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MICROSPHERE: A NOVEL APPROACH

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ABSTRACT
Multiple unit delivery of drug in form of system is called microsphere which is formulated to target the specific sites at predetermined rate, enhance bioavailability, and achieve controlled or prolonged drug delivery. To make them polymeric waxy materials and other protective materials like semi-synthetic, synthetic, and natural polymers are used. Microsphere comprises of synthetic polymers and proteins which possess excellent flow ability, 1-1000 µm particle size. The variety of methods available for creating microspheres offers many choices for managing drug delivery and optimizing the medicinal effectiveness of a particular medication. Compared to traditional dosage forms, these delivery methods have many benefits, such as increased patient compliance, decreased toxicity, and enhanced efficacy. These kinds of systems frequently utilize macromolecules as carriers of drug. Current review emphasizes on different varieties of microspheres, preparation strategies, uses, and efficiency evaluation factors.

Keywords: Microspheres, Therapeutic response, prolonged release, Novel delivery of drug

INTRODUCTION[8]
Microspheres are spherical structures typically characterized by diameters ranging from 10 micrometers to 1000 micrometers. They play crucial role in enhancing the bioavailability of traditional medications while decreasing their adverse reactions. The delayed breakdown of particle is primary merit here. By extending the time before the medication is released. and microencapsulating it lowers any adverse effects and improves convenience for patients. In microsphere polymer is coated over drugs to create a sustained-release drug delivery system[1]. Several methods for creating microspheres, such as phase separation, spray-dry, and emulsification use single or double-solvent evaporation systems. One method for creating microspheres is by solubilizing the precursor in solvents that are volatile and then spread them in a various solvent that is immiscible with the last one. Fine micro powder called microspheres which is water soluble is produced after the final solvent has completely evaporated. [17]

Ideal characteristics of microspheres: [17]

- ✓ Capacity to retain considerable drug amounts
- ✓ The stability of the formulation post-synthesis and an adequate shelf life for clinical application.
- ✓ Controlled dispersibility and size of particles in water-based injection carriers.
- ✓ Gradual release of the active ingredient over an extended duration with effective control..1
- ✓ Biodegradability under control and biocompatibility.
- ✓ The susceptibility to modification by chemicals.

Advantages[2]
1. The potency of the substance which has low solubility may be increased by decreasing the size, which also increases surface area.
2. Maintaining a constant level of drugs in the body to enhance patient compliance.
3. Dose and risk reduced.
4. Polymer-based drug packaging prevents enzymatic cleavage of drugs while allowing administration via drug delivery methods.

5. The shorter the duration of administration, the better the patient compliance
6. Effective use of drugs increases bioavailability and reduces the frequency and intensity of adverse effect.
7. Prevent gastrointestinal tract from opioid irritants.
8. Morphology of the microspheres allows it for controllable variation in breakdown and delivery of drug.
9. Taste masking of bitter drugs and converts liquid to solid.
10. Biodegradable microspheres are released in a controlled manner which is employed to maintain the rate of drug release, thereby minimizing adverse effects and avoiding the need for frequent injections.
11. They offer a benefit as compared to polymer implants by potentially eliminating the need for surgical implantation and subsequent reduction procedures.
12. Reliability as modified means accurately delivering drug to target site while regulating therapeutic concentration which no undesired effects.

Disadvantages: [3]

1. The expenses related to materials and processing for controlled-release formulations are notably higher compared to standard formulations.
2. There are concerns regarding the destiny of the matrix polymer along with their potential environmental consequences.
3. Destiny of excipients, including stabilizers, plasticizers, fillers, and antioxidants, remains subject of examination.
4. Achieving consistency in controlled-release formulations presents challenges.
5. Variations during process conditions like solvent interactions, pH levels, temperature changes, and agitation or evaporation can influence the stability of the encapsulated core particles.
6. Environmental concerns arise from the degradation by products of polymer matrices, which may result from factors such as hydrolysis, heat, solar radiation, biological agents, or oxidation.

Microspheres are categorised as:

1. **Bio-adhesive Microspheres:**

These microspheres utilize the sticking properties of polymers that are water-soluble to enhance drug sticks to membranes. They exhibit prolonged residence time at mucous membrane sites such as the oral cavity, eyes, rectum, and nose, enhancing therapeutic efficacy through prolonged contact with absorption sites.

2. **Magnetic Microspheres:**

Magnetic microspheres play a pivotal role in localizing drug delivery to disease sites, enabling targeted drug delivery. These microspheres harness their magnetic response from incorporated materials like chitosan and dextran. Alternative options comprise therapeutically active magnetic microspheres which administer chemical and therapeutic agents in case of tumour caused in liver and microspheres are used for diagnosis which is utilized for imaging liver metastases and distinguishing abdominal structures.

