IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Formulation And Evaluation Of Bio-Degradable Microsphere

Kumar Nishant[1]*

Thakur Pallav[2]*

Ranjan Himanshu[2]*

Mamgain Shilpa[3]*

1-2 Student, B. Pharma, Dev Bhoomi Institute of Pharmacy and Research, Dehradun

3 Assistant Professor, School of Pharmacy and Research, Dev Bhoomi Uttarakhand University, Dehradun

1) ABSTRACT

Microspheres are spherical particles with diameters typically ranging from tens to hundreds of micrometers, extensively utilized in various fields including pharmaceuticals, biotechnology, and materials science. Among the methods employed for their formulation, solvent evaporation stands outas a versatile and widely adopted technique. This abstract aims to provide a concise overview of the process involved in formulating microspheres via solvent evaporation.

The process begins with the dissolution of a polymer or a blend of polymers in a volatile solvent, forming a homogeneous solution. Optionally, an emulsification or dispersion step may follow to encapsulate hydrophilic substances or control release properties. Subsequently, the polymer solution is subjected to controlled evaporation to remove the solvent gradually. As the solvent evaporates, thepolymer precipitates, leading to the formation of solid microspheres. Parameters such as polymer choice, solvent selection, and processing conditions are carefully optimized to achieve desiredmicrosphere characteristics.

Solvent evaporation offers several advantages including precise control over particle size and morphology, versatility in encapsulating both hydrophobic and hydrophilic substances, and compatibility with various polymers and active ingredients. However, optimization of process parameters is critical to ensure the desired characteristics and performance of the microspheres.

Keywords: microspheres, solvent evaporation, pharmaceuticals, biotechnology, materials science, formulation methods, polymer dissolution, volatile solvent, emulsification, dispersion, controlled evaporation, particle size, morphology, encapsulation, hydrophobic substances, hydrophilic substances, polymer choice, solvent selection, processing conditions, optimization, active ingredients, release properties

2) INTRODUCTION

Microspheres are tiny spherical particles with diameters typically ranging from tens to hundreds of micrometers. They find applications in various fields including pharmaceuticals, biotechnology, cosmetics, materials science, and diagnostics. Due to their unique properties and versatile nature, microspheres have become invaluable tools in research and industry.

The fabrication of microspheres involves a range of techniques, each tailored to specific applications and desired characteristics. These techniques include emulsification, solvent evaporation, spray drying, and precipitation methods, among others. Depending on the intended use, microspheres can be engineered to exhibit controlled release properties, surface modifications for targeting specific tissues or cells, or encapsulation of active ingredients.

In pharmaceuticals, microspheres are extensively used for drug delivery systems due to their ability to encapsulate drugs, protect them from degradation, and control their release kinetics. They enable sustained and targeted delivery of drugs, improving efficacy and patient compliance while minimizingside effects.

2.1 TYPES OF MICROPHERES

1) Bioadhesive Microsphere
2) Magnetic Microsphere
3) Floating Microsphere
4) Radioactive Microsphere
5) Polymeric Microsphere

a) Biodegradable Polymeric Microsphere
b) Synthetic Polymeric Microsphere

➢ Bioadhesive Microspheres

Bioadhesive microspheres are small spherical particles designed to adhere to biological surfaces such as mucosal tissues upon contact. These microspheres are engineered to possess adhesive properties that allow them to bind strongly to the surface of tissues, providing sustained contact and localized delivery of drugs or bioactive agents.

The key characteristic of bioadhesive microspheres is their ability to adhere to biological surfaces through various mechanisms such as electrostatic interactions, hydrogen bonding, van der Waals forces, or specific receptor-ligand interactions. This adhesion prolongs the residence time of the microspheres at the site of application, enhancing the absorption of drugs or bioactive substances across mucosal barriers and improving their therapeutic efficacy.

➢ Magnetic Microspheres

Magnetic microspheres are tiny spherical particles typically ranging in size from nanometers to micrometers, which are infused or coated with magnetic materials. These materials often include ferromagnetic or superparamagnetic substances like iron oxide nanoparticles. The incorporation of magnetic components enables these microspheres to exhibit magnetic properties, allowing themto respond to external magnetic fields.

The primary characteristic of magnetic microspheres is their ability to be manipulated and controlled under the influence of external magnetic fields. When exposed to a magnetic field, these microspheres can be attracted, repelled, or maneuvered within a fluid medium, depending on the strength and orientation of the magnetic field. This unique feature makes magnetic microspheres highly useful in a variety of applications, particularly in targeted drug delivery, magnetic separation, bioseparation, imaging, and sensing.

