



Review Article

Microsponge: A Stable Microscopic Polymeric Delivery System

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ABSTRACT

Microsponge is polymeric delivery system and a drug carrier which have tiny microscopic structure with a larger porous surface. These are micro-sized particle with average diameter of 5-30 micron. The pores of a microsponge are used for entrapment of drug. These are newer technologies which have been used to control the release of medicament from formulation and also it precises the drug in targeted delivery. Microsponges have several advantages like improved stability, extended release, improved bioavailability and précised drug targeting makes it a better carrier for drug than the conventional nanocarrier like liposome. Microsponges are formulated by various approaches in which quasi-emulsion solvent diffusion method. In this two phases (1) Internal organic phase (2) External aqueous phase are prepared separately. The organic phase contains drug and solvent (ethanol) with polymer (1-5% w/v) and outer phase contains water with surfactant (PVA) (0.1-1%w/v). The internal phase is added drop-wise to external phase with high speed continuous stirring that formulate porous microsponge after evaporation. Due to higher ranges of temperature tolerance up-to 130oC and Ph stability from 1-11, microsponge are suitable opportunity for preparing stable formulation of wide range of drug categories. Microsponges were widely used in various drug deliveries like oral, drug delivery, topical drug delivery with uses in diseases like acne, diabetic wound healing, psoriasis, fungal infection, cancer etc.


INTRODUCTION

Microsponges are spherical, porous, microscopic particles. These are polymeric delivery system and a drug carrier which have tiny microscopic structure with a larger porous surface. These are micro-sized particle with average diameter of 5-30

microns¹. Microsponge have unique compression and also have a unique dissolution due to its spongy structure². Microsponge can deliver drug at minimal amount of dose and work efficiently in enhancing stability, modifying drug release and reducing side effects³. These have flexibility to

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entrap a wide range of active ingredients which are mostly used for prolonged topical administration for extended release of drug ⁴ Recently, in oral drug delivery microsponge shows increase rate of solubilisation of poorly water-soluble drug ⁵ As the

pores are very small containing about 2,50,000 pores in a typical 25 micrometer microsphere. ⁶ A 25 micrometer sponge may have internal pore structure equal to 10ft length, making it almost 1ml/gram for drug retention ⁷.

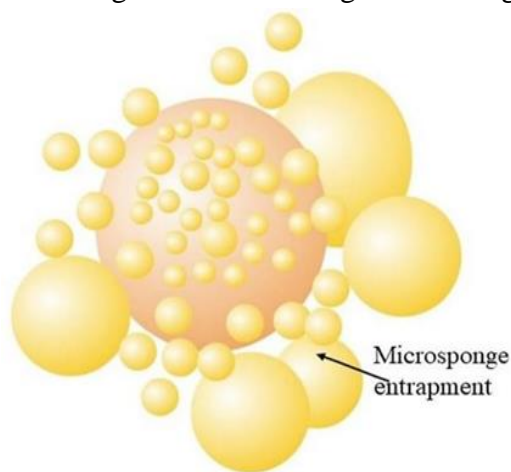


Figure 01: - Structure of microsponge

History Of Microsponge:-

The technology of microsponge was developed by *won* in 1987 and the original patent was assigned to *Advanced Polymer Systems Inc.*⁸ The company worked on many variations of this technique and the technique was applied to various cosmetics as well as OTC and prescription drug ⁹and also in some FDA-approved products such as- Retin A Micro[®] (0.1/0.04% tretinoin) and carac (0.5% FU)¹⁰.

Characteristics Of Microsponge^{11, 12, 13}: -

- Microsponge are stable over wide pH range from ph 1-11 and can withstand temperature up to 130°C.
- These have higher drug payload efficiency that it shows about 50-60% drug entrapment efficiency.
- These are compatible with most ingredient and vehicles.
- Self-sterilizing due to small pore size any bacteria can't pass through it.
- Microsponge can absorb oil up to 6 times of their weight.