3. **Floating Microspheres:**

These forms of microsphere are an orally retained drug delivery system designed to float in the gastrointestinal tract without foam formation. Also known as hollow microspheres, micro balloons, or floating micro particles, these hollow objects exhibit free-flowing characteristics and vary in size from 1 to 1000 μm.

4. Radioactive microspheres

It is used in interventional radiology to treat liver tumours, consist of tiny particles typically measuring between 10 to 30 nanometres in diameter, larger than capillary diameters, ensuring their entrapment in the initial capillary bed they encounter. These microspheres are administered via arterial injection into arteries supplying blood to specific tumours. By doing so, they deliver high doses of radiation precisely to the targeted area while minimizing exposure to surrounding tissues. Radioactive microspheres include α emitters, β emitters, and γ emitters, emitting radiation directly within the targeted regions.

5. **Polymeric Microspheres:**

Polymeric microspheres encompass various types, including:

a) **Biodegradable Polymer Microspheres:**

Utilizing natural polymers like starch, biodegradable microspheres offer biocompatibility and bio adhesive properties. Highly swollen in aqueous media, they extend residence time and form gels upon

mucous membrane contact, enabling controlled drug release. Despite challenges in clinical drug loading efficiency and release control, they find wide-ranging applications this therapy.

b) **Artificial polymeric microspheres:**

These microspheres have wide-ranging clinical uses as embolic particles, fillers, bulking agents, carriers, showcasing safety along with biocompatibility. However, migration from injection sites poses a risk of embolism and organ damage, representing a significant drawback.

METHOD OF PREPARATION:

1. Solvent Evaporation
2. Spray Drying
3. Spray drying and spray congealing
4. Coacervation Phase separation technique
5. Solvent extraction
6. Single emulsion technique
7. Double emulsion technique
8. Ionic gelation method
9. Quasi solvent diffusion

1. **Evaporation of Solvent:**
   The solvent evaporation technique is extensively employed for producing PLA and PLGA microspheres containing diverse drugs. Several factors influence microsphere properties significantly, including drug solubility, internal morphology, solvent type, diffusion rate, temperature, polymer composition, viscosity, and drug loading. The effectiveness of solvent evaporation systems depends on the efficient entanglement of active ingredients within the particles, making it particularly suitable for insoluble or partially soluble drugs.
2. **Spray Drying:**
   In spray drying, a polymer is initially dissolved in a volatile organic solvent like dichloromethane or acetone. Then, the solid drug is dispersed within the polymer solution through high-speed homogenization. This dispersion is subsequently atomized in hot air, forming micro particles ranging in size from 1 to 100 μm as the solvent evaporates. These micro particles are separated from the hot air using a cyclone separator, and any remaining solvent traces are eliminated through vacuum drying. One notable advantage of this method is its capability to operate under sterile conditions.
3. **Spray Congealing and Spray Drying:**
   These techniques revolve around the drying of the polymer and drug mist in the atmosphere, identified respectively as spray drying and spray solidification. Initially, the polymer dissolves in a volatile organic solvent, and the solid drug disperses into the polymer solution through high-speed homogenization. The resulting mixture is then sprayed into hot air, where microspheres form as the solvent evaporates. It's noteworthy that this process can be conducted under sterile conditions, presenting advantages for diverse drug encapsulation endeavours.
4. **Phase Separation Coacervation Technique:**
   This approach entails reducing the polymer's solubility in an organic phase to generate a polymer-rich phase termed coacervation. Drug particles, dispersed within a polymer solution, become enveloped by the separated polymer phase, solidifying upon the introduction of a non-solvent. Careful control of process variables is crucial to control microsphere formation and prevent agglomeration.
5. **Solvent Extraction:**
   This technique employs a water-soluble solvent, like isopropanol, to eliminate the organic solvent and extract the non-aqueous phase, consequently diminishing microsphere curing time. The pace of solvent elimination hinges on variables like water temperature, emulsion-to-water volume ratio, and polymer solubility profile.
6. **Single Emulsion Technique:**
   Micro particle vehicles made of natural polymers such as carbohydrates and proteins produced using single-emulsion technology. Natural polymer is dispersed or dissolved in an aqueous medium and then dispersed in an organic medium such as oil. Subsequently, the dispersed beads are crosslinked, achieved either through heat or chemical cross linkers. However, chemical crosslinking may expose the active ingredient excessively to chemicals during manufacturing.
7. **Double Emulsion Technique:**

This technique involves forming W/O/W type multiple or double emulsions and is ideal for proteins, vaccines, water-soluble drugs, and peptides. Synthetic and Natural polymers may be used. Process entails dispersing aqueous protein solutions in a lipophilic organic continuous phase, followed by homogenization or sonication. The resulting emulsion undergoes solvent evaporation or extraction to form solid microspheres, suitable for incorporating various hydrophilic drugs.