➢ Floating Microspheres

Floating microspheres, also known as gastroretentive microspheres or buoyant microspheres, are small spherical particles designed to remain buoyant in the stomach for an extended period of time after oral administration. These microspheres are typically engineered to have low density and may contain gas-generating agents or porous structures to enhance their buoyancy.

The key characteristic of floating microspheres is their ability to float on the gastric fluid surface,thereby prolonging their residence time in the stomach. This extended gastric retention allows forsustained release and absorption of drugs or bioactive substances, particularly those with limited solubility or stability in the acidic environment of the stomach.

➢ Radioactive Microspheres

Radioactive microspheres are tiny spherical particles that contain a radioactive material, typically a radioisotope, incorporated within their structure. These microspheres are used in various medical applications, particularly in radiation therapy and diagnostic imaging.

In radiation therapy, radioactive microspheres can be designed to deliver localized radiation therapy directly to tumours or cancerous tissues. This targeted approach minimizes damage to surrounding healthy tissues while maximizing the therapeutic effect on the diseased area. This technique is often used in the treatment of liver cancer (hepatocellular carcinoma) or certain typesof metastatic cancer.

➢ Polymeric Microspheres

Biodegradable and synthetic polymeric microspheres are two categories for polymericmicrospheres.

a) **Biodegradable Polymeric Microspheres:-** Biodegradable polymeric microspheres are small spherical particles made from biocompatible polymers that can be broken down and metabolized by biological processes within the body. These microspheres are designed to deliver drugs, proteins, genes, or other bioactive compounds to specific tissues or organs, providing controlled release and targeted therapy.

The key characteristic of biodegradable polymeric microspheres is their ability to degrade overtime into non-toxic byproducts that can be eliminated from the body through natural metabolicpathways. This property makes them ideal for applications where sustained drug release is desired without the need for surgical removal of the delivery system.

b) **Synthetic Polymeric Microspheres**:- Synthetic polymeric microspheres are small spherical particles composed of artificial or synthetic polymers that are engineered for specific biomedical or industrial applications. These microspheres are typically produced through controlled chemical or physical processes, allowing precise control over their size, shape, andcomposition.

The key characteristic of synthetic polymeric microspheres is their versatility and tunability, as they can be designed to meet specific requirements such as drug delivery, imaging,diagnostics, cell culture, or separation techniques. By selecting appropriate polymers and fabrication methods, synthetic polymeric microspheres can exhibit desired properties such as biocompatibility, biodegradability, surface functionality, and controlled release kinetics.

2.2 METHODS OF PREPARATION

1. Solvent evaporation
2. Single emulsion Method
3. Double emulsion technique
4. Solvent extraction

1) Solvent Evaporation

Solvent evaporation is a process commonly used in the formulation of microspheres, which are small spherical particles typically ranging from tens to hundreds of micrometers in size. This process involves the creation of microspheres by dissolving a polymer or a mixture of polymers in a volatile solvent to form a solution. The solution may also contain active pharmaceuticalingredients (APIs) or other desired substances.

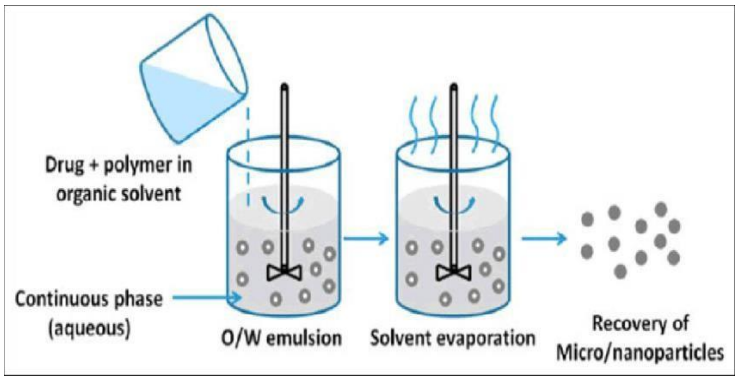

Fig1-solvent evaporation technique

2) Single emulsion techniques

The single emulsion method, also known as the oil-in-water (o/w) emulsion method, is a common technique used in the fabrication of polymeric microspheres for drug delivery and other applications. This method involves the preparation of a primary emulsion consisting of a dispersedphase (typically a polymer dissolved or dispersed in an organic solvent) and a continuous phase (an aqueous solution or dispersion containing emulsifiers).

