International Journal of Pharmaceutical Research and Development

**ISSN Print:** 2664-6862
**ISSN Online:** 2664-6870
**Impact Factor:** RJIF 8.55
IJPRD 2025; 7(2): 223-229
www.pharmaceuticaljournal.net
Received: 15-07-2025
Accepted: 16-08-2025

**M Balasundaresan**
Associate Professor, Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**SK Senthil Kumar**
Principal, Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**P Pravin Kumar**
Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**S Premalatha**
Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**D Priyadharshini**
Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**J Rabbani**
Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**M Ragul**
Final B.Pharm Students, Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

**Corresponding Author:**
**M Balasundaresan**
Associate Professor, Arunai College of Pharmacy, Tiruvannamalai, Tamil Nadu, India

# Microspheres: A brief review

**M Balasundaresan, SK Senthil Kumar, P Pravin Kumar, S Premalatha, D Priyadharshini, J Rabbani and M Ragul**

**DOI:** https://www.doi.org/10.33545/26646862.2025.v7.i2c.183

**Abstract**
Microspheres are spherical, free-flowing, and discrete particulate systems typically ranging from 1 to 1000 micrometers in diameter, used widely as carriers for drugs, enzymes, vaccines, and other bioactive agents. They are designed to deliver therapeutic agents in a controlled and sustained manner, thereby enhancing efficacy, minimizing side effects, and improving patient compliance. Microspheres can encapsulate both hydrophilic and lipophilic drugs and offer targeted delivery, which is particularly advantageous in the treatment of chronic diseases. In pharmaceutical sciences, microspheres serve as an effective system for controlled drug delivery, sustained release, and site-specific targeting. These systems are particularly beneficial for drugs with short biological half-lives, low bioavailability, or narrow therapeutic windows, as they help in maintaining steady plasma drug concentrations over extended periods.

**Keywords:** Microspheres, natural polymers, nanoparticles, bioavailability, half life

## Introduction
A novel drug delivery system can be defined as new approach that combine innovation development, formulation, new technologies, novel methodologies for delivering pharmaceutical compound in the body as needed to safety achieve its desired pharmacological effects [1].

Microspheres are spherical, free-flowing, and discrete particulate systems typically ranging from 1 to 1000 micrometers in diameter, used widely as carriers for drugs, enzymes, vaccines, and other bioactive agents. They are designed to deliver therapeutic agents in a controlled and sustained manner, thereby enhancing efficacy, minimizing side effects, and improving patient compliance. Microspheres can encapsulate both hydrophilic and lipophilic drugs and offer targeted delivery, which is particularly advantageous in the treatment of chronic diseases. In pharmaceutical sciences, microspheres serve as an effective system for controlled drug delivery, sustained release, and site-specific targeting. These systems are particularly beneficial for drugs with short biological half-lives, low bioavailability, or narrow therapeutic windows, as they help in maintaining steady plasma drug concentrations over extended periods.

NDDS is a system for delivering of drug other than conventional drug delivery system. NDDS is a combination of advance technique and new dosage forms which are far better than conventional dosage form.

## Aim
**For drug to reach the targeted site with little or no side effect**

- To minimizes drug degradation & loss.
- To increase bioavailability of the drug.

## Types of drug delivery system
- Targeted drug delivery system.
- Controlled release drug delivery system.
- Sustained release drug delivery system.

**Targeted Drug Delivery System**
Targeted drug delivery is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others [2].

**Sustained releases drug delivery system**
The terms sustained release, prolonged release, modified release, external release or depot formulations are used to identify drug delivery systems that are designed to achieve or extending therapeutic effect by continuously releasing medication over an extended period of time after administering of single dose [3].

**Controlled release drug delivery system**
It is made to release a medication at a predetermined space over an extended length of time, keeping therapeutic levels stable for a longer amount of time.

**Microsphere**
Microspheres are solid spherical particles ranging in size from 1-1000µm.
They are tiny, spherical particles made from proteins or special plastics, which are biodegradable in nature [4].

