

Microsponge: A Novel Approach for Topical Drug Delivery of Anti Rheumatoid Drugs

Krupa Joshi^{1*}, Ashimkumar Sen¹, Vatsal Gujariya²

¹Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Vadodara, Gujarat, India,

²Department of Roganidan Evam Vikriti Vigyan, Parul Institute of Ayurved, Parul University, Vadodara, Gujarat, India

Abstract

Microsponge is one of the developing fields of science innovation, which can be capable of both regulated drug delivery and site-specific administration of drugs. The determination of the particular pharmaceutical formulations and way of distribution for delivery of the medicament is strongly influenced by the physical and chemical characteristics of the microsponge, such as the size of particles, distribution of particle size, transparency, and surface structure. An innovative technique for topical medicine delivery has also emerged: The microsponge. The topical methods further benefit from flexible formulations, more patient participation, increased safety and overall performance, and attractive characteristics. Immunomodulatory rheumatoid arthritis requires long-term therapy to control the condition. Long-term administration of the marketed oral dosage forms may result in liver damage. The topical way may represent a good alternative method for medication delivery with better drug stability, less adverse effects, and less frequent administration. Microsponges have the ability to entrap significant amounts of dosage and may also alter medication release due to its porous and spongy nature.

Key words: Administration, drug delivery, microsponge, rheumatoid arthritis, topical

INTRODUCTION

An immunomodulatory condition called arthritis primarily causes joint inflammation, which can affect one or more joints. It usually affects seniors, but it can occasionally be seen in young children as well. In addition, it occurs more frequently in female patients than in adult men.^[1,2]

Rheumatoid arthritis (RA) is an autoimmune condition that primarily affects the synovial stratum and promotes inflammation and pain inside the joints [Figure 1]. Stiffness, limited joint motion, inflammation, redness of the knee area, and other clinical symptoms are also observed. Long-term treatment therapy is necessary.^[3] Since there is not an effective treatment for arthritic conditions. Medicines called disease-modifying antirheumatic drugs (DMARDs) are used to relieve symptoms.^[4]

DMARDs formulations which are currently available for sale in the market are available in the form of oral medication. The long-term impact of oral drug – delivery results in liver

damage. An alternate option is to use topical medication delivery devices. The medicine can be delivered using a variety of formulations for topical drug administration. Topical formulations including creams, ointments, lotions, gel, emulgel, organogel, and others are often use. Gel comprises a watered-based vehicle that is more compatible with skin and has a higher percentage of permeability through the skin, so gel is the most practical dose form to be applied topically.^[5,6]

Microsponges are oval, porous microspheres that may contain a lot of drugs. It may release medications for such a longer duration and in a regulated manner due to its huge porous surface.^[7,8] Moreover, it is temperature and pH stable over a broad range. Microsponges may distribute drugs uniformly at low dosages and are suitable for small

Address for correspondence: Krupa Joshi, Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Piparia, Vadodara, Gujarat, India. Phone: 9426424547. E-mail: krupaj356@gmail.com

Received: 07-06-2024

Revised: 21-08-2024

Accepted: 07-09-2024

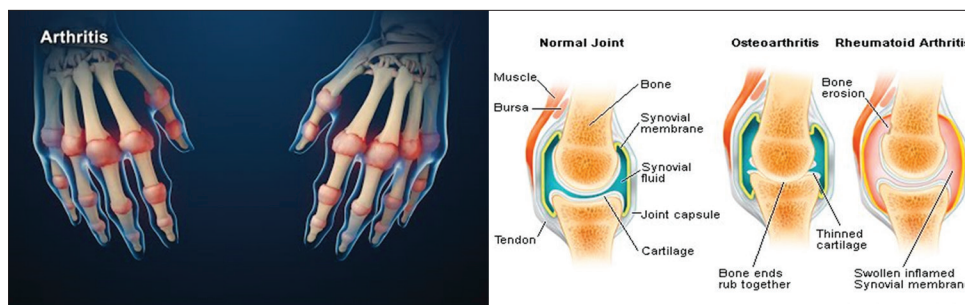


Figure 1: Causes of arthritis

doses of medication, which affects the drug's release rate. Besides that, microsponges can be placed in pharmaceutical formulations such as cream, lotion, gel, and others for topical medication delivery, offering a variety of formulations flexibility based on the physicochemical properties of the medication.^[9,10]

