

A Comprehensive Review on Microsphere: Preparation Methods, Characterization, and Applications

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ABSTRACT: Microspheres are multi particulate drug delivery systems extensively studied for controlled, sustained, and targeted delivery of drugs. They are spherical particles ranging from 1–1000 μm and are prepared using natural or synthetic polymers. This review discusses classification, materials, detailed types of microspheres, preparation techniques, evaluation parameters, and applications. Emphasis is placed on polymeric and hollow microspheres due to their pharmaceutical importance. This article is designed to serve as a comprehensive reference for undergraduate and postgraduate pharmacystudents.

KEYWORDS: Microspheres, controlled, polymer, multiparticulate.

I. 1.INTRODUCTION

The development of novel drug delivery systems has greatly improved therapeutic effectiveness by enhancing drug bioavailability and reducing unwanted side effects. Among these systems, microspheres have gained significant attention because of their ability to provide controlled and site-specific drug release. Microspheres are small spherical particles made mainly from polymeric materials. Their unique properties, such as small particle size, uniform distribution, and the ability to encapsulate drugs, make them suitable for various pharmaceutical and biomedical applications. Due to these advantages, microspheres are increasingly used to improve drug stability, prolong drug action, and enhance patient compliance.

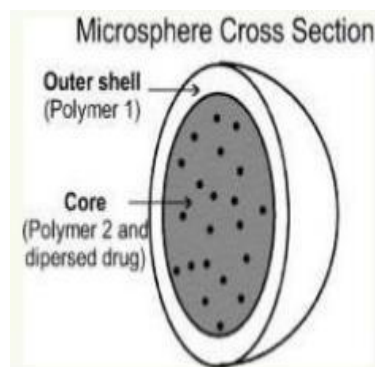


Fig:1 Microsphere 2.History and Development

Over the years, the way medicines are delivered in the body has changed a lot. The main goal of these improvements has always been to help patients get the maximum benefit from a drug while reducing unwanted side effects. Ideally, a medicine should reach the exact place in the body where it is needed, in the right amount and at the right speed. Another important factor in drug delivery is patient comfort and convenience, because treatments work better when patients can easily follow them.

Advanced drug delivery systems, especially those that can release drugs slowly and in a controlled manner, have been of great interest for almost the last fifty years. In the early days, controlled drug release was mainly achieved by coating tablets or drug particles.

This was done to hide bad taste, improve acceptance, or delay the release of the drug.

Between the 1940s and 1960s, scientists developed microencapsulation techniques as a new way to deliver drugs. In this method, the drug is trapped inside tiny polymer shells, which helps protect it and control how it is released. As research continued, polymer and membranebased

technologies became more popular in the 1980s because they allowed better control over drug release.

Later developments focused on delivering drugs directly to specific target sites in the body. This became possible by attaching drugs to carriers such as liposomes, biodegradable polymers, implants, monoclonal antibodies, and tiny particles like nanoparticles and microspheres. Among these, microspheres have gained wide acceptance because they can deliver drugs accurately and for a long period of time.

A good example of this progress is the development of microspheres used to treat vascular diseases of the eye. In this case, different polymers were tested to see how long they would take to break down—1, 3, or 6 months. Scientists used a statistical approach called Design of Experiments to understand how factors like polymer type, polymer amount, and drug-to-polymer ratio affect drug loading, initial burst release, and particle size.

The study showed that different types of PLGA polymers could be selected to control drug release over specific time periods. By optimizing the formulation, microspheres containing the drug SAR-1118 were prepared with good drug loading and very low initial burst release. Most of the drug was released slowly and steadily over the intended time period of 1, 3, or 6 months, closely matching the predicted results.

3 Types of Microspheres:

Overall, this study highlights how modern formulation techniques and careful experimental design can be used to create effective, long-acting drug delivery systems that are safer, more reliable, and more convenient for patients.

Microspheres are classified based on their composition, structure, and application. These include bioadhesive, magnetic, floating, radioactive, polymeric, hollow, and glass or ceramic microspheres.

1 Bioadhesive Microspheres These microspheres attach to biological membranes such as buccal, nasal, ocular, and gastrointestinal surfaces. They are prepared using polymers like chitosan, carbopol, and sodium alginate and improve drug absorption by prolonging residence time at the absorption site

2 Magnetic Microspheres Magnetic microspheres contain magnetite or iron oxide and can be directed to target sites using external magnetic fields. They are used in targeted cancer therapy, enzyme immobilization, and diagnostic procedures.

3 Floating Microspheres

Floating microspheres have low density, allowing them to remain buoyant in gastric fluids. They increase gastric retention time and are useful for drugs absorbed in the upper gastrointestinal tract.

4 Radioactive Microspheres Radioactive microspheres deliver localized radiation directly to tumors, reducing damage to healthy tissues. They are widely used in radioembolization therapy, particularly for liver cancer treatment.