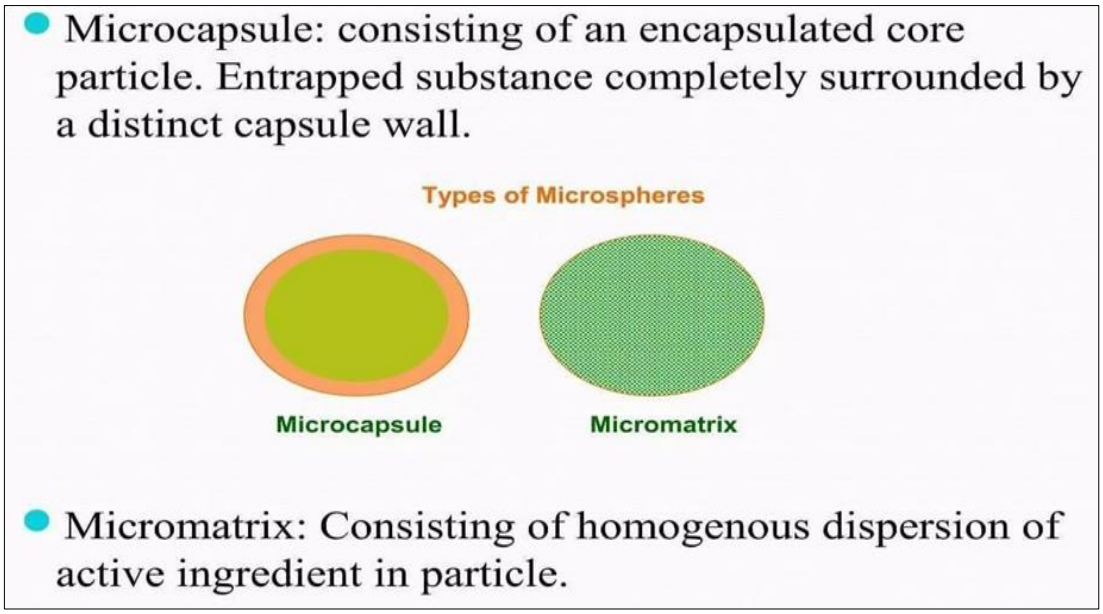


**Fig 1:** General structure and properties of microspheres.

Microsphere improves bioavailability reduces the side effect improves stability decreases dose frequency and targets the drug to specific site at predetermined rate [5].
Oral ingestion is the most common method of drug delivery, but some drugs get absorbed from GIT and have short half-life are eliminated quickly from the blood circulation. To avoid these problems oral controlled delivery systems have been developed they releases medication slowly, maintaining a study level in the body for a longer time [6].

**Types**
**The different types of microspheres are:-**
- Bio adhesive microsphere
- Magnetic microsphere
- Floating microsphere
- Radioactive microsphere
- Polymeric microsphere
  - Biodegradable polymeric microspheres
  - Synthetic polymeric microspheres [5].

**Advantages**
- Increased surface area improve solubility.
- Reduced dose and risk.
- Maintain consistent medication levels.
- Protects medication from breakdown.
- Shorter dosage intervals improve patient compliance [7].

**Disadvantage**
- Microsphere formulations can be more expensive than traditional formulations.
- Scaling up microsphere production while maintaining consistency can be challenging.
- Some microspheres may release their payload too quickly, leading to adverse effects.
- Ensuring uniform microsphere size can be difficult, which may affect performance.

**Limitation**
- Manufacturing challenges
- Food and digestion can affect from the medication is released
- Difficulty in achieving consistent release rates.
- In controlled-release medication have a lot of active ingredients, so if they
- Don’t work properly, it could be harmful.
- Shouldn’t crush (or) chew these. Tablet, take them whole [8].

**Applications**
- **Targeted Drug Delivery:** Microspheres can deliver drugs directly to specific cells or tissues, improving efficacy and reducing side effects.
- **Controlled Release:** Microspheres can release drugs or active ingredients slowly over time, providing sustained

therapeutic effects.

- **Vaccine Delivery:** Microspheres can be used to deliver vaccines and enhance immune response, providing protection against diseases.
- **Cancer Treatment:** Microspheres can be used to deliver chemotherapy drugs directly to tumors, reducing side effects and improving treatment outcomes.
- **Improved Bioavailability:** Microspheres can improve the bioavailability of drugs or active ingredients, making them more effective and reducing the required dosage [9].