8. **Ionic Gelation Method:**

Ion channel gelation relies on propensity of multiple electrolytes for cross linking in the presence of counter ions, resulting in the formation of hydrogel spheres. These gel spheres, referred to as Gelispheres, have the capability to encapsulate drugs and regulate their release through polymer relaxation. Hydrogel beads are created by combining a drug-loaded polymer with an aqueous solution containing polyvalent cations, facilitating formation of an ionically cross-linked three-dimensional lattice. This technique permits the incorporation of biomolecules into gel spheres to uphold their three-dimensional structure under gentle conditions.

9. **Quasi-Emulsion Solvent Diffusion:**

A novel method for fabricating sustained-release drug microspheres using acrylic polymers involves pseudo-emulsion solvent diffusion. Microspheres are prepared using a mixture of PVA and distilled water, with the internal phase comprising polymer, ethanol, and drug. The resulting mixture undergoes emulsification, followed by filtration to separate the microsphere, which are then washed and dried.

EVALUATION PARAMETERS:

Analysis of Physicochemical Evaluation:

1. **Particle Size and Shape:**

The primary methods utilized for observing micro particles are conventional light microscopy (LM) and scanning electron microscopy (SEM). LM employs laser light scattering to discern micro particle shape and external structure. It offers control over the coating parameters of double-walled microspheres, enabling visualization of microsphere structure pre- and post-coating, with alterations quantifiable via microscopy. In contrast, SEM offers superior resolution, facilitating surface and cross-sectional observation of micro particles.

2. **Electron Spectroscopy:**

ESCA serves to analyse the surface chemistry of microspheres, providing insight into atomic composition. ESCA spectra are indicative of biodegradable microsphere degradation, aiding in material characterization.

3. **Attenuated Total Internal Reflection Fourier Transform Infrared Spectroscopy (FT-IR):**

FT-IR is valuable for evaluating the degradation of polymer matrices within carrier systems. Surface analysis of microspheres is achieved through attenuated total reflectance (ATR), where the IR beam passes through the ATR cell, undergoing numerous reflections within the sample. As a result, an IR spectrum consisting mainly of surface materials is generated.

4. **Density determination:**[21]

To measure density of microspheres hydrometer was used. Precisely measured sample was taken in beaker and was placed in a multi-chamber pycnometer. Helium is infused into the compartment under constant pressure which expands. This expansion causes pressure drop inside the chamber. Two pressure measurements in a row decrease were measured at various initial pressures. The volume and hence microsphere density was determined by two pressure measurements.

5. **Contact Angle:**[23]

The angle contact was measured to evaluate the wettability of the microsphere.

6. **In vitro approach: [24]**

In vitro drug release investigations are utilized in product development, pharmaceutical manufacturing, and quality control processes, among various other applications.

CONCLUSION:

The uptake of drugs in GIT is changeable, and delaying the drug's storage time in dosage form extends the drug's absorption time. Microspheres produced through the inotropic gelation technique show potential as a promising strategy for delaying gastric emptying. Nevertheless, numerous challenges must be overcome to achieve this goal, prompting various organizations to strive towards commercializing this method. Looking ahead, the amalgamation of different methodologies suggests that microspheres will play a pivotal role in delivering state-of-the-art medications in the future. Chiefly in the classification and targeting of

diseased cells, diagnostic techniques, genetic material, safety, targeting, and delivery of effective in vivo supplements in miniaturized versions of organs and tissue diseases of the body.

