heating rate of the 15^{o}C/min over a temperature range 25–430^{o}C in atmosphere of nitrogen.

VII] The Release evaluations: The Release mechanism of microsponges. The release can be controlled through the diffusion or the other triggers such as the pH, moisture, temperature

friction. This release technology is available for the absorbent materials or to enhance the product aesthetics. The Microsponge delivery sys-tem can be incorporated into the conventional dosage forms such as lotions, ointments, powder creams, gels, & share the broad package of the benefits. The system can improve its formulation flexibility.

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

IX] The Polymer/monomer composition: Various factors such as the drug loading, microsphere size, polymer composition govern the release of drug from the microspheres. The polymer composition of the MDS can affect the partition coefficient of the entrapped drug between the vehicle & the microsponge system & hence has the direct influence on the release rate of entrapped drug. The release of drug from the microsponge systems of different polymer compositions can be studied by plotting the cumulative % drug release against the time.[1,6,21-22]

APPLICATIONS OF MICROSPONGES

The Microsponge delivery systems are used to enhance the effectiveness, safety, aesthetic quality of the topical prescription, personal care products & the over-the-counter products. The Microsponges can be used in the variety of the applications. Mostly it is used for the topical & recently for the oral administration. There are several patents that have been reported that it can be used as an excipient due to its high loading capacity & also sustained release ability. It offers the formulator the range of alternatives to develop the drug & the cosmetic products. The microsponges are designed to deliver the pharmaceutical active ingredient efficiently at the minimum dose & also to enhance the stability to reduce the side effects & modify the drug release. The Over-the-counter products that incorporate the microsponge drug delivery system include the specialized rejuvenated products, sunscreens & numerous moisturizers.

A]. The Microsponge for topical delivery

The Microsponge system is based on the microscopic, polymer-based microspheres that can suspend, bind or entrap the wide variety of the substances & then be incorporated into the formulated product, such as the powder, gel, liquid, cream. The single microsponge is as tiny as the particle of the talcum powder which is measuring less than one-thousandth of an inch in the diameter. Like the true sponge each microsphere consists of the myriad of the interconnecting voids within the non-collapsible structure that can accept the wide variety of the substances. The outer surface is typically porous, allowing a controlled flow of the substances into & out of the sphere. The several primary characteristics or the parameters of the microsponge system can be defined during the production phase to obtain the spheres that are tailored to the specific product applications & vehicle compatibility. The microsponge systems are made of the biologically inert polymers. The extensive safety studies have demonstrated that the polymers are non- mutagenic, non-toxic non-irritating, non-biodegradable & non-allergenic. As a result the human body cannot convert them into the other substances or break them down. Although they are microscopic in size, these systems are too large to pass through a stratum corneum when incorporated into the topical products. The BPO [Benzoyl peroxide] is commonly used in the topical formulations for the treatment of the acne, with skin irritation as the common side effect. It has been shown that controlled release of the benzyl peroxide from the delivery system to the skin could reduce the side effect while reducing the percutaneous absorption. Therefore the microsponge delivery of the BPO was developed using an emulsion solvent diffusion method by adding an organic internal phase containing the benzoyl peroxide, ethyl cellulose & dichloromethane into the stirred aqueous phase containing the polyvinyl alcohol & by suspension polymerization of the styrene & divinyl benzene. The prepared microsponges were dispersed in to the gel base & microsponge gels are evaluated for the anti-bacterial & skin irritancy. The entrapped system released the drug at the slower rate than the system containing the free benzyl peroxide. The topical delivery system with reduced irritancy was developed successfully.

2. The Microsponge for oral delivery

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, in oral applications. As these pores are very small the drug is in effect reduced to the microscopic particles & the significant increase in the surface area, hence greatly increases the rate of the solubilisation. The controlled oral delivery of the ibuprofen microsponges is achieved with an acrylic polymer, Eudragit RS, by changing their intraparticle density. The sustained release formulation of the chlorpheniramine maleate, by using the powder-coated microsponges are prepared by the dry

impact blending method for the oral drug delivery. The controlled oral delivery of the ketoprofen which is prepared by the quasi-emulsion solvent diffusion method by using Eudragit RS 100 & afterwards the tablets of the microsponges were prepared by the method of direct compression. The results indicated that the compressibility was much improved in the physical mixture of the polymer & drug, due to the plastic deformation of a sponge-like microsponge structure that produces the mechanically strong tablets. The colon-specific, controlled delivery of the flurbiprofen was conducted by using the commercial Microsponge 5640 system. The in-vitro studies exhibited that the compression-coated colon-specific tablet formulations started to

release the drug at the 8 th hour corresponding to the proximal colon arrival time due to the addition of the enzyme by following the modified release pattern while the drug release from the colon-specific formulations prepared by the pore plugging the microsponges showed an increase at the 8 th hour, which was the point of time when the addition of enzyme was made.