The majority of medications available on the market have low water solubility, which makes creating dosage forms challenging. Approaches for solubility enhancement can be used to increase a drug's solubility in water. A further benefit of localized and site-specific medication administration is provided by microsphere-based topical drug delivery. It also avoids first-pass liver metabolism as well as adverse effects following oral administration of medication.^[11]

PREPARATION METHOD OF MICROSPONGE

Liquid-liquid suspension polymerization technique

This technique involves dissolving monomers and additional inert ingredients in a solvent. The solvent is chosen such that it is insoluble with the water-based exterior phase. Afterward, a monomer-containing sample was enabled to dispersion in an outside surfactant-containing aqueous media. The creation of a suspension with small droplets is the outcome of the immiscible phase's dispersion in the water phase. Catalysts, temperatures, or radiations all enhance the polymerization of a monomer to enhance the polymerization of a monomer that is currently in suspension [Figure 2]. As long as the monomer is there, polymerization will occur. After the solvent evaporates, porous, spongy microsphere forms that must be cleaned to get free of contaminants. Furthermore, microsponges are removed from the reaction medium and dried.^[12]

Quasi-emulsion solvent diffusion

Moreover, the quasi-emulsion solvent diffusion technique can be used to create microsponges. Internal organic phase preparations and exterior aqueous phase preparations are steps in this process. Polymer and medication can be

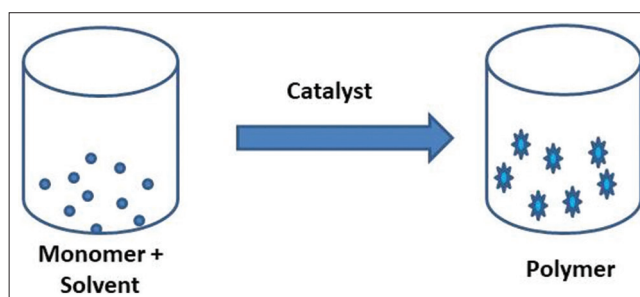


Figure 2: Liquid-liquid suspension Polymerization technique

dissolved concurrently inside a similar organic solvent under the required stirring and temperature conditions to produce the inner phase. The surfactant is dissolved in the watery phase to prepare the outer phase. When the internal phase is added to the external phase dropwise, it forms little droplets that are spread throughout the external phase. A small, porous microsphere is produced by the complete evaporation of an organic solvent [Figure 3]. Afterward, isolated microsponges are washed, followed by drying.^[13]

A drug may be added during production in any of the two ways of preparation I have described if it can endure the alleged experimental situation. If the medication is thermolabile, microsponges are carried out without the drug. Microsponges are submerged in a saturated solution of the medicine for 24 to 48 h to assimilate the medication.

CHARACTERIZATION OF MICROSPONGE

FTIR spectrum

The compatibility between drugs and excipients is investigated using a fourier transform infrared spectrophotometer. The previously dried drugs and excipients are passed through a spectrophotometer, in which the spectrum is recorded between 4000 and 400 cm^{-1} in wavelength. Analysis of the recorded spectrum is used to determine compatibility. Due to the similar function group and inter-molecular interrelations that exist between the atoms, each medicine and excipient have a similar spectrum. Tests can confirm the standard spectrum and show differences.^[14,15]

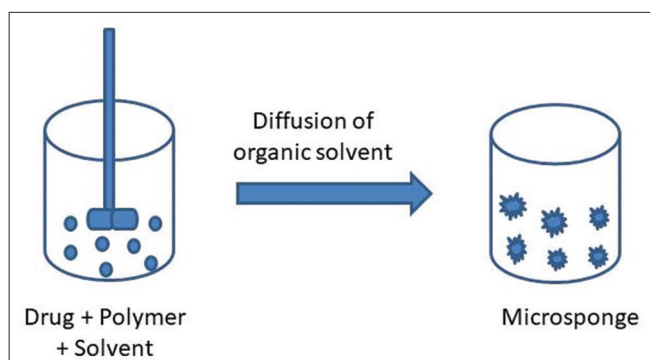


Figure 3: Quasi-emulsion solvent diffusion technique

Differential scanning calorimetry (DSC)

DSC is used to investigate the dynamic activity of excipients such as polymers, medicines, and others. Drug and excipient compatibility is also examined using DSC. A dried sample is pressed between two aluminum plates for the investigation. Moreover, it is heated gradually while being continuously purged with nitrogen. To determine whether the components to be analyzed are amorphous or crystalline, the thermogram acquired using this approach is examined.^[16,17]