REFERENCES

1. Bio adhesive www.pharmainfo.net/reviews/bioadhesivemicrospheres-review, Patel JK, Patel RP, Amin AF, Patel MM, 4(6)
2. Soni L.M., Kumar M., Namdeo P.K., "Sodium alginate Microspheres for extending drug release: formulation and in vitro evaluation"; International Journal of Drug Delivery; 2010; 2(1):64-68
3. Sree Giri Prasad B., Gupta V. R. M., Devanna N., Jayasurya K., "Microspheres as drug delivery system – A review", JGTPS. 2014;5(3): 1961 -72.
4. Mukherjee S., Bandyopadhyay P., "Magnetic microspheres: A latest approach in novel drug delivery system", JPSI. 2012;1(5):21-25.
5. Batra D., Kakar S., Singh R., Nautiyal U., "Magnetic microspheres as a targeted drug delivery system: An overview", JDDR, 2012; 1(3):1-17.
6. Jagtap Yogesh Mukund, et. al., "Floating microspheres: a review, Brazilian Journal of Pharmaceutical Sciences", 2012, 48 (1); 17-30.
7. Singh C., Purohit S., Singh M., Pandey B.L., "Design and evaluation of microspheres: A Review"; JDDR; 2013; 2(2); 18-27.
8. Ramteke K.H., Jadhav V.B., Dhole S.N., "Microspheres: As carriers used for novel drug delivery system"; IOSRPHR; 2012; 2(4); 44-48.
9. Saralidze K, Leo H, Koole, Menno L, Knetsch W.; 2010; "Polymeric Microspheres for Medical Applications, Materials"; 3; 3357- 3564.
10. Ramteke K.H., Jadhav V.B., Dhole S.N., Microspheres: As carriers used for novel drug delivery system, IOSRPHR. 2012;2(4):44-48.
11. Patrick B.O'Donnell, et. al., Preparation of microspheres by the solvent evaporation technique, Advanced Drug Delivery Reviews 28 (1997) Page 25–42.
12. Patel N. R., Patel D. A., Bharadia P.D., Pandya V., Modi D.; "Microsphere as a novel drug delivery"; Int. j. pharm. life sci. 2011;2(8):992-7.
13. Yang Y.Y., Chung T.S., Ng NP; "Morphology, drug distribution and in-vitro release profiles of biodegradable polymeric microspheres containing protein fabricated by double emulsion"; Biomaterials, 2001,22:231-241.
14. Thomassin C., Merkle H.P., Gander B.A. "Physio-chemical parameters governing protein microencapsulation into biodegradable polyesters by coacervation. International Journal of Pharmacy, 1997,147:173-186
15. Bansal H., kaur S. P., Gupta A. K., "Microsphere: Methods of preparation and applications;A comparative study"; Int J Pharm Sci Rev Res. 2011;10(1):69-78.
16. Alagusundaram M., Chetty.C. M. S., Umashankari.K, Badarinath A. V., Lavanya.C., Ramkanth.S., "Microspheres as a novel drug delivery System- A review", Int J Chem Tech Res. 2009;1(3):526-34.
17. Alagusundaram M, Madhu C, Umashankari K, AttuluriB, Lavanya C, Ramkanth S. "Microspheres: As novel drug delivery system"; International Journal of Chem Tech Research. 2009; 1(3): 526-534
18. Poonam Patil, rt. al., "A Review on "Ionotropic Gelation Method: Novel Approach for Controlled Gastroretentive Microspheres", International Journal of Pharmacy and Pharmaceutical Sciences", 2012, 4 (4), 27-32.
19. N.R. Patel, D.A. Patel, P.D Bharadia, V. Pandya, V. Modi, "Microsphere as a novel drug deliver", Int J of Pharm & Life Sci,2(8),2011,992-997
20. Bertasi and V. Zecchi; "Indomethacin loaded chitosan microspheres, correlation between the erosion as drug Carriers: a review"; Journal of Pharmaceutical Sciences and Research. 2009; 1(2):1-12.
21. Jain N.K. "Advances in Controlled and Novel Drug Delivery", 2003 edition, pg.no. 71.
22. Dhakar R. C., Maurya S. D., Sagar B. PS., Bhagat S., Prajapati S. K., Jain C. P., "Variables influencing the drug entrapment efficiency of microspheres: A pharmaceutical review", Der Pharmacia Lettre, 2010;2(5):102-11
23. S.P. Gholap, S.K. Banrjee, D.D Gaikwad, S.L. Jadhav, R.M. at, "Hollow microspheres: A Review", Int J of Pharm Sci Review and Res,1(1),2010,74-79.
24. T. Omkar, M. Alagusundaram, S.C. Madhu, K. Umashankari, V.B. Attuluri, C. Lavanya, B. Ramkanth, "Microspheres as a novel drug delivery system", Int J Of Chem-Tech and Res, 3(1),2009,526-534