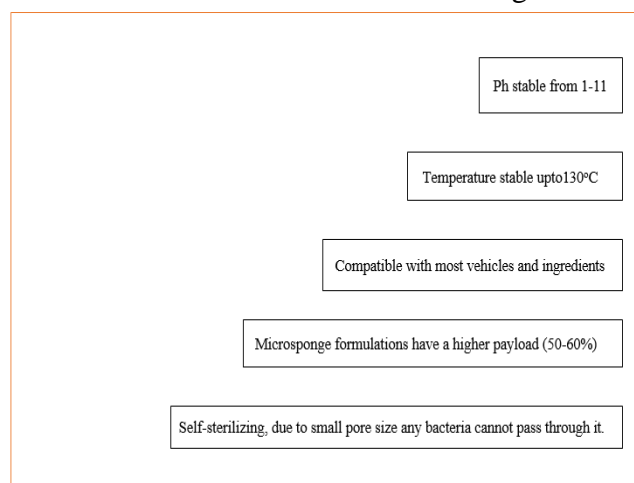


Figure 02: - Characteristics Of Microsponge

Advantages Of Microsponge^{14, 15, 16, 17}: -

- Microsponges have better controlled release of API or drug from the sponge than of microcapsules.
- These are non-allergic, non-irritating, non-toxic and non-mutagenic.
- These have better chemical stability.
- Microsponges can be easily prepared as compared to other nanoparticles like liposome.
- In comparison to ointments these have ability to absorb skin secretion, so this causes less greasiness, lesser sticky and then reduces shine to skin.
- Liquids can be transferred into free flowing powder so it becomes easier to handle.
- These helps in improving the elegance of formulation.

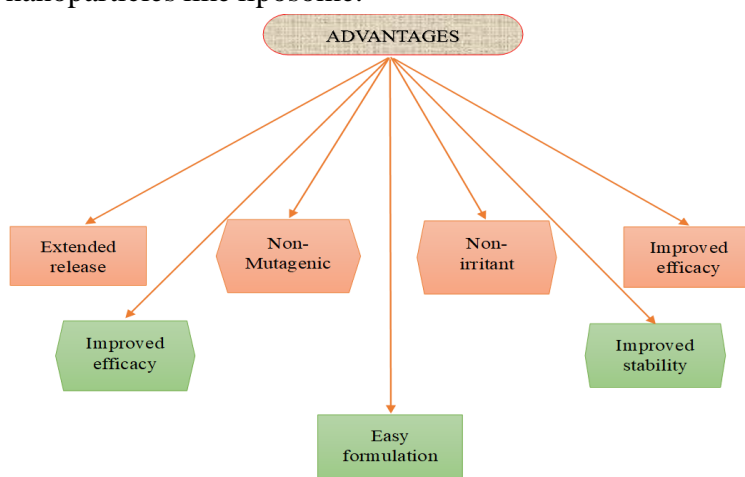


Figure 03:- Advantages Of Microsponges

Mechanism Of Drug Release From Microsponge:-

In microsponge the active ingredients are free to move in and out from the peptides but the release of drug is triggered by some external factors: -

- The external factors that triggers drug release are-
- a. Pressure
 - b. Temperature
 - c. Ph
 - d. solubility^{18, 19}

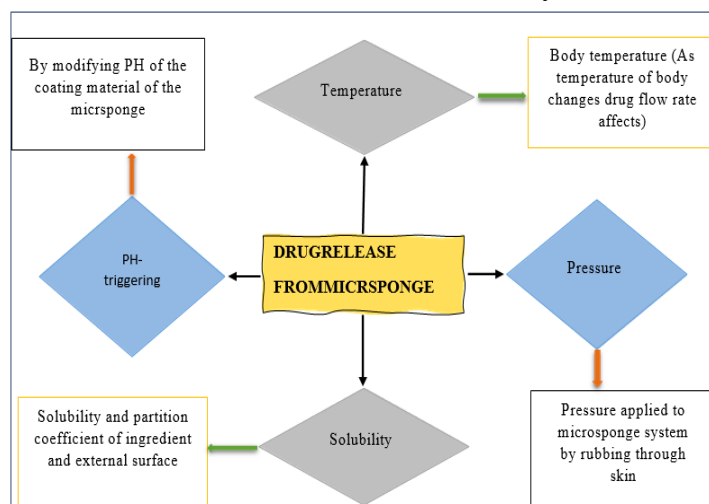


Figure 04: - Mechanism Of Drug Release from Microsponge

1. **Pressure:** - The release from microsponge is triggered by rubbing microsponge through the skin ^{20, 21}.
2. **Temperature:** - When the formulation is applied to skin by changing the temperature of

skin we can regulate drug release from the formulation ²².

