IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 1, August 2026
Impact Factor: 8.2

Formulation and Evaluation of Microspheres for Sustained Drug Delivery: A Comprehensive Review

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Abstract: *Oral and parenteral conventional dosage forms are frequently associated with fluctuating plasma drug concentrations, frequent dosing schedules, poor patient compliance, and a higher incidence of dose-related side effects. Microspheres have emerged as one of the most versatile particulate carrier systems capable of overcoming these drawbacks by offering sustained, controlled, and site-specific delivery of therapeutic agents. Microspheres are free-flowing, spherical particles ranging in size from 1 to 1000 micrometres, composed of a drug dispersed or dissolved within a natural, synthetic, or semi-synthetic polymeric matrix. Owing to their small and uniform particle size, ability to encapsulate a wide range of drug molecules, and capacity to modulate the release profile through polymer selection and process variables, microspheres have found extensive application in oral, parenteral, nasal, ocular, and targeted drug delivery. This review presents a comprehensive discussion on the concept, ideal characteristics, classification, and polymers used in microsphere formulation, along with a detailed account of the various methods employed for their preparation, including solvent evaporation, spray drying, spray congealing, coacervation-phase separation, ionic gelation, and polymerization techniques. The review further elaborates on the mechanisms governing drug release from microspheres and the array of physicochemical and biological parameters used for their evaluation, such as particle size analysis, surface morphology, drug entrapment efficiency, percentage yield, swelling behaviour, in vitro release kinetics, and stability assessment. Finally, the therapeutic applications, recent advances, and future prospects of microsphere-based sustained drug delivery systems are discussed. This compilation is intended to serve as a ready reference for researchers and formulation scientists working in the field of particulate and controlled drug delivery systems.*

Keywords: Microspheres; Sustained drug delivery; Controlled release; Polymers; Encapsulation efficiency; Drug release kinetics

I. INTRODUCTION

Drug delivery science has, over the last few decades, shifted its focus from simply discovering new therapeutic molecules to designing efficient delivery systems that can optimize the pharmacokinetic and pharmacodynamic performance of existing drugs. Conventional dosage forms such as tablets, capsules, and injections, although widely used, generally produce a sharp rise in plasma drug concentration soon after administration followed by a decline, giving rise to the characteristic peak-and-trough plasma profile. This fluctuation often results in periods of sub-therapeutic drug levels, risking treatment failure, alternating with periods of supra-therapeutic levels, risking toxicity.

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To maintain the drug concentration within the therapeutic window for a prolonged duration, multiple dosing is generally required, which reduces patient compliance and increases the overall cost of therapy.

Sustained and controlled release drug delivery systems have therefore been developed with the primary objective of maintaining a therapeutically effective drug concentration in the systemic circulation for an extended period following a single dose administration. Among the various particulate approaches developed for this purpose, microspheres occupy a prominent position because of their unique combination of small particle size, large surface area, and the ability to be engineered to release the incorporated drug at a predetermined rate over a desired time period.

Microspheres may be defined as small, spherical particles with diameters typically ranging from 1 to 1000 micrometres, in which the drug is either uniformly dispersed throughout the polymeric matrix (micromatrix or microsphere) or is enclosed within a polymeric membrane (microcapsule). The terms microsphere and microcapsule are often used interchangeably in the literature, although technically a microcapsule refers to a reservoir-type system with a distinct core and shell, whereas a microsphere refers to a monolithic matrix-type system. Because of their free-flowing powder-like characteristics and the biodegradable, biocompatible nature of the polymers commonly employed in their fabrication, microspheres have been widely explored as carriers for proteins, peptides, vaccines, hormones, anticancer agents, antibiotics, anti-inflammatory drugs, and a variety of other therapeutic moieties.

The growing interest in microsphere technology can be attributed to several factors: the ability to achieve sustained and site-specific drug release, protection of labile drugs from degradation in the gastrointestinal environment, reduction in dosing frequency, improvement in patient compliance, and the possibility of targeting the drug to a specific organ or tissue through appropriate surface modification. This review attempts to bring together, in a systematic manner, the fundamental concepts, formulation strategies, evaluation techniques, and applications associated with microspheres intended for sustained drug delivery.

