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TOPICAL MICROSPONGE GEL

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ABSTRACT
Number of semisolid dosage forms that are used for topical applications among which gels formulations are becoming pre-eminent. The basic network of gel is a combination of a gelling agent and a solvent in which the drug molecules are embedded or entwined evenly. The nature transdermal drug delivery system (TDDS) developed for systemic delivery of drugs using the skin as portal of entry. But TDDS is not practicable for delivery of materials whose final target is skin itself. circulation in significant amounts is an area of research. Mainly drug is entrapped in polymer they act as carriers for drug and show their pharmacological action In This review article discusses Genral replaced with general way how to formulate and development the microsponge gel analysis of mircosponge via DSC, SEM and FTIR, formulation and evaluation of topical microsponge gel. Different method is replaced with by novel method. And finally which parameter used for validation of dosage form.

KEYWORD: Microsponge gel, Transdermal delivery systems, Replace with characterization.

INTRODUCTION

Topical preparations are used for the localized effects at the site of their application by Chasity of drug insight into the rudimentary stratum of skin or mucous membranes or tissue layer. The main advantage of topical delivery system is to bypass first pass metamorphosis.

The topical drug delivery system is generally used where the other system of drug administration flushes it or it is mainly used in pain management, contraception, and urinary incontinence. Topical drug delivery can be specified as the diligence of a drug incorporate formulation to the skin to directly treat dermal disorders (e.g. Acne) or the cutaneous manifestations of a general disease (e.g. Psoriasis) with the intent of confining the pharmacological or other effect of the drug to the surface of the skin or within the skin. Micro sponges are tiny, sponge like spherical particles that consist of a innumerous of interlinking voids within a non-collapsible structure with a large porous surface. Micro sponges consist of non-collapsible structures with a porous surface through which active ingredients are released in a controlled manner depending upon the size.[1]

MICROSPONGE DRUG DELIVERY SYSTEM

The micro sponge technique was grown by Won in 1987, and the original patents were specified to get on Polymer Systems. Micro sponges are porous microspheres having a myriad of unified voids of particle size, embed between 5-300 μm.[4] These micro sponges have capacitance to snare broad range of active ingredients such as emollients, fragrances, essential oils, sunscreens, and anti-infective, anti-fungal and anti-inflammatory agents etc. and are applied as a topical carrier system. Further, these porous microspheres with active ingredients can be compressed into formulations such as creams, gel, lotions and powders and portion extensive package of welfare. Micro sponges consist of non-collapsible structures with a porous airfoil through which active ingredients are liberated in a controlled manner. Depending upon the size.

Micro sponges have the content to Adsorb or load a high degree of active materials into the particle or onto its surface. Its large capacity for entrapment of actives up to 3 times its weight differentiates micro sponges from other types of dermatological delivery systems. Recently, the micro sponge delivery system has been successively addressed for the controlled release of drugs onto the epidermis with assurance that the drug remains chiefly localized and does not enter the systemic circulation in major amounts and circulation in major amounts and resulted in a new creation of highly efficacious and easily tolerated novel products.[3]

Micro sponges for Topical Delivery

The ability of a drug in a topical formulation to permeate the skin and to exert its effect is dependent on two consecutive events. The drug must first diffuse out of the vehicle to the skin surface and then it must permeate

through barrier to the site of action. Both steps are dependent upon the physicochemical properties of the drug; vehicle and barrier. The stratum corneum provides the principal barrier to the percutaneous permeation of topically applied substances.[20]

Objective of the study

- Delivery of drug through topical formulation with the intention overcoming its GI side effect.
- To prepare and evaluate drug with micro sponge using as a polymer.
- To validate the process for various process parameters.
- To study in vitro drug release and permeability study of micro sponge incorporated into gel formulation.

Advantages of topical drug delivery system

- TDS avoid first pass metabolism
- It is convenient and easy to apply
- Achievement of efficacy with lower total daily dosage of drug by continuous drug input.
- Avoid Fluctuation in the drug levels, inter-and intrapatient variations
- Ability to easily terminate medication, when need

Disadvantage of topical drug delivery system

1. Some drugs are poorly permeable through skin.
2. Possibility of allergenic reaction.
3. Drugs which have large particle size not easy to absorb through skin.
4. Enzyme in epidermis may denature the drugs.
5. TDS can be used for drugs which require very small plasma concentration for action.