**Method of preparation**

- Solvent evaporation technique.
- Single emulsion technique.
- Double emulsion technique.
- Phase separation or coacervation technique.
- Spray drying & spray congealing.
- Solvent extraction method.
- Quasi-emulsion solvent diffusion.

**Solvent evaporation technique:** This describes a process for creating microencapsulated or microsphere formulations.

**Here's a simplified overview**

A polymer is dispersed in an organic solvent. The drug is dissolved or dispersed in the polymer solution. The polymer-drug solution is emulsified into an aqueous phase with surfactants or polymers. The organic solvent is removed through heat, reduced pressure, or stirring. As the solvent evaporates, the polymer precipitates at the oil-water interface, forming microspheres or microcapsules. This process is commonly used to create sustained-release or controlled-release formulations, where the drug is encapsulated within a polymer matrix [10].

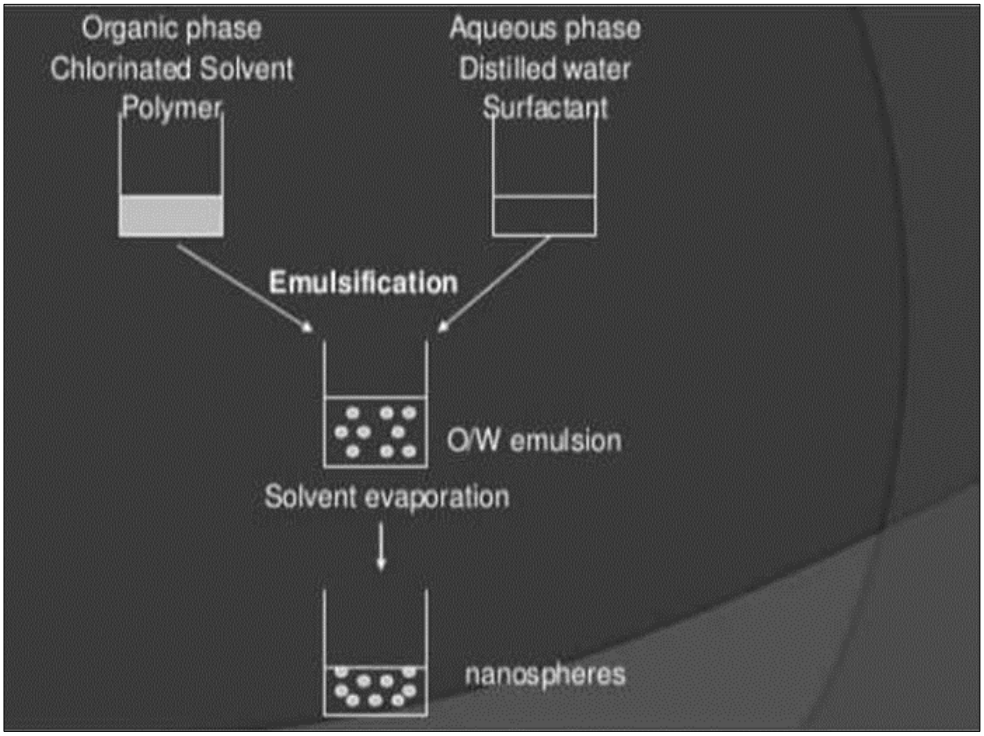


**Fig 2:** Single emulsion technique for microsphere preparation.

**Single emulsion technique**

Natural polymers (like proteins or cabs) are mixed with water. This mixture is then added to oil, creating tiny droplets. These droplets are then hardened using heat or chemicals to create microspheres. Chemicals like glutaraldehyde can be used for cross linking but might affect the active ingredients. The type of surfactants used can impact the final products size, shape, and performance [6].

**Polymer in aqueous solution**

↓

↓ Stir or sonicate

Disperse in organic phase (Oil/Chloroform)

↓

↓ Chemical cross linking or heat denaturation

Microspheres in organic phase

↓

↓ Centrifugation, wash, separation

Microspheres

**Double emulsion technique**

A water solution with the active ingredient (e.g., protein) is mixed with a lipophilic organic phase. The mixture is homogenized or sonicated to create a stable emulsion.