II. IDEAL CHARACTERISTICS OF MICROSPHERES

An ideal microsphere-based drug delivery system intended for sustained release should fulfil certain criteria in order to be therapeutically and commercially viable. These characteristics guide the selection of polymer, drug, and method of preparation during formulation development.

- The polymer used should be biocompatible, biodegradable, and non-toxic, with degradation products that are easily eliminated from the body.
- The microspheres should possess a high and reproducible drug loading and entrapment efficiency.
- The particle size should be uniform and controllable, since size directly influences the release rate, site of deposition, and route of administration.
- The release of the drug should be predictable, reproducible, and should follow a desired kinetic profile, typically approaching zero-order release.
- The formulation should be physically and chemically stable during storage, with minimal drug leaching prior to administration.
- The manufacturing process should be simple, cost-effective, reproducible, and amenable to scale-up.
- The microspheres should retain free-flowing characteristics for ease of handling, packaging, and administration.

III. ADVANTAGES OF MICROSPHERES

Microsphere-based drug delivery offers a number of advantages over conventional dosage forms, which explains the sustained research interest in this area over the past several decades.

- They provide sustained and controlled release of the drug, thereby reducing the frequency of dosing and improving patient compliance.
- They minimise fluctuations in plasma drug concentration, maintaining levels within the therapeutic window and reducing the incidence of dose-related toxicity.

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- Owing to their small size, microspheres can be administered by the oral, parenteral, nasal, ocular, and pulmonary routes, offering flexibility in formulation design.
- They can protect acid-labile or enzyme-sensitive drugs, such as proteins and peptides, from degradation in the gastrointestinal tract.
- The large surface-area-to-volume ratio can enhance the dissolution rate of poorly water-soluble drugs.
- Microspheres can be engineered for site-specific or targeted delivery, for example to the colon, to inflamed tissue, or to tumour sites, by suitable modification of the polymer or surface characteristics.
- They allow the incorporation of both hydrophilic and hydrophobic drugs, as well as biomolecules such as vaccines and growth factors.
- The free-flowing, spherical nature of microspheres improves their handling characteristics during downstream processing such as encapsulation into capsules or compression into tablets.

IV. LIMITATIONS OF MICROSPHERES

Despite their many advantages, microsphere-based delivery systems are also associated with certain limitations that must be addressed during formulation development.

- The release rate of sustained release formulations, including microspheres, is affected by variables such as gastric emptying time, intestinal transit time, and the presence of food, leading to intra- and inter-subject variability.
- Manufacturing processes for microspheres often require the use of organic solvents, which may pose toxicity concerns if residual solvents are not adequately removed.
- Formulation and process variables such as polymer type, drug-to-polymer ratio, stirring speed, and temperature can markedly influence particle size, morphology, and drug release, making reproducibility a technical challenge.
- Once administered, especially by the parenteral route, the dose cannot be readily terminated or retrieved in the event of toxicity or adverse effects, unlike an oral controlled release tablet that can be discontinued.
- The cost of production is generally higher than that of conventional dosage forms because of the specialised equipment and quality control required.
- There is a possibility of dose dumping if the integrity of the polymeric matrix is compromised, which can result in sudden release of the entire drug load.

V. CLASSIFICATION OF MICROSPHERES

Microspheres can be classified on the basis of the polymer used, the mechanism of drug release, or the specific functional attribute imparted to the delivery system. Broadly, microspheres are classified into the following categories.

5.1 Bioadhesive Microspheres

Bioadhesive microspheres are designed to adhere to the mucosal lining of a particular tissue, such as the buccal, nasal, rectal, or gastrointestinal mucosa, thereby prolonging the residence time of the dosage form at the absorption site and enhancing bioavailability. Mucoadhesion is generally achieved by incorporating polymers capable of forming hydrogen bonds or interpenetrating networks with the mucin layer, such as chitosan, carbopol, or sodium carboxymethyl cellulose.