Classification of Topical drug Delivery

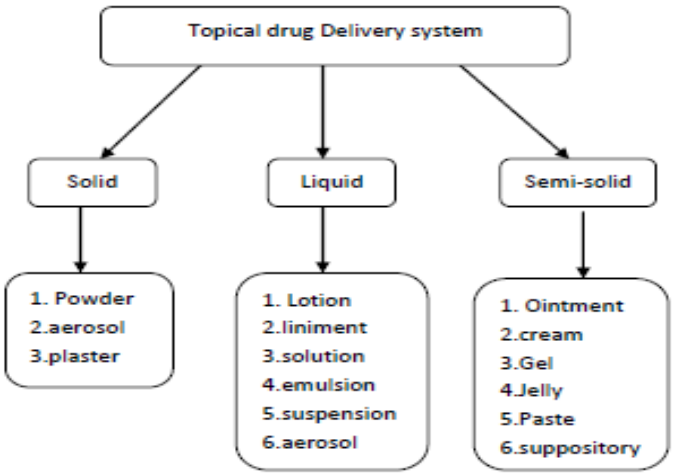

Figure 1: Flowchart of classification of the topical drugs.

STRUCTURE OF GELS

A gel consists of a natural or synthetic polymer forming a three dimensional matrix throughout a dispersion medium or hydrophilic liquid. After application, the liquid evaporates leaving the drug entrapped in a thin film of the gel – forming matrix physically covering the skin. The presence of a network formed by the interlocking of particles of the gelling agent gives rise to the rigidity of a gel. The nature of the particles and the type of form that is responsible for the linkages determine the structure of the network and the property of the gel.[1,8]

Benefits of Micro sponge Technology

Micro sponge technology offers:

- Enhanced product performance.
- Extended release.
- Reduced irritation and hence improved patient compliance.
- Improved product elegancy.
- Improved oil control as it can absorb oil up to 6 times its weight without drying.
- Improved formulation flexibility.
- Improved thermal, physical, and chemical stability.
- Flexibility to develop novel product forms.
- In contrast to other technologies like microencapsulation and liposome's, MDS has wide range of chemical stability, higher payload and are easy to formulate.
- Micro sponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.[20,21,22]

Method of preparation microsponge gel

Liquid-Liquid suspension polymerization

Inward this method of polymerization the monomer is dismissed on with the API in a desirable dissolving agent and so on summed in aqueous stage bearing additives, i.e. surfactant, suspending agents, etc. The polymerization is then novice by sum catalyst or by increasing temperature or irritation. Polymerization of

styrene or methyl methacrylate is ran out in circular bottom flask. A solution of non polar drug is made in the monomer, to which aqueous phase, ordinarily with surfactant and dispersant to further suspension is incorporated. Polymerization is effected, once suspension with the distinct droplets of the coveted size is launched, activating the monomers either by catalysis or increased temperature.(Reaction vessel shown in fig.) if the drug is sensitive to the polymerization conditions, two step process is used. The polymerization is executed utilization replacement porogen and is substituted by the functional substance under mild data based conditions.

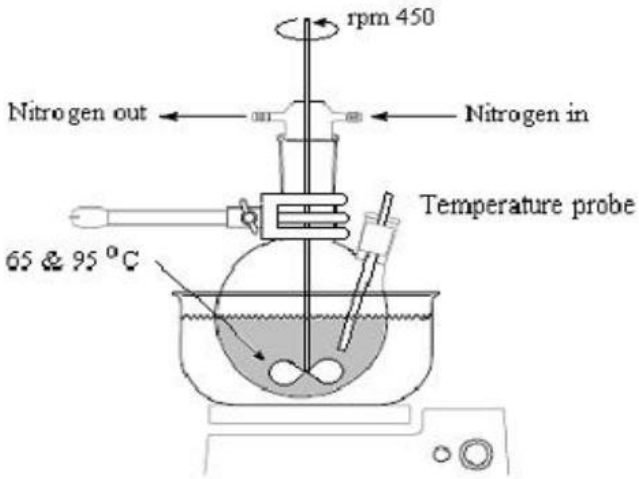

Figure 2: Reaction vessel for preparation of micro sponge by liquid – liquid suspension polymerization.

The various steps in the preparation of micro sponges are summarized as follows

- choice of monomer or compounding of the monomer.
- shaping of concatation monomer as polymerization begins.
- Formation of monomer ladder as result of cross linkage between chain monomer.
- Closing up of monomer ladder to form circular particles00.
- Agglomeration of microsphere lead to constitute of a cluster of the microsphere Binding of bunches lead to the formation of micro sponge.