An aqueous solution (e.g., polyvinyl alcohol) is added, creating a water-in-oil-in-water (w/o/w) double emulsion.

The solvent is removed through evaporation or extraction, leaving behind microspheres with the active ingredient encapsulated [10].

**Polymer in aqueous solution + drug**

↓

↓ Homogenization of sonication

Disperse in organic phase

↓

↓

First Emulsion (W/O)

↓

↓ Addition to large AQ phase

Microspheres in solution

↓
↓ Separation, wash, dry
Microspheres

**Phase separation method**

It is based on principle of reduces polymers solubility, inducing phase separation. Disperse the drug particles in polymer solution. Add incompatible polymers or non-solvent. Polymers phase separates, engulfing drug particles. Solidify polymers to form microsphere [11].

**Aqueous/Organic solution of polymer**

↓
↓ Add drug
Drug dispersed or dissolved in the polymer solution
↓
↓ Phase separation induced by different means
Polymer Rich Globules
↓
↓ Solidify
Microspheres in aqueous/organic phase
↓
↓ Separate, wash and dry
Microspheres

**Spray drying and spray congealing**

Polymer is dissolved in a volatile organic solvent (e.g. Dichloromethane, acetone). Solid drug particles are dispersed in the polymer solution under high-speed homogenization. The dispersion is atomized into a stream of hot air (spray drying) or cool air (spray congealing). Solvent evaporation instantly, forming Microsphere (1-100nm). Microspheres are collected using a cyclone separator Excess solvent is removed by vacuum drying [12].

