Research Article

J. innov.appl. pharm. Sci, 10[2] 2025, 29-33

Journal of Innovations in Applied Pharmaceutical Science [JIAPS]

Content available at: www.saap.org.in ISSN: 2455-5177

INNOVATIVE DRUG DELIVERY USING MICROSHERIC CARRIERS

Meenega Rajesh*, Mekala Bhaskar, Budagala. Gayathri, Chandu Babu Rao

Priyadarshini Institute of Pharmaceutical Education and Research, 5th Mile, Pulladigunta, Guntur-522017.Andhra Pradesh, India

Article History

Received: 22-06-2025
Revised: 19-07-2025
Accepted: 06-08-2025

Keywords:

Microspheres, Types of Microspheres, Methodes of Preparation, Characterization of Microspheres, Application of Microspheres.

Abstract

Microspheres are innovative drug delivery systems that address the limitations of conventional drug therapies. They are free-flowing spherical powders, typically made from biodegradable proteins or synthetic polymers, with particle sizes ranging from 1 to 1000 µm. Microspheres offer significant advantages, such as improved drug bioavailability, reduced side effects, increased stability, and the ability to deliver drugs at a controlled rate to specific target sites. This targeted delivery minimizes the impact on non-target tissues, enhancing therapeutic efficacy. Various types of microspheres exist, including bioadhesive, floating, radioactive, and biodegradable microspheres, each designed for specific applications in drug delivery. They are used in multiple fields such as oral drug delivery, gene therapy, cosmetics, and diagnostics. Microspheres are particularly effective for controlled release and targeted drug delivery, providing a reliable method for achieving optimal drug concentration at the target site, reducing toxicity, and improving overall treatment outcomes. The future of microspheres in drug delivery systems is promising, especially in applications like targeted therapies, diagnostics, and genetic material delivery. As research progresses, microspheres will play a more central role in novel drug delivery technologies, offering smart and efficient solutions for treating various diseases. Their ability to release drugs in a controlled manner at the desired location makes them an ideal alternative to conventional single-unit dosage forms, with the potential to revolutionize therapeutic approaches in medicine.

***Corresponding Author**

Meenega Rajesh

Production and Hosted by

www.saap.org.in

Introduction

Novel drug delivery system delivers a therapeutic substance to the target site in a well-controlled and sustained model [1]. Microspheres or microparticles are defined as a free-flowing spherical particles consisting of polymer matrix and drug. They consist of proteins or synthetic polymers which are biodegradable in nature having a particle size less t33han 200µm [2]. (typically 1 µm to 1000 µm). Microspheres can also be called as microparticles. Microspheres had been explored significantly for their use in the subject of drug transport and various polymers had been utilized for the formulation of the microspheres, which in turn have been assessed for distinctive purposes. Eventually the whole dose and few adverse reactions can be decreased due to the fact that a steady plasma concentration is maintained [3]. Delivery systems (DDS) with the ability to precisely monitor drug release rates or target drugs to particular body sites have had a profound effect on the health-care system. Over the course of treatment, the best drug delivery device delivers drugs at a set pace determined by the body's needs and delivers the active ingredient to the site of action. By binding the drug to a carrier particle such as microspheres, nanoparticles, or lipids, drug carrier technology offers an intelligent approach to drug delivery [4]. Microspheres are spherical particles that range in diameter from 10 µm to 1000 µm. Microspheres are essential for improving the way conventional drugs are absorbed and lessening their side effects. The controlled release of the medicinal content is the primary benefit of using microspheres as a drug delivery mechanism. By postponing the medication's release from dose forms, microencapsulation reduces adverse effects and enhances patient adherence. This method uses emulsion solvent diffusion evaporation to coat an aqueous insoluble coat (polymer) over an aqueous insoluble core (drugs) to create a sustained release drug delivery system. There are various methods for making microspheres, such as phase separation, spray-dry, and emulsification using single or double solvent evaporation systems. One method for creating microspheres is to dissolve the precursor components in volatile solvents and then disperse them in a different solvent that isn't miscible with the first one. A fine powder known as microspheres that is soluble in water will be produced when

the last solvent has completely evaporated. Medication with a brief half-life that is merely transferred from the gastrointestinal tract (GIT) is instantly eliminated from the bloodstream [5].

History of Microspheres

The first dermal filler substance, Zyderm, was debuted in 1982 and was very well accepted. We were all waiting for this material, and it finally arrived. Although it continues to be one of the safest substances injected into the dermis, the initial excitement has subsided due to itsbrief duration. According to the senior author's three decades of experience with all types of autologous grafts, including dermal, fat, cartilage, bone, and tendon, they will fall out in locations where they do not retain their natural biologic function. After a few months, most of these grafting materials leave only a little amount of scar tissue behind.