3. Ph- triggered: - By modifying the ph of the coating material of the microspong system the drug release can also be regulated ²³.

4. Solubility: - Solubility and partition coefficient of ingredients, active material and the chemical composition of the microspunge plays a crucial role in drug release from microspunge drug delivery system ^{24, 25}.

Method Of Microspunge Formation:-

1. Quasi-emulsion solvent diffusion method

^{26,27,28}. _

- ❖ The inner phase is prepared by dissolving the polymer in suitable solvent (ethanol).
- ❖ The drug is added to inner phase and allowed to dissolve for 15 minutes at 35°C under ultrasonication.
- ❖ PVA is dissolved in water to prepare outer phase.
- ❖ The inner phase is then introduced dropwise to outer phase with continuous stirring for 2 hours at 500rpm speed.
- ❖ The preparation is filtered and microspunge is isolated.
- ❖ The isolated microspunge is dried at 40° C to get resulted product.

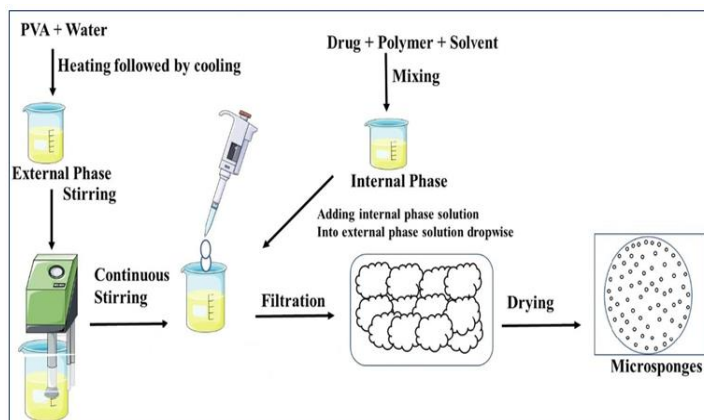


Figure 05: - Quasi-emulsion solvent diffusion method

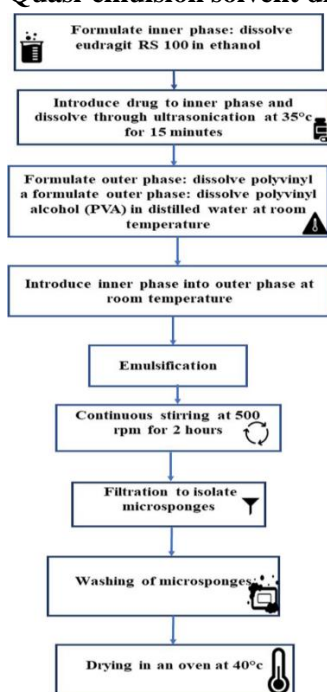
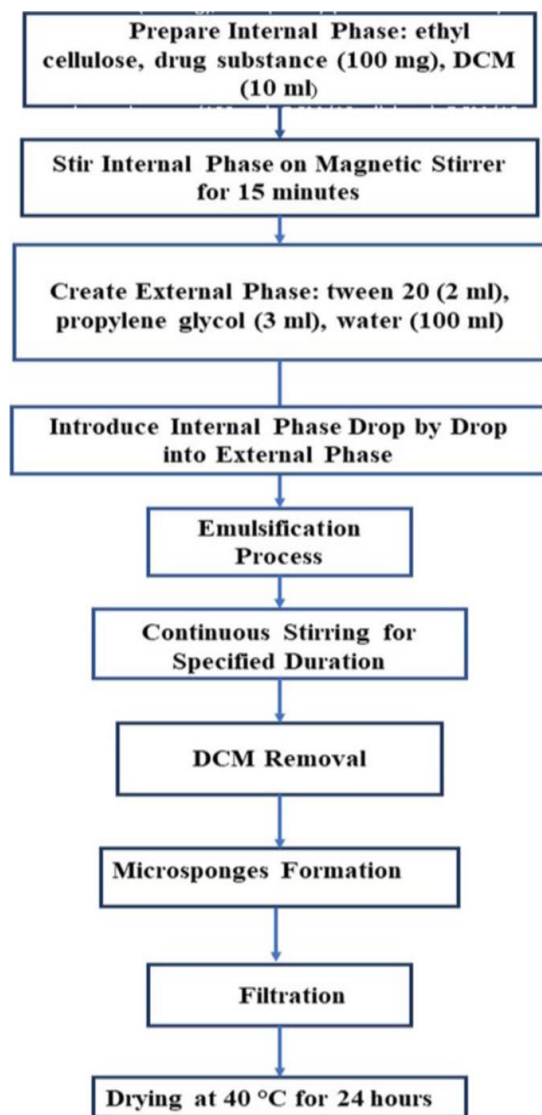