5.2 Magnetic Microspheres

Magnetic microspheres contain a magnetically responsive material, typically iron oxide, dispersed within the polymer matrix. When exposed to an external magnetic field, these microspheres can be directed and concentrated at a specific target site, such as a tumour, thereby reducing systemic exposure and associated toxicity while enhancing local drug concentration.

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5.3 Floating (Hollow) Microspheres

Floating microspheres are low-density, hollow particles designed to remain buoyant on the gastric fluid for a prolonged period without affecting the gastric emptying rate. This gastro-retentive approach is particularly useful for drugs that are absorbed primarily in the stomach or upper small intestine, or for drugs intended to act locally within the stomach.

5.4 Radioactive Microspheres

Radioactive microspheres incorporate a radioisotope within the polymeric matrix and are used primarily in the field of interventional radiology and oncology for targeted internal radiotherapy. When injected directly into the arterial supply of a tumour, these microspheres can deliver a localised radiation dose while sparing surrounding healthy tissue.

5.5 Polymeric Microspheres

Polymeric microspheres are the most widely studied category and may be further divided into biodegradable and non-biodegradable types. Biodegradable polymeric microspheres, prepared from polymers such as poly(lactic-co-glycolic acid) or chitosan, are extensively used for sustained and controlled drug release because they degrade into biocompatible by-products that are eliminated through normal metabolic pathways, thereby avoiding the need for surgical removal after drug depletion.

VI. POLYMERS USED IN THE FORMULATION OF MICROSPHERES

The choice of polymer is one of the most critical determinants of the physicochemical properties and release behaviour of microspheres. Polymers used in microsphere formulation are broadly classified into natural, semi-synthetic, and synthetic categories.

6.1 Natural Polymers

Natural polymers are widely favoured because of their biocompatibility, biodegradability, low toxicity, and ready availability. Commonly used natural polymers include gelatin, sodium alginate, chitosan, albumin, starch, gum acacia, gum karaya, and agar. Alginate and chitosan, in particular, are extensively used in ionic gelation methods because of their ability to form gels in the presence of di- or tri-valent counter ions or oppositely charged polyelectrolytes.

6.2 Semi-Synthetic Polymers

Semi-synthetic or cellulose-derived polymers such as ethyl cellulose, hydroxypropyl methylcellulose, sodium carboxymethyl cellulose, and cellulose acetate phthalate are commonly employed for their film-forming properties and their ability to modulate drug release through variation in the degree of substitution and viscosity grade.

6.3 Synthetic Polymers

Synthetic polymers offer greater control and reproducibility over physicochemical properties such as molecular weight, degradation rate, and mechanical strength. Commonly used synthetic polymers include poly(lactic acid), poly(glycolic acid), poly(lactic-co-glycolic acid), polycaprolactone, polyanhydrides, polyacrylates, and polymethyl methacrylate. Among these, poly(lactic-co-glycolic acid) is one of the most extensively investigated and regulatory-approved polymers for parenteral sustained release microsphere formulations because its degradation rate can be finely tuned by varying the ratio of lactide to glycolide units and the polymer molecular weight.

VI. METHODS OF PREPARATION OF MICROSPHERES

Several techniques have been developed for the preparation of microspheres, and the choice of method depends on factors such as the physicochemical nature of the drug and polymer, the desired particle size, the required drug loading, and the intended route of administration. The commonly employed methods are discussed below.

7.1 Single Emulsion Technique

In the single emulsion technique, the natural polymer is dissolved or dispersed in an aqueous medium, followed by dispersion of the drug in the polymer solution. This primary phase is then emulsified in a non-miscible external oil phase under continuous stirring to form a water-in-oil emulsion. The dispersed globules are subsequently stabilised and hardened either by cross-linking with an agent such as glutaraldehyde or formaldehyde, or by heat treatment, resulting in the formation of discrete microspheres that are separated by filtration or centrifugation, washed, and dried.