Microscopic analysis

A laboratory-scale microscope can be used to perform optical microscopy. A slide may be made by spreading a tiny film of dry microsponge over it and then viewing it with a conventional optical microscope. It is also possible to do size of the particles and particle density analyses. Moreover, an optical microscope and camera may be combined to take pictures of the created Microsponge.^[18]

Scanning electron microscopy (SEM)

SEM is used to examine the three-dimensional morphological characteristics of a manufactured microsponge. A probe used in SEM can only scan conductivity objects. As a result, a prepared microsponge is created by covering it with highly conductive material under predetermined vacuum conditions. Using the picture produced by the scanning probe's movement across the Microsponge's surface, a topographical analysis of the microsponge may be done.^[19]

X-ray diffraction study (XRD)

The provided sample's physicochemical nature is investigated using XRD. Equipment was used on a microsponge sample. Under the required voltage conditions, X-rays of short wavelength are sent to the sample. In a diffractogram, diffracted radiation is detected. By examining the interference pattern, it is possible to determine if the sample's structure is crystalline or amorphous. Furthermore, it may be inferred from the study whether or not the physical nature

of the medication or microsponge was altered throughout processing.^[20]

Percentage yield

The whole ideal mass of the microsponge is made up of the medication, polymers, and various excipients. The mass of the microsponge following the experimental procedure to manufacture the microsponge is really the practical weight of the microsponge. The formula below may be used to get the microsponge % yield.

$$\% \text{ Yield} = \frac{\text{Particle mass of microsponges}}{\text{Theoretical mass of microsponges}} \times 100$$

OR

$$\% \text{ Yield} = \frac{\text{Particle Yield}}{\text{Theoretical Yield}} \times 100$$

Drug content and encapsulation efficiency

A properly weighed amount of microsponge is dissolved in a solvent while being continuously stirred to measure the drug concentration. The solvents have been chosen such that they can dissolve both the medication and the polymer. Moreover therefore, the majority of the material would dissolve in the specific solvent. After filtering, the solution's drug content can be examined by the appropriate analysis method.

Drug content and encapsulation efficiency can be calculated by the following formula.^[21]

$$\text{Actual drug content (\%)} = \frac{M \text{ actual drug}}{M \text{ obtained}} \times 100$$

$$\text{Encapsulation efficiency} = \frac{M \text{ practical}}{M \text{ theoretic}} \times 100$$

where, M actual is the actual drug content of microsponges, M obtained is the weighed amount of powder of microsponges

In vitro drug release study

Franz diffusion cells can be used for artificial insemination drug release studies. The giver and receiver sections are the two it utilizes. A dialysis membrane separates those two chambers. The giver section, which also contains a tiny amount of diffusion medium, is filled with Microsponge that has been precisely weighed. The receiver section is likewise packed with a diffusion medium. A magnetic stirrer is used to support the entire assembly. To replicate the conditions seen in the human body, the receiver section is constantly

stirred and kept at 37°C. To keep the receiver section in good condition, aliquots are removed out and refilled with new diffusion media at regular intervals. Sieve and dilute with a correct quantity of diffusion medium, collected aliquots are then subjected to an analysis.^[22,23]

Stability study

To evaluate the effect of external variables or handling and storage temperature on the composition of microspoon, a stability study should be performed. For a short-term acceleration stability assessment, up maximum 1 month of monitoring can be made of the Microspoon formulation that has been improved. Temperature and relative humidity must meet International Conference on Harmonization standards of 40°C and 75%RH (40±2°C/75% ± 5%RH) for the stability assessment. When the stability research is finished, the gathered samples can be examined for a variety of factors.^[24]

CONCLUSION

Microsponges are a customized dosage form that provides a broad variety of drugs and dosages to be integrated. The quick release of drugs is provided by Microspoon's high porosity. Drug distribution that is regulated and maintained can also be accomplished using modified polymers. Microspoon can be developed to provide anti-rheumatoid medication for topical application, in contrast to the presently available therapy for RA as an oral formulation. Further benefits for site-specific medication delivery may result from this. Moreover, topical distribution can improve the dosage form's effectiveness and safety. Future prospects for the creation of microspoon for external use might provide a successful approach to the treatment of arthritis.