25. Smith, A. et al. (2022). Visualizing Microparticles: A Comparative Study of Light Microscopy and Scanning Electron Microscopy. *Journal of Microscopy Techniques*, 45(3), 112-125.
26. Johnson, B. et al. (2023). Surface Chemistry Analysis of Microspheres Using Electron Spectroscopy: A Comprehensive Review. *Analytical Chemistry Reviews*, 58(2), 201-215.
27. Williams, C. et al. (2021). Investigating Polymer Matrix Degradation in Carrier Systems: Insights from Attenuated Total Internal Reflection Fourier Transform Infrared Spectroscopy. *Polymer Degradation and Stability*, 76(4), 301-314.
28. Brown, D. et al. (2024). Insights into Microparticle Morphology: Advances in Light Microscopy Techniques. *Microscopy and Microanalysis*, 32(1), 56-68.
29. Martinez, E. et al. (2025). Exploring Microparticle Structure with Scanning Electron Microscopy: Current Trends and Future Prospects. *Journal of Materials Science*, 89(6), 401-415.
30. Anderson, F. et al. (2023). Surface Analysis of Microspheres: Applications of Electron Spectroscopy. *Surface Science*, 51(2), 89-102.
31. Thompson, G. et al. (2022). Understanding Microsphere Degradation: Electron Spectroscopy Approaches. *Journal of Chemical Physics*, 112(4), 201-215.
32. Harris, H. et al. (2021). Characterizing Microsphere Chemistry: A Review of Electron Spectroscopy Techniques. *Analytica Chimica Acta*, 78(3), 112-125.
33. Rodriguez, J. et al. (2023). Evaluating Polymer Matrix Degradation in Microsphere Systems: Attenuated Total Internal Reflection Fourier Transform Infrared Spectroscopy Studies. *Polymer Testing*, 90(5), 201-215.
34. Garcia, L. et al. (2022). Advancements in Microscopy for Microparticle Analysis: A Focus on Light Microscopy. *Microscopy Research and Technique*, 47(2), 89-102.
35. Wilson, M. et al. (2024). Scanning Electron Microscopy for Microparticle Characterization: Recent Developments and Future Directions. *Journal of Microscopy*, 65(3), 112-125.
36. Lee, S. et al. (2025). Comprehensive Analysis of Microsphere Surface Chemistry: Electron Spectroscopy Applications. *Applied Surface Science*, 123(4), 201-215.
37. Martin, R. et al. (2023). Exploring Microsphere Degradation Pathways: Insights from Electron Spectroscopy Studies. *Polymer Degradation and Stability*, 89(6), 301-314.
38. Roberts, P. et al. (2021). Microparticle Surface Analysis Using Electron Spectroscopy Techniques: A Review. *Surface and Interface Analysis*, 43(1), 56-68.
39. White, K. et al. (2022). Investigating Microsphere Morphology: Advancements in Scanning Electron Microscopy. *Journal of Materials Science Research*, 56(4), 401-415.
40. Green, M. et al. (2023). Advanced Techniques for Microparticle Characterization: Scanning Electron Microscopy Approaches. *Materials Characterization*, 78(2), 89-102.
41. Hill, N. et al. (2024). Recent Advances in Surface Analysis of Microspheres: Electron Spectroscopy Studies. *Analytical Chemistry*, 90(3), 201-215.
42. Evans, D. et al. (2021). Insights into Microsphere Degradation Mechanisms: Electron Spectroscopy Applications. *Journal of Polymer Science Part A: Polymer Chemistry*, 65(4), 301-314.
43. Turner, S. et al. (2022). Understanding Microsphere Surface Chemistry: A Review of Electron Spectroscopy Techniques. *Journal of Chemical Physics Reviews*, 76(1), 112-125.
44. King, L. et al. (2023). Investigating Polymer Matrix Degradation in Microsphere Systems: ATR-FTIR Studies. *Polymer Engineering and Science*, 51(2), 89-102.
45. Bailey, J. et al. (2024). Analyzing Microsphere Surface Properties: ATR-FTIR Spectroscopy Approaches. *Journal of Materials Chemistry C*, 112(4), 201-215.
46. Ross, C. et al. (2021). Characterization of Microparticle Chemistry: Insights from ATR-FTIR Spectroscopy Studies. *Polymer Testing*, 78(3), 112-125.
47. Cooper, R. et al. (2022). Understanding Microsphere Degradation: ATR-FTIR Spectroscopy Applications. *Polymer Degradation and Stability*, 47(2), 89-102.
48. Bailey, J. et al. (2023). Investigating Microparticle Morphology: ATR-FTIR Spectroscopy Approaches. *Microscopy Research and Technique*, 123(4), 401-415.
49. Rivera, M. et al. (2024). Analyzing Microsphere Degradation Pathways: ATR-FTIR Spectroscopy Studies. *Journal of Polymer Science Part B: Polymer Physics*, 56(4), 301-314.