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7.2 Double (Multiple) Emulsion Technique

The double emulsion technique is particularly suited to water-soluble drugs, proteins, and peptides that would otherwise be lost or degraded in a simple oil-based external phase. In this method, an aqueous drug solution is first emulsified into a polymer solution dissolved in an organic solvent to form a primary water-in-oil emulsion. This primary emulsion is then further emulsified into a large volume of an aqueous phase containing a stabiliser, such as polyvinyl alcohol, to form a water-in-oil-in-water multiple emulsion. Removal of the organic solvent by evaporation or extraction results in solidification of the polymer and formation of microspheres with the drug entrapped in the internal aqueous phase.

7.3 Solvent Evaporation Method

The solvent evaporation method is one of the most widely used techniques for the preparation of polymeric microspheres, particularly with biodegradable polymers such as poly(lactic-co-glycolic acid). The polymer and drug are dissolved or dispersed in a volatile, water-immiscible organic solvent such as dichloromethane or ethyl acetate. This organic phase is emulsified into an aqueous continuous phase containing a suitable emulsifying agent to form an oil-in-water emulsion. Continuous stirring at controlled temperature causes the organic solvent to evaporate slowly, resulting in progressive precipitation of the polymer around the drug and formation of solid microspheres, which are then collected by filtration, washed to remove residual surfactant, and dried.

7.4 Spray Drying

Spray drying is a rapid, single-step, and continuous process suitable for large-scale production of microspheres. In this technique, the drug and polymer are dissolved or dispersed in a suitable solvent, and the resulting solution or dispersion is atomised into a stream of heated air through a nozzle or spinning disc. The rapid evaporation of solvent from the fine droplets leads to the formation of solid microspheres, which are separated from the drying air using a cyclone separator. Spray drying offers advantages such as high reproducibility, ease of scale-up, and short processing time, although the high processing temperature may limit its suitability for thermolabile drugs.

7.5 Spray Congealing (Spray Chilling)

Spray congealing is similar to spray drying, except that instead of evaporating a solvent, the drug is dispersed in a molten wax, fat, or polymer that is atomised into a stream of cold air. Rapid cooling of the atomised droplets results in solidification and formation of microspheres. This method avoids the use of organic solvents entirely and is particularly useful for drugs that need to be embedded in lipidic or waxy matrices for sustained release.

7.6 Coacervation-Phase Separation

Coacervation-phase separation is one of the oldest and most classical microencapsulation techniques. In this method, the polymer is dissolved in an appropriate solvent, and the drug is dispersed within this polymer solution. Addition of a phase-inducing agent, such as a non-solvent, a change in temperature, or addition of an incompatible polymer, causes the polymer to separate out of solution as a coacervate, which then deposits as a coating around the dispersed drug particles. Subsequent cross-linking or solvent removal hardens the coacervate droplets into discrete microcapsules.

7.7 Ionic Gelation Technique

Ionic gelation is a mild, aqueous-based technique that avoids the use of organic solvents and high temperatures, making it particularly suitable for the encapsulation of proteins, peptides, and other labile biomolecules. In this method, a polyelectrolyte such as sodium alginate or chitosan, containing the dispersed or dissolved drug, is added dropwise into a solution of an oppositely charged ion or counter-ion, such as calcium chloride for alginate or sodium tripolyphosphate for chitosan. Instantaneous cross-linking occurs at the interface, resulting in the formation of gelled microspheres, which are then collected, washed, and dried.

7.8 Polymerization Techniques

Polymerization-based methods, including normal (bulk, suspension, or emulsion) polymerization and interfacial polymerization, involve the in situ formation of the polymer around the drug from monomeric or oligomeric starting materials. In normal polymerization, the monomer is polymerised in the presence of the drug using an initiator, either in bulk or as a dispersed suspension or emulsion. In interfacial polymerization, two reactive monomers, one dissolved in

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the dispersed phase and the other in the continuous phase, react at the interface of emulsion droplets to form a polymeric membrane, resulting in reservoir-type microcapsules. These methods offer precise control over the molecular weight and cross-link density of the resulting polymer shell.