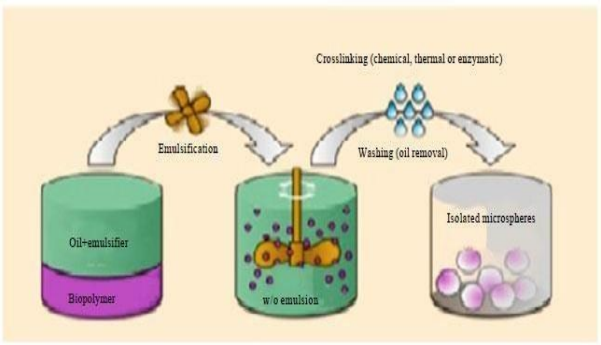

Fig2- Single emulsion technique

3) Double emulsion techniques

The double emulsion technique, also known as the water-in-oil-in-water (w/o/w) emulsion method, is a specialized approach used in the fabrication of polymeric microspheres, particularly for encapsulating hydrophilic drugs, proteins, or other water-soluble bioactive agents within a polymer matrix. This method enables the creation of microspheres with a core-shell structure, where the activeingredient is entrapped within an inner aqueous phase surrounded by a polymer shell, which in turn isdispersed in an external aqueous phase.

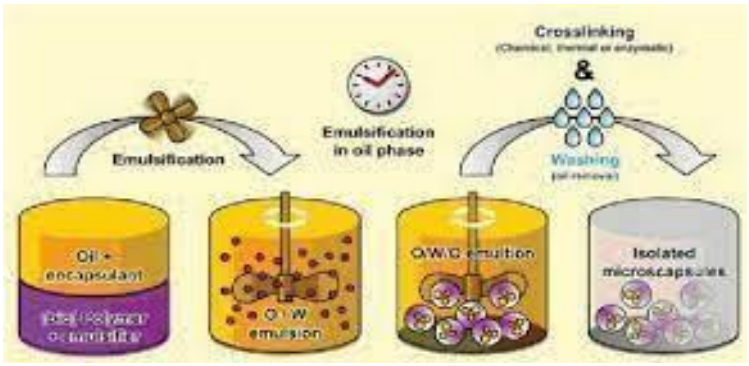

Fig3- Double emulsion technique

5. Solvent extraction

The solvent extraction method, also known as the phase separation or coacervation method, is a techniqueused in the preparation of polymeric microspheres for drug delivery and encapsulation of bioactive compounds. This method involves the formation of a polymer-rich phase around the dispersed droplets ofa drug-containing solution, followed by the removal of the solvent to solidify the polymer and form microsphere.

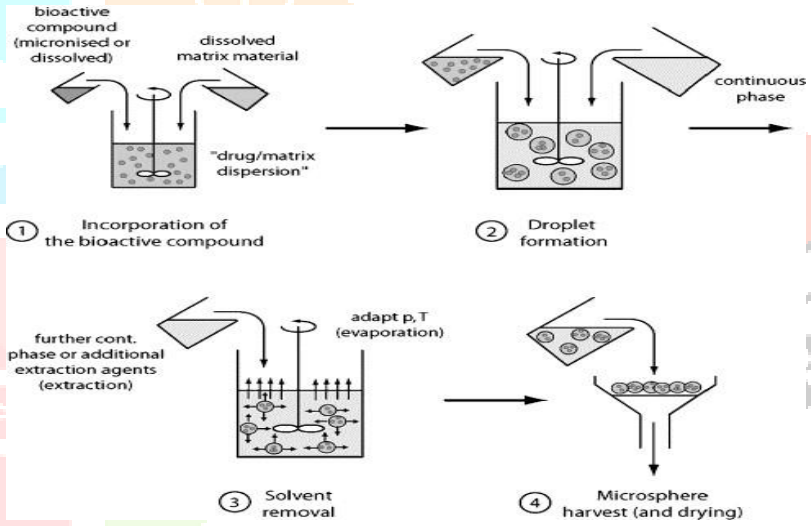

Fig4- Solvent extraction technique

2.3 Evaluation of Microspheres

a. Micro metrics Properties (Particle Size and Shape):-

The techniques most often used to view microparticles are particle size analyzers, scanning electron microscopy (SEM), and conventional light microscopy (LM).

b. Electron Spectroscopy for Chemical Analysis:-

The surface chemistry of the microspheres can be ascertained by electron spectroscopy for chemical analysis, or ESCA.

c. Drug Entrapment Efficiency:-

The aim is to compute the total amount of medication entrapped in the microspheres. It can be calculated using the formula below: Actual content / Theoretical content X 100 equals entrapment.

d. Density Determination:-

A multi-volume cyclometer can be used to determine the microspheres' density.

e. Isoelectric Point:-

Micro electrophoresis can be used to measure the electrophoretic mobility of microspheres in orderto determine the isoelectric point.

f. The angle of Contact:-

The angle of contact is measured to determine the wetting property of a microparticulate carrier.

g. In-vitro Methods:-

Utilizing various suitable dissolving media, the dissolution apparatus used in IP/USP/BP is usedto conduct release studies for different types of microspheres.