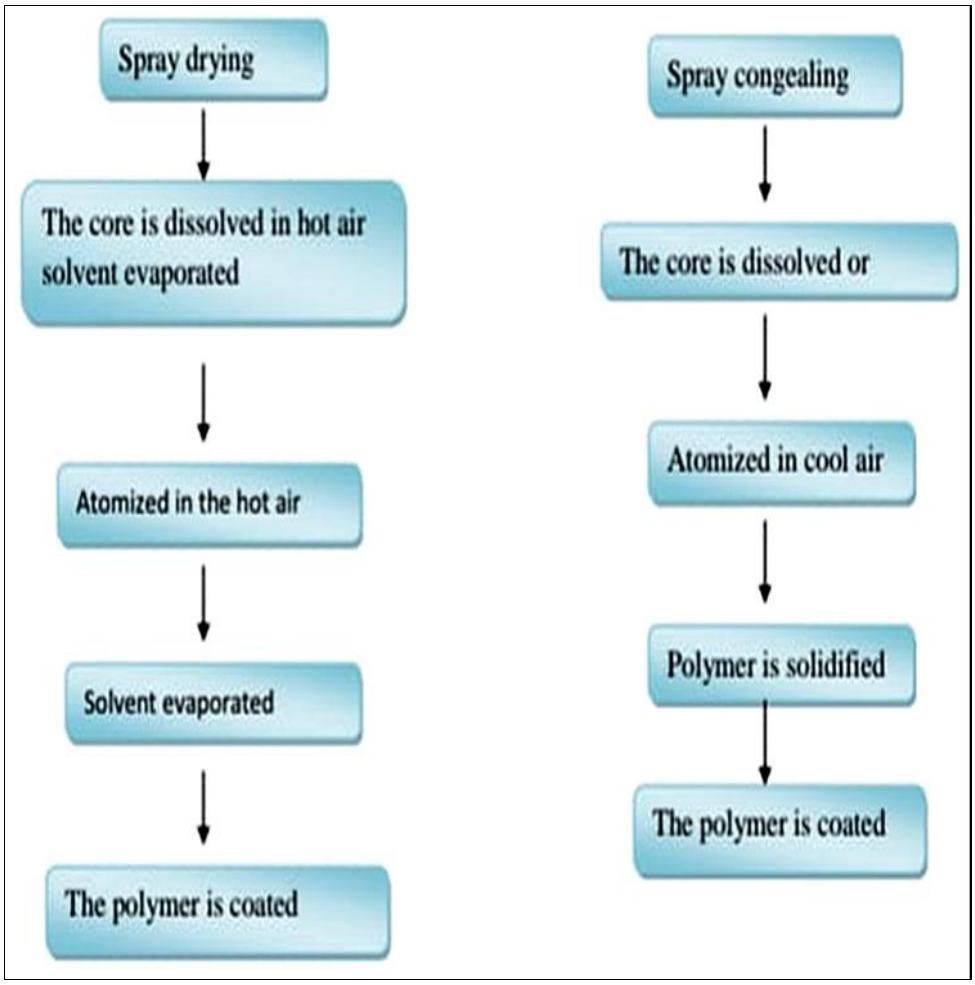


**Fig 3:** Diagrammatic representation of spray drying and spray congealing

**Solvent extraction method**

Dissolve polymer in a water-miscible organic solvent. (e.g.: isopropanol). Mix drug or protein into the polymer solution. Create an emulsion with polymer solution. Add water to extract organic solvent from the emulsion. As the solvent is removed, the microsphere hardens. Collect the formed micro particles [12].

**Drug is dispersed in organic solvent:**

[Water misible organic solvents like isopropanol]
↓
Polymer in organic solvent
↓
Organic phase is removed by extraction with water
↓
Microspheres

**Quasi-emulsion solvent diffusion method:**

Mix drug, ethanol, and polymer at 60 °C. Mix distilled water and polyvinyl alcohol at room temperature. Add internal phase to external phase and stir for 2 hours. Separate micro sponges from the mixture. Wash and dry micro sponges in a vacuum oven at 40 °C [13].