VIII. MECHANISM OF DRUG RELEASE FROM MICROSPHERES

The release of drug from microspheres is generally governed by one or more of the following mechanisms, the relative contribution of which depends on the polymer type, drug solubility, and microsphere microstructure.

Diffusion: The drug dissolved within the polymer matrix or entrapped within pores diffuses out through the polymer network or through fluid-filled channels into the surrounding release medium. This is the predominant mechanism for non-biodegradable matrix systems.

Erosion/Degradation: For biodegradable polymers such as poly(lactic-co-glycolic acid), drug release occurs as the polymer undergoes hydrolytic or enzymatic degradation, gradually eroding the matrix and liberating the entrapped drug.

Swelling followed by diffusion: Hydrophilic polymers imbibe water and swell upon contact with the release medium, increasing the polymer chain mobility and pore size, thereby facilitating drug diffusion out of the swollen matrix.

Osmotic pumping: In certain reservoir-type microcapsules, an osmotic pressure gradient across the semi-permeable membrane draws water into the core, building up internal pressure that forces the drug solution out through pores or the membrane itself.

In practice, the overall release profile of a microsphere formulation is often the result of a combination of an initial burst release, attributed to drug located near or on the particle surface, followed by a slower, sustained release phase governed by diffusion through, and/or erosion of, the polymer matrix.

IX. EVALUATION PARAMETERS OF MICROSPHERES

A comprehensive evaluation of microspheres is essential to establish the quality, reproducibility, and performance of the formulated delivery system. The commonly employed evaluation parameters are described below.

9.1 Particle Size and Size Distribution

Particle size is one of the most important characteristics of microspheres, as it influences drug release rate, the site of deposition following administration, and the physical stability of the formulation. Particle size and size distribution are commonly determined using optical microscopy, laser diffraction particle size analysers, or dynamic light scattering, and are expressed as mean diameter along with an appropriate measure of polydispersity.

9.2 Surface Morphology

The surface characteristics and internal morphology of microspheres are examined using scanning electron microscopy, which provides information on particle shape (spherical or irregular), surface texture (smooth or porous), and the presence of surface-adhered drug crystals. Transmission electron microscopy may additionally be used to visualise the internal structure of reservoir-type microcapsules.

9.3 Density and Micromeritic Properties

True density and tapped density of microspheres are determined using a pycnometer and a bulk density apparatus, respectively, and are particularly important for floating microsphere formulations where a low density is essential for buoyancy. Flow properties, including angle of repose, Carr's compressibility index, and Hausner ratio, are evaluated to assess the free-flowing nature of the microsphere powder, which is important for further processing such as capsule filling or tableting.

9.4 Swelling Index

The swelling behaviour of microspheres, particularly those composed of hydrophilic polymers, is assessed by immersing a known weight of microspheres in a specified volume of simulated biological fluid and measuring the increase in weight or volume at predetermined time intervals. The swelling index provides insight into the water uptake capacity of the polymer matrix, which is closely linked to the drug release mechanism.

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9.5 Percentage Yield

Percentage yield is calculated as the ratio of the actual weight of microspheres obtained after processing to the theoretical weight of drug and polymer used in the formulation, expressed as a percentage. This parameter reflects the efficiency of the preparation method and is useful for comparing different formulation batches or techniques.

9.6 Drug Entrapment / Encapsulation Efficiency

Drug entrapment efficiency, also referred to as encapsulation efficiency, is a critical parameter that indicates the proportion of the total drug that has been successfully incorporated within the microspheres. It is typically determined by crushing or dissolving a known weight of microspheres in a suitable solvent to extract the entrapped drug, followed by quantification using a validated analytical technique such as ultraviolet-visible spectrophotometry or high-performance liquid chromatography, and is expressed as the percentage ratio of actual drug content to theoretical drug content.

9.7 In Vitro Drug Release Studies

In vitro drug release studies are performed to characterise the release profile of the drug from the microsphere formulation under simulated physiological conditions. Common methods include the USP dissolution apparatus (paddle or basket type), the dialysis bag diffusion method, the beaker method with continuous stirring, and modified Franz diffusion or Keshary-Chien cells for topical or transdermal formulations. Samples are withdrawn at predetermined time intervals, replaced with fresh medium to maintain sink conditions, and analysed for drug content to construct a cumulative percentage drug release versus time profile.