2 Quasi-emulsion solvent diffusion

Micro sponges were prepared by quasi emulsion solvent diffusion method. Inward this method the internal stage consists of suitable polymer fadded out in an organic solvent then added as plasticizer and followed by the addition of API Below ultra-sonication at 35^0C for 15 min. The internal phase was then swarmed into the exteraneous phase after one hour of scarmonger by mechanical stirrer at a rate of 500 rotations per minute (rpm); the microsponges were shaped referable to the remotion of organic solvent from the scheme. The microsponges were separate out and dehydrate at 40°C for nightlong. The fictional microsponge was assessed for production yield, charging efficiency, particle size and, FTIR, differential scanning calorimetry, and scanning electron microscopy.[15]

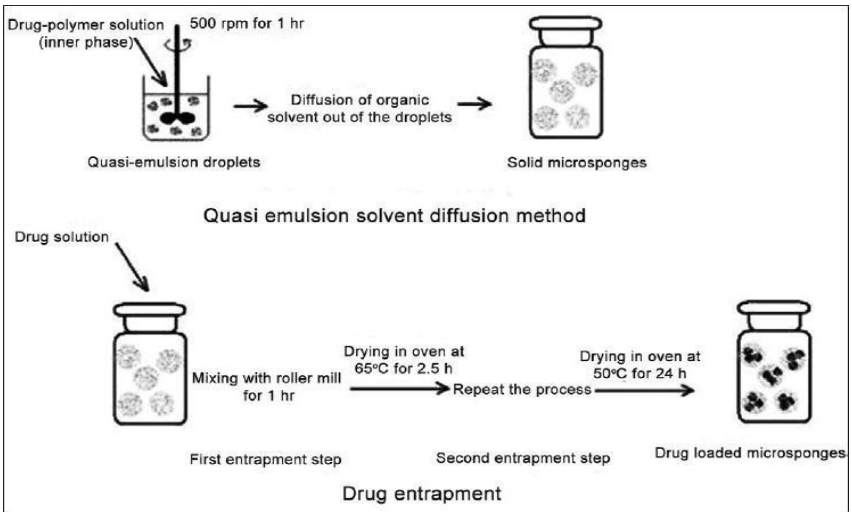

Figure 3: Quasi-emulsion solvent diffusion method.

GELS AS PHARMACEUTICAL DOSAGE FORM

The term 'Gel' was innovates in the recent 1800 to name about semisolid material granting to their physiological property rather than molecular composition.

The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. Gels are a substantially dilute cross-linked system, which show no flow when in the steady-state. They consist of a two component semi-solid system rich in liquid. Their one characteristic feature is the presence of continuous structure providing solid like properties. Gels have become a premier materials used for drug delivery formulations due to its biocompatibility, network structure, and molecular stability of the incorporated bioactive agent.[23,24]

Method of preparation of micro sponges

The microspoges was set up by quasi emulsion solvent diffusion method. It is two tread process methods. In first tread, internal phase was organized by dissolving the polymer in suitable solvent then the drug was incorporated into the solution of polymer and dissolved under ultrasonication at 35°C for 15 min. The outer phase was set up by dissolving the into the distilled water and the procedure was carried out at room temperature. The inner phase was then poured into the outer phase drop wise and the mixture was continuously stirred using mechanical stirrer at 1000 rpm for 2hr after the shaping of micro sponges the mixture was strained to separate the drug loaded micro sponge. The product was Rinsed and dried in oven at 40°C.[4,15]

CHARACTERIZATION OF MICROSPONGES[19]

- **Particle size determination**

Charged and uncharged partical size of analysis microsponges can be done by laser light diffractometry or any other worthy method. The values can be explicit for whole formulations as base size scope. Cumulative percentage drug passing from microsponges of dissimilar particle size will be plotted opposite time to survey event of particle size on drug release. Particles greater than 30µm can transmit granules tone and therefore particles of sizes betwixit 10 and 25µm are preferred to use in terminal topical formulation.

- **Morphology and surface topography of microsponges**

For morphology and surface topography, prepared micro sponges 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 micro sponge particle can also be taken to illustrated is ultra structure.

- **Determination of loading efficiency and production yield**

The loading efficiency (%) of the micro sponges can be calculated according to the following equation

Production yield = final obtained mass of micro sponges × 100

Initial mass of polymer and drug

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 micro sponge obtained.

- **Compatibility studies**

Compatibility of drug with reaction accessory 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 Calorimetry (DSC). For DSC approximately 5mg 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)**

Resiliency (viscoelastic properties) of micro sponges 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.

- **Kinetics of release**

To determine the drug release mechanism and to compare the release profile differences among micro sponges, the drug released amount versus time.