3 .METHODS. AND PROCEDURES

3.1 Materials and Equipment:

S.No.	Ingredients
1	Active pharmaceutical ingredient (API)
2	Polymers
3	Organic solvent
4	Surfactant

Equipment

S.No.	Equipment
1	Stirring apparatus
2	Rotary evaporator or vacuum pump
3	Emulsification device
4	Microsphere hardening solution
5	Filter paper or membrane
6	Drying apparatus

3.2 Procedure to formulate microsphere by solvent extraction Method

1) Weighing = Weigh the desired amount of polymer and API according to the formulation requirement.
2) Polymer Dissolution = The polymer should dissolve in the organic solvent. Until the polymer is fullydissolved, stir the mixture.
3) API Dissolution (if applicable) =Dissolve the API in the polymer solution. Ensure homogeneous mixing by stirring.
4) Emulsification = Dropwise addition of the polymer-API solution, homogenized by homogenization or ultrasonication, and continuous stirring into an aqueous phase (with surfactant added if necessary) yields an emulsion. As a result, an oil-in-water (O/W) emulsion is created.
5) Solvent Extraction = Stir the emulsion continuously so that the solvent can permeate into the outer aqueous phase and cause the microspheres to solidify. This can be made easier by eliminating the solvent with a vacuum pump or rotary evaporator.
6) Microsphere Hardening = Transfer the formed microspheres into a non-solvent for the polymer, commonly referred to as the hardening solution. This induces solidification and hardening of the microspheres.
7) Separation = Filter the microspheres from the hardening solution using filter paper or membrane to separate them from the liquid phase.
8) Washing (Optional) = Rinse the microspheres with a suitable non-solvent to remove any remaining traces of the solvent or impurities.
9) Drying = Dry the microspheres using a suitable drying method, such as freeze-drying or air drying, to obtain a powder or solid form.
10) Characterization = Characterize the microspheres for size, morphology, drug loading, and other relevant parameters using techniques like microscopy, particle size analysis, and drug contentanalysis.
11) Storage = Store the formulated microspheres in appropriate conditions to maintain stability until further use.

4. FUTURE ASPECT

1. Precision Medicine and Personalized Therapeutics

Tailoring microsphere formulations for specific patient populations or even individual patients.

Customizing drug release profiles to match patient needs and optimize therapeutic outcomes.

2. Advanced Drug Delivery Systems

Incorporating advancements in nanotechnology to enhance the drug delivery capabilities of microspheres.

Developing smart microspheres that respond to specific physiological cues for targeted and controlleddrug release.

3. Combination Therapies

Formulating microspheres that can deliver multiple therapeutic agents simultaneously, enablingcombination therapies for complex diseases.

Integrating diagnostics and therapeutics within a single microsphere system for real-time monitoring and treatment adjustments.

4. Imaging and Diagnostics

Developing imaging-capable multifunctional microspheres for improved diagnostic uses.

Developing microsphere-based contrast materials for use in magnetic resonance imaging (MRI),computed

tomography (CT), and ultrasound.

5. Biodegradable and Sustainable Materials

Continued focus on environmentally friendly materials and processes for the synthesis of microspheres.

Exploring biodegradable and renewable polymers to address sustainability concerns in the pharmaceutical and biomedical industries.

6. Innovative Manufacturing Techniques

Advancements in microsphere fabrication methods, including microfluidics, 3D printing, and bottom-up assembly approaches.

Scalable and cost-effective manufacturing processes to meet the demand for large-scale production.

7. Targeted Delivery Systems

Designing microspheres with improved targeting capabilities for specific tissues or cells.

Incorporating ligands and targeting moieties for enhanced precision in drug delivery.

8. Regulatory Considerations

Addressing regulatory challenges associated with the approval and commercialization of microsphere- based therapies.

Establishing standardized testing protocols and quality control measures for ensuring the safety and efficacy of microsphere products.

5. CONCLUSION

The current review article claims that microspheres are a better drug delivery method that can solve problems with conventional dosage forms. Microspheres are essential to novel drug delivery systems, particularly in the areas of diseased cell sorting, diagnostics, gene and genetic materials, safe, targeted, specific, and effective in vitro delivery, and supplements as tiny replicas of diseased organs and tissues inthe body.