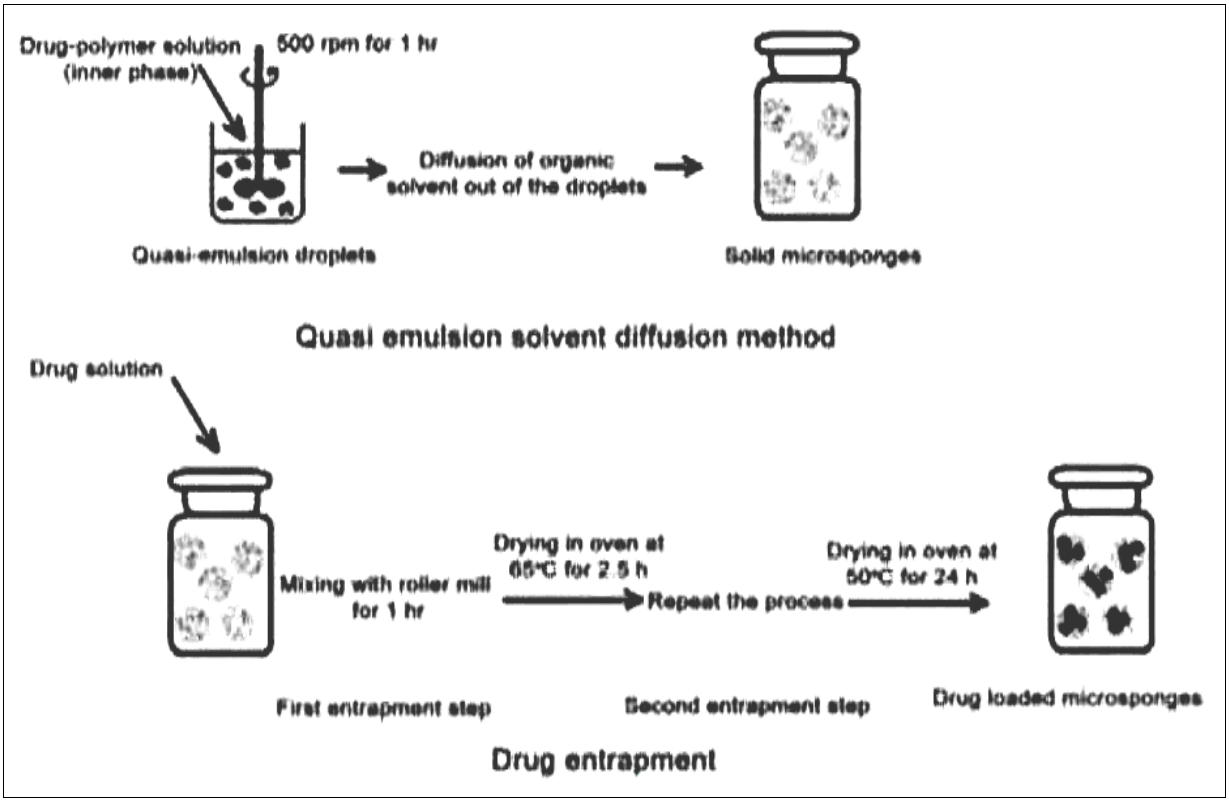


**Fig 4:** Quasi-emulsion solvent diffusion method for microsponge preparation.

**Polymers**

**Microspheres usually use polymers**

- Natural polymers
- Synthetic Polymers

**Natural polymers**

- **Carbohydrates:** Agarose, Carrageenan, Chitosan, Starch
- **Proteins:** Albumin, Collagen and Gelatin
- **Chemically modified carbohydrates:** Poly dextran, Poly starch

**Synthetic polymers**

**Biodegradable polymers:** Lactides, Glycosides & their co-polymers, Poly anhydrides, Poly alkyl cyanoacrylates.

**Non-biodegradable polymers:** Polymethyl methacrylate (PMMA), Glycidyl methacrylate, Acrolein, Epoxy Anions: Tripolyphosphate (TPP-), sodium sulfate.

**Common polymers utilized in beads technology:-**

- Sodium Alginate
- Chitosan
- Carboxy Methyl Cellulose [14]