Types of Microspheres

Microspheres are classified into different types. They are of following

1. Bioadhesive microspheres
2. Magnetic microspheres
3. Floating microspheres
4. Radioactive microspheres
5. Polymeric microspheres
   I. Biodegradable polymeric microspheres
   II. Synthetic polymeric microspheres

1. Bioadhesive microspheres

Sticking of drug to the membrane by using the watersoluble property of the water-soluble polymers is called adhesion. Sticking or adhesion of drug delivery system to the mucosal membrane such as buccal, nasal, ocular, rectal etc can be termed as bioadhesion. This type of microsphere provides prolonged residence time at the target site and provide better therapeutic action [6].

2.0 Magnetic microsphere

This type of delivery system is important because it allows the drug to be delivered to the exact location where it is needed. A smaller amount of magnetically targeted drug will replace a larger amount of freely circulating drug in this condition. Chitosan, dextran, and other integrated materials used in magnetic microspheres have magnetic responses to a magnetic field [7, 8].

2.1 Therapeutic magnetic microspheres:

These are used to administer a chemotherapeutic agent to liver tumors. Drugs like proteins and peptides can also be targeted through this system [9].

3. Floating microspheres:

Because the bulk density of floating kinds is lower than that of gastric fluid, they float in the stomach without slowing down the pace at which the stomach empties. The medication is released gradually at the desired pace if the stomach material is floating in the system, lengthening the duration of gastric residency and causing more variations in plasma concentration. By producing a sustained therapeutic impact, this approach lowers the frequency of dose. [10]

4. Radioactive microspheres

Radioembolization treatment involves inserting 10-30 nm microspheres, which are larger than capillaries, into the first capillary bed they encounter. They are injected into the arteries that supply the targeted tumor. Radioactive microspheres provide targeted radiation doses without harming neighbouring healthy tissues. There are three different types of radioactive microspheres: those that emit α, β, and γ. The subset of microspheres that interact radioactively is usually treated similarly to non-radioactive microspheres. Radioactive microspheres contain radio-nuclides in addition to matrix material, allowing for targeted delivery to certain tissues or organs. Radioactive microspheres can provide significant radiation doses to specific areas in small numbers without injuring surrounding tissue [11.12].

Polymeric Microspheres

The different types of polymeric microspheres can be classified as follows and they are biodegradable polymeric microspheres and synthetic polymeric microspheres [15].

I. Biodegradable Polymeric Microspheres:

Natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also bioadhesive in nature. Biodegradable polymers prolongs the residence time when contact with mucous membrane due to its high degree of swelling property with aqueous medium, results gel formation. The rate and extent of drug release is controlled by concentration of polymer and the release pattern in a sustained manner. The main drawback is in clinical use drug loading efficiency of biodegradable microspheres is complex and is difficult to control the drug release.

II. Synthetic Polymeric Microspheres

The interest of synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulking agent, fillers, embolic particles drug delivery vehicles etc and proved to be safe and biocompatible. But the main disadvantage of these kinds of microspheres, are tend to migrate away from injection site and lead to potential risk, embolism and further organ damage.

Methods of Microspheres

The choice of technique depends upon the nature of polymer as well as nature of drug and the duration of therapy. The most important physical and chemical factors that may be controlled in microsphere manufacture are

Tecniques for Miceospheres Preparation

1. Solvent evaporation
2. Single emulsion technique
3. Double emulsion technique
4. Phase separation coacervation technique
5. Spray drying and spray congealing
6. Solvent extraction

1. Solvent evaporation

Solvent evaporation is carried out in a manufacturing vehicle phase. The microcapsule coating is first dispersed in a volatile solvent which is immiscible with the liquid manufacturing vehicle phase. In a coating polymer solution, a core material to

be microencapsulated is dissolved or dispersed. To obtain acceptable size microcapsule, agitation is performed so that the core material mixture is dispersed in the liquid manufacturing vehicle phase [13].

2. Single emulsion technique

The microparticulate carriers of natural polymers i.e. those of proteins and carbohydrates can be prepared by single emulsion technique. The natural polymers are dissolved or dispersed in aqueous medium followed by dispersion in non-aqueous medium such as oil. In the next step, cross linking can be achieved either by means of heat or by using the chemical cross linkers. The chemical cross-linking agents used are glutaraldehyde, formaldehyde, acid chloride etc [14].