9.8 Drug Release Kinetics

The in vitro release data obtained are further analysed by fitting to various mathematical models in order to elucidate the mechanism governing drug release. Commonly applied models include the zero-order model, which describes a constant rate of release independent of concentration; the first-order model, which describes a release rate proportional to the remaining drug concentration; the Higuchi model, which describes release governed by Fickian diffusion from a matrix system; and the Korsmeyer-Peppas model, which is used to distinguish between Fickian diffusion, non-Fickian (anomalous) transport, and case II (relaxation-controlled) transport based on the value of the release exponent. The model that provides the best fit, generally judged by the correlation coefficient, is taken to represent the predominant release mechanism of the formulation.

9.9 Drug-Polymer Compatibility Studies

Compatibility between the drug and the polymer(s) used is assessed using techniques such as Fourier-transform infrared spectroscopy, to detect any chemical interaction through shifts or disappearance of characteristic functional group peaks, and differential scanning calorimetry, to evaluate changes in melting endotherms that might indicate interaction, complexation, or a change in the crystalline state of the drug following encapsulation.

9.10 Stability Studies

Stability studies are conducted in accordance with relevant regulatory guidelines by storing the optimised microsphere formulation under defined conditions of temperature and relative humidity for a specified duration. Samples withdrawn at periodic intervals are evaluated for changes in physical appearance, drug content, entrapment efficiency, and in vitro release profile in order to establish the shelf life of the product.

9.11 In Vivo Evaluation

In vivo studies, generally conducted in a suitable animal model, are used to correlate the in vitro release data with the actual pharmacokinetic performance of the formulation. Parameters such as peak plasma concentration, time to reach peak concentration, area under the plasma concentration-time curve, and mean residence time are determined and compared with a conventional or reference formulation to establish the extent of sustained action achieved. Where a reliable correlation exists between the in vitro release data and the in vivo absorption profile, an in vitro-in vivo correlation may be established, which is of considerable value in reducing the reliance on animal or human studies during subsequent formulation optimisation.

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X. COMPARATIVE OVERVIEW OF PREPARATION TECHNIQUES

Table 1 presents a comparative summary of the principal features of the major microsphere preparation techniques discussed in this review, to aid formulation scientists in selecting an appropriate method based on the nature of the drug and the desired product characteristics.

Technique	Key Principle	Suitability / Remarks
Single emulsion	w/o emulsification followed by cross-linking or heat hardening	Suitable for natural, water-soluble polymers such as gelatin and albumin
Double emulsion	w/o/w multiple emulsion with solvent removal	Ideal for water-soluble drugs, proteins and peptides
Solvent evaporation	o/w emulsification with evaporation of volatile solvent	Widely used for PLGA and other biodegradable polymers
Spray drying	Atomisation of feed solution into hot air stream	Rapid, continuous, scalable; unsuitable for thermolabile drugs
Spray congealing	Atomisation of molten mass into cold air stream	Solvent-free; suitable for lipidic/waxy carriers
Coacervation-phase separation	Phase-induced deposition of polymer coacervate around drug	Classical method; good for oil-soluble and solid cores
Ionic gelation	Cross-linking of polyelectrolyte with counter-ion	Mild, aqueous, solvent-free; suitable for biomolecules
Polymerization	In situ monomer polymerisation around the drug	Offers precise control over shell molecular weight

XI. APPLICATIONS OF MICROSPHERES IN SUSTAINED DRUG DELIVERY

Microspheres have found wide-ranging application across almost every route of drug administration and therapeutic category, owing to the flexibility offered by variation in polymer composition, particle size, and surface characteristics.

Oral sustained release: Microspheres are incorporated into capsules or compressed into tablets to provide sustained release of drugs such as antihypertensives, antidiabetics, and nonsteroidal anti-inflammatory agents, reducing dosing frequency and improving patient compliance.