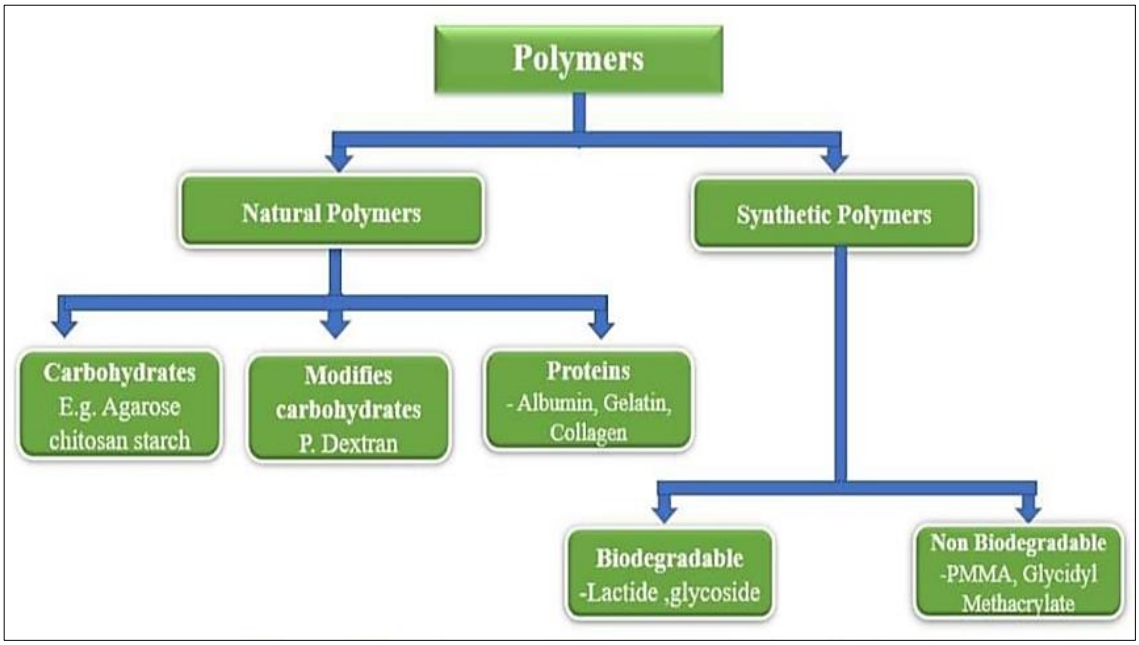


**Fig 5:** Diagrammatic representation of spray drying and spray congealing techniques for polymer coating.

**Mechanism of microsphere**

Most of the drug delivery via micro particles inhibits the formation of a matrix-like internal solid dispersion morphology structure. The drug can be insoluble in the matrix of polymer, and it is released through erosion. First, water diffuses into the matrix, dissolving the resulting near the device's surface. The resulting osmotic pressure gets alleviated by forming a channel to the surface and releasing a predetermined amount of drug in the initial drug burst.

Drug release from the microspheres occurs by a general mechanism including;

- Dissolution
- Diffusion,
- Polymer degradation,
- Hydrolysis/erosion [14]

**Evaluation**

**Particle size and shape**

The predominant methodologies employed to visualize microspheres encompass Conventional Light Microscopy (LM) and Scanning Electron Microscopy (SEM). Both techniques are adept at elucidating the morphology and external architecture of these microspheres. Light Microscopy (LM) affords meticulous control over coating parameters, particularly in the context of double-walled microspheres. The structural attributes of the microspheres can be visualized both pre- and post-coating, with alterations readily quantifiable via microscopic analysis. In contrast, SEM offers superior resolution relative to Monogonal Fluorescence Microscopy, which is utilized for the structural characterization of multi-walled microspheres. Additionally, techniques such as laser light scattering and multi-size Coulter counting, alongside instrumental methodologies, can be employed to comprehensively characterize the size, shape, and morphology of the microspheres [14].

**Swelling index**

To determine the swelling index, measure how much the microspheres expand when placed in a specific liquid. To do this, take dried microspheres (roughly half the weight of a grain of table salt) and let them soak overnight in buffer solution inside a measuring cylinder. After swelling, use the following formula to calculate the swelling index [14].

$$Swelling\ index = wf - wo/\text{wo} \times 10$$

**Entrapment efficiency**

To measure the encapsulation efficiency (or percent entrapment) of the microspheres, first lyse the washed microspheres. Then, analyze the resulting lysate to determine the amount of active ingredient present, following the relevant method described in the monograph. Use the following formula to calculate the percent encapsulation efficiency [14].

$$\%EE = Actual\ drug\ content/Theoretical\ drug\ content \times 100$$

**The percentage yield**

The percentage yield is calculated by dividing the weight of the microspheres obtained from a batch by the total weight of the drug and polymer used to make that batch, then multiplying the result by 100 [15].

$$\%\ Yield = Practical\ yield/theoretical\ yield \times 100$$

**Isoelectric point**

Micro electrophoresis is an instrument used to measure the electrophoretic mobility of microspheres, which helps in determining their isoelectric point. This is done by calculating the average velocity of the microspheres at various pH level based on the time it takes for the particles to travel a distance. Using this information, the electrical mobility of the particles can also be calculated. Electrophoretic mobility is influenced by factors such as the surface charge, ionizable groups, and the ability of the Microspheres to absorbs ions [14].

**Attenuated total reflectance Fourier transform infrared (FT-IR) Spectroscopy**

FT-IR (Fourier Transform Infrared Spectroscopy) is used to assess the degradation of the polymer matrix in the carrier system. The surface composition of the microspheres is analyzed using Attenuated Total Reflectance (ATR). In this technique, a beam of infrared light passes through an ATR crystal and reflects multiple times through the sample, generating IR spectra that mainly represent the surface material. Combined, ATR-FTIR provides detailed information about the surface characteristics of the microspheres [16].

**Electron spectroscopy for chemical analysis (ESCA)**

This technique is used to analyze the surface chemistry of microspheres. ESCA (Electron Spectroscopy for Chemical Analysis) provides important information about the atomic composition on the surface of biodegradable microspheres [17].

**Density determination**

The density of microspheres can be measured using a device called a multi-volume pycnometer. A precisely weighed sample is placed into a cup inside the pycnometer. Then, helium gas is introduced at a constant pressure, and allowed to expand into the chamber. This causes a drop in pressure, which is measured. Two pressure readings are taken at different starting pressures. Using these readings, the volume of the sample is calculated, and from that, its density is determined [18].