Figure 06: - Chart showing Quasi-emulsion solvent diffusion method

2. Quasi-emulsion solvent evaporation^{29,30}:-

- ❖ Dichloromethane, ethyl cellulose, and drug are mixed together to form internal phase and the internal phase is stirred on magnetic stirrer for 15 minute.
- ❖ In a separate container external phase is prepared by mixing surfactant and plasticizer in water.
- ❖ Internal phase is added drop-wise to external phase for emulsification followed by continuous stirring for 1 hour.
- ❖ Thus dichloromethane was eliminated and suspension is filtered and then dried for 24 hour at 40° C to obtain microsponge.



3. Liquid-liquid suspension polymerization^{31,32}:-

- ❖ Non-polar active ingredients are dissolved with monomer in a suitable solvent.
- ❖ The solution is then dispersed in aqueous phase with surfactant and suspending agents helps in the formation of suspension.
- ❖ Formation of ladder is occurred by cross-linking between chained monomers.
- ❖ The ladder then folds to form spherical particles and agglomeration of spheres causes formation of microspheres.

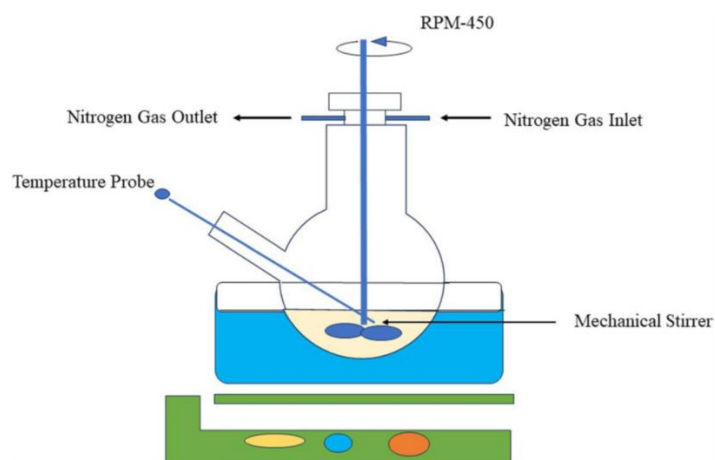


Figure 07: - Liquid-liquid suspension polymerization method

4. Water in oil emulsion solvent diffusion³³: -

- ❖ The internal aqueous phase containing emulsifying agent is disseminated in organic polymeric solution.

- ❖ The w/o emulsion then disseminated in exterior phase containing PVA to formulate double emulsion

- ❖ This approach is suitable for both water and oil soluble drugs.