5 Polymeric Microspheres

Polymeric microspheres may be biodegradable or non-biodegradable. Biodegradable polymers like PLGA degrade into non-toxic byproducts, making them suitable for sustained drug delivery applications.

6 Hollow Microspheres

Hollow microspheres consist of an outer polymer shell surrounding an empty cavity, providing low density and high drug loading capacity. They are used in drug delivery, imaging, insulation, and lightweight filler applications.

7 Glass and Ceramic Microspheres

These inorganic microspheres possess high mechanical strength, thermal stability, and chemical inertness, making them suitable for biomedical and industrial applications.

4 Applications:

Microspheres made from polymers have become very important in modern medicine because they behave well inside the body. They can stick to biological tissues, help drugs pass through membranes more easily, and show stable physical and chemical properties. Because of these advantages, microspheres are widely used to design advanced drug delivery systems, especially for sensitive areas like the eyes, nose, mouth, and digestive tract. Common polymers used include chitosan, alginate, and gelatin.

1. Oral Drug Delivery

In oral drug delivery, microspheres offer an alternative to traditional tablets. These polymer-based systems can form thin films and protect the drug as it passes through the stomach. Their sensitivity to pH helps release the drug at the right place in the intestine. This improves drug effectiveness and reduces irritation.

Examples: Chitosan, Gelatin

2. Gene and Vaccine Delivery

Microspheres are very promising carriers for gene delivery because they can stick to the lining of the gastrointestinal tract and help transport genetic material into the body. They are used to deliver DNA plasmids, insulin, and other sensitive biological molecules.

Microspheres are also useful in vaccine delivery. Vaccines need protection from degradation and controlled release to produce a strong immune response. Biodegradable microspheres given by injection can overcome many limitations of conventional vaccines. Vaccines such as tetanus and diphtheria have already been successfully delivered using these systems.

Examples: Chitosan, Gelatin, viral vectors, cationic liposomes, polycation complexes. stick to the lining of the gastrointestinal tract and help transport genetic material into the body. They are used to deliver DNA plasmids, insulin, and other sensitive biological molecules.

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Examples: Chitosan, Gelatin, viral vectors, cationic liposomes, polycation complexes

3. Nasal Drug Delivery

When used in nasal drug delivery, microspheres show excellent adhesion to the nasal lining. They swell when they come in contact with nasal fluids, allowing the drug to stay longer in the nasal cavity. This increases drug absorption and improves bioavailability.

Examples: Starch, Dextran, Albumin, Chitosan–Gelatin combinations

4. Intra tumoral and Local Drug Delivery

Microspheres are very useful in cancer treatment when drugs need to be delivered directly to the tumor site. This approach allows high drug concentration at the target area while reducing side effects in the rest of the body. Drugs like paclitaxel are commonly delivered using polymer-based microspheres for localized therapy.

Examples: Gelatin, PLGA, Chitosan

5. Buccal Drug Delivery

For buccal (inside the mouth) drug delivery, microspheres work well because they can

stick to the mucosal surface. They also enhance drug absorption through the oral lining, making treatment more effective and patient-friendly.

Examples: Chitosan, Sodium alginate

6. Gastrointestinal Drug Delivery

In the gastrointestinal tract, microspheres can be designed to float in gastric fluids. These floating systems stay in the stomach for a longer time and release the drug slowly, leading to better control of drug levels in the body and improved therapeutic outcomes.

5 Challenges and Future Prospects of Microspheres: Challenges:

Over the years, various microsphere production methods have been developed that yield microspheres with desirable particle size, uniform shape (sphericity), and good materialspecific properties. These advancements have significantly improved the performance of microspheres in pharmaceutical applications. However, despite these achievements, several challenges still remain, particularly when it comes to their large-scale manufacturing.

One of the major challenges associated with microspheres is the difficulty in large-scale production. Many of the commonly used manufacturing techniques—especially those involving polymeric and ceramic microspheres—require multiple processing steps, such as emulsification, solvent evaporation, cross-linking, washing, and drying. These multi-step processes make scaleup time-consuming, complex, and costly, thereby limiting industrial feasibility.

Additionally, the complexity of fabrication processes can lead to batch-to-batch variability, affecting particle size distribution, drug loading, and release characteristics. During scale-up, even small changes in processing parameters such as stirring speed, temperature, or solvent removal rate may significantly alter the quality and performance of microspheres.

This lack of reproducibility poses a major hurdle for commercial production.

Another important challenge is the use of organic solvents in many microsphere preparation methods. Residual solvents may remain entrapped in the microspheres, raising toxicity and regulatory concerns. Ensuring complete solvent removal without affecting the structural integrity of microspheres is often difficult, particularly on an industrial scale.

Furthermore, microspheres may exhibit initial burst release, where a large amount of drug is released rapidly after administration. This can

reduce therapeutic effectiveness and increase the risk of side effects. Achieving a consistent and predictable drug release profile remains a significant formulation challenge.