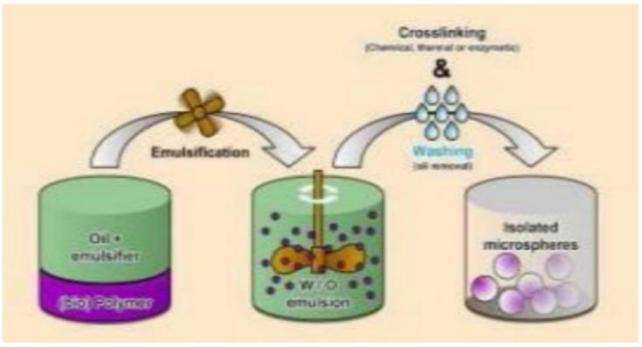


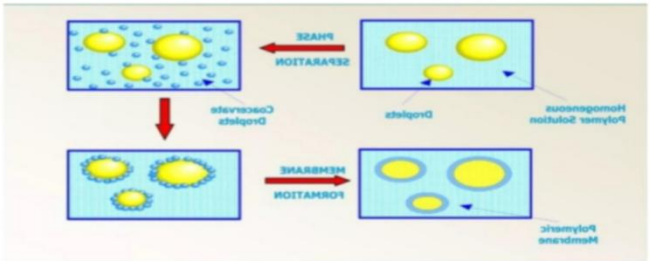
Figure: 1. Single emulsion technique

Double Emulsion Technique

It is the creation of several emulsions, i.e. W/O/W is prepared by pouring the primary w/o emulsion into an aqueous polyvinyl alcohol solution. This w/o/w emulsion shall be put at constant stirring for 30 min. Slowly add some water to the emulsion for a duration of 30 min. Collection of microcapsules by filtration and dry under vacuum. It is ideally suited for water-soluble medicines, peptides, proteins and vaccines. Natural as well as synthetic polymers can be used for this process. The aqueous protein solution is distributed in a continuous organic lipophilic phase. This protein solution will contain active ingredients [15].

Phase separation coacervation technique

Specifically made to prepare the reservoir type of the system, that is, to encapsulate pharmaceuticals that are soluble in water, like as proteins and peptides, and medications that are hydrophobic, like steroids. The medication or protein in a matrix-type device is soluble in the polymer phase. The method works on the basis of reducing the polymer's solubility in the organic phase to influence the development of the coacervates, a polymer-rich phase.



Phase: 3. Phase separation coacrvation technique

5. Spray Drying Technique

This was used to prepare polymeric blended microsphere loaded with ketoprofen drug. It involves dispersing the core material into liquefied coating material and then spraying the mixture in the environment for solidification of coating followed by rapid evaporation of solvent.

Characterization of Microspheres

1. Particle size and shape

LM provides a control over coating parameters in double walled microspheres. SEM provides higher resolution when compared to LM. The Samples can be analyzed through SEM. The sample is scanned in parallel lines using a centered electron beam. Microspheres are placed on a sample holder for SEM characterization followed by coating with a conductive metal like platinum or zirconium using a sputter coater. The sample is scanned with a fine electron beam. The surface properties of the sample are obtained from the secondary electrons leaked from the sample surface.

2. Electron spectroscopy for chemical analysis

The electron spectroscopy for chemical analysis (ESCA) is used to determine the surface chemistry of the microspheres. It is also used for the determination of the atomic composition of the surface. The surface degradation of the biodegradable microspheres can be determined using the ESCA spectra.

Evalusion of Microspheres

1. Particle size and shape:

Scanning electron microscopy (SEM) and conventional light microscopy (LM) are commonly used to study microparticles, revealing their external structure and form. LM allows control over coating settings, while SEM offers higher resolution. Conflocal fluorescence microscopy characterizes multiplewalled microspheres, while laser light scattering and multisize Coulter counter can also be used [16].

2. Electron spectroscopy for chemical analysis:

Confocal fluorescence microscopy evaluates structural features of microspheres with many walls. In addition to instrumental approaches, multisize microspheres can be examined for size, shape, and morphology. Coulter Counter and Laser Light Scattering [17.18].

Mechanisam of Microspheres

The majority of drug delivery via microparticles prevents the formation of a matrix-like internal solid dispersion morphology structure. The drug may be insoluble in the polymeric matrix, and it is released by erosion. First, water diffuses into the matrix, dissolving the resulting near the device's surface. The resulting osmotic pressure is alleviated by forming a channel to the surface and releasing a predetermined amount of drug in the initial drug burst. [19]

Advantages of Microspheres [20-21]

1. Decreased size of microsphere contributes increased surface area thereby increases the potency of the poorly soluble material.
2. Dose frequency and adverse effects can be reduced.
3. Increased patient compliance.