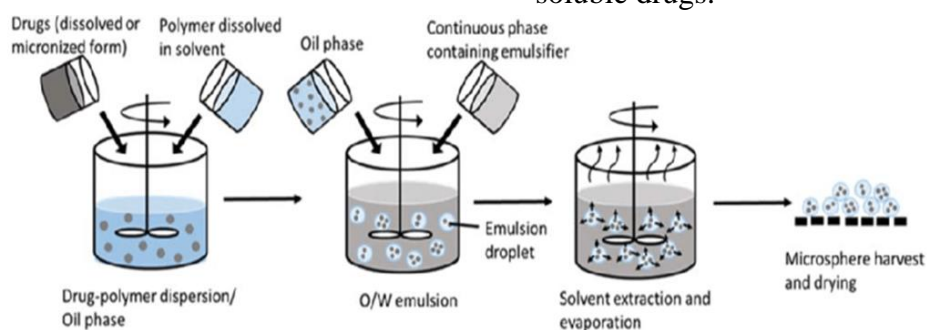


Figure 08:-Water in oil emulsion solvent diffusion method

5. Oil in oil emulsion solvent diffusion³⁴:-

- The interior phase is made up of volatile organic fluid. The volatile solvent is mainly dichloromethane.
- The external phase is prepared by polymer span 80 and poly actide-glycolic acid.
- The internal phase is added dropwise to external phase with continuous stirring.

- ❖ Porogens like hydrogen peroxide or sodium bicarbonate is disseminated in polymeric solution to form uniform dispersion.

- ❖ The dispersion is then re-dispersed in aqueous phase containing PVA.

- ❖ Then hydrogen peroxide is added that causes creation of linked pores.

6. Addition of porogen³⁵: -

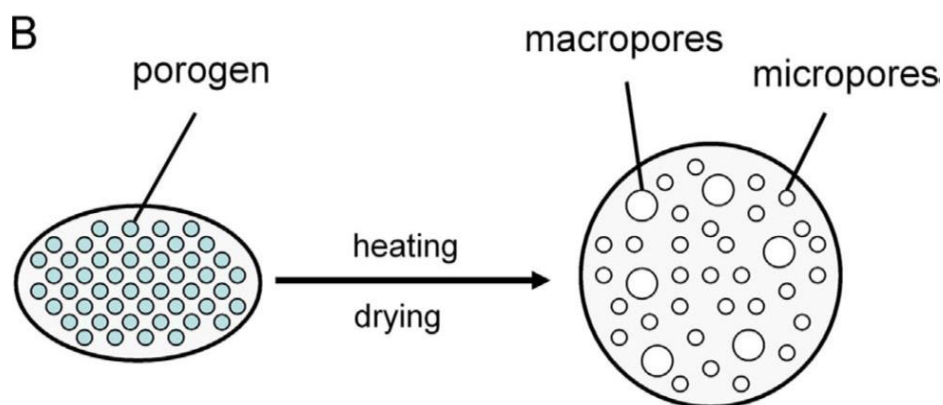


Figure 09: - addition of porogen method of preparation

7. Lyophilisation³⁶:-

- The microsponges are lyophilized after incubating in chitosan hydrochloride solution.
- By lyophilisation rapid removal of solvent occurs. But due to rapid solvent elimination cracking, shrinkage may occur.

8. Vibrating orifice aerosol generator (VOAG)³⁷:-

- ❖ VOAG was first reported for the preparation of lipid bilayered mesoporous silica particles.
- ❖ Tetra ethyl ortho silicate, ethanol, water and dil. HCl were refluxed to prepare stock solution for formation of core.
- ❖ The stock solution is diluted with solvent containing surfactant and stirred to form mono dispersed droplets. The droplets were encapsulated in liposome.

Evaluation Parameters Of Microsponge:-

- a. Particle size determination
- b. Morphology and surface topography
- c. Determination of loading efficiency and production field
- d. Drug entrapment

1. Particle size determination³⁸-

For particle size distribution optical microscope is used. Diffractionometry can also be used to determine the particle size of microsponges.

The texture and stability of a formulation are affected by particle size.

2. Morphology³⁹-

For determination of morphology or surface morphology scanning electron microscopy is used. The sample was mounted directly on to the SEM sample holder using double sided stucked tape. The images were recorded at different resolutions.