Microspheres are superior to current technology in a number of ways. Not only does microsphere formulation prove to be a more potent and effective drug delivery system in in vivo settings, but it also proves to be an efficient carrier for innovative drug delivery systems**.**

Reference

1. Rajput S, Agrawal P, Pathak A, Shrivasatava N, Baghel SS, Baghel RS. A review on microspheres:methods of preparation and evaluation. World journal of pharmacy and pharmaceutical sciences. 2012;1:422- 38.

2. Saini S, Kumar S, Choudhary M, Nitesh, Budhwar V. Microspheres as controlled drug delivery system: an updated review.International journal of pharmaceuticalsciences and research. 2018;9(5):1760-8.

3. Patel KS, Patel MB. Preparation and evaluation of chitosan microspheres containing nicorandil. International journal of pharmaceutical investigation. 2014;4(1):32. doi: 10.4103/2230- 973X.127738; PMID: 24678460.

4. .Chaware P, Sharma S, Bhandari A, Garud A, Garud N. Bioadhesive Microspheres: A Review onPreparation and In-Vitro Characterization. World Journal of Pharmaceutical Research. 2014;4(2):423-36.

5. Farah Hamad Farah, et. al., Magnetic Microspheres: A Novel Drug Delivery System, Analytical andPharmaceutical Research. 2016;3(5):1-10. DOI: 10.20959/wjpps20179- 10054.

6. Jagtap Yogesh Mukund, et. al., Floating microspheres: a review, Brazilian Journal of Pharmaceutical Sciences, 2012;48(1):17-30.

7. Urs Hafeli, et. al., Review: Radioactive Microspheres for Medical Applications, Cleveland ClinicFoundation, Radiation Oncology Department T28, page 1-29.

8. Lachman LA, Liberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Varghese Publishng House, Mumbai, India: 1991, 3rd edition; P-414-415.

9. Ketie Saralidze, et. al., Polymeric Microspheres for Medical Applications, Materials, 2010, 3, Page3537- 3564.

10. E Veena Rani, et. al., Preparation and Evaluation of Aspirin Loaded Microspheres by Solvent Evaporation Technique, Journal of Medicine and Biology, 2019;1 (1):27- 32.

11. Jayaprakash S, Halith S M, Mohamed Firthouse P U, Kulaturanpillai K, Abhijith, Nagarajan M.Preparation and evaluation of biodegradable microspheres of methotrexate. Asian JPharm,3;2009,26-29.

12. Sinha V R, Bansal K, Kaushik R, Kumria R, Trehan A. Polycaprolactone microspheres and nanospheres, International Journal of Pharmaceutics (2004) 278 1–23

13. Sinha V R,Singla A K,Wadhawan S,Kaushik R,Kumria R,Bansal K, Dhawan S, Chitosan microspheres as a potential carrier for drugs, International Journal of Pharmaceutics274;2004, 1–33.

14. Saravana Kumar K, et. al., A Review on Microsphere for Novel drug delivery System, Journal of Pharmacy Research, 2012;5(1):420-424. Doi: 10.52711/2231- 5713.2021.00025.

15. Yadav R, Bhowmick M, Rathi V, Rathi J, Design and characterization of floating microspheres forrheumatoid arthritis, Journal of Drug Delivery and Therapeutics 2019; 9(2-s):76-81.

16. Patel NR, Patel DA, Bharadia PD, Pandya V and Modi D: Microsphere as a novel drug delivery, Int.J.Pharm. Life Sci. 2011; 2(8): 992-7.

17. Singh C, Purohit S, Singh M and Pandey BL: Design and evaluation of microspheres: A Review,Jour.Of Drug Deli. And Res. 2013; 2(2): 18-27.

18. Prashant VV, Moy AC, Mathew ST and Mathapan R: Microspheres: An overview, Int. J. Res. Pharm. Biomed. Sci. 2011; 2: 3328. 14 Prasad SGB, Gupta VRM, Devanna N and Jayasurya K: Microspheres as drug delivery system – A review, JGTPS. 2014; 5(3): 1961 -72.

19. Bort R, Mace K, Boobis A, Gomez-Lechon MJ, Pfeifer A, Castell J: Hepatic metabolism of diclofenac:role of human CYP in the minor oxidative pathways. Biochem Pharmacol. 1999 Sep 1;58(5):787-96

20. Kadam N. R. and Suvarna V, Microspheres: A Brief Review, Asian Journal of Biomedical and Pharmaceutical Sciences, 2015;3(4):13-15.

21. Virmani Tarun and GuptaJyoti, Pharmaceutical Application of Microspheres: An Approach for the Treatment of Various Diseases; International Journal of Pharmaceutical Sciences and Research, 2017; 8(1): 3257- 3259. DOI: 10.13040/IJPSR