**Angle of contact**

Contact angle measures how water interacts with microparticles. It shows whether microspheres in terms of hydrophilicity or hydrophobicity. The angle of contact is measure at the solid/air/water interface. The angle of contact is measured using a droplet is placed in a cell on an inverted microscope [19].

***In vitro* methods:-**

- Beaker method
- Dissolution method

**Beaker method**

In this method, the dosage form is attached to the bottom of a beaker containing a liquid medium, which is stirred evenly using an overhead stirrer. The volume of the medium typically, and the stirring speed is set between 60 and 300 rpm. Samples are taken at specific time intervals to measure the amount of drug dissolved in the medium.

**Dissolution apparatus**

A standard USP or BP dissolution apparatus is used to study the *in vitro* drug release profile, using rotating elements such as the paddle (apparatus 41, 42, 43) or basket (apparatus 44, 45). The dissolution medium volume typically, and the rotation speed is set between 50 and 100 rpm [16].

**Conclusion**

Microspheres have been discovered to be a better option for medication delivery when compared to several other forms of drug delivery systems. Different kinds of procedures for preparation are being studied. It contains microspheres used in gene delivery, nasal delivery, oral delivery, and other microsphere applications. Microspheres will play a major role in medicine in the future.

**Reference**


1. Chavan A, *et al*. A review on micro emulsion and microsphere: A promising optimizing technique for advanced drug delivery system. Acta Biomed. 2024;95(1).
2. Gupta M, Sharma V. Targeted drug delivery system: A review. Res J Chem Sci. 2011;1(2):135-6.
3. Dixit N, *et al*. Sustained release drug delivery system. Indian J Res Pharm Biotechnol. 2013;1(3):305-310.
4. Kaushtubh, *et al*. A review on microsphere and its application. Asian J Pharm Res. 2019;9(2):123-129.
5. Athira K, *et al*. Microspheres as a novel drug delivery system: A review. Int. J Pharm Sci Rev Res. 2022;75(1):160-166.
6. Kataria S, *et al*. Microsphere: A review. Int. J Res Pharm Chem. 2021;1(4):1184-97.
7. Yadav M, *et al*. A review on microsphere as a promising drug carrier. J Drug Deliv Ther. 2024;14(7):120-128.
8. Singh C, *et al*. Design and evaluation of microsphere: A review. J Drug Deliv Res. 2013;2(2):18-27.
9. Ingle TKG, *et al*. The current trends in microspheres: A review. J Drug Deliv Ther. 2023;13(1):183-194.
10. Patel, *et al*. A review on microsphere: Types, methods of preparation, process variables and applications. Am J PharmTech Res. 2020;10(4):124-140.
11. Alagusundaram M, *et al*. Microsphere as a novel drug delivery system: A review. Int J ChemTech Res. 2009;1(3):526-534.
12. Mangnale M, *et al*. A review on microsphere: Method of preparation and evaluation. IJPPR Human. 2021;20(3):486-497.
13. Kadam NR, Suvarna V. Microsphere: A brief review. Asian J Biomed Pharm Sci. 2015;5(47):13-19.
14. Abrar A, *et al*. Formulation and evaluation of microspheres of antiulcer drug using Acacia nilotica gum. Int. J Health Sci. 2020;14(2):10-17.
15. Samantha MS, *et al*. A review of microspheres as a novel drug delivery system. Asian J Pharm Clin Res. 2021;14(4):3-11.
16. Savale SK. Formulation and evaluation of microspheres with aceclofenac. WJPMR. 2016;2(4):181-187.
17. Das MK, *et al*. Microsphere as a drug delivery system: a review. Int J Curr Pharm Res. 2019;11(4):34-41.
18. Sah H, Ganarajan G. Microspheres: types, preparation, evaluation and application: A review. Int. J Res Appl Sci Eng Technol. 2023;2(6):260-267.
19. Gurung BD, *et al*. An overview on microspheres. Int. J Health Clin Res. 2020;3(1):11-24.