3. The Microsponge for Bone & Tissue Engineering Bone-substitute

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 compounds were obtained. The final composites appeared to be the porous & acted as the microsponges. The Basic fibroblast growth factor [bFGF] incorporated in the collagen sponge sheet was sustained released in a mouse sub-cutis according to the biodegradation of the sponge matrix & exhibited the local angiogenic activity in the dose-dependent manner. The injection of the collagen microsponges by incorporating the bFGF induced the significant increase in the blood flow in the murine ischemic hind limb which could never have been attained by a bolus injection of the bFGF. These results suggest that the significance & therapeutic utility of the type I collagen as the reservoirs of the Basic fibroblast growth factor [bFGF] [1, 23-30]

Table No-1: Marketed Products based on Microsponge Drug Delivery System [1,31-32]

PRODUCT NAME	MANUFACTURER	ADVANTAGES
Retinol cream	Biomedic	The retinol molecule is kept in the microsponge system to protect the potency of vitamin A. This helps to maximize the retinol dosage, while reducing the possibility of irritation. Retinol is a topical vitamin A derivative, which helps

		maintain healthy skin, hair, and mucous membranes.
EpiQuin micro	Skin Medica Inc	The Microsponge® system entrap hydroquinone and retinol. The microsponges release these ingredients into the skin gradually throughout the day, which may minimize skin irritation
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+8 dimethacrylate cross-polymer porous microspheres.
Oil control lotion	Fountain Cosmetics	Feature-light lotion microsponges that absorb oil on the skin's surface during the day, for a matte finish.Eliminate shine for hours with this feature-weight lotion. The natural-antibiotic Skin Response Complex soothes inflammation and tightness to promote healing, Acne-Prone, oily skin conditions
Ultra guard	Scott Paper	Microsponge system that contains dimethicone to help protect a baby's skin from diaper rash
Micro peel plus	Biomedic	The MicroPeel® Plus,stimulates cell turnover through the application of salicylic acid in the form of microcrystals using Microsponge® technology.The MicroPeel® Plus aggressively outperforms other superficial chemical peels by freeing the skin of all dead cells, while doing no damage to the skin.

Sports cream RS and XS	Embil Pharmaceutical.	Topical analgesic-anti-inflammatory and counterirritant actives in a Microsponge® Delivery System (MDS) for the management of musculoskeletal conditions

CONCLUSION

Over the conventional topical drug delivery, the Microsponge drug delivery system is advantageous due to the properties like, simple ingredients, ease manufacturing & wide range of drugs that can be entrapped. For the topical delivery of drugs like anti-acne, anti-inflammatory, anti-fungal, anti-dandruffs, antipruritics, rubefacients etc, the microsponge drug delivery system is originally developed. The microsponge drug delivery have the hopeful prospect in the various pharmaceutical applications in the coming years by the virtue of their exclusive properties like elegancy , efficient carrier characteristics ,small size, enhanced product performance & the extended release, reduced irritation, improved physical, chemical & thermal stability so flexible to develop the novel product forms. The microsponge delivery system can further be incorporated into the conventional dosage forms such as the lotions, ointments, creams, powder & gels. Hence the microsponges represent the promising approach for the controlled drugs delivery.

REFERENCES

1. D'souza JI. The Microsponge Drug Delivery System: For Delivering an Active Ingredient. Controlled Time Release 2008; 6(3): 62.

2. Shaha V, Jainl H, Krishnal J, Patel P, Microsponge drug delivery: A Review. Int. J. Res. Pharm. Sci, 2010; 1(2): 212-218.

3. Jelvehgari M, Siahi-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.

4. Tansel C., Baykara T. The effects of pressure and direct compression on tabletting of microsponges. Int. J. Pharm. 2002;242:191–95.