4. Drug packaged with polymer prevent drug fromenzymatic cleavage therefore the drug can be protected from various enzymes.
5. Enhances bioavailability.
6. Microspheres have a consistent and long-lasting therapeutic impact.

Disadvantages of Microspheres

1. Reproducibility is less.
2. The cost of materials and processing is high compared to conventional preparations.
3. Change in process variables such as change in temperature, pH, solvent addition and evaporation/agitation may influence the stability of core particles.
4. The fate of polymer matrix and additive [22].

Applications of Microspheres

Microspheres in vaccine delivery an ideal vaccine must meet the following criteria: effectiveness, safety, ease of use, and cost. Biodegradable vaccine delivery systems for vaccines administered through the parenteral route may be able to overcome the limitations of conventional vaccines [23].

1. Improved antigenicity by adjuvant action
2. Modulation of antigen release
3. Stabilization of antigen.

The microspheres have been extensively studied and used for the targeting purposes. Various cells, cell lines, tissues and organs can be imaged using radio labelled microspheres. The particle size range of microspheres is an important factor in determining the imaging of particular sites. The particles injected intravenously apart from the portal vein will become entrapped in the capillary bed of the lungs. This phenomenon is exploited for the scintiographic imaging of the tumour masses in lungs using labelled human serum albumin microspheres

Fucture Challenges

Future challenges of microspheres look bright particularly in the area of medicinal field because of its wide spectrum of application in molecular biology, eg: microsphere based genotyping platform is used to detect six single nucleotide polymorphism, yittrium-90 microspheres is used to prevent tumour after liver transplantation and it's advanced way in delivery of vaccines and proteins

Conclusion

The absorption of medicine in the gastrointestinal tract is highly variable, with the duration a dosage form stays in the stomach influencing the absorption rate. Ionotropic gelation of microspheres holds promise as a strategy for prolonged gastric retention. By using gel-like microspheres, drugs can be retained in the stomach for extended periods, which may enhance their absorption by slowing down their release. However, this approach faces challenges such as ensuring stability, controlled drug release, and safe degradation or clearance of the microspheres from the body. Despite these obstacles, many companies are working to commercialize this method, recognizing its potential in improving drug delivery. Microspheres are expected to play a key role in the future of drug delivery by integrating various strategies, particularly in areas like diseased cell sorting, diagnostics, and targeted gene delivery. These microspheres can also enhance the safe and efficient in vivo delivery of drugs, ensuring they are released only at the site of action to minimize side effects. Additionally, microspheres may serve as miniature models of diseased organs and tissues, which could be used in research for developing new treatments. Overall, while challenges remain in perfecting this technology, microspheres show great potential in revolutionizing drug delivery, especially in precision medicine and gene therapy, by providing more targeted, effective, and safe treatment options.

Author Contributions

All authors are contributed equally

Financial Support

None

Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

Acknowledgements

None

References

1. Nama S, Chandu BR, Awen BZ, Khagga M. Development and validation of a new RP-HPLC method for the determination of aprepitant in solid dosage forms. Tropical Journal of Pharmaceutical Research. 2011;10(4):491-7. https://doi.org/10.1016/j.ijbiomac.2019.10.233
2. Wong CY, Al-Salami H, Dass CR. Microparticles, microcapsules and microspheres: A review of recent developments and prospects for oral delivery of insulin. International journal of pharmaceutics. 2018 Feb 15;537(1-2):223-44. https://ioppublishing.org/contacts/
3. Chowdary KP, Rao YS. Mucoadhesive microspheres for controlled drug delivery. Biological and pharmaceutical Bulletin. 2004;27(11):1717-24. https://doi.org/10.1248/bpb.27.1717 https://periodicos.ufv.br/reves
4. Dara SR. An Overview of the Use of Natural Indicators in Acid-Base Titrations. UPI Journal of Pharmaceutical, Medical and Health Sciences. 2024 Jul 23:29-35. http://dx.doi.org/10.52711/2231-5713.2021.00025
5. Munin A, Edwards-Lévy F. Encapsulation of natural polyphenolic compounds; a review. Pharmaceutics. 2011 Nov 4;3(4):793-829. https://doi.org/10.3390/pharmaceutics3040793
6. Kiranmai M, Renuka P, Brahmaiah B, Chandu BR. Vitamin D as a promising anticancer agent.. https://doi.org/10.1021/bm049316f
7. Yawalkar AN, Pawar MA, Vavia PR. Microspheres for targeted drug delivery-A review on recent applications.