REFERENCES

1. Kwok C, Anderson L, Greene J, Johnson D, O'Dell J, Robbins M. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum* 2002;46:328-46.
2. Di Benedetto DB, Zhou X, Reynolds M, Ogale S, Best JH. Assessing methotrexate adherence in rheumatoid arthritis: A cross-sectional survey. *Rheumatol Ther* 2015;2:73-84.
3. Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: Pathological mechanisms and modern pharmacologic therapies. *Bone Res* 2018;6:15.
4. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: A review. *JAMA* 2018;320:1360-72.
5. Khullar R, Saini S, Seth N, Rana A. Emulgels: A surrogate approach for topically used hydrophobic drugs. *Int J Pharm Biol Sci* 2011;1:117-28.
6. Purnamawati S, Indrastuti N, Danarti R, Saefudin T. The role of moisturizers in addressing various kinds of dermatitis: A review. *Clin Med Res* 2017;15:75-87.
7. Embil K, Nacht S. The microspoon® delivery system (MDS): A topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. *J Microencapsul* 1996;13:575-88.
8. Nacht S, Katz M. The microspoon: A novel topical programmable delivery system. *Drugs Pharm Sci* 1990;42:299-325.
9. Chadawar V, Shaji J. Microspoon delivery system. *Curr Drug Deliv* 2007;4:123-9.
10. Newton DW. Biotechnology frontier targeted drug delivery. *US Pharmacist* 1991;16:38-51.
11. Vyas LK, Tapar KK, Laddha BH, Lahoti AO, Nema RK. Formulation and development of anti-blemish preparation using microspoon technology. *J Chem Pharm Res* 2010;2:562-71.
12. Pushpa K, Kiran MS. A comprehensive review on novel microsponges drug delivery approach. *Asian J Pharm Clin Res* 2016;9:25-30.
13. Orlu M, Cevher E, Araman A. Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges. *Int J Pharm* 2006;318:103-17.
14. Anilkumar JS, Mano B, Sawant SS. Development and evaluation of fenoprofen microsponges and its colonic delivery using natural polysaccharides. *Int Publ Am J Pharm Sci Nanotechnol* 2014;1:27-42.
15. Charde MS, Ghanawat PB, Welankiwar AS, Kumar J, Chakole RD. Microspoon A novel new drug delivery system: A review. *Int J Adv Pharm* 2013;2:63-70.
16. Roaa AN, Hussein AA. Preparation and evaluation of meloxicam microsponges as transdermal delivery system. *Iraqi J Pharm Sci* 2014;23:62-74.
17. Rizkalla CM, latif Aziz R, Soliman II. *In vitro* and *in vivo* evaluation of hydroxyzine hydrochloride microsponges for topical delivery. *AAPS PharmSciTech* 2011;12:989.
18. Pawar AP, Gholap AP, Kuchekar AB, Bothiraja C, Mali AJ. Formulation and evaluation of optimized oxybenzone microspoon gel for topical delivery. *J Drug Deliv* 2015;2015:261068.
19. Osmani RA, Aloorkar NH, Thaware BU, Kulkarni PK, Moin A, Hani U, et al. Microspoon based drug delivery system for augmented gastroparesis therapy: Formulation development and evaluation. *Asian J Pharm Sci* 2015;10:442-51.
20. Bhatia M, Saini M. Formulation and evaluation of curcumin microsponges for oral and topical drug delivery. *Prog Biomater* 2018;7:239-48.
21. Salah S, Awad GE, Makhlof AI. Improved vaginal retention and enhanced antifungal activity of miconazole microsponges gel: Formulation development and *in vivo* therapeutic efficacy in rats. *Eur J Pharm Sci* 2018;114:255-66.
22. Mathew ST, Devi SG, Prasanth VV, Vinod B. Formulation and *in vitro-in vivo* evaluation of ketoprofen-loaded albumin microspheres for intramuscular administration.

J Microencapsul 2009;26:456-69.

23. Mohan KV, Veena NM, Manjula BP. Formulation and evaluation of microsponges for topical drug delivery of Mupirocin. Int J Pharm Technol Res 2013;5:1434-40.
24. ICH-Technical Coordination. Stability Testing

Guidelines: Stability Testing of New Drug Substances and Products. London: ICH-Technical Coordination.

Source of Support: Nil. **Conflicts of Interest:** None declared.