5. Ruckenstein E, Hong L. Concentrated emulsion polymerization pathway to hydrophobic And hydrophilic Microsponge molecular reservoirs. Chem. Mater. 1992;4:1032-1037.

6. Chadawar V, Shaji J. Microsponge delivery system. Current Drug Delivery 2007;4:123-129.

7. Cevher E and Araman A, "Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges." Int J Pharm 318 (2006) 103-113.

8. D'souza JI, Masvekar RR, Pattekari PP, Pudi SR and More HN. Microspongic delivery of

fluconazole for topical application. Indo-Japanese Int. Conference on Adv. Pharm. Res. and

Tech., 2004: 76.

9. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Control of Prolonged Drug Release and Compression Properties of Ibuprofen Microsponges with Acrylic Polymer, Eudragit RS, by Changing Their Intraparticle Porosity. Chemical & pharmaceutical bulletin 1992, vol.40(1),196-201.

10. Grimes PE: A microsponge formulation of hydroquinone 4% and retinol 0.15% in the treatment of melasma and post inflammatory hyper-pigmentation. Cutis, Vitiligo and Pigmentation Institute of Southern California, Los Angeles, Vol. 74(6), 2004,362-368.

11. Nanda S; Kaur M; Sood N; Nagpal S; Microsponge drug delivery system: an overview; World Journal of Pharmacy and Pharmaceutical Science; 2013; 2(3): 1032-1043.

12. Brunton LL; Lazo J S; Parker K L; Goodman and Gilman's "The Pharmacological Basis of Therapeutics". 2006; 11th Edition; 1021

13. Vyas SP; Khar RK; Targeted and Controlled Drug Delivery-Novel Carrier System; New Delhi; CBS Publication: 453. 2002

14. Tansel Cl; Preparation and in-vitro evaluation of modified release ketoprofen microsponge; II Farmaco; 2003; 58: 101-106.

15. Jain N; Sharma PK; Banik A; Recent advance on microsponge delivery system; International Journal of Pharmaceutical Science Review and Research; 2011; 8(2): 13-23

16. Kaity S; et.al, Microsponge: A novel strategy for drug delivery system; J Adv Pharm Technol Res; 2010; 1(3): 90-283.

17. Jadhav N; Patel V; Mungekar S; Karpe M; Kadam V; Microsponge delivery system: an update review, current status and future prospects; world Journal of Pharmacy and Pharmaceutical Science; 2013; 2(6): 6463-6485.

18. Christensen MS, Natch SJ. Invest. Dermato, 1983; 69:282.

19. Sato T, Kanke M, Schroeder G, Deluca P: Porous biodegradable microspheres for controlled drug delivery, Assessment of processing conditions and solvent removal techniques, Pharm Res. 1988; 5:21-30.

20. Guyot M. and Fawaz F: Microspheres- Preparation and physical characteristics, Int J Pharma 1998; 175:61-74.

21. Shyam S. M., Vedavathi T. Novel approach: microsponge drug delivery system. Int. J. Pharm. Sci.Res.vol. 3(4), 2012, 967-980.

22. Martin A, Swarbrick J, Cammarrata A. In: Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences, 1991; 3,527.

23. 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.

24. D'souza JI, In-vitro Antibacterial and Skin Irritation Studies of Microsponges of Benzoyl Peroxide, Indian Drugs. 2001, 38(7): 23.

25. 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.

26. 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.

27. Jain V., Singh R., Dicyclomine-loaded Eudragit based microsponge with potential for colonic delivery Preparation and characterization. Tropical Journal of Pharmaceutical Research, 9(1): 67-72, (2010).

28. 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.

29. Shaheen S Z, Bolla K, Vasu K & Singara C M A. Antimicrobial activity of the fruit extracts of Coccinia indica, African Journal of Biotechnology Vol. 8(24) (2009), 7073-707.

30. Park W H, Lee S J and Moon H I. Antimalarial Activity of a New Stilbene Glycoside from Parthenocissus tricuspidata in Mice, Antimicrobial Agents and Chemotherapy. 52(9) (2008): 3451–3453.

31. Rossi S, editor; Australian Medicines Handbook 2006, Adelaide; Australian Medicines Handbook; 2006.

32. Baselt R. Disposition of Toxic Drugs and Chemicals in Man, 8th edition, Biomedical Publications, Foster City, CA, 2008, 29-31.