Journal of Drug Delivery Science and Technology. 2022 Sep 1;75:103659. https://doi.org/10.1016/j.jddst.2022.103659

8. Hwisa NT, Gindi S, Rao CB, Katakam P, Rao Chandu B. Evaluation of Antiulcer Activity of Picrasma Quassioides Bennett Aqueous Extract in Rodents. Vedic Res. Int. Phytomedicine. 2013;1:27. https://doi.org/10.1016/j.ijpharm.2018.06.015
9. Sudharsan MS, Praveen Kumar M, Gokul V, Pazhamalai V, Hariharan NM, Saravanan M. Stimuli-Responsive Hybrid Microgels for a Sustainable Future: A Comprehensive Review of Classification, Synthesis, and Multifaceted Applications. Polymers for Advanced Technologies. 2025 Jan;36(1):e70087. https://doi.org/10.1002/pat.70087
10. Andrianov AK, Payne LG. Polymeric carriers for oral uptake of microparticulates. Advanced drug delivery reviews. 1998 Dec 1;34(2-3):155-70. https://doi.org/10.1016/S0169-409X(98)00038-6
11. Development of microspheres for Rani, E. V. (2019). Preparation and evaluation of aspirin loaded microspheres by solvent evaporation technique. Journal of Medicine and Biology, 1(1), 27-32. https://doi.org/10.1021/acsbiomaterials.4c01249
12. Qiao Z, Yuan Z, Zhang W, Wei D, Hu N. Preparation, in vitro release and antibacterial activity evaluation of rifampicin and moxifloxacin-loaded poly (D, L-lactide-co-glycolide) microspheres. Artificial Cells, Nanomedicine, and Biotechnology. 2019 Dec 4;47(1):790-8 https://doi.org/10.1080/21691401.2019.1581792
13. Khafoor AA, Karim AS, Sajadi SM. Recent progress in synthesis of nano based liposomal drug delivery systems: A glance to their medicinal applications. Results in Surfaces and Interfaces. 2023 May 1;11:100124. https://doi.org/10.1016/j.rsurfi.2023.100124
14. Cai Z, Jiang H, Lin T, Wang C, Ma J, Gao R, Jiang Y, Zhou X. Microspheres in bone regeneration: Fabrication, properties and applications. Materials Today Advances. 2022 Dec 1;16:100315. https://doi.org/10.1016/j.mtadv.2022.100315
15. Agnihotri N, Soni G, Chanchal DK, Khan A, Tiwari S. A Review on Microspheres a Novel Drug Delivery System for Multiparticulate Drug Release. Int. J. Life Sci. Rev. 2019;5:6-15. http://dx.doi.org/10.13040/IJPSR.0975-8232.IJLSR.5(1).6-15
16. Yawalkar AN, Pawar MA, Vavia PR. Microspheres for targeted drug delivery-A review on recent applications. Journal of Drug Delivery Science and Technology. 2022 Sep 1;75:103659. https://doi.org/10.1016/j.jddst.2022.103659
17. Sailaja AK, Anusha K. Review on microspheres as a drug delivery carrier. Int. J. Adv. Pharm. 2017 May 30;6:96-102. https://doi.org/10.7439/ijap.v6i5.4152
18. Raj H, Sharma S, Sharma A, Verma KK, Chaudhary A. A novel drug delivery system: Review on microspheres. Journal of Drug Delivery and Therapeutics. 2021;11(2-S):156-61. http://dx.doi.org/10.22270/jddt.v11i2-s.4792
19. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Preparation of multiple unit hollow microspheres (microballoons) with acrylic resin containing tranilast and their drug release characteristics (in vitro) and floating behavior (in vivo). Journal of Controlled Release. 1991 Aug 1;16(3):279-89. https://doi.org/10.1016/0168-3659(91)90004-W.
20. Win KY, Teng CP, Ye E, Low M, Han MY. Evaluation of polymeric nanoparticle formulations by effective imaging and quantitation of cellular uptake for controlled delivery of doxorubicin. Small. 2015 Mar;11(9-10):1197-204. https://doi.org/10.1002/smll.201402073
21. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: importance and enhancement techniques. International Scholarly Research Notices. 2012;2012(1):195727 .https://doi.org/10.5402/2012/195727
22. Hwisa, NT; Gindi, S; Rao, CB; Katakam, P, Rao Chandu, B. 2013.Evaluation of Antiulcer Activity of Picrasma Quassioides Bennett Aqueous Extract in Rodents.Vedic Res. Int. Phytomedicine vol 1.pg no : 27 https://www.researchgate.net/publication/248995990