3. Production yield^{40,41}-

The production yield of microsponges can be calculated using formula.

$$x = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100$$

4. Drug content⁴²-

To measure drug content in microsponge 100 mg of precisely weighted microsponge is mixed in 100 ml of 6.8 ph phosphate buffer. The mixture is filtered through 0.45 μm membrane filter and sample is analyzed at suitable wavelength using UV.

$$\text{Drug content} = \frac{\text{Actual amount of drug}}{\text{Weighed amount of sponge}} \times 100$$

5. Entrapment efficiency^{43,44}-

Drug entrapment efficiency is assessed through solvent extraction method.

10 mg of precisely weighed microsponge is dissolved in 5ml of methanol using magnetic stirrer for 20 min.

20 ml of freshly prepared PBS is added and heated at 45-50°C .Till the formation of clear solution. Methanol is evaporated and cooled at 25°C and filtered.

The drug concentration is measured by UV.

$$DEE = \frac{\text{Actual drug content of sponge}}{\text{Theoretical drug content of sponge}} \times 100$$

Application Of Microsponge in Different Pharmaceutical Formulation:-

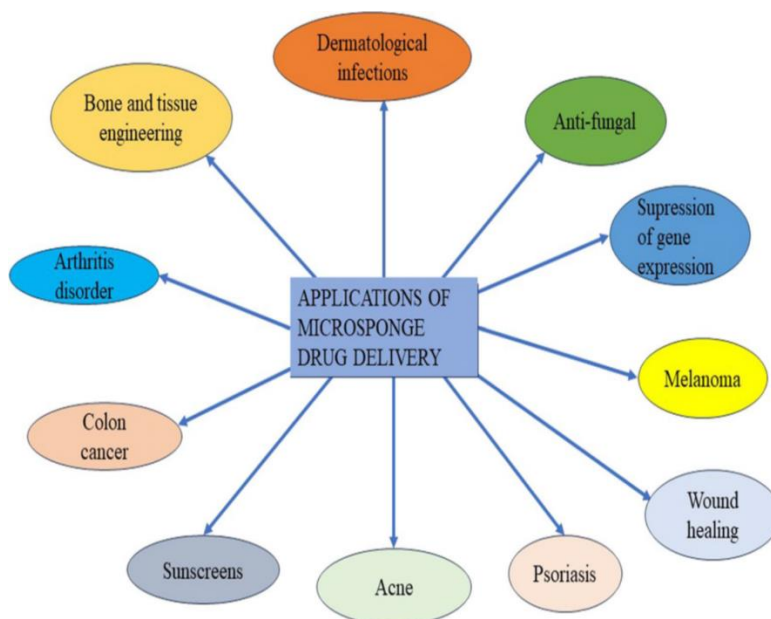


Figure10:- Application of microsponge

1) Microsponge for oral drug delivery:-

- Microsponge helps to maintain the drug in protected condition and protected release under regulated condition in lower GIT ⁴⁵.
- Microsponge increases absorption of medicament through small and large intestine by extending transit time ⁴⁶.
- There produced mechanically robust tablets of ketoprofen by quasi-emulsion solvent diffusion method of sponge formation. That prove plastic deformation of microsponge enhances compressibility ⁴⁷.
- Fluoribiprofen shows notable augmentation in drug release during 8th hour due to inclusion of enzyme in colon results in colon-targeting ⁴⁸.

2) Microsponge for topical delivery: -

- Fluocinolone acetonide, a corticosteroid is employed in dermatology to eliminate skin irritation and improve inflammatory condition ⁴⁹.

- By incorporating benzoyl peroxide in microsponge its percutaneous absorption lowers which causes lessen in skin-irritation ^{50, 51, 52}.
- Microsponge can be formulated in creams, gels, powders, lotions.
- Hydroquinolone bleaching creams shows prolong release to minimize skin irritation ⁵³.
- Zinc pyrithione, selenium sulphide when formulated in microsponge to be use in anti-dandruff shampoo shows reduction in unpleasant odour with lowered irritation with extended safety and efficacy ⁵⁴.