IDENTIFICATION AND CHARACTERIZATION OF DRUG

- Description
- Melting point
- Solubility
- Ultraviolet spectrum
- (FTIR) studies
- Particle size analysis[19]

CHARACHTERIZATION OF GEL

- **Calibration of eye piece micrometer**

One division of stage micro meter = 10µm

C = (SM X 100) / EM ..... Equation no (1)

Where, C = correction factor

SM = reading of stage micro meter which coincides with reading of occulo meter

The average particle size was determined using the equation

D (mean) = Σnd / Σn .... Equation no (2)

Where,

n = no of microsponge observed,

D = mean size range

- **Production yield**

The production yield of microsponge was determined by calculating accurately the initial weight of raw material and the last weight of microsponge obtained after drying.
Production yield = final obtained mass of micro sponges × 100
Initial mass of polymer and drug.

- **Theoretical drug content**

Drug content was determined by calculating assuming that the entire API present in the polymer solution used gets entrapped in API microsponges, and no loss occurs at any stage of preparation of API microsponge.

- **Practical drug content**

Drug content was done by following procedure. Weighed amount of API microsponges equivalent to quantity of the API was dissolved in suitable solvent. The solution was Shake continuously for complete dissolution of API in dich solution was filtered and further diluted to make a solution. The absorbance of solution was measured at maximum absorbance using blank and calculated for the percent of drug present on the sample.

- **Scanning electron microscope (SEM)**

Scanning electron microscopy has been used to determined particle size distribution. Surface topography, texture, and to examine the morphology of fractured or sectioned surface. SEM is probably the most commonly used method for characterizing the drug delivery system. Owing in the large simplicity of sample preparation and ease of operation. SEM studies uses scanning electron microscope. Dry API were placed on an electron microscope brass stub and coated with platinum coating. Picture of API microsponge were taken by random scanning of the stub.

- **Differential scanning calorimetry (DSC)**

Thermogram of API micro sponge formulation was obtained using differential scanning calorimeter outfitted with an intercooler. Indium standard was implied for calibrating DSC enthalpy and temperature scale. Microsponge samples were kept in aluminium pan hermetically and heated at constant rate .

EVALUATION OF MICROSPONGE GEL[17,21]

- Visual inspection
- PH measurement
- Spreadibility studies
- Tube extrudability
- Viscosity measurement:
- In vitro drug release

VALIDATION OF PROCESS PARAMETERS[15]

- **VALIDATION**

The documented evidence of proving high degree of assurance that any procedure, process, equipment, material, activity or system actually leads to expected result.

- **PROCESS VALIDATION**

"Process validation is establishing documented evidence which provides a high degree of assurance that a specified process will consistently produce a product meeting its pre-determined specifications and quality characteristics.

Process validation is both us FDA or U.S requirement. Similar requirements are included in the world health organization (WHO), the pharmaceutical inspection co-operation scheme and the European Union (EU) requirements along with those of Australia, Canada, Japan and other international authorities.

Reason for Process Validation

The possible reason of performing process validation may include:

- New product or existing products as per SUPAC changes.
- Change in site of manufacturing.
- Change in batch size
- Change in equipment.
- Change in process existing products.
- Change in composition or components.
- Change in the critical control parameters.
- Change in vendor of API or critical excipients.
- Change in specification or input material.
- Abnormal trends in quality parameters, of product through review during annual product review.

Benefits of process validation

- Consistent through output
- Reduction in rejections and re work
- Reduction in utility cost
- Avoidance of capital expenditures.
- Reduced testing in process and finished goods.
- Easier maintenance of equipment.
- Improve employee awareness of processes.
- More rapid automation.

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REFERENCES

1. Ashni Verma, Sukhdev Singh, Rupinder Kaur, Upendra K Jain; Topical Gels as Drug Delivery Systems. Int. J. Pharm. Sci. Rev. Res., Nov – Dec 2013; 23(2): 60, 374-382.
2. Ansel HC, Popovich NG Loyd VA, Pharmaceutical Dosage Forms and Drug Delivery Systems, 9, B. I. Publications, New Delhi, 2005; 407-408.
3. Riyaz Ali Osmani, Nagesh H. Aloorkar, Ajit S. Kulkarni, Bhargav R. Harkare, Rohit R. Bhosale, A new cornucopia in topical drug delivery: micro sponge technology, Asian journal of pharmaceutical science andtechnology, 2014; 4: 48-60.