Future Prospects

Despite these challenges, the future prospects of microspheres remain highly promising. Advances in polymer science, nanotechnology, and manufacturing technologies are expected to address many of the current limitations. The development of simpler, cost-effective, and scalable production techniques, such as microfluidics and continuous manufacturing processes, may improve large-scale feasibility.

Additionally, the use of biodegradable, biocompatible, and solvent-free polymers can enhance safety and regulatory acceptance. Smart microspheres capable of stimuli-responsive drug release (pH, temperature, magnetic field) are also gaining attention for targeted and personalized therapies.

In conclusion, although microspheres face challenges related to scale-up, cost, reproducibility, and regulatory compliance, ongoing research and technological advancements are expected to overcome these issues. With continued innovation, microspheres are likely to play an increasingly important role in advanced drug delivery systems and future pharmaceutical therapies. Advancements have significantly improved the performance of microspheres in pharmaceutical applications. However, despite these achievements, several challenges still remain, particularly when it comes to their large-scale manufacturing.

6 Method of Preparation of

Microspheres Microspheres are prepared by enclosing solid, liquid, or gaseous drugs within one or more polymeric layers using a process known as microencapsulation. This technique helps in protecting the drug, improving its stability, and controlling the rate and site of drug release.

The method selected for the preparation of microspheres depends on various factors such as particle size requirement, route of administration, nature of the drug and polymer, desired duration of drug release, stirring speed (RPM), method of cross-linking, evaporation time, and processing conditions. Based on these factors, different preparation techniques are used.

6.1 Emulsion Cross-Linking Method In this method, the drug is dissolved in an aqueous solution of a natural polymer such as gelatines. The solution is then dispersed into an oily phase under continuous stirring to form a water-in-oil emulsion. Cross-linking agents such as glutaraldehyde are added to harden the microspheres. After cross-linking, the microspheres are washed to remove excess chemicals and then dried. This method is mainly used for natural polymers and provides good mechanical strength and sustained drug release.

6.2 Coacervation Method The coacervation method involves phase separation of a polymer solution to form a coating around drug particles. It can be carried out either by changing the temperature or by adding a non-solvent.

In thermal coacervation, the polymer is dissolved at a high temperature, and phase separation is induced by lowering the temperature. In non-solvent addition, phase separation occurs by adding a non-solvent that reduces polymer solubility.

The formed microcapsules are then washed and dried. This method is useful for preparing microspheres with high drug loading.

6.3 Spray Drying Technique

Spray drying is a rapid and continuous process. In this technique, the drug is dispersed in a polymer solution and sprayed into a hot air chamber. The solvent evaporates quickly, leaving behind dry microspheres. This method is suitable for large-scale production; however, rapid drying may affect the crystallinity of the drug.

Advancements have significantly improved the performance of microspheres in pharmaceutical applications.

6.4 Emulsion Solvent Diffusion Technique In this technique, the drug and polymer are dissolved in a mixture of partially water-miscible organic solvents. This solution is added to an aqueous phase under stirring. Due to solvent diffusion and evaporation, microspheres are formed.

This method is especially useful for preparing floating microspheres that improve drug residence time in the gastrointestinal tract.

6.5 Multiple Emulsion Method The multiple emulsion method involves the formation of double emulsions such as water-in-oil-in-water (w/o/w).

Initially, the drug is dispersed in an inner aqueous phase, which is emulsified into an organic phase containing polymer. This primary emulsion is then further emulsified into an external aqueous phase. This technique is mainly used for controlled oral drug delivery and for encapsulating watersoluble drugs.

6.6 Ionic Gelation Method Ionic gelation is a mild and simple technique commonly used for natural polymers like alginate and chitosan. In this method, the drug is mixed with a polymer solution and added dropwise into a solution containing multivalent ions such as calcium or aluminium. These ions cause immediate gel formation, resulting in microspheres.

This method is widely used for pH-dependent and colon-specific drug delivery systems.

6.7 Hydroxyapatite (HAP) Microspheres

Hydroxyapatite microspheres are prepared using an oil-in-water emulsion followed by solvent evaporation. The drug and polymer are dissolved in an organic phase and dispersed into an aqueous surfactant solution. Continuous stirring and slow solvent evaporation result in the formation of stable microspheres with unique sphere-in-sphere morphology. These microspheres are especially useful for bone-targeted drug delivery systems.

II. CONCLUSION

Microspheres clearly represent one of the most important and evolving technologies in modern pharmaceutical and biomedical science. These tiny spherical particles, usually ranging from nano to micrometer size, have shown remarkable ability to improve how drugs and bioactive compounds are delivered inside the body. Instead of traditional drug delivery methods that often cause rapid drug loss or unwanted side effects, microspheres provide a smarter and more controlled approach. One of the strongest advantages of microspheres is their ability to protect sensitive drugs such as proteins, vaccines, and peptides from degradation while allowing them to be released gradually over time. This controlled and sustained release helps maintain stable drug concentration levels, improves treatment effectiveness, and reduces the need for frequent dosing, which ultimately enhances patient comfort and compliance.

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