3) Microsponge in cosmetics: -

Microsponge helps in dismantling uniformity and improves covering power so colorful cosmetics can be prepared with microsponge ⁵⁵.

4) Microsponge for bone and tissue engineering: -

Two aqueous dispersion tricalcium phosphate granules and powdered calcium hydroxyapatite and prepolymerised polymethyl metha acrylate with methyl methaacrylate monomer liquid.

A collagen sheet encapsulating basic fibroblast growth factor (bFGF) when injected subcutaneously causes increase in blood rate^{56, 57, 58}.

Uses Of Microsponge For Various Diseases

- i. **For psoriasis-** Momentasonefuroate is used in microsponge by emulsion solvent diffusion method shows initial rapid drug release effect with 29-30% drug release during first hour to 78-95 % drug release after 8 hour^{59,60,61,62}.
- ii. **For skin infection-** Mupirocin microsponge incorporated in emulgel base could provide sustained drug release till 24 hours. In draize patch test these formulation are stable and safe use. This causes slow release and shows prolonged therapeutic effect⁶³.
- iii. **For diabetic wound healing-** Nevibolol-loaded microsponge shows double effect of vasodilation with controlled and sustained release so promote faster healing. In in-vitro study 80% drug release shows within 8 hour and rapid and significant wound healing⁶⁴.
- iv. **For fungal infection-** Voriconazole prepared using quasi-solvent diffusion method shows high encapsulation efficiency than conventional fluconazole gel and shows greater zone of inhibition⁶⁵.
- v. **For acne-** Benzoyl peroxide microsponge had a high drug loading capacity, sustained drug release and improved stability over conventional formulations. The microsponge gel shows greater reduction in acne lesions and skin irritation^{66, 67}.
- vi. **Atopic dermatitis-** Nargenin 1% microsponge gel have 82% entrapment and shows faster healing, reduced earflap thickness, lower WBC counts as compared to plain gel. The main benefit is three-fold greater drug deposition onto skin⁶⁸.
- vii. **Hyperpigmentation-** glabrid microsponge using ethyl cellulose then formulated in gel causes reduction in melanin density⁶⁹.

For skin cancer- 5- fluorouracil (5-FU) shows better surface area and pore volume and have improved texture and it shows 5.5 times increase in skin deposition and lessen skin irritation^{70, 71}.

For Herpes- acyclovir loaded microsponge emulgel causes improved drug penetration than commercial formulation⁷².

x. **For arthritis-** diclofenac used in microsponge shows prolonged release for arthritis on topical application^{73, 74}.

CONCLUSION

The microsponge delivery system is a unique technology for the controlled release of macroporous beads, loaded with an active agent, offering a potential reduction in side effects while maintaining their therapeutic efficacy. The microsponge delivery system is a novel, unique and emerging technology for controlled and prolonged release of drug. These are valuable drug matrix substance with several beneficial advantages like having good physical, chemical and thermal stability and allow greater flexibility in dosage from manufacturing and drug entrapment. Microsponges drug delivery system is very emerging pharmaceutical application for controlled release system, it reduces irritancy, reduces toxicity and compatible with most of ingredient and vehicles. Synthesized through techniques like quasi-emulsion solvent diffusion, they found use in dermatological and oral drug delivery. Now a days it can also used for tissue engineering and controlled oral delivery using biodegradable polymers, especially for colon specific delivery. These were mainly used in cosmetics, but due to its versatility it is source of interest in drugs of various field like NSAIDs, cancer, arthritis, acne, Diabetic wound etc. Due to its stability over wide range of temperature and pH range it is suitable area of research for various sensitive drugs and its ability to control drug and it can also be controlled drug delivery and biopharmaceutical



drug delivery. Due to its larger pore area it is main choice for enhance drug entrapment and control release rate of drug from sphere. Microsponges represent a promising frontier in drug delivery, with potential across pharmaceutical and cosmetic domains. MDS holds a promising future in various pharmaceutical applications in the coming years as they have unique properties like extended release, reduced irritancy, small size, self sterilize and compatible with most of vehicles and ingredients, so flexible to develop novel product forms.

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