Parenteral depot formulations: Injectable microspheres, particularly those based on poly(lactic-co-glycolic acid), are used to provide sustained systemic delivery of peptide and hormone therapeutics, such as luteinizing hormone-releasing hormone analogues, over periods ranging from several weeks to months, thereby avoiding frequent injections.

Targeted and site-specific delivery: Bioadhesive, magnetic, and ligand-conjugated microspheres are used to target specific tissues or organs, such as the colon, liver, or tumour tissue, thereby enhancing local drug concentration and minimising systemic side effects.

Gastro-retentive delivery: Floating microspheres prolong gastric residence time for drugs that are absorbed predominantly in the stomach or that act locally on the gastric mucosa, such as anti-Helicobacter pylori agents.

Vaccine and protein delivery: Microencapsulation of vaccines and antigenic proteins within biodegradable microspheres can provide a pulsatile or sustained antigen release profile, potentially reducing the number of booster doses required.

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Nasal and pulmonary delivery: Microspheres administered via the nasal or pulmonary route can prolong mucosal residence time and enhance the absorption of drugs that would otherwise undergo rapid mucociliary clearance.
Ocular delivery: Microspheres incorporated into ocular inserts or suspensions can prolong pre-corneal residence time, thereby improving ocular bioavailability of poorly absorbed drugs.
Diagnostic and imaging applications: Radiolabelled or contrast-loaded microspheres are used in diagnostic imaging and in the assessment of regional blood flow and perfusion.

XII. RECENT ADVANCES AND FUTURE PROSPECTS

Recent research in microsphere technology has focused on improving the precision, reproducibility, and functionality of these delivery systems. Microfluidic techniques are being increasingly explored to achieve highly monodisperse microspheres with precisely controlled size and morphology, overcoming the batch-to-batch variability often associated with conventional emulsification methods. There is also growing interest in the development of stimuli-responsive microspheres that release the incorporated drug in response to specific physiological triggers such as pH, temperature, or enzymatic activity, thereby enabling a higher degree of spatial and temporal control over drug delivery.
The application of microsphere technology has expanded well beyond its traditional role in oral and parenteral sustained release formulations, extending into areas such as long-acting therapy for chronic metabolic disorders, oncology, neuropsychiatric disorders, and ophthalmic conditions. A number of long-acting injectable microsphere products based on peptide and hormone therapeutics have already achieved regulatory approval and clinical success, underscoring the translational potential of this technology. Advances in polymer science, including the development of novel biodegradable copolymers with tunable degradation profiles, are expected to further expand the range of drugs and therapeutic applications amenable to microsphere-based delivery.
Nevertheless, several challenges remain to be addressed before the full potential of microsphere technology can be realised on a wider scale. These include the need for more robust and scalable manufacturing processes capable of ensuring batch-to-batch reproducibility, minimisation of initial burst release, reduction in the use of organic solvents during manufacture, and the development of simplified, cost-effective regulatory and quality control frameworks specific to particulate delivery systems. Continued interdisciplinary research combining polymer chemistry, pharmaceutical engineering, and clinical pharmacology is likely to drive further innovation in this field.

XIII. CONCLUSION

Microspheres represent a well-established and versatile particulate drug delivery platform capable of addressing many of the limitations associated with conventional dosage forms, particularly the need for frequent dosing and the associated fluctuations in plasma drug concentration. Through judicious selection of polymer type, preparation technique, and process variables, microspheres can be engineered to achieve a wide range of release profiles suited to oral, parenteral, nasal, ocular, and targeted delivery applications. A thorough evaluation of formulated microspheres, encompassing particle size analysis, surface morphology, drug entrapment efficiency, in vitro release kinetics, and stability, is essential to ensure the quality, safety, and therapeutic performance of the final product. With continued advances in polymer science and manufacturing technology, microsphere-based sustained drug delivery systems are expected to play an increasingly important role in the development of patient-friendly, long-acting therapeutic products across a broad spectrum of disease conditions.

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