4. Vyas LK, Tapar KK, Laddha BH, Lahoti AO and Nema RK. Formulation and development of anti-blemish preparations using microsponge technology. J. Chem. Pharm. Research, 2010; 2(5): 562-571.
5. Uche DOV, Sol-gel technique: A veritable tool for crystal growth, Advances in applied science research, 2013; 4(1): 506-510.
6. Mohan kumar V, Veena NM, Manjula BP.; Formulation and Evaluation of Micro sponges For Topical Drug Delivery of Mupirocin, International Journal of PharmTech Research, July-Sept 2013; 5(3): 1434-1440.
7. Rekha. U, b. p. Manjula et al; Formulation and evaluation of micro sponges for topical drug delivery of mometasone furoate, International Journal of Pharmacy and Pharmaceutical Sciences, 23 July 2011; 3: 133- 137.
8. Rajendra Jangde, Micro sponges for colon targeted drug delivery system: An overview, Asian J. Pharm. Tech. year, 2011; 1(4): 87-93.
9. Lachman L, Lieberman H.A, kaning J.L., theory and practice of industrial pharmacy. 4th Indian edition, 1991, verghese publication house, 534-56.
10. Mithal B.M., and saha R.N., "A handbook of cosmetics" ,1st edition vallabh prakashan Delhi, 2003; 11-17, 21-22, 37-38, 61-89, 90-93, 177, 214-215.
11. Gupta p., Garg S., Recent advances in semisolid dosage form for dermatological application. Pharmaceutical technology, March 2002; 144-162.
12. Yerram Chandramouli1, Shaik Firoz1, R. Rary System, International Research Journal of Pharmaceutical and Biosciences, 24 Jan 2016.
13. Katkade Mayur1, Kalkotwar Ramesh2, Jain Nitin 1, Patil Prashant1, Gadakh Rajendra2, Naikwade Jeevan1, ethyl cellulose based microsponge delivery system for anti-fungal vaginal gels of tioconazole, international research journal of pharmacy, Oct 2011; 64 – 69.
14. Vyas SP, Khar RK, Targeted and controlled drug delivery- Novel carrier system: New Delhi: CBS publication, 2002, pages no 453-95.
15. 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, 2012; 5(1): 12.
16. Riyaz Ali M. Osmani, Nagesh H. Aloorkar, Dipti J. Ingale, Parthasarathi K. Kulkarni, Umme Hani, Rohit R. Bhosale, Dandasi Jayachandra Dev: Microsponge based novel drug delivery system for augmented arthritis therapy, Saudi pharmaceutical journal, 2015; 562-572.
17. Mahajan Aniruddha G, jagtap Leena S,Chaudhari Atul L, Mali Prabha R, Formulation and evaluation of microsponge drug delivery system using indomethacin, international research journal of pharmacy, 2011; 2(10): 64-69.
18. Karthika.R, Elango.K, Ramesh Kumar.K, Rahul.K, formulation and evaluation of lornoxicam microsponge tablets for the treatment of arthritis, international journal of pharmaceutical innovations, March ‒ April 2013; 3(2): 29-40.
19. Carter SJ, Disperse system In: Cooper and Gunn's Tutorial Pharmacy, 6, CBS Publishers and Distributors, New Delhi, 2000; 68-72.
20. Lieberman HA, Rieger MM, Banker GS, Pharmaceutical dosage form: Disperse system, 2, Marcel Dekker, New York, 2005; 399-421. (Charchterstic gel)
21. 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, 2011; 3(8): 170- 183.
22. Madhu Sharma, Baibhav Joshi. Microsponges: A comprehensive Review. The Global J Pharm Res, 2012; 1(3): 359-377.
23. Setty C.M., Babubhai S.R. and Pathan I.B., Development of valdecoxib topical gel, effect of formulation variables on the release of valdecoxib, International Journal of Pharmacy and Pharmaceutical Science, 2010; 2(1): 70-73.
24. Penzes T., Blazso G., Aigner Z., Falkay G. and Eros I., Topical absorption of piroxicam from organogels-invitro and invivo correlations, International Journal of Pharmaceutics, 2005; 298: 47-54.
25. Bhasha SA, Khalid SA, Duraivel S, Bhowmik D, Kumar KS, Recent trends in usage of polymers in the formulation of dermatological gels, Indian Journal of Research in Pharmacy and Biotechnology, 2013; 1(2): 161-168.
26. Thakur V, Prashar B, Arora S, Formulation and in vitro Evaluation of Gel for Topical Delivery of Antifungal Agent Fluconazole Using Different Penetration Enhancers, Drug Invention Today, 2012; 4(8): 414-419.